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Editorial

REVERSING TYPE 2 DIABETES: MECHANISMS, FACTORS, AND STRATEGIES FOR LONG-TERM REMISSION

Dr. Santosh Kumar Swain [1], Dr. Pradip Kumar Behera[2]

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, â-cell dysfunction, and hyperglycemia. It is a significant public health concern, affecting millions of people worldwide. As per International Diabetes Federation (IDF) 537 million adults (20-79 years) were living with diabetes in 2021 representing 10.5% of the world's population in this age group. This number is predicted to rise to 643 million (11.3%) by 2030 and 783 million (12.2%) by 2045. Diabetes was responsible for 6.7 million deaths in 2021 (1 every 5 seconds.). Over 3 in 4 adults with diabetes live in low- and middle-income countries with poor health care infrastructure making the management of the disease still difficult.[1] Historically, Diabetes mellitus, particularly Type 2 diabetes (T2DM), has long been perceived as a chronic and incurable disease, managed primarily through medication and lifestyle changes aimed at symptom control rather than remission. However, recent research suggests that T2DM can be reversed, particularly in its early stages, with sustained lifestyle modifications and targeted interventions. This editorial explores the mechanisms behind the reversal of T2DM, the factors influencing long-term remission, and strategies that have shown promise in clinical practice.

Mechanisms of Type 2 Diabetes Reversal :

1. Restoration of Insulin Sensitivity :

Insulin resistance is the hallmark of T2DM, where cells in muscles, fat, and the liver become less responsive to insulin, leading to elevated blood glucose levels. Reversing T2DM involves restoring insulin sensitivity in peripheral tissues. Weight loss, particularly through calorie restriction or bariatric surgery, has been shown to improve insulin sensitivity. Studies suggest that a reduction in liver and pancreatic fat is crucial for restoring insulin sensitivity[2]. As hepatic fat decreases, the liver's ability to regulate glucose production improves, reducing fasting blood glucose levels.

2. Improved β-Cell Function :

Pancreatic β-cells, responsible for insulin secretion, become dysfunctional in T2DM. Chronic exposure to hyperglycemia, free fatty acids, and inflammatory cytokines leads to β-cell exhaustion. Evidence suggests that early intervention with lifestyle changes can restore β-cell function. A key mechanism for this restoration is the reduction of glucotoxicity and lipotoxicity, which damage β-cells. In studies involving intensive lifestyle changes, β-cell function improved in patients who achieved significant weight loss, supporting the idea that β-cell dysfunction is at least partially reversible [3].

3. Gastrointestinal Hormone Modulation :

Bariatric surgery, particularly Roux-en-Y gastric bypass (RYGB), has been shown to induce diabetes remission independently of weight loss. This suggests that changes in gastrointestinal hormones, such as glucagon-like peptide-1 (GLP-1), play a role in diabetes reversal. GLP-1 improves insulin secretion and inhibits glucagon

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release, helping to lower blood glucose levels. The enhancement of GLP-1 signaling post-surgery offers insights into how gut hormones may be leveraged to achieve remission [4].

4. Reduction of Inflammation :

Chronic low-grade inflammation is associated with obesity and T2DM. Adipose tissue, particularly visceral fat, secretes pro-inflammatory cytokines like TNF-á and IL-6, which contribute to insulin resistance. [5]Weight loss and dietary changes can reduce inflammation, thereby improving insulin sensitivity and â-cell function. A diet rich in anti-inflammatory foods, such as fruits, vegetables, and omega-3 fatty acids, may promote diabetes reversal by modulating the inflammatory response.

Factors Influencing Long-Term Remission:

1. Duration of Diabetes :

The duration of T2DM plays a critical role in determining the likelihood of remission. Patients with a shorter duration of disease are more likely to achieve remission, as their â-cell function is less compromised. Studies suggest that individuals diagnosed within five years of disease onset have the highest chances of achieving long-term remission with lifestyle interventions or bariatric surgery [6] Once â-cell function declines significantly, reversal becomes more challenging, underscoring the importance of early intervention.

2. Weight Loss and Maintenance :

Sustained weight loss is a key factor in achieving and maintaining T2DM remission. Studies like the DiRECT (Diabetes Remission Clinical Trial) have demonstrated that achieving at least 10-15% weight loss can lead to remission in approximately 46% of individuals after 12 months [7] The challenge lies in maintaining this weight loss over time. Relapse into hyperglycemia often occurs when weight is regained, highlighting the need for long-term strategies to sustain a healthy weight.

3. Dietary Composition :

Specific dietary patterns have been associated with improved glycemic control and diabetes remission. Low-carbohydrate diets, Mediterranean diets, and very low-calorie diets (VLCDs) have all shown promise in achieving remission. VLCDs, typically involving 600-800 kcal/day, can result in rapid weight loss and significant improvements in insulin sensitivity and â-cell function.[8] While these diets can induce remission, their sustainability remains a challenge for many patients.

4. Physical Activity :

Regular physical activity improves insulin sensitivity and supports weight loss maintenance. Exercise enhances glucose uptake in muscles, independent of insulin, and reduces hepatic glucose production. Both aerobic and resistance training have been shown to improve glycemic control and may contribute to diabetes reversal when combined with dietary changes.[9] Long-term adherence to an exercise regimen is crucial for maintaining remission.

5. Psychological and Behavioral Factors:

Achieving and maintaining diabetes remission requires significant lifestyle changes, which can be difficult for many patients. Psychological factors, including motivation, self-efficacy, and social support, play a critical role in long-term success. [10] Behavioral interventions, such as cognitive-behavioral therapy (CBT) and motivational interviewing, can help patients overcome barriers to lifestyle change and sustain their efforts toward remission.

Strategies for Long-Term Remission:

1. Bariatric Surgery :

Bariatric surgery, particularly RYGB and sleeve gastrectomy, has been shown to induce long-term remission in a significant proportion of patients with T2DM. The mechanisms behind this include weight loss, changes in gut hormones, and improved insulin sensitivity. Long-term studies have shown that up to 50-80% of patients

maintain remission for five years or more following surgery (3). Bariatric surgery should be considered in patients with obesity (BMI >35 kg/m²) who are unable to achieve remission with lifestyle interventions alone.

2. Very Low-Calorie Diets (VLCDs) :

VLCDs have been shown to induce rapid diabetes remission by promoting significant weight loss and reducing fat in the liver and pancreas. The DiRECT study demonstrated that 46% of patients achieved remission after one year on a VLCD. The challenge with VLCDs is their sustainability; transitioning to a long-term, less restrictive eating pattern while maintaining weight loss is essential to prevent relapse.

3. Low-Carbohydrate and Ketogenic Diets :

Low-carbohydrate diets, including ketogenic diets, have been shown to improve glycemic control and may lead to remission in some patients. These diets reduce the need for insulin by limiting dietary glucose intake, which can help reduce insulin resistance. However, long-term adherence to these diets can be challenging, and the effects on cardiovascular health remain a topic of ongoing research.

4. Behavioral and Psychological Support :

Given the significant lifestyle changes required for T2DM remission, behavioral support is essential. Structured weight management programs, support groups, and behavioral counseling can help patients stay motivated and overcome challenges. Psychological interventions that address emotional eating, stress, and other behavioral factors can improve the likelihood of long-term success.

5. Pharmacological Support :

While lifestyle changes are the cornerstone of diabetes reversal, pharmacological interventions may also play a role, particularly in patients struggling to achieve remission. GLP-1 receptor agonists and SGLT2 inhibitors have shown promise in improving glycemic control and promoting weight loss. These medications may be used as adjuncts to lifestyle interventions to enhance the likelihood of remission.

Conclusion

The concept of T2DM reversal challenges the traditional view of the disease as a lifelong condition. Mechanisms such as improved insulin sensitivity, restored â-cell function, and reduced inflammation play key roles in achieving remission. Factors such as the duration of diabetes, weight loss, dietary composition, and physical activity significantly influence the likelihood of long-term remission. While bariatric surgery, VLCDs, and low-carbohydrate diets have shown promise in inducing remission, sustaining these changes requires ongoing behavioral and psychological support. Future research should focus on identifying strategies to enhance long-term maintenance of remission and explore the role of novel pharmacological agents in supporting lifestyle changes.

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Original Article

SERUM PROCALCITONIN AND C-REACTIVE PROTEIN LEVELS AS PREDICTIVE MARKERS FOR MORTALITY IN SEPTIC SHOCK : A TWO-YEAR OBSERVATIONAL STUDY

Dr. Amitav Mohanty[1], Dr. Ganitya Bhusan Bhuyan[2]

Abstract :

Aim : The aim of this study was to investigate and evaluate the clinical significance of C-reactive protein (CRP) and serum procalcitonin (PCT) in patients with septic shock.

Method : Seventy-two patients with septic shock were divided two groups based on treatment outcomes-mortality (n = 42) and survival (n = 102) groups. As a control group, 40 sepsis patients without septic shock were selected. PCT, CRP, and SOFA scores were evaluated within twenty-four hours of admission.

Results : The mortality group had highest PCT, CRP, and SOFA scores, followed by survival and control groups. In determining the prognosis of patients with septic shock, the sensitivity and specificity of PCT were 67.9% and 46.5%, while those of CRP were 83.3% and 81%.

Conclusion : CRP and PCT levels may indicate a patient's prognosis.

Keywords : PCT, CRP, septic shock, SOFA

Introduction :

Sepsis has been defined as a potentially fatal illness of the human body caused by inappropriate host immune system responses in a variety of infectious circumstances. Statistics show that around 18 million novel cases are reported worldwide each year, with an annual increase of 8% [1, 2]. Sepsis is distinguished by its sudden onset and critical stage. Its mortality rate has been estimated up to about 20-30 percent high, accounting for 30-50 percent of total hospital mortality, significantly outnumbering patients with myocardial infarction [2,3].

During the initial few hours of triage, prompt diagnosis and treatment of septic conditions with particular antibiotics is critical [2]. The indiscriminate and nonspecific use of antibiotics leads to an increase in infection and resistance, elevating odds of healthcare expenses and mortality [3, 4]. More efficient and prompt diagnosis of the causal pathogen, as well as appropriate antibiotic therapy, have a promising future in resolving this issue [5].

Sepsis is a pathological condition known as Systemic Inflammatory Response Syndrome (SIRS), which manifests as a widespread inflammatory response impacting several organ systems. Scientific progress in the field of molecular biology has facilitated the identification of pertinent biomarkers for the timely detection of sepsis [8]. White blood cell count (WBC), Interleukin-1 (IL-1), and C-Reactive Protein (CRP) are the established biomarkers employed in the diagnostic process of sepsis. In comparison to CRP, PCT has superior prognostic and diagnostic efficacy, effectively discerning between bacterial and viral meningitis [9, 10]. The gold standard for confirming bacteraemia presence and responsible pathogen identification is blood culture. However, due to the time delay associated with this method, the rapid testing of a biomarker is highly valuable in facilitating the early identification of sepsis [11].

The objective of this study was to examine the expression and clinical relevance of C-reactive protein (CRP) and Procalcitonin (PCT) in individuals diagnosed with septic shock, with the intention of offering more precise and sensitive clinical markers.

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Materials and Methods :

This descriptive observational study was conducted on 144 patients for two years at the Medical Intensive Care Unit of Apollo Hospital, Bhubaneswar, India.

The patients were divided into two groups- survival group (SG) (n = 102) and mortality group (MG) (n = 42), with a control group (CG) consisting of 40 sepsis patients without shock, treated during the same time period.

Inclusion and exclusion criteria

This study included patients who met the diagnostic criteria for septic shock, had complete medical records, were e" 18 years old, were expected to spend more than 72 hours in the intensive care unit, and provided written consent.

This study excluded patients with irreversible illness during ICU admittance, psychiatric disorders, cardiopulmonary resuscitation, pregnancy or immune system diseases, haematological diseases, the need for long-term glucocorticoid therapy, long-term immunosuppressant use, and refusal to sign an informed consent form.

Study procedure

All study participants' demographic information, clinical examinations, details of fundamental investigations,and medical history were recorded on a standard form. Using an immunochromatographic assay and a commercially available test reagent, serum procalcitonin was measured and interpreted according to the manufacturer's instructions.

Statistical Analysis

The obtained data was entered into a Microsoft Excel spreadsheet and evaluated with Statistical Package for the Social Sciences (SPSS) version 24.0 International Business Management USA. In terms of percentages, qualitative data was conveyed. The Mean and Standard Deviation were utilised to convey quantitative data. Using the Chi-square/Fisher's exact test, an association between two qualitative variables was observed. Using the Pearson correlation test, correlations between qualitative variables were determined.

Results :

The baseline characteristics of the three groups, including age, sex, weight, and disease history, were comparable (Table 1).

Table 1. Baseline data

	Death group	*Survival group*	*Control group*	*P value*
Male	22	50	20	0.3
Female	20	52	20	
Age	52.2	52.4	53.7	0.3
Weight	61.5	60.1	61.2	0.9
BMI	21.4	21.5	21.9	0.8
Infections				
Urinary system	16	24	14	0.2
Respiratory system	10	24	8	
Digestive system	8	28	10	
Other	8	26	8	
Hypertension	12	16	10	0.7
Diabetes	10	10	6	0.8

The MG demonstrated high SOFA scores as compared to the SG, whereas the SG demonstrated high SOFA scores as compared to the CG. Patients with septic shock exhibited a positive correlation between SOFA and PCT scores (r = 0.33, r = 0.34), whereas CRP scores exhibited a negative correlation (r = -0.10).PCT had sensitivity of 66.8%, specificity of 45.4% and an AUC of 0.81%, while CRP had a sensitivity of 82.2%, specificity of 80.3% and AUC of 0.52.

Discussion :

Sepsis is a critical medical condition characterised by the presence of several organ dysfunctions [13]. It arises when the body's innate immune regulatory system is activated by a pathogen, resulting in widespread inflammatory responses throughout the body. The aforementioned process frequently entails an exaggerated response to pathogens, disrupting the equilibrium between anti-inflammatory and pro-inflammatory substances, resulting in significant death of T cells and ultimately leading to dysregulation of the body's immune response [14]. The available data indicate that the global yearly occurrence of sepsis in

adults is around 300 cases per 100,000 individuals, with a corresponding fatality rate ranging from 19.3% to 47.2%. Research in clinical practice has indicated that individuals diagnosed with sepsis frequently encounter exorbitant healthcare expenses, with an estimated daily expenditure of 11,000 RMB per person. This financial burden places significant strain on both patients' families and society as a whole [15, 16]. The implementation of timely diagnosis and intervention is crucial in mitigating patient mortality rates and enhancing patient prognosis [17].

Sinha et al. [15] included forty patients between the ages of 18 and 84, with a male:female ratio of 2.33:1. Similarly, Todi S et al. and Martin GS et al. reported that sepsis is more common in men [16,17]. Khan AA et al.'s study found that 53.34% of the total 60 patients were male, while 46.66% were female. 30% of male patients and 23.33% of female patients were younger than 50 years old [13].The results of this study demonstrated that CRP and PCT levels in the MG were higher as compared to those in the SG. The levels of the SG were higher as compared to those in the CG. This indicated that CRP and PCT levels increased substantially with sepsis progression.

A retrospective studyconducted on 201 sepsis patients revealed that the mean CRP and PCT levels of the patient with clinically fatal outcomes were 110.94 mg/L and 11.03 ìg/L, respectively. The mean CRP and PCT levels of the SG were 56.93 mg/L and 1.39 ìg/L, respectively [21].

In this study, it is hypothesised that CRP and PCT are commonly used clinical laboratory indicators that reflect the body's inflammatory response. An abnormal elevated level indicates an inflammation state in the subjects. PCT is produced by kidneys, lungs, and other organs during an inflammatory response and then enters the bloodstream. It will be detected in blood samples within 2-4 hours of infection onset and will reach its apogee within 6 to 24 hours [22, 23]. CRP is an acutely sensitive and highly sensitive phase protein. It is sensitive to the body's inflammatory response. Consequently, CRP and PCT levels will vary in blood samples of septic shock patients with varying clinical outcomes [24].

