ORISSA PHYSICIANS JOURNAL

ESTABLISHED IN 2005 | Vol. 21, No. 1, 2025 | www.apiodisha.com

ISSN 0973-2853

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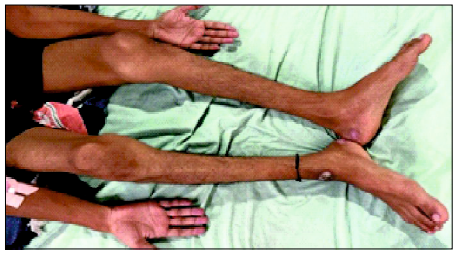
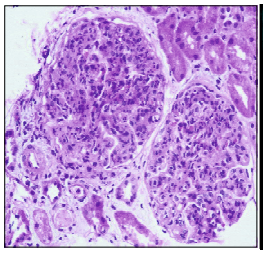
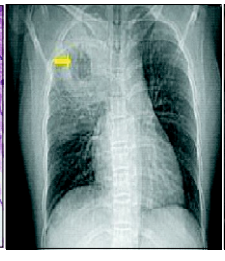
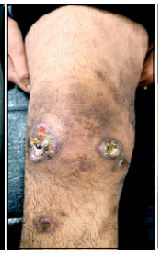
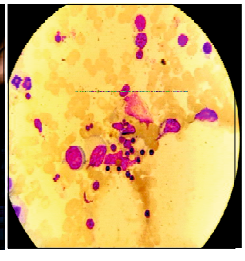

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ESTABLISHED IN 2005 Vol. 21 No. 1, 2025 www.apiodisha.com

ISSN 0973-2853

ORISSA PHYSICIANS JOURNAL
Official Journal of API, Orissa Chapter

Subscription information

Orissa Physicians Journal is published annually. The annual subscription is Rs.100.00. The journal is despatched within India by surface mail.

Edited, Printed & Published by

Dr. Pradip Kumar Behera
for the Association of Physicians of India,
Orissa State Branch,

Advertorial enquiry

Dr. Pradip Kumar Behera, Hon Editor, OPJ

Printed at

Graphic Art Offset Press, Nuapatna, Cuttack-1.
Website : www.apiodisha.com

OPJ Vol.21, No. 1 * 2025

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Editorial

BEYOND THE STETHOSCOPE : ARTIFICIAL INTELLIGENCE – THE NEXT ERA OF INTERNAL MEDICINE

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

Introduction :

Over the past decade, rapid advances in computing, data science, and algorithmic modelling have brought the promise of artificial intelligence (AI) into the forefront of internal medicine. From predictive analytics and clinical decision support systems to remote monitoring and personalized medicine, AI offers the potential to transform how internal medicine physicians diagnose, treat, and manage patients. Artificial Intelligence (AI) refers broadly to algorithms and systems that can perform tasks traditionally thought to require human intelligence—e.g., reasoning, pattern recognition, prediction, decision-making. In medicine, this often involves processing large volumes of clinical data (electronic health records, imaging, genomics, wearable sensors) to derive insights. In the domain of internal medicine, where patient heterogeneity is large, comorbidities are common, and decisions often hinge on integrating multiple data streams, the promise of AI is especially compelling.

Application Domains in Internal Medicine

Diagnostics and Decision Support:

One of the earliest and most visible applications of AI is diagnostic assistance—helping physicians identify diseases and choose management paths. For example, the survey of internal medicine physicians found that 68% of respondents reported using AI tools in their practice, and that 80% believed AI improved diagnostic accuracy.[1] AI models analyzing electronic health record (EHR) data can identify patients at risk of complications such as sepsis, heart failure exacerbation, or acute kidney injury ahead of time. In internal medicine subspecialties like gastroenterology, AI has been applied for polyp detection during colonoscopy, image based interpretation of endoscopic findings, and risk stratification of gastrointestinal disease.

Thus, AI has the capacity to act as a second reader, flagging findings for physicians, or even generating preliminary impressions of complex cases.

Risk Prediction and Preventive Medicine :

Preventing disease progression and avoiding complications is core to internal medicine practice. AI enables more refined risk stratification. Using ML models on large datasets, one can identify which patients with e.g., hypertension, diabetes, or chronic kidney disease are at heightened risk of progression, enabling clinicians to tailor interventions earlier. AI-enabled clinical decision support systems (CDSS) integrate demographics, labs, imaging, genomics, and wearable data to provide personalized risk estimates (for adverse events, hospital readmissions). Remote monitoring technologies using AI can detect early signs of deterioration in chronic disease patients, enabling early intervention.[2] This shift from reactive to proactive care aligns with the goals of internal medicine: maintaining health, preventing complications, and managing chronic conditions longitudinally.

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Personalized Medicine and Therapeutic Optimization :

Internal medicine is increasingly embracing precision/personalized medicine—tailoring therapies to individual patient profiles (genetic, phenotypic, lifestyle). AI-driven models can predict which patients will respond favorably to specific drugs, or who may suffer adverse effects, thereby optimizing therapeutic choices and reducing trial & error.[3]

Work-flow Efficiency, Documentation & Administrative Functions :

Beyond core clinical decision tasks, AI systems are increasingly applied in the background—helping physicians reduce administrative burden, streamline workflows, and improve documentation accuracy. A scoping review found that AI technologies (such as NLP, speech recognition) can improve clinical documentation accuracy and speed across settings. [2] By automating charting, coding, summarizing clinical notes, and assisting with triage, AI frees up physician time to focus more on patient interpersonal care—a key concern in internal medicine.

Monitoring and Longitudinal Care :

Internal medicine often involves long term management of patients with chronic multisystem diseases. AI-enabled remote patient monitoring (RPM) systems monitor vital signs, activity, and other sensor data, detecting early signs of decompensation or non adherence. Continuous data and AI processing allow for dynamic adjustment of care plans, personalized follow up intensity, and timely alerts to clinicians when issues arise.

Subspecialty Specific Applications :

While many applications cross internal medicine broadly, some subspecialties have especially active AI adoption:

- Cardiology : AI for ECG interpretation, arrhythmia detection, heart failure risk modelling.
- Endocrinology : AI for predicting progression of diabetic complications, insulin dosing automation.
- Gastroenterology : AI for polyp/lesion detection in endoscopy, risk stratification of GI cancers.
- Pulmonology/critical care : AI for predicting respiratory failure, optimizing ventilator settings.
- Nephrology : AI for predicting acute kidney injury, chronic kidney disease progression.

Hence, the internal medicine domain is rich with opportunity for AI across the spectrum from generalist to subspecialist care.

Challenges, Limitations & Barriers :

Despite the immense promise, AI adoption in internal medicine faces substantial hurdles. These can be grouped into technical, clinical, regulatory/ethical, and human factors.