This study also analysed the differences in SOFA scale scores between patients with septic shock. The difference in scores between the three patient groups in the study confirms the validity of the disparities in PCT and CRP levels between the three patient groups.

Conclusion :

In conclusion, the expression of PCT and CRP has a significant correlation with the prognosis and diagnosis of patients and can be used as essential indicators to reflect patients' prognoses. The novel aspect of this investigation is the correlation between CRP and PCT and the SOFA scores, confirming the viability of PCT and CRP as prognostic indicators for septic shock patients. As a consequence of the limited sample size, the results are insufficiently exhaustive. In addition, there was no long-term monitoring. In future, we will conduct clinical studies with larger samples, a longer follow-up period, and more indicators in order to provide better benchmarks for enhancing the clinical outcome of septic shock patients.

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Original Article

CORRELATION OF NEUTROPHIL-LYMPHOCYTE RATIO, PLATELET-LYMPHOCYTE RATIO AND GAMMA GLUTAMYLTRANSFERASE WITH SEVERITY OF ACUTE ISCHEMIC STROKE

Dr. Bharath Vikhil Karnati[1], Dr. Sasidhar Ch[2], Dr. Debasis Pathi[2], Dr. Pradip Kumar Behera[3], Dr. K.P. Tripathy[4]

Abstract :

Background : The acute ischemic stroke (AIS) is a devastating disease and remains one of the leading cause of death and disability worldwide**.** Neutrophil-to-lymphocyte ratio (NLR),Platelet-lymphocyte ratio(PLR) and gamma glutamyl transferase(GGT) are markers of acute systemic inflammation and we want to evaluate whether admission NLR, GGT, PLR levels correlate with the early stroke severity using modified Rankin scale.

Material And Methods : This is a cross-sectional study carried out in the Department of General Medicine and Neurology KIMS,Bhubaneswar.57 patients with acute ischemic stroke during the period of May 2023 to July 2023 were recruited into the study. Complete blood count was done in all cases. NLR, PLR and GGT were calculated from CBC. Modified Rankin Scale(mRs) was evaluated in all patients at the time of discharge. NLR,PLR and GGT were analysed with mRs grade for any correlation using Kruskal-Wallis analysis

Results : The median age of study subjects was 64.2(IQR:58.0-72.0) years with males of 33(57.9%) and females of 24(42.1%). Median PLR for grade 2 was 8.57 (IQR: 5.52-14.20), grade 3 was 10.97(IQR:8.0-18.93),grade 4 was 16.09(IQR:11.15-18.75) and grade 5 was 11.19(IQR:10.32-17.56) with a significant p value of 0.047.Median NLR for grade 2 was 2.10(IQR:1.87-3.13) ,grade3 was 3.09(IQR:2.31-5.10),grade 4 was 2.83(IQR:2.35-7.08) and grade 5 was 3.54(IQR:2.15-4.71) with a P value of 0.221 and median GGT for grade 2 was 33(IQR:20-41),grade 3 was 37(IQR:17.50-44.50),grade 4 was 23(IQR:15.00-66.00)with a P value of 0.932.

Conclusion : Platelet lymphocyte ratio has shown significant P value of 0.047 correlating well with the severity of acute ischemic stroke on basis of mRs.Therefore, Platelet lymphocyte ratio can be used as a simple cost effective tool in addition to mRs to predict the severity of acute ischemic stroke.

Key Words : Cerebro-vascular Accident, Stroke Severity, Modified Rankin Scale, acute systemic inflammation

Introduction :

Acute ischemic stroke (AIS) is a severe medical condition caused by an obstruction in blood flow to part of the brain, leading to neuronal death and substantial functional impairment. This condition is a leading cause of global mortality and long-term disability, placing a significant burden on healthcare systems worldwide.[1] Rapid identification of AIS severity and prognostic factors is essential for effective management and therapeutic decision-making. Recent studies highlight the role of systemic inflammation in AIS pathophysiology, suggesting that inflammation markers may offer valuable insights into patient outcomes [2]

Among these markers, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and gamma-glutamyl transferase (GGT) have emerged as potential biomarkers for assessing inflammatory response and predicting stroke severity. Elevated NLR is associated with adverse clinical outcomes in various diseases, representing a hyper-

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inflammatory state that may exacerbate ischemic injury. For instance, Ying et al. nd Li H et al found NLR to be predictive of short-term prognosis in stroke patients with intracranial atherosclerosis. [1,3] Similarly, PLR reflects the immune response balance, integrating both pro-inflammatory and anti-inflammatory processes during stroke and indicating the potential severity of the ischemic event. GGT, though primarily considered a liver enzyme, is associated with oxidative stress and inflammatory pathways, factors relevant in AIS contexts [3]. The Modified Rankin Scale (mRs) provides a structured way to measure disability and dependency in stroke patients, offering a framework for linking these inflammatory markers to clinical severity [4,5] This study investigates the relationships between admission levels of NLR, PLR, and GGT and early AIS severity, aiming to enhance the understanding of AIS-related inflammatory processes and improve prognostic accuracy.

Materials and Methods :

Study Design and Setting :

This cross-sectional observational study was conducted in the Department of General Medicine and Neurology at KIMS, Bhubaneswar, over a period from May to October 2023. A cross-sectional design was selected to explore associations between biomarkers (NLR, PLR, GGT) and the severity of acute ischemic stroke (AIS), assessed via the Modified Rankin Scale (mRs) upon discharge.

Study Population :

Fifty-seven adult patients with AIS were enrolled. Inclusion criteria included adults aged 18 years or older, with a confirmed AIS diagnosis through imaging, and who presented within 24 hours of stroke onset. Exclusion criteria comprised patients with hemorrhagic stroke, recent infections, autoimmune disorders, liver disease, or other chronic conditions that could independently alter inflammation markers. These criteria were designed to minimize confounding effects on the measured biomarkers.

Data Collection :

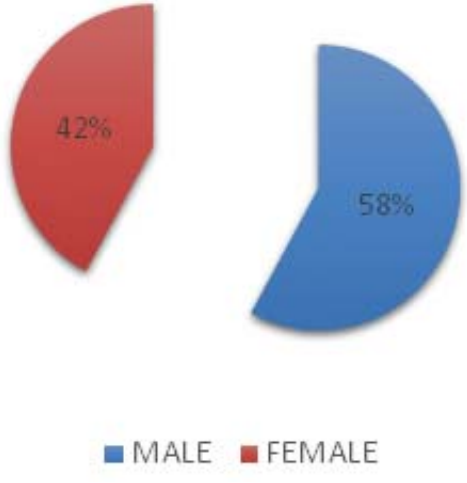
Upon admission, patient demographic information (age, gender) and clinical history were recorded. Stroke severity was evaluated by a neurologist using the mRs scale, ranging from 0 (no symptoms) to 6 (death), as an objective measure of functional impairment (Ying et al., 2021).Neutrophil, lymphocyte, and platelet counts were obtained from CBC results to calculate NLR (neutrophils divided by lymphocytes) and PLR (platelets divided by lymphocytes). GGT levels, measured in U/L, were assessed through enzymatic assays performed in the hospital laboratory.

Statistical Analysis :

Data were analyzed to evaluate correlations between mRs grades and biomarkers (NLR, PLR, and GGT). Descriptive statistics summarized demographic characteristics and biomarker levels, with means, medians, or interquartile ranges (IQRs) for continuous variables. Due to non-normal distributions, the Kruskal-Wallis test was used to assess differences in NLR, PLR, and GGT across mRs grades. Statistical significance was defined by a p-value <0.05. Statistical analyses were performed using SPSS -24 software, and graphs such as box plots were used to represent data visually.

Results :

A total of 57 patients were recruited to the study with median age of the study subjects being 64.2 years (IQR: 58.0-72.0), with 33 males (57.9%) and 24 females (42.1%).(Fig 1). Most subjects were in mRs Grade 2(n =19) followed by Grade 3 (n=17) and Grade 5(n=14) and least subjects were in Grade 4(n=7).



(Fig 1. Gender Distribution in study group)

The distribution of Inflammatory markers (PLR, NLR and GGT) among study subjects with grades of mRs is shown in the Table 1 .

Variables	Grade 2 (n=19)			Grade 3 (n=17)			Grade 4 (n=7)			Grade 5 (n=14)			P Value
	Median	IQR		Median	IQR		Median	IQR		Median	IQR		
GGT(U/L)	33.00	20.00	41.00	37.00	17.50	44.50	23.00	15.00	66.00	23.00	21.75	64.25	0.932
Neutrophil-Lymphocyte ratio	2.10	1.87	3.13	3.09	2.31	5.10	2.83	2.35	7.08	3.54	2.15	4.71	0.221
Platelet-Lymphocyte ratio	8.57	5.52	14.20	10.97	8.00	18.93	16.09	11.15	18.75	11.19	10.32	17.56	0.047

Correlation of Inflammatory Markers with mRs :

Platelet-Lymphocyte Ratio (PLR)

The median PLR values were as follows:

- Grade 2: 8.57 (IQR: 5.52-14.20)
- Grade 3: 10.97 (IQR: 8.0-18.93)
- Grade 4: 16.09 (IQR: 11.15-18.75)
- Grade 5: 11.19 (IQR: 10.32-17.56)

The difference in PLR across the mRs grades was statistically significant (p = 0.047).

Neutrophil-Lymphocyte Ratio (NLR)

The median NLR values were:

- Grade 2: 2.10 (IQR: 1.87-3.13)
- Grade 3: 3.09 (IQR: 2.31-5.10)
- Grade 4: 2.83 (IQR: 2.35-7.08)
- Grade 5: 3.54 (IQR: 2.15-4.71)

The correlation between NLR and mRs grades was not statistically significant (p = 0.221).

Gamma-Glutamyl Transferase (GGT)

The median GGT values were:

- Grade 2: 33 (IQR: 20-41)
- Grade 3: 37 (IQR: 17.50-44.50)
- Grade 4: 23 (IQR: 15.00-66.00)

The analysis showed no significant correlation between GGT levels and mRs grades (p = 0.932).

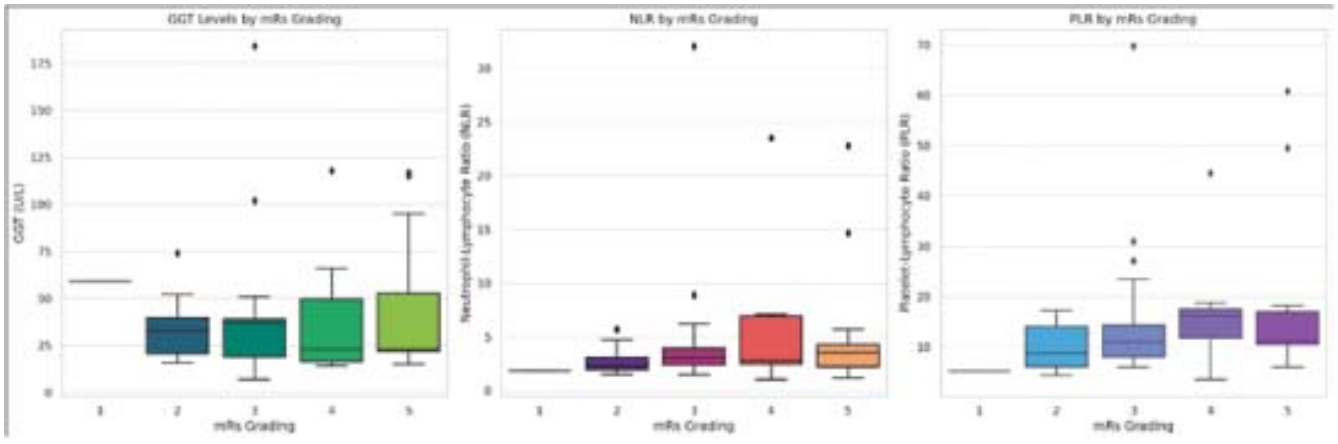


Fig 2: showing the correlation of NLR, PLR and GGT with mRs Grades.

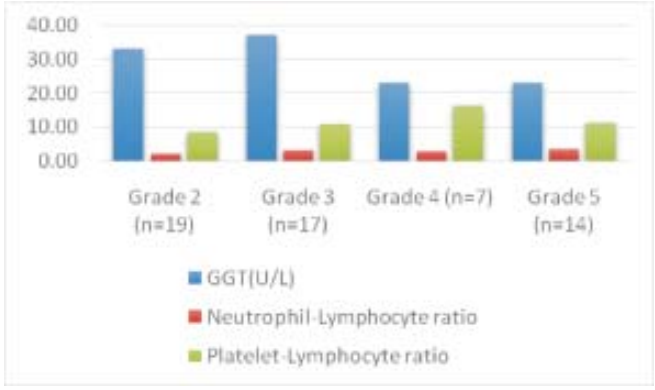


Fig 3 Bar Chart showing inflammatory markers under study with grades of mRs

Discussion :

This study aimed to determine the correlation between neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and gamma-glutamyl transferase (GGT) with the severity of acute ischemic stroke (AIS), using the Modified Rankin Scale (mRs) as a measure of stroke severity. The findings indicate that while PLR correlates significantly with stroke severity, NLR and GGT did not show a statistically significant relationship with mRs grades, thus underscoring PLR's potential utility as a predictive biomarker in AIS severity evaluation.

Acute ischemic stroke is primarily caused by the obstruction of blood flow to brain tissues, which leads to neuronal injury and ischemic inflammation. Recent studies have highlighted that the inflammatory response plays a significant role in AIS progression and outcomes. with markers like NLR, PLR, and GGT increasingly recognized for their potential to predict stroke severity and prognosis.[6,7]

The NLR reflects the balance between neutrophils, which are involved in the acute inflammatory response, and lymphocytes, which are key players in adaptive immunity. High NLR levels have been linked to more extensive brain damage and poorer outcomes due to the pro-inflammatory effects of neutrophils, which release proteolytic enzymes and reactive oxygen species that can exacerbate neuronal injury. [6] in this study, NLR did not correlate significantly with mRs scores, suggesting that its prognostic role might depend on the timing of measurement, as NLR levels can fluctuate with the evolution of inflammation following a stroke. Previous studies have shown mixed results regarding NLR's predictive accuracy for stroke severity; for instance [7,8].Goyal et al. (2018) noted that elevated NLR was associated with poor outcomes specifically in large-vessel occlusion strokes, highlighting the potential influence of stroke subtype on NLR's predictive utility.[9]

PLR, showed a significant association with stroke severity in this study, aligning with findings from other research suggesting that platelet-related markers reflect both inflammation and thrombosis in stroke. [10,11] Platelets are central in thrombotic processes and can release inflammatory mediators that contribute to ischemic brain injury. Elevated PLR levels may therefore indicate a higher thrombotic and inflammatory state, which could contribute to worse stroke severity as observed on the mRs scale [12] . The ability to R through a routine complete blood count (CBC) test also makes it an accessible and practical tool for initial stroke assessment in clinical settings.

Gamma-glutamyl transferase (GGT), a marker of oxidative stress and liver function, has been associated with cardiovascular risk factors such as hypertension, diabetes, and metabolic syndrome, which are also risk factors for AIS [11,12] . While GGT levels have been linked to stroke recurrence and poor outcomes, this study found no significant correlation between GGT levels and mRs scores, suggesting that GGT may have more relevance as a predictor of chronic vascular health rather than acute stroke severity. Additionally individual metabolic factors and lifestyle variables might influence GGT, making it less specific to the acute inflammatory response in AIS.

The significant correlation between PLR and AIS severity observed in this study suggests that PLR could be incorporated as a prognostic tool in clinical settings, supplementing the Modified Rankin Scale.[13,14]. Since PLR is a simple, cost-effective marker, it could be especially beneficial in settings where resources are limited, enabling early risk stratification for stroke patients. Given its association with both thrombotic and inflammatory pathways, PLR may help identify patients at higher risk of severe outcomes, allowing for more targeted and intensive monitoring and care during the acute phase of stroke

Comparative Biomarkers and Future Research Directions :

While PLR demonstrated significance in this study, other biomarkers, such as the Systemic Immune-Inflammation Index (SII), have shown promise in AIS prognosis but often require more complex calculations or specific assays[15] . Compared to PLR, which is derivedc CBC data, these advanced indices might be less feasible in some healthcare contexts. Future research should explore the combined utility of PLR with other inflammatory and thrombotic markers to enhance predictive accuracy for AIS outcomes. Additionally, exploring how inflammatory markers like NLR and GGT fluctuate over the acute and subacute phases of stroke could yield insights into their utility in predicting long-term functional outcomes and recovery trajectories.