Technical Challenges :

- **Data Quality, Bias & Heterogeneity:** Medical data often contains missing values, inconsistent formatting, bias (e.g., populations under represented). Models trained on one dataset may not generalize.
- **Explainability and Transparency:** Many AI models, especially deep learning, are "black boxes," making it difficult for clinicians to trust or understand how conclusions were reached. Explainable AI (XAI) is increasingly pertinent
- **Domain Adaptation & Transfer Learning:** Models may perform well in a development environment but degrade in real world different hospital settings. Need for domain adaptation techniques.
- **Integration with Existing Systems:** AI tools must integrate with existing EHRs, workflows, clinician interfaces; otherwise they become burdens rather than enablers.[4]
- **Data Privacy, Security and Federated Learning:** Sharing large volumes of sensitive patient data across institutions raises privacy risks. Federated learning can help but is complex to implement.

Clinical/Operational Challenges :

- **Workflow Disruption:** Introducing AI tools may disrupt existing workflows; if poorly designed, they may increase clinician burden or cause alert fatigue.
- **Physician Trust and Acceptance:** Physicians may question the accuracy, transparency, or relevance of AI outputs—and some fear job displacement. The survey of physicians found concerns: 55% worried about interpretability and transparency.
- **Evidence of Clinical Benefit:** Many AI tools are validated retrospectively; fewer have been proven in prospective, real world trials. Without robust evidence of improved patient outcomes, adoption remains cautious.
- **Maintenance and Monitoring:** AI models may "drift" over time (changes in practice patterns, patient populations, data capture). Monitoring, recalibration, and governance are needed.
- **Cost, Infrastructure and Implementation:** AI adoption requires investment in infrastructure, training, change management; cost may be prohibitive for many institutions. The physician survey found cost was a major barrier (59%).

Ethical, Legal & Social Challenges :

- **Bias and Equity:** AI models may perpetuate or amplify biases (racial, gender, socioeconomic). Without careful design and oversight, AI could worsen disparities.
- **Accountability and Liability:** If an AI system makes a wrong recommendation that leads to harm, who is liable—developer, institution, physician?
- **Patient Autonomy & Transparency:** Patients should know when AI is influencing their care; how to explain AI output and maintain trust?
- **Regulatory Compliance:** Medical grade AI tools must meet regulatory standards (e.g., FDA in the U.S., CE marking in Europe). Continuous updates and "learning systems" pose new regulatory challenges.
- **Data Ownership and Consent:** Use of large EHR/sensor/genomic datasets raises questions about data ownership, patient consent, and secondary uses.

Human and Professional Challenges :

- **Skill Atrophy:** Over-reliance on AI may erode clinicians' core diagnostic reasoning and procedural skills. A recent study in colonoscopy suggested routine AI assistance may reduce human detection skills.
- **Change Management & Education:** Clinicians need adequate training to use AI tools effectively, understand their limitations, and interpret outputs. The physician survey found lack of training was the top barrier (73%). [5]
- **Interdisciplinary Collaboration:** Effective AI deployment requires close collaboration between clinicians, data scientists, informaticians, IT specialists. Cultural silos can hinder progress.

Future Directions and Emerging Trends :

Looking ahead, several trends are poised to shape the integration of AI into internal medicine practice. The recent surge in LLMs (like GPT-style models) opens new possibilities for summarizing clinical notes, generating treatment plans, patient communication, and interactive decision support. However, questions about reliability, hallucinations, and domain adaptation remain. As clinical adoption penetrates deeper, the demand for tools whose outputs can be understood, audited, and validated will grow. [6] Future AI systems will combine genomics, proteomics/metabolomics, imaging, wearable/sensor data, EHR records, environmental/social determinants to provide more holistic patient insights. AI will increasingly be used to create adaptive treatment pathways, predictive interventions, real time monitoring and adjustment of therapies based on dynamic patient data. Institutions will increasingly adopt AI systems embedded in the care loop that learn from outcomes, adapt, and improve over

time (and across institutions). As AI becomes a standard tool rather than novelty, regulatory frameworks will evolve (e.g., oversight of "learning" algorithms, continuous monitoring, performance tracking). Ensuring that AI tools reduce rather than exacerbate disparities will become a central focus—development of bias-mitigation, representativeness in data, fairness audits, patient consent models. The future is likely one where AI augments human physicians rather than replaces them—leveraging machine speed, scale, pattern recognition while leaving human judgment, context, empathy in the loop.

Conclusion :

The integration of artificial intelligence into internal medicine is no longer a distant future—it is happening now. From diagnostic support to risk prediction, personalized therapeutics to workflow optimization, AI offers internal medicine physicians powerful tools to enhance care. However, the promise comes with caveats: technical limitations, evidence gaps, ethical and equity concerns, workflow disruption, and the need for robust implementation. The ideal future is one of "augmented medicine" – where physicians retain central roles of judgment, empathy, and patient relationship, while AI systems handle data heavy, pattern recognition, prediction tasks at scale.

For internal medicine practitioners, the imperative is twofold: first, to engage proactively with the evolving AI ecosystem (understand, evaluate, adopt wisely) and second, to ensure that deployment of AI remains patient-centred, equitable, transparent, and safe. Over the next decade, the most successful internal medicine practices may be those that harness AI not as a gimmick but as a strategic, integrated partner in delivering high-quality, personalized, preventive, and effective care.

Although challenges remain, the time is ripe for internal medicine to evolve—not simply with technology, but through it, to deliver better outcomes for patients. As the adage goes: "The better we leverage data and tools, the more we can focus on what only human physicians can do."

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Original Article

CORRELATION OF PLATELET INDICES WITH GLYCEMIC CONTROL AS ASSESSED BY HbA1c IN PATIENTS OF TYPE 2 DIABETES MELLITUS

Dr. Piyali Sengupta[1], Dr. Subhashree Mishra[2], Dr. Karlapudi Sai Shree[3]

Abstract :

Background:

Type 2 Diabetes Mellitus (T2DM) is associated with platelet hyperactivity, contributing to vascular complications. Platelet indices such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Plateletcrit (PCT), and Platelet Large Cell Ratio (PLCR) reflect platelet morphology and activation. Evaluating their relationship with glycated hemoglobin (HbA1c) may help identify simple, cost-effective markers of vascular risk in diabetes.

Material and Methods:

A hospital-based cross-sectional study was conducted with a total of 203 T2DM patients aged >18 years. Complete blood counts, including platelet indices, were analyzed using the SYSMEX XN-1000 hematology analyzer, and HbA1c was measured. Patients were grouped based on HbA1c levels (<7.5%, 7.5–10%, >10%). Statistical analysis was performed using SPSS version 24.0, with $p < 0.05$ considered significant.

Results:

The mean age of participants was 61.7 ± 12.0 years, with a male-to-female ratio of 1.5:1. The mean HbA1c level was 8.8 ± 2.7%, while the mean MPV, PDW, PCT, and PLCR were 11.4 ± 1.7 fL, 15.2 ± 3.8 fL, 0.28 ± 0.11%, and 38.9 ± 11.8%, respectively. Although mild variations in platelet indices were noted across the three HbA1c groups (<7.5%, 7.5–10%, >10%), these differences did not reach statistical significance ($p > 0.05$). No consistent trend was observed between worsening glycemic control and platelet activation markers.

Conclusion:

Platelet indices did not show a significant association with glycemic control. However, they remain simple, inexpensive hematological markers that may complement HbA1c in assessing vascular risk in T2DM.

Keywords:

Type 2 Diabetes Mellitus; Platelet Indices; Mean Platelet Volume; HbA1c; Glycemic Control

Introduction :

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion, leading to persistent hyperglycemia. It has become one of the most significant global health challenges, with its prevalence rising rapidly in both developed and developing countries. Chronic hyperglycemia in T2DM is associated with microvascular and macrovascular complications, largely due to endothelial dysfunction and platelet hyperactivity, which contribute to atherothrombosis and cardiovascular morbidity (1,2).

Platelets play a crucial role in the pathogenesis of vascular complications in diabetes. Alterations in platelet morphology and function, particularly in indices such as **Mean Platelet Volume (MPV)**, **Platelet Distribution Width (PDW)**, **Plateletcrit (PCT)**, and **Platelet Count (PC)**, have been observed in diabetic patients and are considered markers of platelet activation (3,4). **Glycated hemoglobin (HbA1c)**

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reflects long-term glycemic control and is a well-established predictor of diabetic complications (5).

Evaluating the relationship between platelet indices and HbA1c can provide insights into the link between glycemic control and thrombogenic risk. As these indices are easily obtainable from routine blood counts, they may serve as simple, cost-effective indicators of vascular risk in patients with Type 2 Diabetes Mellitus (6).

Material and Methods :

The present study was carried out in the Dept of Internal Medicine, Kalinga Institute of Medical Sciences,Odisha, India as a hospital based cross sectional study during the period from September 2019 to August 2021. Type 2 DM patients (>18 years of age) coming for follow-up or newly diagnosed DM patients (Diagnosed as per ADA 2017 criteria) attending outpatient Dept or admitted to wards were enrolled after obtaining informed consent . Clinical history was collected and thorough examination was done. Routine investigations were carried out with special emphasis on complete blood count and serum HbA1c . Patients with history of chronic disease like Connective tissue disease, Thyroid disorder, malignancies, any known platelet disorder and patients on anti-platelet drugs were also excluded. Complete blood count analysis which includes estimation of haemoglobin, total leucocte count, total platelet count and platelet indices like MPV, PWD, PCT and PLCR was done by SYSMEX XN 1000 (Sysmex corporation, Japan) automated haematology analyser. All the clinical and laboratory data were recorded in a pre-designed case report form.

Statistical Analysis :

Data collected under the study was scrutinised, codified and entered into the IBM SPSS Statistics, 24.0 software (www.spss.co.in) for analysis. Categorical variables like Haemoglobin, FBS, PPBS, HbA1C, Duration of diabetis, Hypertension, Total Platelet count, MPV, PDW, PCT, PLCR, and HbA1C were studied by using frequency procedure. Pearson's correlation coefficient was used for analyzing association between platelet indices and HbA1c. Mann–Whitney U test for comparison between groups. $p < 0.05$ considered statistically significant.

Results:

A total of 203 cases of Type 2 diabetes were included in the study with a mean age of 61.7±12.0 years and male to female ratio of 1.5:1. Among the study population the mean age of male patients was higher than the female patients.(64.4±11.3 years vs 57.5±11.9 years). Table 1 shows the demographic and clinical characteristics of study participants.

Demographic / clinical characteristics		N(%)
Gender	Male	122(60%)
	Female	81(40%)
Age	<40 yrs	6(3%)
	40-60 yrs	71(35%)
	>60 yrs	126(62%)
Hypertension	yes	142(70%)
	No	61(30%)
Duration of DM	<6 Years	116(36.5%)
	6-10 years	96(47%)
	>10 years	33(16.5%)
Lab parameters		Mean±SD
FBS in mg/dl		165.2±80.5
2hr PPBS in mg/dl		248.7±93.9
HbA1C		8.8±2.7
Duration of DM in years		8.0±5.2
Hb in gm/dl		10.3±2.0
Total platelet count in Lakhs / πl		236.4±112.6

Table 1 showing demographic and clinical characteristics among study participants

The platelet indices like MPV, PDW, PCT and PLCR were specifically considered in the present study to assess their correlation with HbA1c. The mean value of MPV, PDW, PCT and PLCR in the study population were found to be 11.4±1.7, 15.2±3.8, 0.28±0.11 and 38.9±11.8 respectively. Distribution of platelet indices in different ranges among the study subjects has been shown in Table 2.

Table 2 Classification of Platelet indices (N=203)

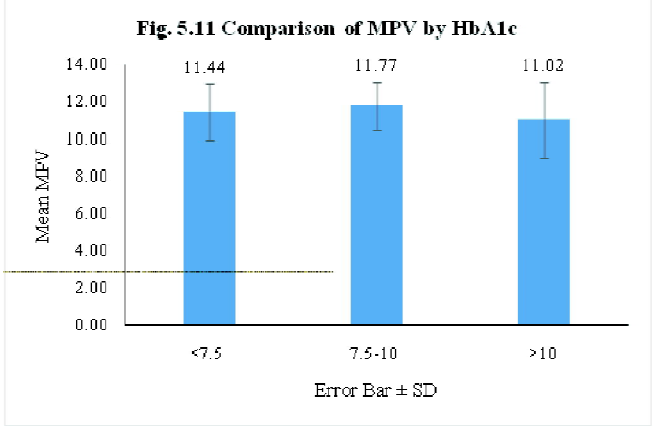
Platelet Indices	Range	No.	%
MPV	<7	0	0
	7-9.5	28	13.8
	>9.5	175	86.2
	Mean ± SD	**11.4 ± 1.7**	
PDW	<9	0	0
	9-17	134	66
	>17	69	34
	Mean ± SD	**15.2 ± 3.8**	
PCT	<0.17	40	19.7
	0.17-0.35	116	57.1
	> 0.35	47	23.2
	Mean ± SD	**0.28 ± 0.11**	
PLCR	<13	0	0
	13-43	130	64
	>43	73	36
	Mean ± SD	**38.9 ± 11.8**	

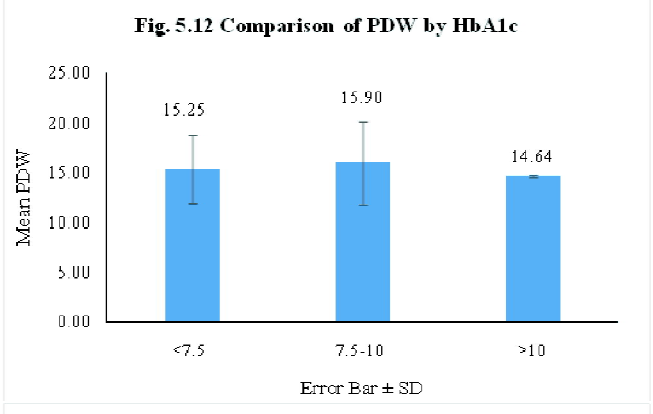
Table 2 showing the distribution of Platelet indices among study subjects.