Limitations and Future Perspectives :

The cross-sectional design of this study and its relatively small sample size limit the broader applicability of the findings. Expanding this research with larger, multicenter studies could validate PLR's predictive utility and clarify the roles of NLR and GGT in AIS prognosis. Moreover, longitudinal studies that assess these inflammatory markers over time could help determine their relevance to different stages of AIS recovery and guide clinicians in refining prognostic assessments.

Conclusion :

This study supports the role of PLR as a promising, cost-effective biomarker for assessing AIS severity. While PLR demonstrated significant correlation with mRs, the lack of significance in NLR and GGT correlations emphasizes the need for further research to define the optimal use of inflammatory markers in stroke prognosis. Ultimately, integrating simple yet predictive biomarkers like PLR with clinical scales like the mRs may facilitate better-informed decision-making in stroke care, aiming to improve patient outcomes through early and targeted interventions.

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Review Article

NAVIGATING CARDIOVASCULAR CARE : THE EXPANDING CLINICAL APPLICATIONS OF NT-PROBNP

Dr. Srikanta Sharma[1], Dr. Soumit Sharma[2], Dr. Rajesh Ranjan Behera[3], Dr. Lalatendu Mohanty[4]

Abstract :

N-terminal pro-B-type natriuretic peptide (NT-proBNP) has become an indispensable biomarker in the diagnosis, prognosis, and management of cardiovascular diseases (CVDs), particularly heart failure (HF). Over the last two decades, its role has expanded significantly beyond the initial use as a tool for diagnosing acute heart failure, demonstrating increasing utility in a variety of clinical settings. Importantly, NT-proBNP levels correlate with the prognosis of patients with chronic and acute HF, making it a valuable predictor of adverse outcomes, including rehospitalization and mortality. Its inclusion in guidelines for diagnosing HF with reduced and preserved ejection fraction (HFrEF and HFpEF) has solidified its role as a frontline biomarker in cardiovascular care. As clinicians and researchers continue to explore its full potential, NT-proBNP promises to play a central role in the future of cardiovascular medicine, guiding more personalized and effective patient care.

Key Words : NT-proBNP, Heart failure, Cardiovascular disease, Biomarker, Acute coronary syndrome, Atrial fibrillation,

Introduction :

B-type Natriuretic Peptide (BNP) is one of the nine distinct natriuretic peptides, among which seven originate from the atria. The Atrial Natriuretic Peptide (ANP) is synthesized by atrial myocytes, while BNP is predominantly produced in the ventricles. Additionally, C-type Natriuretic Peptide (CNP) is generated within the vasculature, and D-type Natriuretic Peptide (DNP) is present in plasma. The precursor, pre-proBNP, is a 134-amino acid prohormone that undergoes enzymatic cleavage by corin, yielding ProBNP, which is subsequently split into biologically active fragments, including NT-proBNP and BNP—a 32-amino acid peptide. Upon release, these natriuretic peptides (NPs) interact with and activate the NPRA (Natriuretic Peptide Receptor A) primarily, with a lesser affinity for NPRB and NPR-C receptors. This receptor binding initiates a conformational change that leads to receptor dimerization and activation, facilitating the conversion of guanosine triphosphate (GTP) to cyclic guanosine monophosphate (cGMP). Elevated intracellular cGMP levels activate cGMP-dependent protein kinase (PKG), triggering physiological responses such as natriuresis, vasodilation, increased glomerular filtration rate (GFR), enhanced renal blood flow, improved ventricular relaxation, anti-fibrotic and antithrombotic effects, and inhibition of the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous activity. The degradation of NPs is mediated by neutral endopeptidase (NEP), commonly known as neprilysin. Notably, NT-proBNP is exclusively excreted through renal pathways.

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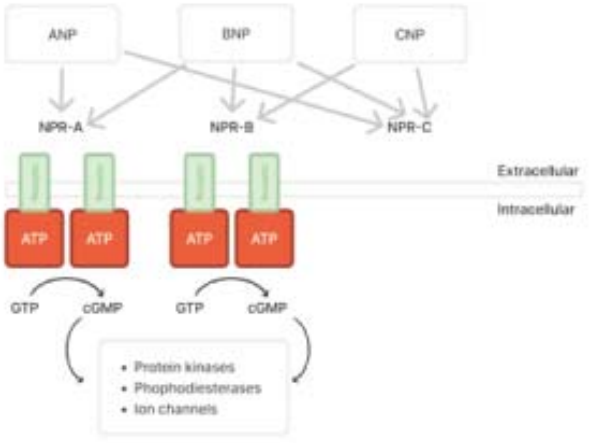
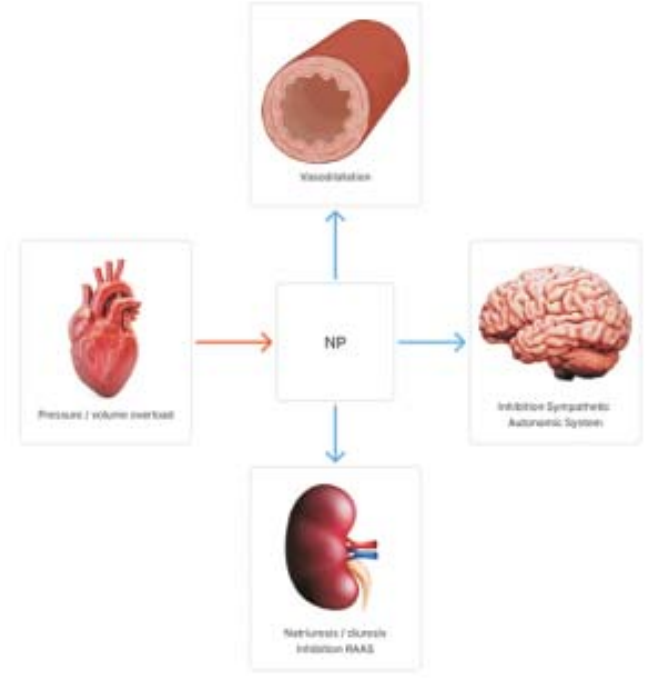


Physiology of natriuretic peptide



Physiological Effect of NP

The N-terminal prohormone fragment of B-type Natriuretic Peptide (NT-proBNP) is a ventricular-derived peptide released in response to increased myocardial stress and wall tension. It is a critical biomarker in cardiovascular medicine, integral for diagnostic evaluation, risk stratification, therapeutic management, and prognostication in various cardiac pathologies. Although the last decade has seen the emergence of several promising biomarkers, such as galectin-3, copeptin, myeloperoxidase, and soluble ST2 (suppression of tumorigenicity 2), most have not yet been adopted into routine clinical practice. In contrast, NT-proBNP remains a gold standard, widely utilized in cardiovascular care, as its concentrations are reflective not only of heart failure (HF) but also of myocardial injury, systemic inflammation, hemodynamic stress, and fibrosis.

Natriuretic peptides (NPs) exhibit protective effects beyond cardiac function, influencing multiple organ systems through the cGMP-dependent protein kinase G (PKG) signaling pathway. Experimental studies have demonstrated their involvement in modulating immune responses, lipid metabolism, and thermoregulation.

European clinical guidelines advocate for age-specific diagnostic thresholds due to observed variations in NT-proBNP and BNP levels, noting a 10 pg/mL variance in BNP and up to a 100% difference in NT-proBNP concentrations between males and females [1][2]. These discrepancies are attributed to hormonal influences on gene expression, sex-specific differences in body composition, and the potential contribution of extra-cardiac sources of natriuretic peptides, notably those originating from the female reproductive system[3][4].

Clinical Applications :

1. Heart Failure (HF)

Guideline 2024	Recommendation	Class of evidence
2024 American Heart Institute of America / Heart failure society of America	Confirm the diagnosis of HF. Assess the severity of HF. Assess the prognosis of HF	1A 1A 1A

Heart Failure with preserved ejection fraction (HFpEF) constitutes approximately half of all HF cases. Despite sharing a poor prognosis with heart failure with reduced ejection fraction (HFrEF), HFpEF poses diagnostic challenges. Natriuretic peptides remain the most utilized biomarkers for HF diagnosis, with elevated levels serving as a key diagnostic criterion independent

of left ventricular ejection fraction (LVEF) [5]. NT-proBNP has a high negative predictive value (0.94–0.98), making it particularly useful for excluding HF, though its positive predictive value is comparatively lower (0.64–0.67). Age-specific NT-proBNP thresholds are recommended: >450 pg/mL for patients under 50, >900 pg/mL for those aged 50–75, and >1800 pg/mL for individuals over 75 [6][7][8][9]. Conversely, NT-proBNP levels below 300 pg/mL effectively rule out HF, while levels falling between normal and HF constitute a diagnostic "gray zone."

Risk Stratification :

NT-proBNP is instrumental in identifying individuals at risk of developing HF, enabling targeted preventive interventions. Measurement of natriuretic peptides (NP) in high-risk populations, such as those with arterial hypertension or type 2 diabetes mellitus, can aid general practitioners in identifying patients with elevated ventricular diastolic pressure, thereby accelerating the implementation of preventative strategies including medication titration or novel therapies to mitigate HF progression. Trials like PONTIAC [10] and STOP-HF [11] have demonstrated that NT-proBNP measurement in at-risk populations, including those with diabetes, facilitates early detection and more aggressive prevention strategies, subsequently reducing HF incidence [12]. Moreover, NT-proBNP is predictive of HF onset, supporting clinicians in creating targeted intervention plans. Wang et al. reported in the Framingham Offspring Study that asymptomatic individuals with mildly elevated BNP levels, adjusted for cardiovascular risk factors, have an increased risk of death, cardiovascular events, HF, atrial fibrillation, and stroke or transient ischemic attack.

McKie et al. confirmed in a general population from Olmsted County, MN, that higher BNP and NT-proBNP levels correlate with increased mortality. A recent meta-analysis of 40 studies involving 95,617 individuals without a history of cardiovascular disease found NT-proBNP levels to be strong predictors for first-onset HF, coronary cardiomyopathy, and stroke. NT-proBNP levels also exhibited superior predictive power for coronary cardiomyopathy and stroke compared to HDL cholesterol and C-reactive protein levels. NT-proBNP levels above 400 pg/mL significantly heightened the risk of cardiovascular events.

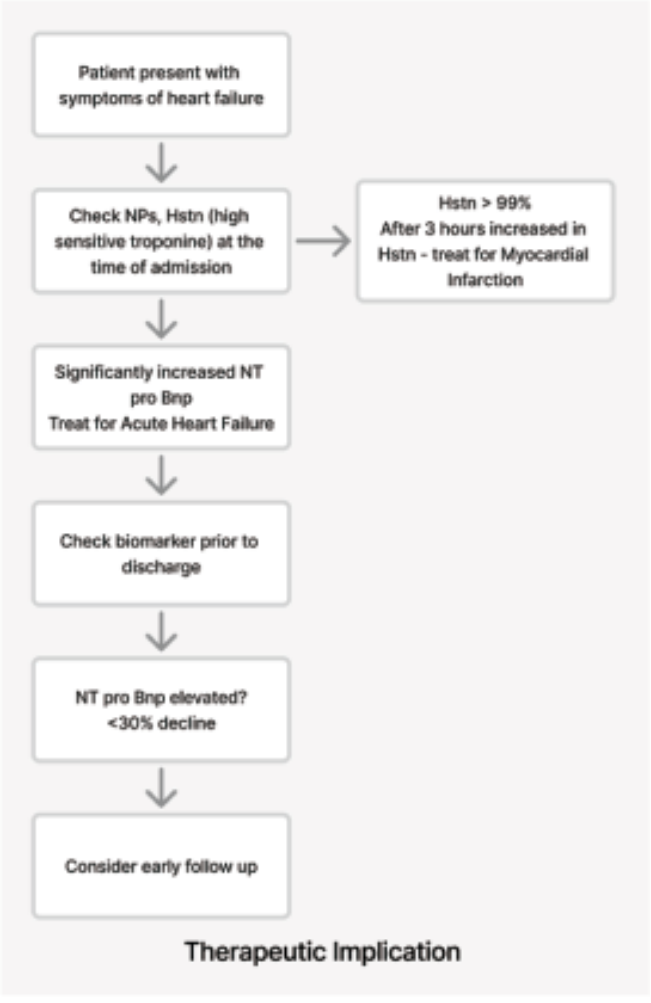
Research has also explored dietary influences on cardiac hemodynamics. Data from the National Health and Nutrition Examination Survey (NHANES) (1999–2004) linked a high-quality diet (low sodium and sugar intake) to lower NT-proBNP levels. Both the Mediterranean and DASH diets are associated with reduced NT-proBNP concentrations, likely due to their effects on oxidative stress and inflammation. Excessive salt intake activates the renin–angiotensin–aldosterone system (RAAS), leading to fluid retention and ventricular expansion, subsequently increasing NT-proBNP levels. Long-term n-3 fatty acid consumption has been shown to prevent age-related diastolic dysfunction, evidenced by lower NP levels.

Clinical Use in Heart Failure :

NT-proBNP is valuable in both acute and chronic HF for diagnostic and prognostic purposes. Elevated NT-proBNP levels enhance diagnostic accuracy, particularly in cases with ambiguous dyspnea. NPs help confirm or exclude acute HF, as well as chronic HF, HFpEF, and HFrEF [13][14]. However, NT-proBNP levels in HFpEF patients can occasionally be misleading; up to 20–25% of HFpEF cases present with low NP levels despite elevated pulmonary wedge pressures, potentially due to genetic, obesity-related, or other confounding factors [15][16]. Nevertheless, NT-proBNP is effective in ruling out HF in emergency settings due to its high negative predictive value and its ability to expedite clinical decision-making.

Therapeutic Value :

NT-proBNP levels correlate with left ventricular filling pressure and are instrumental in monitoring intravenous therapy response, assessing hemodynamic congestion, and guiding treatment in HF patients. Studies indicate that therapies aimed at reducing NT-proBNP levels correspond with improved clinical outcomes [17][18][19]. Pre-discharge NT-proBNP measurement, once optimal fluid balance is achieved, can guide follow-up care intensity and frequency. Lower discharge NT-proBNP levels or a substantial reduction post-therapy are associated with better patient outcomes [20][21][22].



Plasma NT-proBNP levels correlate with E/e', an echocardiographic index of left ventricular filling pressure, and are inversely related to right ventricular ejection fraction while directly relating to intraventricular pressure. Secondary analysis of the RELAX trial revealed that NT-proBNP is linked with left atrial enlargement and increased E/e' ratio. Therapeutic benefits for HFrEF include ACE inhibitors [23], ARBs [24], spironolactone [25], beta-blockers [26], and cardiac resynchronization therapy [27], all of which decrease BNP levels alongside improved cardiac remodeling and outcomes. In contrast, the I-PRESERVE trial on irbesartan use in HFpEF showed increased morbidity and mortality, coinciding with rising NT-proBNP levels.

Troughton et al. in patients with symptomatic chronic HFrEF(<40%) [28] French multicenter study(STARS -BNP) [29], and Berger et al. favored NP guided therapy. The TIME-CHF trial suggested that BNP-guided therapy reduced mortality in younger patients but not older ones, likely due to age-related renal dysfunction and comorbidities. This indicates the necessity for intensive therapy in patients with high biomarker levels.

In chronic HF management, NP-guided therapy has shown a 20–25% reduction in mortality [30]. However, evidence remains divided on its efficacy relative to high NP levels, suggesting that NP measurements are better suited for assessing hemodynamic status rather than symptoms. Misuse in patients without significant congestion may lead to adverse effects such as hypotension and renal dysfunction. The debate continues, with large studies showing mixed results regarding NP-guided interventions [31-39].

Hence an important question remains: should there be individualized target NP values? considering age, sex, renal function, body mass index, and genotype. Due to this uncertainty no authorized guidelines recommend, Class-Level of Evidence as 1A, by serial measurement of NP to guide titration of therapy in chronic HF.

Prognostic Value :

NT-proBNP remains a robust prognostic marker in both acute and chronic HF, irrespective of LVEF. Elevated levels are associated with increased mortality and worse outcomes [40][41][42][43]. For example, in patients with dyspnea and preserved LVEF, resting NT-proBNP levels are significantly correlated with elevated wedge pressures during peak exercise [44][45]. The STRONG-HF study demonstrated that NT-proBNP-guided intensive therapy improves patient outcomes, with those showing greater NT-proBNP reductions after acute HF treatment exhibiting better prognosis [20][21]. Failure to reduce NT-proBNP levels by 30% post-treatment is linked with significantly higher mortality. For chronic HF, elevated NT-proBNP levels predict recurrent hospitalizations and poorer long-term outcomes, with levels exceeding 5000 pg/mL indicating poor prognosis as per the PROTECT trial. Data from the Val-HeFT study indicate that both baseline and 3-month NT-proBNP changes are powerful predictors of future outcomes.

2. Hypertrophic Obstructive Cardiomyopathy (HOCM) :

In individuals diagnosed with hypertrophic obstructive cardiomyopathy (HOCM), NT-proBNP levels serve as a valuable biomarker for distinguishing HOCM from other etiologies of left ventricular hypertrophy. Elevated concentrations of NT-proBNP are associated with increased obstruction of the left ventricular outflow tract, greater septal wall thickness, and heightened risk of adverse clinical events, such as sudden cardiac death and progression to heart failure [48]. Serial monitoring of NT-proBNP allows clinicians to track disease evolution and evaluate therapeutic effectiveness, as reductions in NT-proBNP levels typically indicate successful management and improved outcomes.

3. Acute Coronary Syndrome (ACS) :

NT-proBNP has gained prominence as a biomarker in the diagnostic, therapeutic, and prognostic assessment of coronary artery disease (CAD). In the context of acute coronary syndrome (ACS), NT-proBNP levels are reflective of left ventricular dysfunction due to myocardial ischemia and increased myocardial wall stress [49][50]. Elevated NT-proBNP concentrations post-myocardial infarction are predictive of higher mortality rates and increased risk of subsequent cardiovascular events. Moreover, NT-proBNP measurements are instrumental in evaluating coronary wall stress during procedures such as balloon inflation in coronary interventions, providing additional insight into patient condition and procedural outcomes [51].

4. Stable Coronary Artery Disease (CAD) :

In patients with stable coronary artery disease, NT-proBNP levels are elevated even in the absence of acute ischemic episodes. The levels of NT-proBNP in this population correlate with the severity and extent of coronary stenosis, offering critical prognostic information regarding disease progression and long-term outcomes [52].

5. Valvular Heart Diseases :

Valvular pathologies, which contribute to either volume or pressure overload in the left ventricle, lead to elevated NT-proBNP concentrations. NT-proBNP is strongly correlated with parameters such as left atrial enlargement and left ventricular dysfunction, where higher values signify increased severity of the valvular disease [53][54]. In patients undergoing valve surgery, whether repair or replacement, NT-proBNP levels can guide the optimal timing for surgical intervention and are predictive of postoperative recovery and outcomes [55][56].

Limitations of NT-proBNP :

NT-proBNP concentrations are subject to variability influenced by several demographic, physiological, and pathological factors, such as age, sex, obesity, renal function, and ethnicity. In elderly individuals and females, NT-proBNP levels are typically elevated, whereas obese patients tend to have lower levels, which may result in underdiagnosis in this population [55]. Furthermore, a range of comorbidities including chronic obstructive pulmonary disease (COPD), pulmonary embolism, obstructive sleep apnea, severe pneumonia, burn injuries, chemotherapy, and sepsis can significantly increase NT-proBNP levels. Dietary factors, such as high intake of sodium and sugar, may also contribute to elevated NT-proBNP levels. Pharmacological interventions, particularly beta-blockers, diuretics, and ACE inhibitors, can alter NT-proBNP concentrations, complicating the interpretation of these measurements in clinical practice [57][58].

To enhance the diagnostic and prognostic utility of NT-proBNP, it is recommended that its levels be interpreted alongside other clinical evaluations, serial monitoring, and individualized patient characteristics. Developing more advanced assays with greater specificity and sensitivity may help address some of these current limitations and improve the accuracy and reliability of NT-proBNP as a biomarker.

Conclusion :

NT-proBNP has established itself as an indispensable biomarker in the management of diverse cardiovascular pathologies, demonstrating its capacity to reliably reflect hemodynamic stress on the myocardium irrespective of the specific underlying disease. Its broad utility spans the diagnosis, prognosis, and management of heart failure, coronary artery disease, hypertrophic cardiomyopathy, and valvular heart disorders. Despite its lack of specificity for a singular condition, NT-proBNP's primary strength lies in its

ability to effectively exclude heart failure in patients presenting with dyspnea, thereby streamlining diagnostic pathways and reducing unnecessary interventions. Beyond its diagnostic capabilities, NT-proBNP offers comprehensive prognostic insights across a spectrum of cardiovascular conditions, encompassing both chronic and acute heart failure, stable coronary artery disease, acute coronary syndromes, hypertrophic cardiomyopathy, and valvular diseases. Its application in these varied clinical scenarios highlights NT-proBNP's robust role in guiding treatment strategies, improving patient outcomes, and supporting targeted therapeutic decision-making.

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Review Article

AN INTEGRATED APPROACH TO ANTICOAGULANT INDUCED BLEEDING : A BRIEF REVIEW

Dr. Biswajit Bhuyan

Abstract :

Anticoagulant therapy is the cornerstone in the management of thromboembolic disorders, yet it carries a significant risk of bleeding complications, which can be life-threatening. This review explores an integrated approach to managing anticoagulant-induced bleeding, focusing on the latest strategies for prevention and treatment. Emphasis is placed on the role of reversal agents, such as vitamin K antagonists, direct oral anticoagulant (DOAC) reversal agents, and the use of prothrombin complex concentrates (PCC) and fresh frozen plasma (FFP). This brief review aims to guide clinicians in optimizing outcomes for patients on anticoagulants, ensuring prompt and effective intervention in the event of bleeding while maintaining therapeutic anticoagulation.

Keywords : Anticoagulants, Bleeding, reversal agents, DOACs, Prothrombin complex concentrates, Thromboembolism.

1. Introduction :

Bleeding can be a life threatening complication of anti-coagulant drugs requiring urgent attention. The approach to an anti-coagulant drug induced bleeding patient requires proper history taking, physical assessment, lab investigations, other supportive measures and antidote to prevent significant morbidity and mortality.

2. Classification of anticoagulants :[1]

2.1 Heparin and Heparinoids :

Unfractionated Heparin(UFH), Low molecular weight Heparin(LMWH), Fondaprinux, Danaparoid.

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2.2 Vitamin K antagonist :

Warfarin ,Acemocoumarol,Dicoumarol.

2.3 Direct thrombin inhibitors :

Dabigatran, Argatroban, Bivalirudin, Lepirudin.

2.4 Factor Xa inhibitors :

Apixiban, Rivaroxaban, Betrixiban, Edoxaban.

3. Major bleed and supportive measures :

According to ISTH a major bleed is defined as any bleeding causing fall in Hb>2gm/dl or requiring transfusion or bleeding in critical sites such as intra-cranial, intra-occular, intra-spinal, retroperitoneal or causing compartmental syndrome [2] A major bleed generally warrants cessation of the anti-coagulant drug and hemostatic measures. A meticulous history focusing on type of anticoagulation, timing of last dose, concurrent anti platelet use and renal/liver impairment should be taken in each patient presenting with bleed. Whenever possible local hemostatic measures like local compression, nasal packing should be initiated. All anticoagulant and antiplatelet drugs should be put on hold in cases of major bleeding with close monitoring of vital signs. Activated charcoal can be used if the last dose of the anticoagulant was taken within within 2-3 hours. Tranexamic acid can serve as an useful adjunct to control bleeding but caution has to maintained in hematuria[3] Transfusion with PRBC/FFP/RDP may be given according to requirments.Preliminary investigations include a complete blood count(CBC), renal function tests(RFT) for all patients. For patients on VKA antagonist PT, INR should be sent along with other routine investigations. APTT can be helpful in UFH induced bleeding while estimation anti-factorXa levels can provide the degree of anticoagulation in LMWH associated bleeding.Tests for the anti-coagulant

activity of DOACS are much more complex ,not easily available and requires specialized/reference laboratory.

4. Management of bleeding to specific Anticoagulants :

4. 1 Heparin and Heparinoids :

The incidence of major bleeding with UFH is around 2-3% from various studies[4] The half life of UFH is around 45-60 minutes and is monitored by APTT levels with target therapeutic range between1.5-2.5.Due to short half life of UFH bleeding can often be controlled by temporarily stopping the drug. Protamine sulphate derived from the sperm of salmon completely neutralizes the action of UFH and can be used in cases of bleeding.1mg of protamine sulphate neutralizes around 100 units of UFH[5] It must be given slowly (<5mg/minute) because of the risk of anaphylaxis and bronchospasm. Because of the short half life of protamine sulphate repeated injections may be required .Bleeding with LMWH is more difficult to manage as protamine sulphate only neutralizes 60% of LMWH. In cases of ongoing bleeding with LMWH despite protamine sulphate rFVIIahas been used with good results[6] APTT is not reliable in cases of LMWH hence estimation of anti-factorXa should be done.Renal impairment increases the risk of bleeding with both UFH and LMWH .Due to the longer half life of LMWH there is a risk of bio-accumulation in cases of renal impairment and hence increased chances of bleeding than UFH. Protamine sulphate cannot reverse bleeding caused by Fondaparinux and hence other strategies(APCC /rFVIIa/Hemodialysis) should be utilized.

4.2 VKA antagonist :

VKA antagonist such as coumadin derivaties are one of the most commonly used anti-coagulation used world widein atrial fibrillation, prosthetic heart valves and ischemic stroke. Owing to oral formulation, low cost ,ease of monitoring and excellent efficacy they are the mainstay of anticoagulation in the developing world. They inhibit post translational modification of Vitamin -K dependent factors (Factor II, VII, IX, and X) causing anti-coagulant activity.Warfarin and other coumadin derivatives have a narrow therapeutic window predisposing to increased risk of major bleeding specially intracerebral hemorrage(ICH).Risk factors for warfarin associated bleeding are summarized in Table 1[7] The anticoagulant activity is monitored by International Normalised ratio(INR) with a target INR between 2.0-3.0 and higer values in cases of prosthetic hart valves. Various modalities to treat warfarin associated bleeding are summarized below.

4.2(a) Vitamin K :

Can be given by orally or intravenously ;however intravenous route is the preferred route in cases of major bleeding. The ACCP (American college of chest physicians) recommend 5 to 10mg of Injection Vitamin K intravenously slowly over 30 minutes to reverse warfarin associated bleeding along with APCC/PCC .[8]

4.2(b) Prothrombin complex concentrate(PCC) :

There are two types of Prothrombin complex concentrate(PCC); 3 factor PCC and 4 factor PCC.The later contains F VII in addition to factor II, IX, and X.Various studies have shown the favorable efficacy of 4 factor PCC in quickly reversing prolonged INR ,reducing mortality without causing volume overload.The ACCP recommends 4 factorPCC along with Vitamin K for prompt reversal of Warfarin associated coagulopathy.Furthermore it doesn't require blood group matching and can be readily given.The recommended dose is 25U/KG to 100U/KG depending upon the product used[9]

4.2(c) FFP :

It contains majority of the clottting factors including Vitamin K dependent factors and can correct the coagulopathy,however large volumes of FFP (>2L) required is required for correction causing risk of volume overload and transfusion reactions. Use of FFP is not preferable in this setting and can be only used if other measures are not available.

Stepwise algorithm for warfarin reversal is summarized in Figure 1.

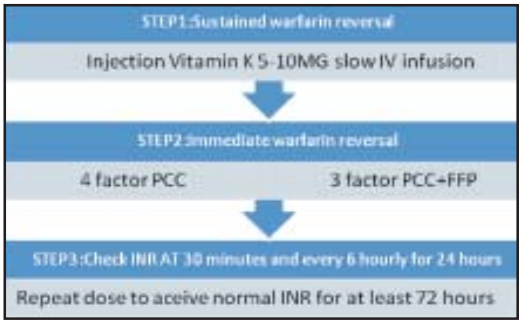

Figure 1: Stepwise algorithm for warfarin reversal

Table1: Risk factors for Warfarin associated bleeding

1. Concomitant anti-platelet use.
2. Poor hypertension control.
3. Advanced age>65Years.
4. Cerebral amyloid angiopathy.
5. Genetic polymorphism (CYP2C9).

4.3 Warfarin associated ICH: ICH is the commonest major hemorrhagic manifestation of Warfarin leading to mortality.Markers of poor prognosis in ICH are a)Failure to lower INR rapidly b)Midline shift c)Large intraventricular extension c) Large volume of bleed[10].

4.4 DOACS AND DIRECT THROMBIN INHIBITORS :

All direct thrombin inhibitors are parenteral anticoagulants except dabigatran. For parenteral agents no specific antidote is aavailable and bleeding has to be managed by stopping the drug and other conservative measures. For dabigatran a TT(Thrombin time),Ecarin clotting time (ECT) may be sent in cases of bleeding although availability of specialised laboratory is a concern[11].Idarucizumab, a specific reversal agent for dabigatran, is a monoclonal Fab antibody fragment that binds to dabigatran and completely reverses its anticoagulant effect within minutes.The final report of the Reversal Effects of Idarucizumab on Active Dabigatran trial analyzed outcomes in 503 patients who received idarucizumab for reversal of dabigatran in the setting of major bleeding (301 patients in group A) or urgent surgery (202 patients in group B). Of the 203 evaluable patients with major bleeding, 134 (67.7%) had complete cessation of bleeding within 24 hours (the median time to hemostasis was 2.5 hours)[12].Its availability is restricted to very few centres in the world. In institutions or countries having no access to Idarucizumab,4 Factor PCC may be used in case of dabigatran induced bleeding.Due to the low protein binding of Dabigatran hemodialysis is an option to remove the drug although insertion of dialysis catheter is technically challenging in a bleeding patient[13].

4.5 Reversal of direct factor Xa inhibitors :

Bleeding with these agents are difficult to manage owing to challenges in lab monitoring as well as limited antidote and availability of the same.They are known to cause gastrointestinal and genito urinary bleeds and hence should be used in caution these kind of patients[14].Anti factorXa levels may give an assessment of anticoagulant activity of these agents.Andexanet alfa is an inactive form of factor Xa that acts as a “decoy” via binding and sequestering the factor Xa inhibitors, which also include fondaparinux and LMWH. The interim report of the Prospective, Open-Label Study of Andexanet Alfa in Patients Receiving a Factor Xa Inhibitor Who Have Acute Major Bleeding study examined the efficacy and safety of andexanet alfa in managing major bleeding in 228 patients who were taking a factor Xa inhibitor. Of 132 patients adjudicated for efficacy, good or excellent hemostasis was achieved at 12 hours in 109 patients (83%, 95% confidence interval, 75-89). At 30 days, 24 patients (11%) had a thrombotic event and 27 (12%) died[15].It has been approved by the FDA for DOACS reversal although although its availaibility is confined to very centres.4 factor PCC may be used if Andexanet alpha is not available.

5.0 Conclusion :

Bleeding due to anticoagulant especially ICH can be life threatening .A high index of suspicion and timely reversal of the bleeding episodes is required to prevent significant morbidity and mortality.With more and more physicians shifting towards DOAC therapy it is imperative to have antidotes and laboratory facilities available along with supportive care for major bleeding.