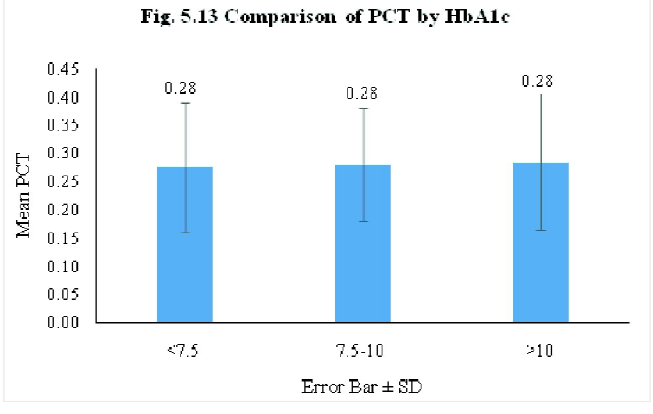
The HbA1C level among the study participants was classified into 3 groups i.e. <7.5, 7.5-10 and >10. Platelet parameters were analysed for any significant correlation with HbA1c level. In the present study the mean MPV, PDW, PCT and PLCR did not show any significant correlation with HbA1c level (p>0.05).

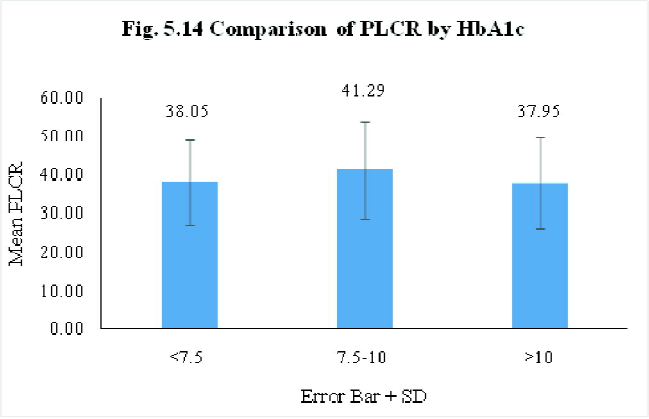
Table 5.13 Comparison of Platelet indices by HbA1c Level

	HbA1c	N	Mean	SD	ANOVA p value
MPV	<7.5	92	11.44	1.55	0.062
	7.5-10	53	11.77	1.32	
	>10	58	11.02	2.06	
	Total	203	11.41	1.67	
PDW	<7.5	92	15.25	3.69	0.210
	7.5-10	53	15.90	3.39	
	>10	58	14.64	4.16	
	Total	203	15.25	3.77	
PCT	<7.5	92	0.28	0.12	0.902
	7.5-10	53	0.28	0.10	
	>10	58	0.28	0.12	
	Total	203	0.28	0.11	
PLCR	<7.5	92	38.05	11.09	0.219
	7.5-10	53	41.29	12.71	
	>10	58	37.95	11.82	
	Total	203	38.87	11.77	









Discussion :

In the present study, platelet indices — Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Plateletcrit (PCT), and Platelet Large Cell Ratio (PLCR) — were analyzed across three HbA1c categories (<7.5%, 7.5–10%, and >10%) in patients with Type 2 Diabetes Mellitus (T2DM) to evaluate their relationship with glycemic control. Although the mean values of platelet indices showed minor variations among the groups, these differences were not statistically significant ($p > 0.05$). This finding suggests that, within this study population, platelet morphology and activation markers were not strongly correlated with HbA1c levels.

Platelets play a crucial role in the pathogenesis of diabetic vascular complications, as chronic hyperglycemia induces oxidative stress, non-enzymatic glycation of platelet membrane proteins, and increased platelet turnover, all of which contribute to enhanced platelet reactivity and aggregation (7,8). Larger and more reactive platelets, reflected by elevated MPV and PDW, are considered potential markers of increased thrombogenicity in diabetes (9). Several studies have demonstrated a positive correlation between platelet indices and HbA1c, supporting the hypothesis that poor glycemic control enhances platelet activation (10,11).

However, the results of the present study are in contrast with these findings. No significant association was observed between HbA1c and MPV, PDW, PCT, or PLCR. Similar results have been reported by Kodiatte et al. (12), who found no significant correlation between MPV and HbA1c among patients with T2DM. Likewise, Demirtas et al. (13) and Hekimsoy et al. (14) reported that platelet indices may not consistently reflect glycemic control, suggesting that other metabolic and inflammatory factors might influence platelet morphology. Differences in study populations, sample sizes, glycemic ranges, and laboratory methods could also account for these discrepancies.

The absence of a significant relationship in this study could be attributed to multiple factors. Firstly, all participants were known diabetics under varying treatment regimens, which may have altered platelet function independently of HbA1c. Secondly, confounding factors such as lipid levels, obesity, and low-grade inflammation — all of which influence platelet reactivity — were not specifically controlled. Thirdly, the cross-sectional design limits the ability to assess dynamic changes in platelet indices over time with variations in glycemic control.

Despite the lack of statistical significance, a mild trend was observed toward higher MPV and PDW values in the moderate HbA1c group (7.5–10%) compared with the well-controlled group (<7.5%). This may indicate that platelet activation increases in the early stages of deteriorating glycemic control but platelets become dysfunctional in longstanding, poorly controlled diabetes, leading to inconsistent trends. Such non-linear associations have also been noted in prior research (15).

Overall, although this study did not find a significant correlation between platelet indices and HbA1c, the potential role of these hematological markers as indicators of diabetic vascular risk cannot be excluded. Given their simplicity, cost-effectiveness, and routine availability, platelet indices could still serve as adjunctive markers in risk stratification when interpreted alongside clinical and biochemical parameters. Longitudinal studies with larger sample sizes and comprehensive metabolic profiling are warranted to clarify the prognostic significance of platelet indices in diabetes.

Conclusion :

In this study, no significant correlation was found between platelet indices (MPV, PDW, PCT, and PLCR) and HbA1c levels among patients with Type 2 Diabetes Mellitus. Although minor variations were observed, these

did not reach statistical significance. The findings suggest that platelet morphology and activation are not solely dependent on glycemic control and may be influenced by other metabolic and inflammatory factors. Nevertheless, platelet indices remain simple, cost-effective parameters that may complement HbA1c in assessing vascular risk. Larger, longitudinal studies are needed to validate their prognostic significance in diabetic patients.