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Case Report

BRAIN ABSCESS IN TETRALOGY OF FALLOT : A RARE CASE REPORT

Dr. Raja Ram Mohan Pal[1], Dr. L.K. Dash[2], Dr. B.L. Parija[3], Dr. B. Samantaray[4], Dr. S.K. Jangid[5]

Abstract :

A case of uncorrected TOF presenting as a right tempero-occipital brain abscess in a 17yr old boy.Brain abscess is a rarely occurring fatal complication accounting for 5-18.7% of the population with cyanotic congenital heart disease. Cyanotic heart diseases are associated with right to left shunt that bypasses pulmonary circulation & results in tissue hypoxia &cyanosis.The most common cyanotic congenital anomaly seen is the TOF. The patient was managed conservatively on intravenous antibiotics &Antiepileptics patient fully recovered & then referred to Cardio-thoracic Surgeons for the repair of the defect. The purpose of reporting this case is to highlight the importance of early detection & correction of cardiac defects to prevent serious complication resulting morbidity &mortality .

Introduction :

TOF is a cyanotic congenital heart disease characterized by four anatomical features as overriding of aorta , Right ventricular hypertrophy, ventricular septal defect, pulmonary artery stenosis. It accounts for approximately 7-10%of infants with congenital heart disease & affects about 1 in 3500 live births, TOF complications like heart failure, cerebral thrombosis, cerebral abscess, seizure,endocarditis.

Case Summary :

A 17 year old boy presented with c/o- high grade fever with chills & rigor since last 10 days,headache,blurring of vision & vomiting since last 10 days,seizure 2 episodes on the day of admission, O/E-clubbing +, neck rigidity +,CBC-WBC 19000,N-90%,ECG shows – sinus arrhythmia,RA enlarged, Twave inversion (iii,avr,v1,v2) 2DECHO SHOWS- Lt to Rt shunt, overriding of aorta,large VSD, no ASD, PDA, no PAH, EF- 60%. MRI BRAIN + contrast-right side tempero-occipital region shows irregular ring enhancing abscess size-45 X 38 X 24mm with surrounding vasogenic edema extending to the right occipital parietal & temporal deep white matter. Impression- RT tempero-occipital region brain abscess with ventricullitis .our final diagnosis Untreated TOF with Brain abscess, patient was managed with inj MEROPENEM 1gm iv TDS,inj VANCOMYCIN 500mg IV TDS, inj PCM 1gm IV SOS, inj LEVETIRACETAM 500mg iv TDS ,Patient showed marked improvement within 3 days, he was discharged on day 10 with oral antibiotics for further 2 weeks .On follow up after 1 month the patient fully recovered & no neurological deficits or seizure were observed he was referred to CARDIAC surgeons for correction of TOF.

Discussion :

Tetralogy of fallot (TOF) is a congenital heart disease that combines four major development defects of the heart, it is also known as cyanotic heart disease due to underlying right -to- left sided shunt present with cyanosis in early childhood. Complication of untreated TOF such as improper growth & development of the child, delayed milestones, secondary polycythemia, severe infective endocarditis & brain abscess has been reported as rare manifestation. Brain abscess is a infectious disease more commonly seen in developing countries where infections are endemic,sanitation is poor, basic tertiary care hospitals are not that adequate in numbers leading to late detection of disease causing fatal complications.

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There are many factors responsible for the occurrence of brain abscess in CCHD patients, bypassing the pulmonary circulation, the blood in these patients is not filtered by normal alveolar phagocytes. This increases the probability of direct entrance of pathological micro-organisms into the circulation of brain, due to this brain might be hypo-perfused due to severe hypoxemia & metabolic acidosis resulting from secondary polycythemia ,allows the pathogens to seed such under perfused regions ,leading to hematogenous spread from a distant source is attributed to cerebral abscess. Brain abscess is three times more common in men than women, even though rare in occurrence ,it is potentially fatal & is associated with high morbidity especially affecting people in their forties. Mortality in untreated patients ranges from 27.5 % - 71 %.This case of 17 yr old male with TOF who presented with brain abscess represents a remarkable medical challenge, emphasizing the critical significance of early detection & treatment in context of uncommon clinical scenario, TOF itself is a complex congenital heart condition characterized by four structural defects within the heart when coupled with brain abscess the situation becomes complicated.

Empirical medical therapy is an exclusive treatment for cases where the size of abscess is less than 2 cm in diameter, the patient is neurologically stable and being monitored by repeated CT scans.

Larger or deep-seated abscesses should be aspirated immediately and repeatedly. Following aspiration, the patient should be started on appropriate antibiotic therapy specifically targeting the organism discovered in culture .

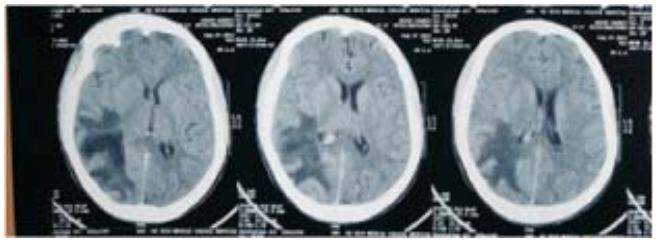

Fig 1 CECT Brain showing SOL with surrounding edema in Rt Temporo-occipital area

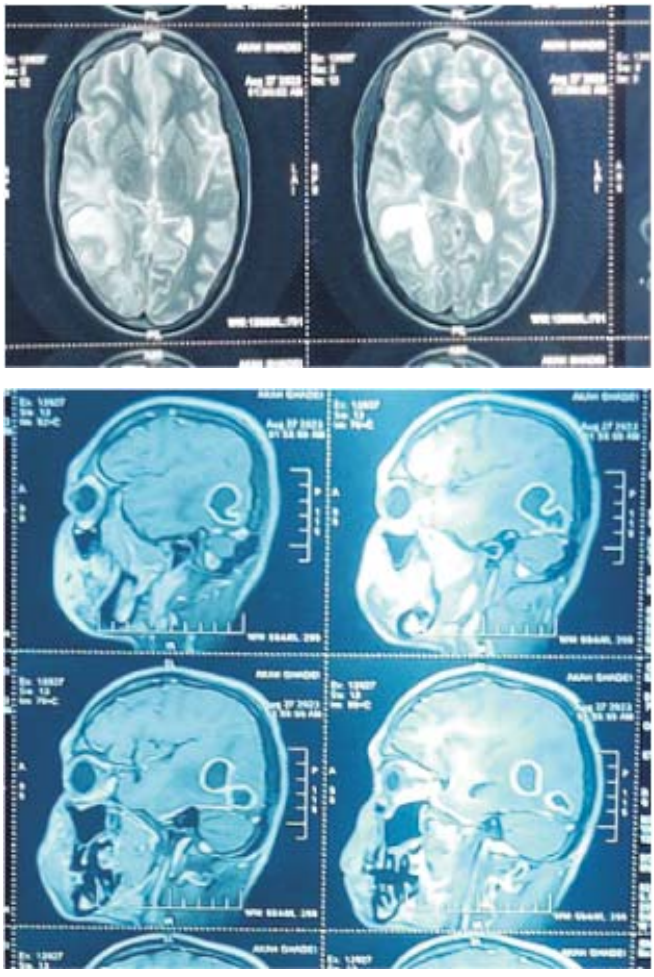

Fig 2, 3 MRI Brain with contras Showing right side tempero-occipital region shows irregular ring enhancing abscess with surrounding vasogenic edema

Conclusion :

Considering the fact that brain abscess complicates uncorrected cyanotic congenital heart disease(CCHD),physicians must hold a high index of suspicion for potentially dealing with a case of CCHD related brain abscess to avoid unnecessary dely in diagnosis & management. Most importantly,parents of children diagnosed with (CCHD) should be counseled on how to recognize serious signs & symptoms of brain abscess & when to seek urgent medical attention.

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Case Report

MOGAD WITH UNILATERAL OPTIC NEURITIS : A RARE CASE REPORT

Dr. Suvam Saswat Rout[1], Dr. Jibanjyoti Das[2], Dr. Susanta Kumar Bhuyan[3], Dr. Premakanta Mohanty[4], Dr. Namita Mohapatra[5]

Introduction :

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a demyelinating disorder of the central nervous system (CNS) distinct from multiple sclerosis (MS) and aquaporin 4 (AQP4) immunoglobulin G (IgG) antibody-associated neuromyelitis-optica spectrum disorder (NMOSD).IgG autoantibodies targeting myelin oligodendrocyte glycoprotein (MOG), a minor transmembrane surface protein found on the outermost lamellae of CNS myelin and oligodendrocytes [1].Annual incidence of MOGAD worldwide is approximately 1.6–4.8 per million people, with a prevalence estimated at 1.3–2.5 per 100,000 people [2].The median age of onset is 20–30 years [3].Optic neuritis (ON) is the most common initial manifestation of MOGAD in adults (~30–60%), followed by transverse myelitis (~10–25%), but unilateral involvement of Optic Nerve is quite rare

Case Description :

A 30-year-old female was admitted with complaints of

- ❖ sudden onset blurring of vision in left eye for 4 days.
- ❖ not associated with fever, headache, vomiting, seizure, orbital pain or any focal neurological deficits.
- ❖ Not a k/c/o DM, HTN, TB, Thyroid disorders.
- ❖ The patient had normal vitals at presentation and general-examination revealed no abnormality.

Neurological-Examination :

Visual acuity of 1/60 in left eye and no improvement with pinhole and 6/6 in right eye. Fundoscopy was normal in both eyes.Normal higher function, other cranial nerve functions, motor, sensory, cerebellar and autonomic functions.

CSF Study	Value
Glucose	52 mg
Protein	35 mg
Cells	2 /mm3
OCB	Absent
Culture	negative

INVESTIGATIONS :

Parameters	Value
Hb	11 g/dl
RFT	WNL
LFT	WNL
TFT	WNL
ESR	**40 mm/hr**
FBS	88 mg/dl
ANA	Negative
AQP4 ab	Negative
MOG ab	**POSITIVE**

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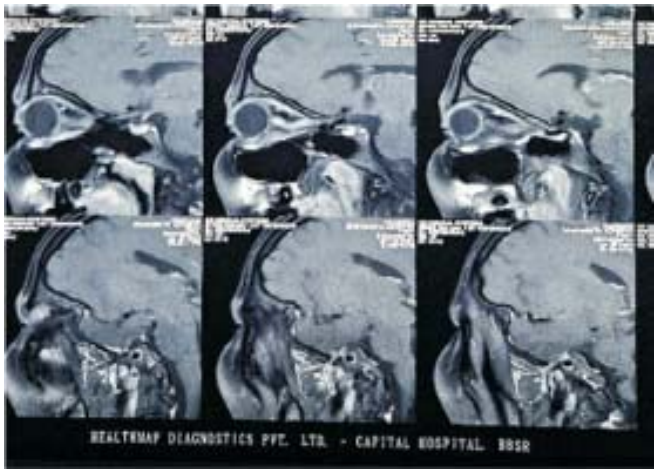

Fig. 1 **MRI-Orbit** showed T2 hyperintensity with differential enhancing seen in intra-orbital part of left optic-nerve suggestive of Optic-Neuritis.

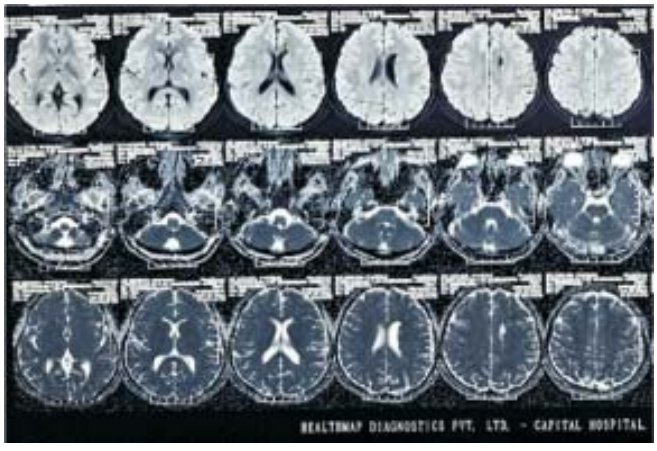

Fig 2 .MRI-Brain showed multiple small nodular subependymal lesions in left lateral ventricle suggestive of grey matter heterotopia.

Management :

The patient was started with pulse dose methylprednisolone (1gm) for 5 days followed by 1 mg/kg oral steroid with tapering dose along with Azathioprine 50mg daily. Injection Rituximab 1g given 2 doses at 14 days interval to prevent relapse and patient showed gradual improvement at 6 month follow up.

Conclusion :

ON is the most common relapsing syndrome in both adults and children with MOGAD, occurring in 28-91% of relapsing cases, and may be recurrent unilateral, contralateral or simultaneous bilateral ON. [1]Patients with ON at onset can also develop other, non-ON relapsing syndromes such as transverse myelitis, aseptic meningitis and cerebral cortical encephalitis with seizures . [1]Compared with AQP4-IgG-positive NMOSD and classical MS, the prognosis of MOGAD is optimism.

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Case Report

TAKAYASU ARTERITIS PRESENTING AS STROKE – A RARE CASE REPORT

Dr. Girija Prasad Bisoi[1], Dr. Jagannath Sadangi[2], Dr. Nihar Ranjan Sahoo[3], Dr. Samir Kumar Behera[4]

Introduction :

Takayasu arteritis is an inflammatory vascular disease of unknown etiology that mainly affects the aorta and its branches and the pulmonary arteries. Stroke in young people is a rare manifestation of the disease. In the progressive stage of arterial wall fibrosis and thickening.cerebrovascular events such as transient

patients.

Case report :

A 34 yr female presented to emergency department with sudden onset weakness of both left upper limb and lower limb with right sided deviation of mouth for 1 day.She had been complaining of headache and both shoulder pain with feeling of pain and numbness in her left arm past month. On examination patient was conscious oriented with PR of 85bpm in right arm, Pulse is feeble in left upper limb.BP was 136/86mmhg in right upper limb and 80/50mmhg in left upper limb .right lower limb BP was 148/82mmhg,in left lower limb it was 144/80mmhg . Bruit was present over the carotid artery. Left sided weakness was there with positive Babinsky on left side. Other systemic examination was unremarkable.

Laboratory testing shows normal CBC. Normal LFT and RFT.ESR was 60mm in 1st hour. CRP was 18. Normal ECG and chest X-ray.

In NCCT Brain- acute infarct in Frontal, parietal and right ganglio capsular region (right MCA territory)

In chest and neck and brain CT angiography- Near complete luminal occlusion of left common carotid artery ,near complete occlusion of left subclavian artery at ostium. Occlusion of brachiocephalic trunk and mild luminal narrowing of thoracic aorta was there

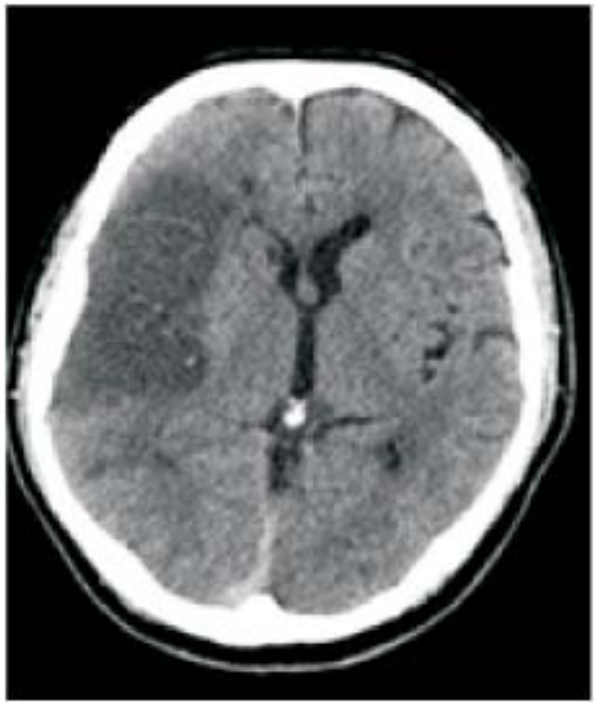
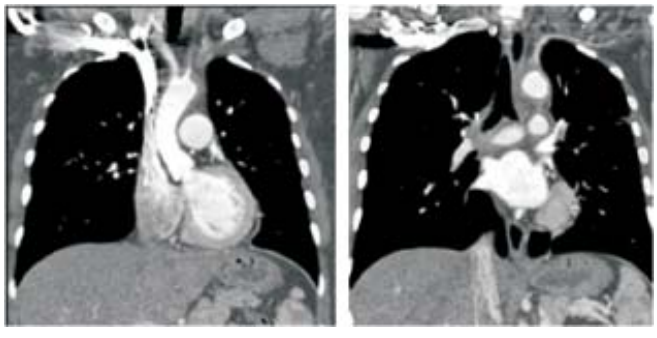


Fig 1 NCCT Brain Showing acute infarct in Frontal, parietal and right ganglio capsular region



[Fig 2 and 3 CT Angiography showing near complete occlusion of Left Common carotid and left subclavian Artery]

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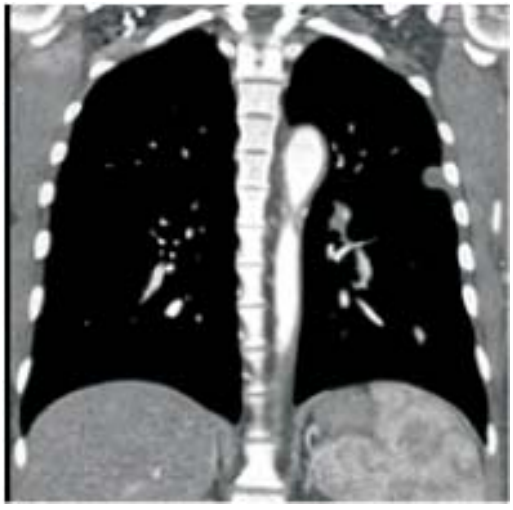

Fig 4. Showing mild luminal narrowing of thoracic aorta.

Given the clinical examination,laboratory results and CT angiography a provisional diagnosis of Takayasu arteritis was made and the patient was started on high dose steroid and methotrexate. Subsequently the patient had normalise ESR AND CRP. Previously for acute infarct the patient was given Aspirin and Atorvastatin with physiotherapy as the patient was presented beyond window period.

Conclusion :

Young patients with stroke as initial presentation should be evaluated for Takayasu arteritis. Early identification of the disease is important as continuous medical treatment along with timely intervention will halt inflammation and disease progression to the permanent stenotic phase.

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Case Report

A CASE SERIES OF A MULTIDENOMINATE MIMICKER OF ENCEPHALOPATHY : STEROID-RESPONSIVE ENCEPHALITIS ASSOCIATED WITH AUTO-IMMUNE THYROIDITIS (SREAT)

Dr. Jayshree Sahu[1], Dr. Tony Mathew Austin[2], Dr. Sagnika Tripathy[3]

Introduction

Steroid Responsive Encephalitis Associated with Auto-immune Thyroiditis (SREAT) ,as the name suggests, is an autoimmune complex neuro-endocrine disorder, which most often than not is associated with a thyroid disorder and has a rare occurrence with an estimated prevalence of 2.1 in 1 Lakh. Previously known as Hashimoto encephalopathy, it was first described in 1966 by Lord Brain[1]. The disease shows a female preponderance with cases being reported in patients aged 14- 70 years, average age being 40-53 years[2].Clinical manifestations of SREAT are varied and nonspecific, with majority of cases run a fluctuating course with features such as cognitive impairment, seizures including status epilepticus, myoclonus, tremor, ataxia, sleep disturbance, headache, depression and/or psychosis[2,3,6]. Occurance of focal neurological deficits has been described as well. Due to lack of any specific diagnostic investigations SREAT is mainly a diagnosis of exclusion. SREAT is considered in the setting of encephalopathy with high anti TPO Ab titers and responsiveness to glucocorticoid therapy[2,3,4].Here we present a series of 3 such cases, with varied presentations, yet with the same diagnosis, showing the need to address the disease as a rare, yet curable, form of encephalopathy.

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Case Details :

CASE - 1 :

37 year female presented with complain of sudden onset loss of consciousness, opsoclonus and myoclonic jerk of both lower limb, of 7 days duration. Her myoclonic jerks were subacute in onset and progressed over few weeks hampering her movements completely. Before our assessment patient was treated as psychosis and conversion disorder without any improvement in her condition.There was no history of substance abuse nor family history of similar illness.Her mother had informed about irregular menstrual cycles and considerable gain of weight in the past few Years.

She was cold with an axillary temperature of 34.4 degree Celsius and had a heart rate of 55 beats per minute. There was bilateral pitting pedal edema and facial puffiness. At the time of examination, patient had a GCS of 10, and had sluggish deep tendon reflexes. There were no evidence of meningeal irritation. Rest of the physical examination was normal.

Her routine blood investigations, ABG, CT and MRI of brain were normal. Electro-Encephalograph (EEG) showed no significant abnormality. CSF examination revealed increased levels of proteins with normal WBC count, sugar, ADA levels and normal opening pressure. Antinuclear bodies were negative. Serum copper and ceruloplasmin level was normal. Her thyroid profile was suggestive of hypothyroidism with total T3 levels at 0.56 ng/dl, fT3 levels at 1.6 pg/ml, total T4 levels at 4.2 mcg/dl, fT4 levels at 0.85ng/dl, and a TSH of 18.6mIU/L. Further testing of serum

anti-TPO antibody showed strong positivity with an absolute value of 1210IU/ml.

With this clinical profile, positive anti-TPO antibodies, normal metabolic, infectious, structural and other autoimmune parameters, she was diagnosed with Hashimoto encephalopathy and was started on pulse IV steroid therapy with 1gm methyprednisolone once daily for five days, along with levothyroxine supplementation and anti-epileptic. By day 3 of steroid therapy she showed signs of improvement, with a GCS score of 13 and decreased frequencies of opsoclonus and myoclonus. By day 5, she had a GCS of 15 with occassional myoclonic jerks and no further episodes of opsoclonus. Her anti-epileptics were gradually tapered, and oral prednisolone at 1mg/kg was started. She was discharged on day 14, with tapering dose of oral prednisolone.

		Observed	Normal			Observed	Normal
HEMATOLOGY	Haemoglobin (g/dl)	13.4	12-16	**SEROLOGY**	Sodium (mEq/L)	138	135-145
	RBCCount (millions/mm3)	4.6	4.2-5.4		Potassium (mEq/L)	4.3	3.5-5.0
	WBCcount (permm3)	8412	4000-11000		Calcium (mmol/L)	2.3	2.2-2.6
	PCV(%)	42%	36-47%		Urea (mg/dL)	22	<30
	ESR (mm/1sthr)	18	<20		Creatinine (mg/dL)	0.8	<1.2
					Fasting Glucose (mg/dL)	96	106
URINE	Casts	Nil			HbA1c (%)	5.4	<5.6
	Glucose	Nil			Total Bilirubin (mg/dL)	1.0	<1.2
	Protein	Nil			Direct Bilirubin (mg/dL)	0.14	0.3
	RBC	Nil			SGOT (IU/L)	34	<40
	Bacteria	Nil			SGPT (IU/L)	32	<40
	Cultureand Sensitivity	Nogrowth			ALP (IU/L)	156	<150
					Total Protein (g/dL)	6.8	6-8
					Albumin (g/dL)	4.1	3.5-5.0

CSF	Glucose (mg/dL)	46	<60	**THYROID PROFILE**	S.TSH (mIU/L)	18.6	0.5-5.0
	Protein(g/dL)	0.6	<0.45		TotalT3 (ng/mL)	0.56	0.8-2.0
	Cytology (cells/mm3)	3 cells	<5		fT3 (pg/mL)	1.6	2.7-3.9
	ADA(IU/L)	2.6	<10		TotalT4 (mcg/dL)	4.2	4.5-9.5
	AutoImmune-encephaliti-spanel	-ve			fT4 (ng/dL) AntiTPO (IU/mL)	0.85 1210	0.9-1.75 <34

MISCELLANEOUS	HIV	Non Reactive	
	HBsAG	Non Reactive	
	CRP (mg/dL)		
	LDH (IU/L)	280	<350
	D-Dimer (mcg/ml)	0.1	<0.5

RADIOLOGY	
Chest Xray	NormalImpression
USGabdomen	NormalImpression
CT Brain	NormalImpression
MRI Brain	NormalImpression
EEG	NormalImpression

CASE - 2 :

20 year old male presented with myoclonic jerk of lower limb of 4 days duration,not preceeded by fever, trauma or seizures. There were no aggravating or relieving factors, and all episodes occurred at random. He had no significant personal or family history with immunizations given for age. On examination, he had normal appearance, with all vital signs normal. Thyroid appeared normal on examination. Systemic examinations of all major systoms yielded normal findings. Suspicious of myoclonic epilepsy, our patient was started on loading dose of Sodium Valproate, followed by maintenance dose. Routine blood investigations were normal. He had a TSH value of 12mIu/L, albiet for a normal T3 and T4 values, consistent with subclinical hypothyroidism. His MRI brain along with MR angiogram of cranial vessels and EEG were normal. Any secondary cause of seizure could not be found. His CSF findings were normal. Serum anti-TPO titers were highly elevated to 2192 IU/ml.

Based on this Hashimoto encephalopathy diagnosis was made and was treated like case1.His jerks decreased in frequency by 2nd day, and completely stopped by day 6. His Anti-epileptic dose was tapered orally, with oral thyroxine supplementation.

		Observed	Normal			Observed	Normal
HEMATOLOGY	Haemoglobin (g/dl)	15.1	14-18	**SEROLOGY**	Sodium (mEq/L)	143	135-145
	RBC Count (millions/mm3)	5.6	4.7-6.1		Potassium (mEq/L)	4.6	3.5-5.0
	WBCcount (permm3)	10880	4000-11000		Calcium (mmol/L)	2.5	2.2-2.6
	PCV(%)	46	38-49		Urea (mg/dL)	18	<30
	ESR(mm/1sthr)	6	<15		Creatinine (mg/dL)	0.5	<1.2
					Fasting Glucose (mg/dL)	102	106
URINE	Casts	Nil			HbA1c (%)	4.9	<5.6
	Glucose	Nil			Total Bilirubin (mg/dL)	1.0	<1.2
	Protein	Nil			Direct Bilirubin (mg/dL)	0.2	0.3
	RBC	Nil			SGOT (IU/L)	26	<40
	Bacteria	Nil			SGPT (IU/L)	18	<40
	Cultureand Sensitivity	Nogrowth			ALP (IU/L)	180	<150
					Total Protein (g/dL)	7.5	6-8
					Albumin (g/dL)	4.9	3.5-5.0
CSF	Glucose (mg/dL)	41	<60	**THYROID PROFILE**	S.TSH (mIU/L)	12	0.5-5.0
	Protein (g/dL)	0.55	<0.45		TotalT3 (ng/mL)	1.5	0.8-2.0
	Cytology (cells/mm3)	1 cell	<5		fT3 (pg/mL)	3.1	2.7-3.9
	ADA(IU/L)	1.2	<10		TotalT4 (mcg/dL)	8.3	4.5-9.5

	AutoImmu-neencephal-itispanel	-ve			fT4 (ng/dL)	1.14	0.9-1.75
					AntiTPO (IU/mL)	2192	<34

MISCELLANEOUS	HIV	Non Reactive	
	HBsAG	Non Reactive	
	CRP (mg/dL)		
	LDH (IU/L)	180	<350
	D-Dimer (mcg/ml)	0.01	<0.5

RADIOLOGY	
Chest Xray	NormalImpression
USGabdomen	NormalImpression
CT Brain	NormalImpression
MRI Brain	NormalImpression
EEG	NormalImpression

CASE - 3 :

A 42 year old female with sudden episode of loss of consciousness followed by unresponsiveness, with no history of fever, trauma or convulsions. There were no history of any known medical disease or substance abuse. On examination, our patient was stuperous with a GCS of 10, and normal vital signs except for a heart rate of 58 beats per minute. She had a smooth diffusely enlarged thyroid.

Detailed CNS examination revealed hypotonia, sluggish deep tendon reflexes and withdrawal plantar reflexes, bilaterally. There were no evidence of any meningeal irritation, and fundoscopy was normal. Other system examinations were normal. Her CT brain was normal without evidence of any bleed or any space occupying lesion. Apart from neutrophilic leucocytosis, her hematological and biochemical parameters were normal, including serum electrolytes. Considering the possibility of encephalitis, she was started on antibacterials and antivirals, as per hospital protocol. CSF study was normal, barring a mild increase in total protein. S. TSH was raised to 25mIU/L with fT3 1.8 pg/ml and fT4 0.76ng/ml. MRI of her brain was normal and so was her sleep EEG. Further evaluation revealed a serum Anti-TPO level of 1872 IU/ml. Following no clinical response to anti-bacterials by day 3, and new found evidence of Hashimoto Encephalopathy, she was started on intravenous pulse steroid, to which she reponded by end of Day 6 by regaining her consciousness. Subsequently, FNAC from her thyroid swelling was suggestive of Lymphocytic Thyroiditis. She was hence discharged with a diagnosis of Hashimoto's Thyroiditis with SREAT, and was put on maintenance dose of oral steroid and oral Levothyroxine.

		Observed	Normal			Observed	Normal
HEMATOLOGY	Haemoglobin (g/dl)	12.1	12-16	**SEROLOGY**	Sodium (mEq/L)	136	135-145
	RBCCount (millions/mm3)	4.3	4.2-5.4		Potassium (mEq/L)	3.5	3.5-5.0
	WBCcount (permm3)	13100	4000-11000		Calcium (mmol/L)	2.2	2.2-2.6
	PCV(%)	38%	36-47%		Urea (mg/dL)	12	<30
	ESR (mm/1sthr)	22	<20		Creatinine (mg/dL)	0.9	<1.2
					Fasting Glucose (mg/dL)	88	106
URINE	Casts	Nil			HbA1c (%)	5.5	<5.6
	Glucose	Nil			Total Bilirubin (mg/dL)	0.6	<1.2
	Protein	Nil			Direct Bilirubin (mg/dL)	0.1	0.3
	RBC	Nil			SGOT (IU/L)	39	<40
	Bacteria	Nil			SGPT (IU/L)	38	<40
	Cultureand Sensitivity	Nogrowth			ALP (IU/L)	180	<150
					Total Protein (g/dL)	6.1	6-8
					Albumin (g/dL)	3.6	3.5-5.0
CSF	Glucose (mg/dL)	46	<60	**THYROIDPROFILE**	S.TSH (mIU/L)	25	0.5-5.0
	Protein(g/dL)	0.6	<0.45		TotalT3 (ng/mL)	0.45	0.8-2.0
	Cytology (cells/mm3)	3 cells	<5		fT3 (pg/mL)	1.8	2.7-3.9
	ADA(IU/L)	2.6	<10		TotalT4	4.1 (mcg/dL)	4.5-9.5

	AutoImmune-encephaliti-spanel	-ve			fT4 (ng/dL)	0.76	0.9-1.75
					AntiTPO (IU/mL)	1872	<34

MISCELLANEOUS	HIV	Non Reactive	
	HBsAG	Non Reactive	
	CRP (mg/dL)		
	LDH (IU/L)	320	<350
	D-Dimer (mcg/ml)	0.7	<0.5

RADIOLOGY

Chest Xray	NormalImpression
Chest Xray	NormalImpression
USGabdomen	NormalImpression
CT Brain	NormalImpression
MRI Brain	NormalImpression
EEG	NormalImpression

FNAC Thyroid Presence of lymphoid cells in all stages of maturation a long with follicular cells in sheets in ahemorrhagic background. Impinging of lymphocytesin to the follicular cell clusters seen. Presence of few epitheloidcells and few fibro blasts. Nodysplastic/malignantcels seen.

Discussion :

SREAT, a form of nonvasculitic auto-immune inflammatory meningoencephalopathy,includes a wide spectrum of neurological features ranging from cognitive decline, psychosis, stroke like symptoms, myoclonus, tremors, autonomic features, cerebellar involvement and extrapyramidal features.

Sometimes, it may present with an acute encephalopathy, and may have a relapsing and remitting course. Common differential diagnoses when these conditions are excluded are Creutzfeldt-Jakob disease, rapidly progressive dementias, and paraneoplastic and non-paraneoplastic limbic encephalitis.This diagnosis is usually considered in patients with the above neurological symptoms, accompanied by either a euthyroid state or mild hypothyroidism, normal or non-specific MRI and CSF findings and an increased serum and/or CSF levels of thyroid antibodies (anti-TPO and/ or anti- TG) [7]. Treatment with corticosteroids is almost always successful, although relapse may occur if this treatment is ceased abruptly[5]. Other forms of immune-modulation, such as intravenous immune-globulin and plasma exchange, may also be effective[5].