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Review Article

ROLE AND RELEVANCE OF AN INTERNIST IN THE ERA OF INCREASING SUB-SPECIALIZATION IN MEDICINE

Dr. Lalatendu Mohanty

Abstract :

The rapid growth of medical subspecialization has transformed healthcare delivery, creating unprecedented opportunities for disease-specific advances. However, this trend raises concerns about fragmentation of care, duplication of services, and loss of holistic patient-centeredness. Internists provide unique value in diagnostic reasoning, management of multimorbidity, coordination of specialist input, and addressing social determinants of health. Evidence demonstrates that while subspecialists improve outcomes in discrete conditions, internists enhance system efficiency, reduce fragmentation, and improve care for complex, multi-morbid patients. Despite their centrality, internists face challenges including declining workforce interest, misaligned payment incentives, scope erosion, and burnout. Strategies to strengthen the internist's role include team-based care, value-based payment reform, training in systems medicine, and integration with subspecialists. Internists remain indispensable in contemporary medicine. Preserving and amplifying their role requires aligning incentives, redesigning training, and leveraging their expertise in integrative and patient-centered care. Collaboration between internists and subspecialists is essential for achieving high-quality, equitable, and efficient healthcare.

Keywords : Internal Medicine, Subspecialization, Generalist Care, Healthcare Coordination, Multimorbidity, Social Determinants of Health

Introduction :

The history of modern medicine has been marked by remarkable advances in knowledge and technology, leading to increasing subspecialization across nearly every discipline. While subspecialists offer deep expertise in narrowly defined domains, theneedsofaging populations and rising multimorbidity require integrative, comprehensive, and longitudinal approaches tocare. Internists, as generalist physicians trained in the breadth of adult medicine, are uniquely positioned to fulfill this role. This review explores the role and relevance of internists in the era of increasing subspecialization, considering historical trends, clinical roles, outcomes evidence, challenges, and future directions.

Historical Perspective and Work force Trends

Subspecialization in medicine accelerated in the second half of the 20th century, driven by advances in diagnostics, therapeutics, and technology. Internal medicine became both the foundation for subspecialty training and a discipline in its own right.

Workforce data reveal a persistent trend: a majority of internal medicine graduates pursue subspecialty training, contributing to shortages of generalist internists in many countries. The emergence of hospital medicine in the 1990s further diversified the career paths available to internists, redefining their in patient roles.While this evolution reflects medicine's complexity, it has also generated tension between specialist depth and generalist breadth.

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Core Roles of the Internist in the Subspecialization Era

Diagnostic Synthesis and Undifferentiated Illness

Internists excel in managing complex presentations, integrating cross-system knowledge, and navigating diagnostic uncertainty. Their ability to contextualize investigations and synthesize data across domains is indispensable in cases where patients present with atypical or multisystem symptoms.

Care Coordination and Clinical Stewardship

With patients frequently engaging multiple specialists, internists serve as coordinators who reconcile treatment plans, prevent duplication, and prioritize interventions according to patient goals. This stewardship role is critical for patient safety and cost-effectiveness.

Chronic Disease Management and Longitudinal Care

Internists provide long-term management of prevalent chronic diseases such as diabetes,heart failure, COPD, and CKD. Longitudinal relationships foster preventive care, continuity, and shared decision-making, directly influencing outcomes and patient satisfaction.

Addressing Social Determinants of Health

Internists increasingly address non-biomedical determinants of health, including socioeconomic status, housing, and nutrition.Policy statements underscore the internist'srole in screening for social needs and linking patients to community resources.

Inpatient and Hospitalist Medicine

The rise of hospitalists reflects the adaptability of internists to system demands. Hospital-based internists manage acute admissions, provide consultative expertise, and coordinate discharges, reinforcing their integrative function within hospital systems.

Education, Research, and Leadership

Internists contribute substantially to medical education, quality improvement, and systems- level leadership. Their broad perspective informs curricula,policy debates,and innovationsin health services research.

Outcomes Evidence: Generalist vs Specialist Care

Comparative studies highlight complementary strengths. Subspecialists achieve superior outcomes in focused, high-acuity conditions (e.g., oncology, interventional cardiology). Conversely, internists improve outcomes in multimorbid patients by reducing fragmentation and enhancing continuity. Collaborative care models that integrate generalist coordination with subspecialist expertise yield the most favorable results.

Challenges Facing Internists

- Work force Decline:Many residents prefer subspecialties, producing a generalist shortage.
- Incentive Misalignment**:**Cognitive,integrative care is undervalued compared to procedural interventions.
- Scope Erosion: Subspecialists encroach on domains traditionally managed by internists.
- Burnout: Administrative burdens and systemic inefficiencies contribute to stress and attrition.

Opportunities and Strategic Directions

1. Team-based Care: Empowering multidisciplinary teams under internist leadership.
2. Payment Reform: Rewarding coordination, complexity management, and prevention.
3. Training Reform : Emphasizing systems medicine, multimorbidity management, and ambulatory continuity.
4. Generalist–Specialist Integration : Developing co-management clinics and shared decision frameworks.
5. Digital Health Integration : Utilizing telemedicine and decision support to extend internists' impact.
6. Community and SDOH Partnerships : Linking healthcare to public health and social services.

Future Directions

Internists will increasingly serve as leaders of integrated care, population health initiatives, and precision medicine applications for multimorbid patients. Their ability to bridge specialties and maintain person-centeredness ensures their enduring relevance.

Conclusion

While subspecialization has advanced disease-specific care, it cannot substitute for the integrative functions of internists. Internists' roles in diagnostic reasoning, care coordination, chronic disease management, and system leadership are vital for contemporary healthcare. Preserving their value requires strategic investments in workforce development, payment reform, and integrated practice models. Ultimately, internists remain essential to a healthcare system that is coherent, equitable, and centered on the needs of the whole patient.

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Review Article

TRIPLE AGONISTS FOR OBESITY: THE DAWN OF A NEW ERA IN WEIGHT MANAGEMENT

Dr. Meghanad Meher

Abstract :

Obesity is a chronic, relapsing disease that contributes to increased morbidity, mortality, and healthcare costs worldwide. Despite lifestyle interventions and pharmacotherapy, sustained weight loss remains challenging. Incretin-based therapies, particularly glucagon-like peptide-1 receptor agonists (GLP-1RAs), have transformed the landscape of obesity treatment. However, newer agents targeting multiple receptors—such as dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) agonists and triple GLP-1/GIP/glucagon agonists—demonstrate unprecedented weight loss efficacy, sometimes approaching that of bariatric surgery. This review summarizes the mechanisms of action, clinical trial evidence, safety, and future directions of dual and triple agonists for obesity.

Keywords : Obesity, GLP-1, GIP, glucagon, Tirzepatide, Retatrutide, Incretin therapy, weight loss

Introduction :

The global prevalence of obesity has nearly tripled since 1975, with more than 1 billion adults affected worldwide [1]. Obesity is associated with type 2 diabetes, cardiovascular disease, fatty liver disease, cancer, and reduced life expectancy. Current pharmacological options—including Orlistat, Phentermine, Topiramate, Liraglutide, and Semaglutide—offer modest to substantial weight loss, but many patients experience weight regain, tolerability issues, or limited accessibility [2].