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Case Report

PARAPLEGIA AS THE PRIMARY PRESENTATION OF ACUTE MYELOID LEUKEMIA : A RARE CASE REPORT

Dr. J. Mallick[1], Dr. D. Panda[2], Dr. A. Mishra[3], Dr. R.K. Sen[4], Dr. B.K. Behera[5]

Abstract :

Herein,we report a rare presentation of a case with acute myeloid leukemia (AML), who presented as acute flaccid paraplegia with a certain sensory level. On thoracic spine magnetic resonance imaging(MRI), anepidural mass compressing the spinal cordat the level of the thoracic spine segment T2 – T8 was found. AML panel showed AML1-ETOt(8;21).

Keyword : AML, Paraplegia

Introduction :

AML is a rapidly progressive myeloid neoplasm characterized by the clonal expansion of primitive hematopoietic stemcells in the bonemarrow[1]. Clinicalfeatures include pallor, easy fatigability ,lethargy, Bleeding and fever. Organ Infiltration is less frequent Compared to ALL. Although neurological symptoms usually present late, it ranges from muscle weakness, paresthesia, hypoesthesia to fecal and urinary incontinence. Paraplegia due

To epidural mass is an extremely rare presentation of undiagnosedl eukemia[2].The thoracic region is the most frequently involved region, followed by the lumbar region. The sacral cord is the rarest region implicated[3]. Here, we present a case of AML presenting with paraplegia at the initial diagnosis.

Case Report :

A 14-year-old boy presented with acute onset tingling of both legs, and subsequently developed inability to move both lower limbs and urinary and fecal incontinence. There was no associated history of trauma, fever and tuberculosis.

On physical examination patient was pale, afebrile, anicteric, no lymphadenopathy or hepatosplenomegaly. Respiratory, cardiovascular, and abdomen examination were unremarkable. There was vertebral tenderness in the mid – thoracic region.

Examination of both lower limbs revealed decreased tone, power of 0/5 and absent reflexes with bilateral Babinski sign positive.

There was loss of all modality of sensations from few centimeters below the clavicle. Cranial nerves examination were normal.

Complete blood count showed :

Hb-7.3gm/dl, TLC–32000/µL (N88%, L4.1%, M6.9%, Immaturegranulocyte 19.3%) Peripheral blood film showed anisocytosis and neutrophilic leukocytosis and thrombocytopenia (78000 / µL). Reticulocyte count – 0.064 x 10^6/ µL.

Lactate Dehydrogenase (LDH) serum assay was 729U/L.

Bone marrow aspiration cytology stained with Leishman stain was consistentwithacute promyelocytic leukemia (APML) FAB – AML M3.

Cerebro spinal fluid analysis was negative formalignant cells.

Magnetic resonance imaging of the whole spine was obtained; MRI showed D2 to D8 level extramedullary epidural soft tissue space occupying lesion (SOL) compressing the cord dorsally with signal alteration as T1 isointense and T2 intermediate suggestive of (S/O) chloroma.

AMLpanelshowedAML1-ETOt(8;21). Patient was commenced on supportive therapy and induction chemotherapy after being referred to hematology.

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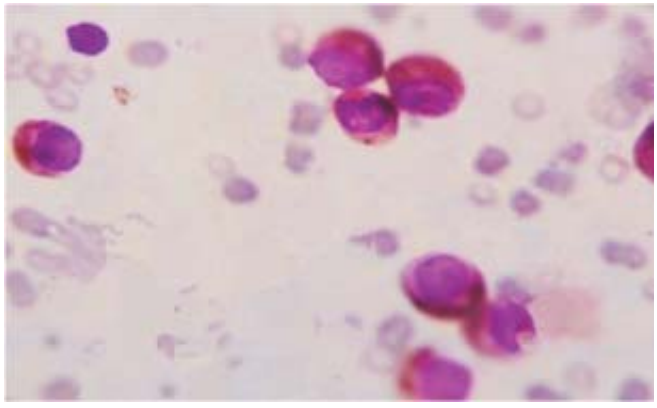

Discussion :

Leukemic cell invasion of the central nervous system(CNS) in patients with AML has been reported in ~3% cases but is lower compared with the incidence in children and adults with acute lymphocyticleukemia (ALL)[4]. Involvement of the CNS mayresultacutelyfrom the disease at the diagnosis, as in the index case; from relapse of the disease or from complications of agents used in treatment. The presence of certain factors has been associated with increased risk of neurological complication. These include hyperleukocytosis, high level of lactatede hydrogenase and high expression of CD56[5].Ina single institution study of 290 pediatric patients withAML, the authors found significant relation between CNS involvement in patients with AML having the cytogenetic abnormality Inv16, t[8:21] or, AMLM4, M5subtype[6]. The authors concluded that CNS

involvement is common in those with favorable cytogenetics. As mentioned above, the peripheral blood film, bonemarro was pirationcytology, cytogenetics of the index patient was in keeping with AMLM3 witht [8:21] subtype, and LDH1729U/L therefore belonged to a high risk group for CNS involvement. Several mechanisms have been putforward to explain the pathogenesis of CNS involvementinleukemia, this includes contamination of the CSF through the choroid plexus or infiltration of the cerebral parenchyma through brain capillaries; direct extension of aggregates of leukemic cells called chloroma, from the bone marrow through the cortical bones into the spinal cord, may cause symptomsas a result of mass effect on neural tissue[7].

Hyperleukocytosis with thrombos is may result inleukostasis and consequently poor CNS perfusion. Intracranial hemorrhage with focal neurological deficit may also arise. Hemorrhage into the spinal canal can occur following diagnostic procedures in cases presenting with thrombocytopenia[7]. In the index case, the CSF was negative formalignant cells and the MRI scan showed features S/O myeloid sarcoma.

Relatively small tumor in this region may manifest with profound symptoms. The involvement of CNS may be without symptoms. In symptomatic patients, the clinical picture will depend on which part of the CNS is involved. Features of advanced disease include irritability, headache, seizure, symptoms of raised intracranial pressure andcord compression. Amongst theleukemia, AML is the most common leukemiato produce cord compression; however, it is a rare initial presentation of AML[3]. The patient may present with pain in the back, abdomen, lower limbs and perianal region. Muscle weakness to paraplegia may also be present. Fecal and urinary incontinence often represents dangerous signs as in all cases of cord compression[8]. Therefore, the physician needs to have a high index of suspicion of AML in young patients presenting with neurological symptoms, and make every effort to diagnose it. Early identification and prompt intervention can prevent the development of irreparable neurological complications. Therefore,the presence oflaboratory evidenceofAMLcanbe usedto commence active treatment and prevent further delay.

Conclusion :

Myeloidleukemiablast cells can form solid masses that in vade organs, potentially causing sudden disability, as highlighted in a case report. Early diagnosis and intervention are crucial to reduce morbidity and mortality. Myeloid sarcoma should be considered in all acute myeloidleukemia (AML) cases, particularly when specific morphological, cytogenetic, and immuno histochemical predictors are present. CNS involvement is a rare initial presentation of AML, and it may occur through direct extension of leukemic aggregates, compressing neural tissue. Importantly, normal MRI results do not exclude spinal cord involvement, and delayed recognition can lead to severe neurological complications.

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Case Report

BICKERSTAFF BRAINSTEM ENCEPHALITIS : A RARE CASE PRESENTATION

Dr. Hrushikesh Mohanta[1], Dr. Subhankar Mishra[2], Dr. S.K. Jangid[3], Dr. K.K. Chand[4]

Introduction :

Bickerstaff's encephalitis is an acute demyelinating pathology, affecting the brainstem, and occurring few days after an infectious episode. The main symptoms are ataxia, ophthalmoplegia, and altered consciousness. Guillain-Barré syndrome (GBS), Miller-Fisher syndrome, and Bicker-Staff Brainstem Encephalitis (BBE) have some similarities, including the presence of anti-ganglioside antibodies. Together with GBS and Miller-Fishersyndrome, these 3 syndromes form a spectrum of postinfectious demyelinating diseases.

Case Summary :

A 53-year-old woman with no history of diabetes or high blood pressure experienced double vision and difficulty swallowing for 2 months, as well as recurrent falls and unsteady gait for1month. Patient had past h/o febrile episode 2month ago which subsided after3 days of medication.At presentation the patient appeared drowsy, with vitals of BP-130/84mmhg, pulse rate- 98/min, RR-18/min,temp-98^{0}F,spO2-93%with room air .CNS examination revealed nonresponsive plantar reflexes, bilateral 3rd nerve palsy, bilateral 6th cranial nerve palsy,bulbarweakness,impaired tandem gait,and bladder incontinence. Decreased muscle tone and diminished deep tendon reflexes were also observed.

On Investgation, Serum sodium-133mmol/l, potassium-3.6mmol/l, creatinine-1.1mmol/l. MRI of the brain showed demyelinating features, and CSF analysis revealed lymphocytic pleocytosis. An autoimmune encephalopathy profile demonstrated the presence of IgG anti GQ1b antibodies.

The patient was diagnosed with Bickerstaff encephalitis and received IVIg and other supportive treatments. Her condition improved, and she was discharged after a 16-day hospital stay.

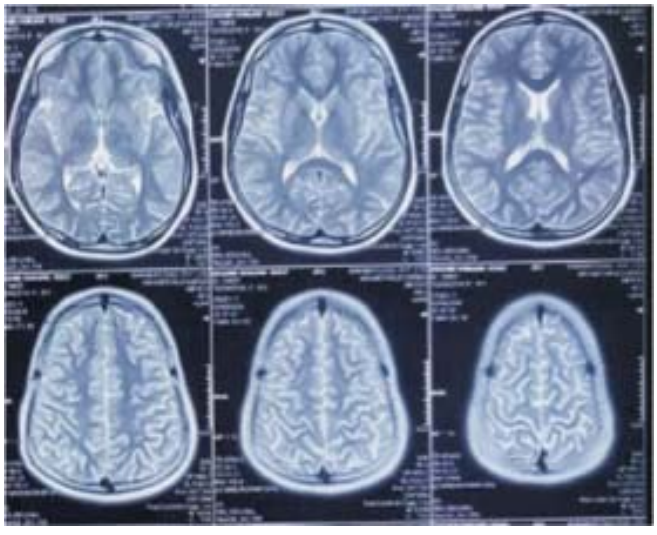

Fig. 1 MRI Brain showing Demyelinating lesions.

Discussion :

Although the exact pathogenesis remains unclear,it is presumably related to an immunereaction, triggered by a previous infection from pathogens like Campylobacterjejuni, Mycoplasmapneumonia or Haemophilus influenzae. Together with GBS and Miller-Fisher syndrome, these 3 syndromes form a spectrum of post-infectious demyelinating diseases. One diagnostic difference is the presence of impaired consciousness in BBE, whereas individuals with MFS exhibit a flexion response and maintain alert consciousness. Serum antiganglioside antibodies (anti-GQ1b) are found in two-thirds of patients. However,

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the absence of these antibodies does not rule out the diagnosis. Most patients can be managed by immunotherapy, using plasmapheresis or intravenous immunoglobulin either singly or in combination.

Conclusion :

The prognosis for typical Bickerstaff's encephalitis is good in the majority of cases. Early diagnosis and prompt management are crucial for improving outcomes and giving clinicians a better under standing when dealing with this rare presentation.

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Case Report

ADULT ONSET STILLS DISEASE IN A PATIENT WITH HASHIMOTO'S THYROIDITIS, A RARE CO-EXISTENCE OF AUTO-INFLAMMATION AND AUTOIMMUNITY: - A CASE REPORT

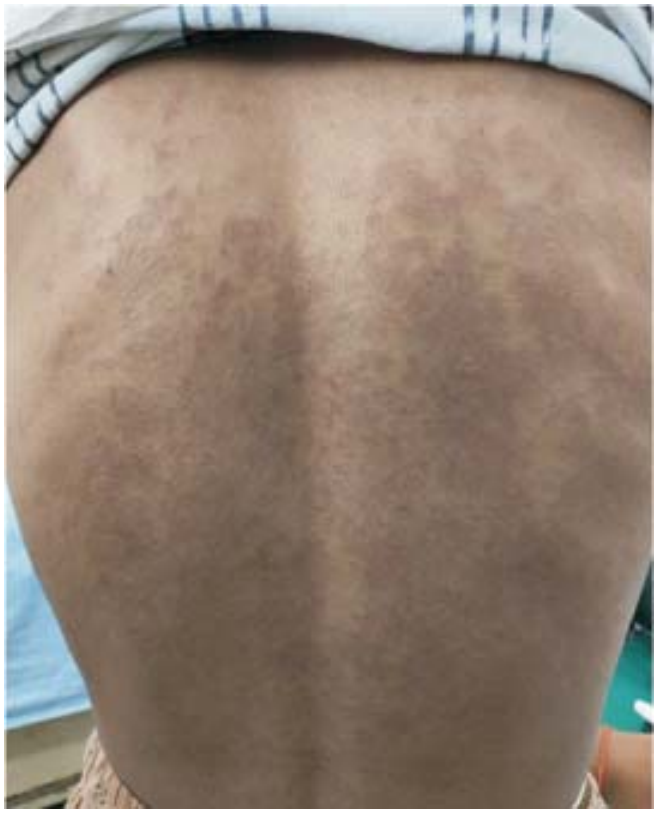
Dr. Tony Mathew Austin[1], Dr. Jayshree Sahu[2], Dr. Sagnika Tripathy[3]

Introduction :

Adult Onset Still's Disease (AOSD) is the adult variant of systemic Juvenile Idiopathic Arthritis (sJIA), a sub-category of JIA, both being characterized by arthritis, fever, evanescent erythematous rash, generalized lymphadenopathy and/or serositis. The condition is associated with elevated inflammatory markers, leucocytosis with neutrophilia, and thrombocytosis. The differentials to be ruled out includes malignancies especially leukemia, infections, and other autoimmune disorders(1). Here we present a case of new onset AOSD, already diagnosed with hypothyroidism, which when evaluated further was consistent with Hashimoto's Thyroiditis, a rare co-existence of autoimmune and autoinflammatory disease.

Case Details :

A 30 year old male, with past history of hypothyroidism on tablet thyroxine 50 micrograms, presented with multiple joint pain for 3 months, intermittent high grade fever for 4 weeks, myalgia and generalised weakness, and rash over back of his trunk for 3 weeks. The arthralgias was marked over bilateral knee, ankles, right shoulder and right proximal interphalangeal joints, and his febrile episodes were high grade with 2-3 peaks per 24 hours, mostly towards evening hours, each episode lasting for 1-2 hours, and associated with marked myalgia, followed by sweating and normal inter-febrile periods. The rash over the back of his trunk was initially erythematous and non-pruritic, which later changed its color to tan- like at the time of presentation. Prior to the onset of arthralgia 3 months ago, patient does remember of an episode of fever with sorethroat, which was managed conservatively. At the time of examination, he was febrile, with pallor and generalised significant lymph node enlargement, tender abovementioned joints and a midline neck swelling which moved on deglutition.



Laboratorical investigation findings are tabulated herewith.