GLP-1 receptor agonists such as semaglutide have set new benchmarks for obesity management, achieving ~15% mean weightloss in STEP trials[3]. However,the search for greater efficacy has led to the development of multi-receptor agonists, which leverage complementary mechanisms of GLP-1,GIP, and glucagon to enhance weight reduction, metabolic outcomes, and energy expenditure.

1. Mechanistic Basis for Multi-Agonist Therapies

1.1 GLP-1Receptor Agonists

Glucagon-like peptide-1 (GLP-1) is an incretin hormone secreted by intestinal L-cells in response to nutrient intake. Pharmacological GLP-1 receptor agonists (GLP-1RAs) act through multiple pathways to promote weight loss and improve glycemic control. Centrally, GLP-1RAs act on hypothalamic appetite centers and reward circuits, therebySuppressing appetite and enhancing satiety. Peripherally ,they delay gastric emptying, leading to reduced caloric intake, and exert direct effects on pancreatic â-cells to enhance glucose-dependent insulin secretion while simultaneously suppressing glucagon release. These combined mechanisms contribute not only to weightloss but also to improved glycemic parameters[1].

1.2 GIP Receptor Agonists

Glucose-dependent insulinotropic polypeptide (GIP) is another incretin hormone secreted by K-cells ofthe proximal small intestine[1].Historically, GIP was thought to promote a diposity, but recent studies indicate a more complex role in energy balance. GIP receptor agonism stimulates insulin secretion in a glucose-dependent manner, complementing GLP-1 effects. Preclinical models suggest that GIP signaling may also improve adiposet issue function and enhance insulin sensitivity, potentially mitigating weightgain. When combined with GLP-1, GIP agonism appears to enhance satiety and produce synergistic effects on weight reduction and glucose regulation[4][1].

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1.3 Glucagon Receptor Agonists

Glucagon, secreted by pancreatic a-cells, has long been recognized for its hyper glycemic effects viastimulation of hepatic glucon eogenesis. However,glucagon receptor activation also increases energy expenditure through thermogenesis in brown adipose tissue and skeletalmuscle. Inaddition, glucagon agonismmay reduce hepatic steatosis and improve lipid metabolism, offering potential benefits for patients withobesity-related non-alcoholicfatty liver disease (NAFLD). The challenge has been balancing these favorable metabolic effects with the risk of hyperglycemia, which can be countered by concurrent GLP-1 receptor activation[1]

2. Triple Agonists for Obesity

2.1 GLP-1/GIP/Glucagon Triple Agonists

The concept of triple agonists builds on the success of dual incretin therapies by simultaneously targeting GLP-1, GIP, and glucagon receptors. This approach seeks to maximize clinical benefits through the complementary actions of appetite suppression (GLP-1), enhanced insulinotropic activity (GIP), and increased energy expenditure coupled with hepatic fat reduction (glucagon). Together, these mechanisms provide a more comprehensive metabolic intervention compared with single- or dual-agonist strategies.

Retatrutide (LY3437943) is the most advanced triple agonist in clinical development. In a phase 2 randomized trial reported in 2023, adults with obesity achieved a mean weight loss of up to 24.2% at 48 weeks, a result that exceeded outcomes with tirzepatide, the leading dual agonist [7]. Beyond weight reduction, retatrutide demonstrated broad cardiometabolic improvements, including significant reductions in blood pressure, glycated hemoglobin (HbA1c), and hepatic fat content[7]. Gastrointestinaladverseeffects—predominantlynausea, vomiting, and diarrhea – werethemost commonlyreportedevents,mirroring thoseseenwith GLP-1receptor agonists. Importantly, these effects were generally manageable and did not lead to excessive treatment discontinuation [7].

Other investigational triple agonists, such as SAR441255, are currently undergoing clinical evaluation. While long-term safety and efficacy data remain limited, early findings suggest that this therapeutic class may provide surgical-level weight reduction combined with improvements in metabolic health.

3. Comparison with Bariatric Surgery

Bariatric surgery remains the gold standard for achieving and sustaining significant weight loss, with procedures such as Roux-en-Y gastric bypass producing 25–30% reductionsinbaselinebodyweight. The magnitude of weight loss observed with triple agonists like retatrutide approaches this benchmark, raising the possibility of a non-surgical alternative for patients with severe obesity[8].

4. Safety and Tolerability

Common:Nausea, vomiting, diarrhea, constipation.

Rarebutserious : Pancreatitis, gallstones, potential risk for thyroid C-cell tumors (from rodent studies).

Long-termunknowns : Cardiovascular outcomes, cancer risk, and durability of weight loss beyond 2–3 years.

Ongoing cardiovascular outcome trials (e.g., SURPASS-CVOT, SURMOUNT- MMO) will clarify safety.

5. Comparative Effectiveness

Orlistat : 3–5% weightloss, poortolerability[2] Liraglutide (3.0 mg): ~8% weight loss [2]

Semaglutide (2.4mg) : ~15% weightloss (STEPtrials)[3] Tirzepatide : ~20–22% weight loss[5]

Cotadutide : upto 10% weightloss[6] Retatrutide : upto 24% weight loss[7]

Table1 below summarizes efficacy of major agents.

Drug/Class	Trial(s)	Mean Weight	KeyNotes
Orlistat	XENDOS	3–5%Loss(%)	Limitedefficacy,GIside effects
Liraglutide(3.0 mg)	SCALE	8%	Dailyinjection
Semaglutide(2.4mg)	STEP 1–5	14–15%	Weeklyinjection
Tirzepatide(dualGIP/GLP- 1)	SURMOUNT- 1	15–22.5%	Weeklyinjection,FDA approved
Cotadutide(dualGLP- 1/glucagon)	Phase2	5–10%	Improvesliver fat
Retatrutide(triple agonist)	Phase2	20–24%	Under investigation

6. Future Perspectives

Cardiovascular outcomes : Trials under way to establish reductions in MACE (major adverse cardiovascular events).

NAFLD/NASH treatment : Multi-agonists show potential in reducing hepatic steatosis and fibrosis.

Personalized medicine : Identifying responders vs. non-responders through biomarkers.

Accessibility and cost : High cost may limit widespread adoption; health policies must address affordability.

Beyond obesity : Potential roles in obstructive sleep apnea, PCOS, and aging-related metabolic decline.

7. Conclusion :

Dual and triple agonists herald a paradigm shift in obesity management. Tirzepatide has already surpassed previous pharmacological options, while triple agonistssuchas retatrutide show promise of surgical-level weight loss without invasive intervention. As evidence matures, these agents may redefine therapeutic goals in obesity and related metabolic disorders. Ensuringlong-termsafety,affordability, and accessibility will be key to their successful integration into clinical practice.

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Case Report

CARDIAC AMYLOIDOSIS WITH DILATED CARDIOMYOPATHY: A RARE CASE PRESENTATION

Dr. Abhilash Patnaik[1], Dr. Biplabi Biswakeshari Mohanty[2], Dr. Smita Priyadarshini[3], Dr. Anup Kumar Budhia[4], Dr. Bijayalaxmi Parija[5]

Abstract :

Cardiac amyloidosis is a serious and under diagnosed disorder characterized by extracellular deposition of amyloid proteins in the myocardium, resulting in restrictive cadiomyopathy, arrhythmias and progressive heart failure. This presentation explores a rare case of cardiac amyloidosis with diagnostic challenges, key features, and management approaches.