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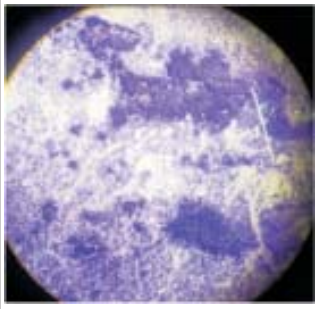
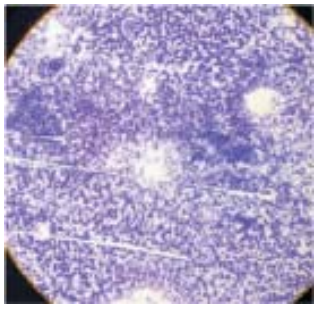
Total Count	16000 per mm3	S. Albumin	2.2 g/dL
Differential Count	N88, L10	Ferritin	4200 microgram/L
Haemoglobin	9 gm/dL	LDH	980 U/L
Platelet Count	501000 per mm3	AST	125 IU/L
ESR	125 mm/1st hour	Procalcitonin	0.03 ng/ml
CRP	278 mg/dl	ANA	negative
RA factor	8 IU/L (-ve)	Anti-CCP	12 IU/L (-ve)
S. TSH	8 mIU/L	fT3, fT4	Normal
Blood Culture	No growth	MP (ICT)	Negative
Urine Culture	No growth	Widal Test	Negative
Induced Sputum Culture	No growth	Scrub Typhus IgM	Negative
Dengue NS1, IgM	Negative	Leptospira IgM	Negative
2D Echo	No vegetations	HBV, HCV, HIV	Negative
Lymph Node FNAC	Reactive changes	Peripheral Smear	Normocytic Normochomic Anemia, with neutrophilic leucocytosis and Thrombocytosis
FNAC throid Swelling	Presence of lymphoid cells in all stages of maturation along with follicular cells in sheets. Impinging of lymphocytes into the follicular cell clusters seen. Presence of few epitheloid cells and few fibroblasts. No dysplastic/ malignant cels seen.	Under 40x 	Under 100x 

He was diagnosed with Adult Onset Still's Disease according to Yamaguchi's criteria, without any complication, against a backdrop of Hashimoto's thyroiditis. He was hence commenced on oral prednisolone at 60 mg once daily for 5 days, during the course of which his fever subsequently improved. He was then put on titrated dose of steroid upto 10 mg, on which he was maintained. His dose of thyroxine was left unadjusted. At the time of discharge, he was afebrile for more than 48 hours and intensity of his arthralgia had diminished to a score of 3 on visual analogue scale (VAS), down from 8 at the time of admission.

Discussion :

AOSD, is a diagnosis often underlooked, due to similarities with many other diseases (infectious, autoimmune and neoplastic), as well as owing to its rarity, with an annual incidence of around 3-4 per million

adults. The disease shows a slightly female preponderance. Just like sJIA, AOSD is also of autoinflammatory in origin, unlike other sub-categories of JIA which are of autoimmune in nature, marked with elevated IL-1,6 and 18 levels(2,3). Among the clinical features, arthralgia and myalgia are present universally in almost all cases, with arthritis limited to few cases at onset. The pattern of fever usually is of intermittent in nature, and shows more than 2 peaks per day rising to more than 39 degree Celsius, touching the baseline in between, lasting for more than 3 days. The evanescent rash characteristically involves any part of the trunk or extremities and is salmon pink in appearance, often being migratory and non-pruritic. Face is usually spared. Other systemic features include lymphadenopathy, hepatosplenomegaly, serositis and sore throatOwing to its non-specific nature, and striking similarities with other diseases, it should be often considered a diagnosis of exclusion, and approached likewise. Exclusion of infections and malignancy hence becomes imperative prior to the diagnosis. The most accepted diagnostic criteria is that of Yamaguchi's (as tabulated below), wherein more than 5 features of which atleast 2 being major criteria, clinches the diagnosis (4).

Major Criteria	Minor Criteria
Fever of atleast 39 degree Celsius, for atleast one week	Sore throat
Arthralgias or Arthritis, for atleast 2 weeks	Lymphadenopathy
Nonpruritic salmon colored eash (usually over trunk or extremities, while febrile)	Hepatomegaly or Splenomegaly
Leukocytosis (more than 10000/mm3) with granulocyte predominance	Abnormal liver function tests
	Negative tests for anti-nuclear antibody and rheumatoid factor.

Another close differential of exclusion is WIssler-Fanconi syndrome, also known as "subsepsis allergica" (according to French and German literatures), another autoinflammatory disease, which is similar to AOSD in most ways (hence sometimes used synonymously with AOSD). The management is targeted against the inflammatory pathology (4). Hence the first choice would be preferably corticosteroids. For maintenance, the lost effective dose of corticosteroid may be given, unless patients adverse effects against corticosteroids, wherein steroid sparers like methotrexate, azathioprine, DMARD's and anti IL-6 antibody (tocilizumab) (4). Of late, newer medications against IL-1 beta like canakinumab, and combined IL-1A and IL-1 beta antagonist like rilonacept have been approved(5). The complications of the entity includes Macrophage Activation Syndrome (MAS, the most life threating complication), TMA, DIC, tenosynovitis, cyst formation, severe joint destructions and deformities, and long term steroid adversities.

Conclusion :

Though rarely encountered and least looked, the possibility of AOSD should be sought out in all cases of prolonged spiking fevers with arthralgias, as it is a completely controllable disease, which if missed can have long term musculoskeletal sequelae and dangeous complications.

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Case Report

DELAYED NEUROPATHY (OPIDN) AND NEPHROTIC SYNDROME FOLLOWING ORGANOPHOSPHOROUS POISONING : A RARE CASE REPORT

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Introduction :

Organophosphorous poisoning is common and can present as acute cholinergic crisis, intermediate syndrome, organophosphate-induced delayed neuropathy (OPIDN), acute kidney injury and rarely nephrotic syndrome. OPIDNisacentral-peripheral distalaxonopathy which usually develops7–20 days after exposure to an OPagent. Glomerular, endothelial and tubular cell damage mediated by OP compound contributes to the development of AKI commonly and rarely nephrotic syndrome.

Case Summary :

Discussion :

A young female patient 31 years, presented to the EmergencyDepartment with alleged history of ingestion of an OP compound on date 04/04/2024 at her residence at around 12 midnight due to a family quarrel. She was initially taken to a nearby hospital where Gastriclavage was done and then referred to AIIMS Bhubaneswar and admitted to the ICU on the same day, where she received Atropine and PAM and empirical antibiotics for first 5 days and then gradually as her condition improved she was shifted to ward and then discharged with stable vitals. Her stay at AIIMS BBSR from 05/04/24 to 11/04/24 was uneventful butserumcholinesterase value 676.7 IU/L.. On day 10th of her ingestion of the OP compound she developed progressive bilaterallower limb weakness, facial puffiness and generalized swelling of body and again bought to the ER department.

Onexamination: Patient was conscious oriented and cooperative. Her BP was 180/90mmh gandrestvitals were normal. There was facial puffiness and bilateral pitting ankle oedema, mild pallor, no icterus, no cyanosis, no Clubbing, no lymphadenopathy. There was normal vehicular breath sounds heard over all lung fields with occasional crepitation, S1S2 heard with nomurmur, abdomen was soft vaguetenderness overall quadrants and non distended. On examination of CNS her Higher mental functions, cranial nerves and sensory examinations werenormal.Spasticitywas present in bilateral lowerlimbs withpowerof 2/5 around bilateralhips,knees and ankles. Lower limb reflexes were brisk with bilateral plantar non-responsive. Investigations revealed nephrotic range proteinuria(3gm/day), serum cholesterol(358mg/dl), hypoalbuminemia(2.4mg/dl) and serum creatinine(1.8mg/dl), urea(50mg/dl) .CSF analysis was done but that doesn't revealed any abnormality , Nerve conduction study and nerve conduction velocities showed increased latencies with normal amplitudes with bilateral carpeltunnelsyndrome.werenormal. USG suggestedmildascites. MRI(brain andspine), ANA, C3, C4, 2D ECHO serum electrolytes were normal Kidney biopsy was not taken.

Patient was managed with broad spectrum antibiotics, Atropine continuous in fusion started ataninitially rate of 3ml/hr with gradual tapering till 0.5ml/

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hr and given till 23/04/24 suspecting intermediate syndrome and OP induced delayed polyneuropathy with myelopathy. Inj Solumedro l1g IVOD for 3 days started on after discussion with Neurology and Nephrology departments. Strict BP control with antihypertensives and statins for dyslipidaemiawasgiven andPatients weakness improvedovertime andcholinesterase value increasedtill 896 IU/L.

Conclusion :

The mechanism of OPIDN has been linked to neuropathy target esterase (NTE), now known as PNPLA6. OPIDN can present with myelopathic features as early as 7days after ingestion of agents like chlorpyrifos. These lead to more potent inhibition of NTE than acetylcholinesterase and subsequentaging resulting in neuro degenerative conditions. Malathion toxicity should be considered in patients with proteinuria and AKI due to its direct cytotoxicity to tubular, glomerular and Bowman's capsule epithelial cells and decreased intravascular volume. OP Poisoning causingAKI with Nephrotic syndrome with OPIDN is a rare case report. Corticosteroids may be beneficial for patients with nephrotic syndrome and AKI associated with malathion exposure and as a neuroprotective drug in OPIDN. Patients may require prolonged and extensive rehabilitation.

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Pictorial CME

GRIP THAT WON'T LET GO : DIAGNOSTIC CLUES FROM A CHALLENGING HANDSHAKE IN MYOTONIC DYSTROPHY

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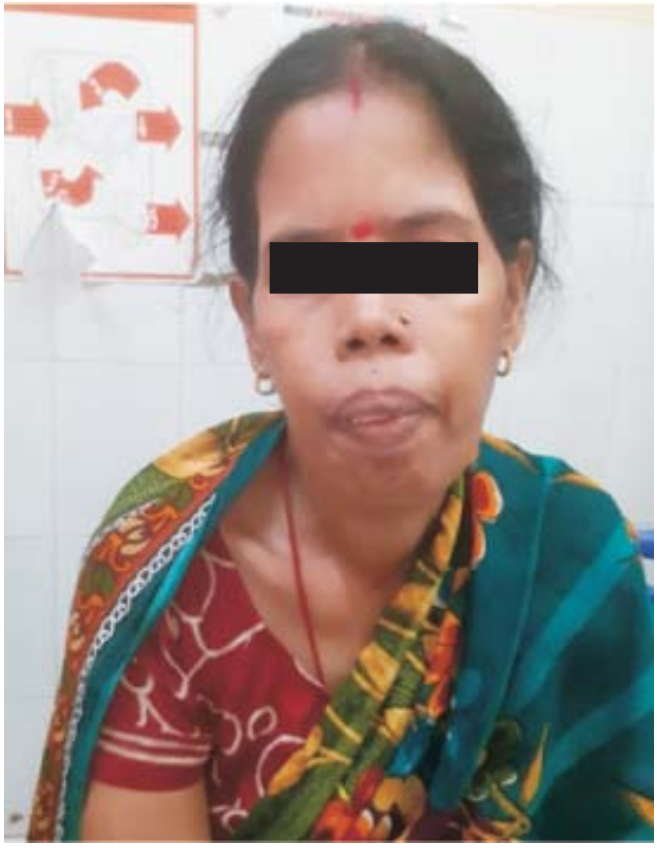
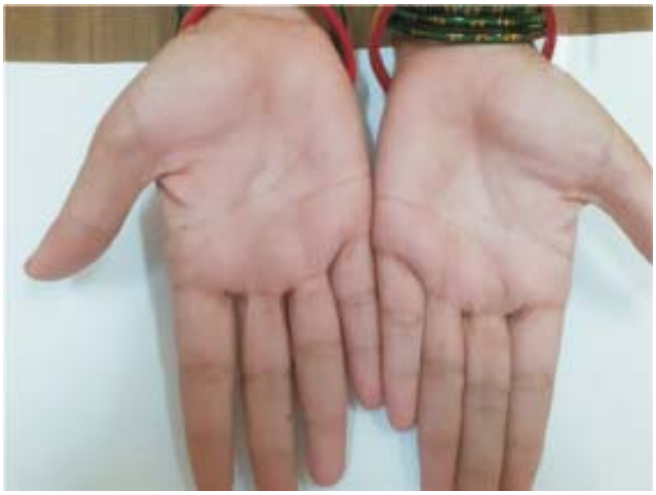
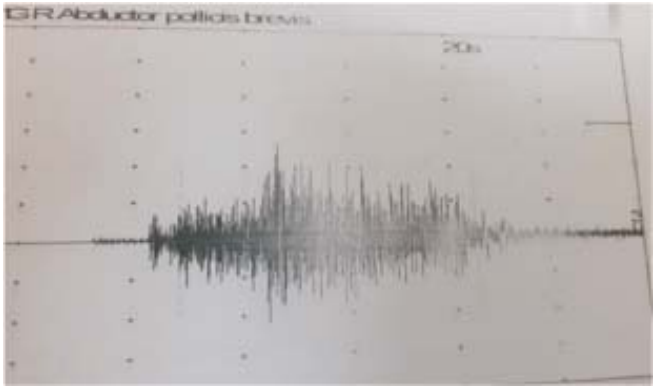


[The Hatchet Face :
Typical of Myotonic Dystrophy]



The Hypothenar and Thenar Atrophy with purcusion myotonia.



(The EMG with Dive Bomber sound heard during Insertional Activity)

A 35 year female house wife, married with three children presented with progressive weakness of hand grip for 2 year, not able raise the arm above the shoulder due to progressive weakness for 1 year ,and difficulty in standing up from squatting position for last 6 months. On examination the vitals were stable without any other

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significant general examination findings. On Neurological examination, there was wasting of temporal muscles and muscles of back of neck and around shoulder girdle. Hand muscles (Both thenar and Hypothenar) were atrophic with handgrip myotonia as evidenced by delayed release of hand shake and percussion myotonia over thenar eminence positive. There was proximal weakness in lower limbs and waddling gait. She was evaluated keeping Myotonic dystrophy as a Differential diagnosis. The EMG showed no fibrillation or fasciculation during spontaneous activity and dive Bombwer sound heard during observation of insertional activity. On voluntary activity there was small amplitude short duration polyphasic waves confirming myogenic etiology.The case was diagnosed as Myotonic Dystrophy (DM 1) , counshelled regarding the prognosis and long term outcomeand put on standard pharmacological agents with advice for regular follow-up.

Myotonic Dystrophy (DM) is a complex, multisystemic, autosomal dominant disorder and the most common form of adult muscular dystrophy. It is characterized by progressive muscle wasting and weakness, along with myotonia, which is a delayed relaxation of muscles following contraction. There are two major types of myotonic dystrophy: DM1 (Steinert's disease) and DM2 (Proximal Myotonic Myopathy), each caused by different genetic mutations. Both types affect various organ systems beyond the muscles, making it a disorder with widespread clinical manifestations.

DM1 commonly presents in adulthood with distal muscle weakness (affecting the hands, forearms, and feet), myotonia, and early cataracts. Facial muscle involvement leads to a characteristic "hatchet" face with ptosis (drooping of the eyelids) and frontal balding. Additional symptoms include cardiac conduction abnormalities, respiratory dysfunction, endocrine disturbances (such as insulin resistance), gastrointestinal issues, and cognitive impairment.

DM2 generally has a later onset and a milder course than DM1, and it affects proximal muscles (those closer to the trunk of the body) more than distal ones. Myotonia is often present but may be milder and less noticeable than in DM1. Patients with DM2 may experience muscle pain, stiffness, and weakness, particularly in the neck, shoulders, hips, and thighs. DM2 shares many of the same multisystemic features as DM1, including cardiac, endocrine, and gastrointestinal involvement, though the risk of congenital onset and cognitive impairment is lower in DM2.

Myotonic dystrophy affects more than just skeletal muscles. Cardiac manifestations, such as arrhythmias and conduction defects, are a major cause of morbidity and mortality, necessitating regular ECG monitoring. Respiratory muscles can also be affected, leading to complications like sleep apnea and hypoventilation. Endocrine disturbances include insulin resistance, thyroid dysfunction, and gonadal atrophy, which may cause infertility in men. Cataracts are a common early sign, particularly in DM1. Cognitive and psychiatric issues, such as difficulty with executive functioning and increased rates of depression, are more prominent in DM1.

Diagnosis is confirmed through genetic testing, and a multidisciplinary approach to management is essential. There is no cure, but treatment is directed toward managing symptoms and preventing complications. Physical therapy and assistive devices can help with mobility, while cardiac monitoring, respiratory support, and endocrinological management are critical for systemic complications.

Myotonic dystrophy requires a holistic approach to care, given its widespread impact on multiple organ systems. Early diagnosis and individualized care plans can help optimize patient quality of life and delay the progression of symptoms.

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