Introduction :

Cardiac amyloidosis is an infiltrative cardiomyopathy caused by the extracellular deposition of misfolded amyloid fibrils within the myocardium. These insoluble protein deposits disrupt normal myocardial architecture, impair diastolic function, and eventually lead to restrictive heart failure.

It is most commonly associated with two major types;

Light-chain (Al) amyloidosis - Due to plasma cell dyscrasia producing monoclonal light chains.

Transthyretin (ATTR) amyloidosis - Due to misfolded transthyretin protein, which may be hereditary (variant ATTR) or age related (wild type ATTR).

Clinically, cardiac amyloidosis presents with features of heart failure, restricted physiology, low-voltage ECG despite ventricular thickening on echocardiography, and often associated systemic manifestations like neuropathy, nephrotic syndrome, hepatomegaly etc

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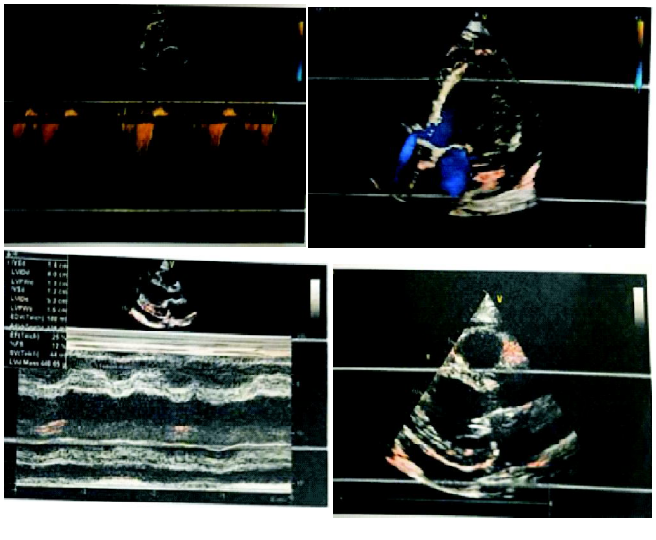
The condition often underdiagnosed because its presentation mimic other forms of hypertrophic and restrictive cardiomyopathy. Advances in imaging like cardiac MRI, Bone Scintigraphy, Biomarkers like NT pro BNP, Troponins have improved detections, while new therapies like e.g. TAFAMIDIS, PATISIRAN, INOTERSEN targeting amyloid fibril formation and stabilization are changing the disease course. [1][2][3].

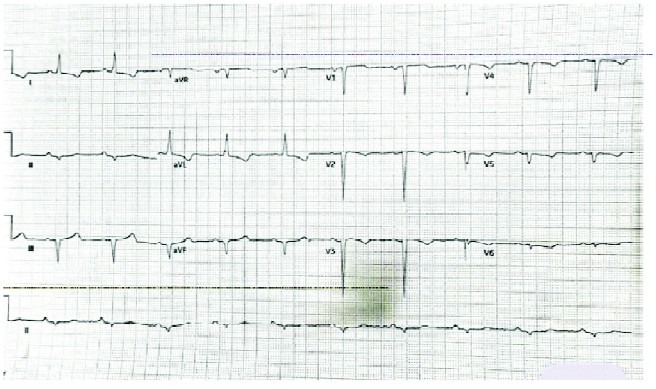
In this case, however, we describe a genotype-phenotype mismatch of a patient with the Transthyretin (TTR) genotype presenting with dilated cardiomyopathy (DCM) and heart failure with reduced ejection fraction.

Case Report

A 55 year-old male with no previous medical history, presented with progressive exertional dyspnea and fatigue for 1 month. It was associated with swelling over both legs followed by face. There was history of orthopnea and Paroxymal nocturnal paroxysmal during this period.



On general examination patient was having mild degree of pallor and pitting edema over both legs, there was no icterus, clubbing, cyanosis or lymphadenopathy and JVP was not raised. BP -110/ 70 mm/hg, Pulse rate 76 beats/min regular in rhythm, normal in volume and character, arterial wall was just palpable, there was no radio radial or radio femoral delay and all peripheral pulses were symmetrical felt. Temp-98.4 F at right axilla, Resp Rate -28 cycle/ min Abdomino-thoracic type (using of accessory respiratory muscle), Spo2- 88% in Room air. On Respiratory system

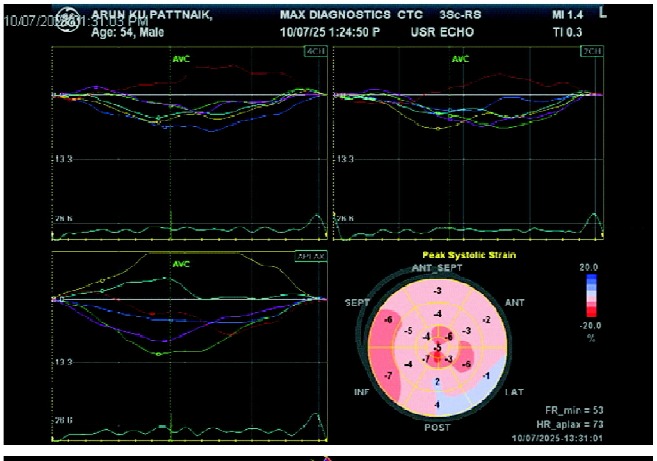


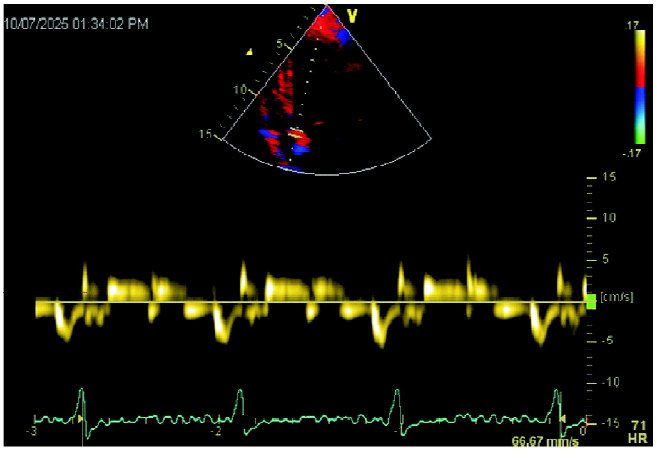
examination Bilateral coarse crepitation over all lung areas. Cardiovascular system examination revealed apex beat shifted to left 6th intercostal space half inch lateral to mid clavicular line and ill sustained in character. On percussion cardiac dullness markedly enlarged from 2nd intercostal space to 6th intercostal space on left side. On auscultation first heart sound was soft with a pansystolic soft blowing, high pitch murmur heard at mitral area, radiating towards axilla, second heart sound p2 component was loud at 2nd intercostal space on left side. On examination of abdomen Liver enlarged 2 cm below right costal margin, smooth and tender, spleen not palpable and there was no evidence of free fluid in abdomen.

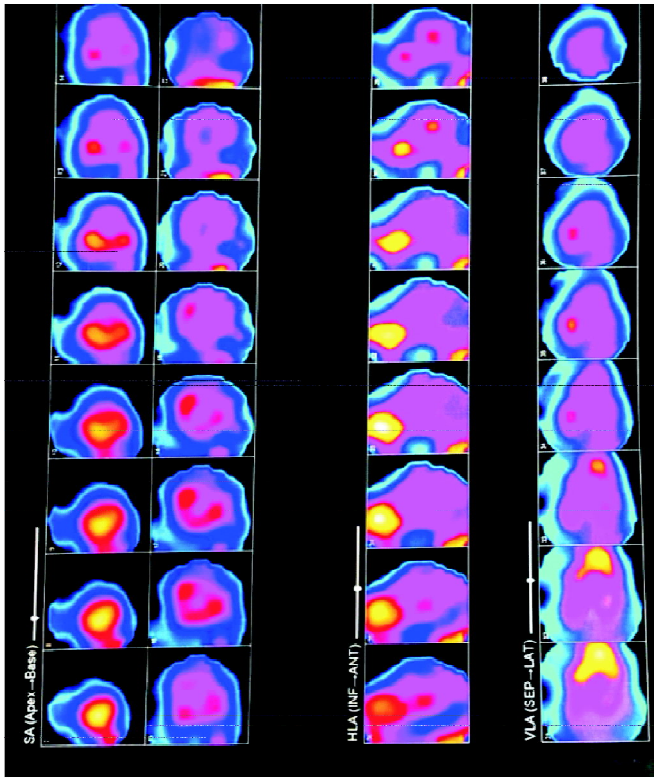
Investigations revealed Hb-10.2 gm %, MCV-80fl, MCH-26pg, MCHC-32gms%, TLC-8936/mm^3, Platelet counts -1.76 lakh. Serum urea-55 mg/dl, serum creatinine-1.45 mg/dl, serum uric acid – 6.88mg/dl. Total-bilirubin-1.1mg/dl, Direct bilirubin-0.48mg/dl, ALT-34UL, AST-45U/L, Total protein-7.62 gm/dl, Serum Albumin-4.39gm/dl, serum globulin-3.23gm/dl. NT PRO-BNP-3268, CPK-MB-4.08 NG/ML, CPK: Creatine kinase-217U/L, HbA1c-6.9%, FBS-168mg/dl,PPBS-188-mg/dl. Lipid profile showed Total cholesterol-203mg/dl, triglyceride-122mg/dl, LDL-124mg/dl, HDL-42 mg/dl, VLDL-15mg/dl. TSH-34 UIU/ml, FT3-2.1 pg/ml, FT4-0.43 ng/ml.

Chest X Ray showed B/L Non Homogenous consolidations, Bat's wing pattern in peri-hilar area with Kerley A & B lines and Cardiomegaly (cardiothoracic ratio>0.5). **ECG** showed low voltage in limb leads and poor R-wave progression in precordial leads.

On 2D Echo there was Eccentric left ventricular hypertrophy, sever left ventricular systolic dysfunction (ejection fraction -19%), Diastolic dysfunction of grade 2(increased LV filling pressure), valves and interatrial septum were thick There was markedly reduced global longitudinal strain (1.1%) with relative apical sparing[2]. **Technetium pyrophosphate (PYP)** scan strongly showed visual grade >2 and H/ CL ratio. 1.5 were positive for cardiac transthyretin amyloidosis (ATTR).[5]. **Cardiac MRI** showed T1 shortening with diffuse subendocardial enhancement of







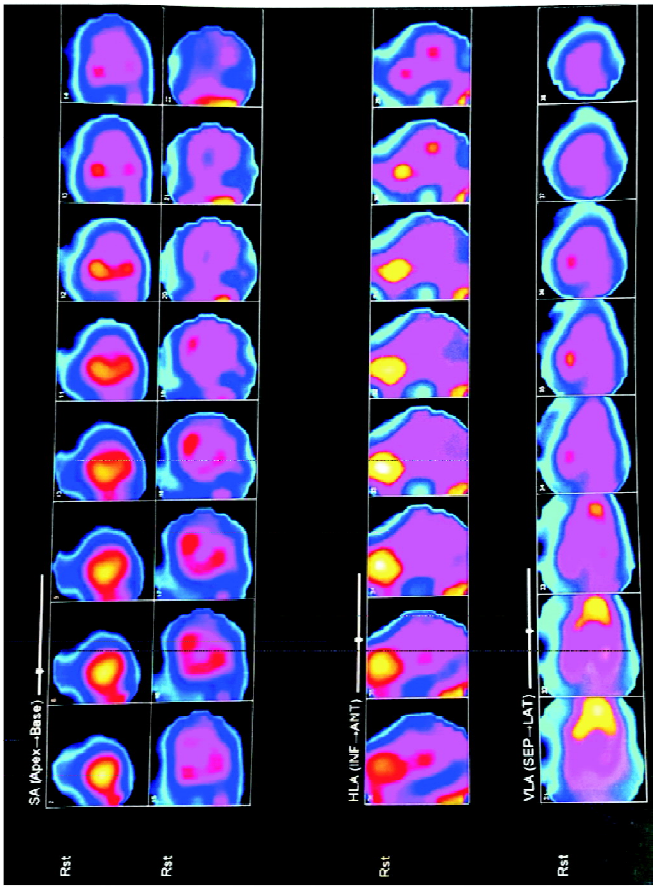
the LV myocardium .Mild similar diffuse subendocardial enhancement was seen in rest of cardiac chambers, finding suggest likely myocardial amyloidosis. **Tissue biopsy** demonstrated Congo red positivity with apple green birefringence under polarized light microscopy, confirming amyloid deposits. [2][5].

Management and Outcome

Patient was treated symptomatically with Diuretics, Beta –blockers , SGLT2 inhibitors, ACE inhibitor/ARBS/ARNI (Sacubitril-valsartan) and Dobutamine infusion. The patient's heart failure was refractory to optimal medical therapy. After conservative management patient left ventricle ejection fraction-increased from – 19% to 35 % within 4 months. Chemotherapy was initiated for AL type, while ATTR patients may benefit from Tafamidis and emerging therapies[1].

Discussion :

The diagnosis relies on integrating clinical suspicion, advanced cardiac imaging (echo, MRI, PYP scan), and definitive tissue pathology[5][2]. Genetic testing is important for guiding treatment in hereditary forms[3]. ECG features—including low voltage and pseudo-infarct patterns—are frequently present in both primary AL and hereditary ATTR cases[2]. Typical findings included ventricular hypertrophy, diastolic dysfunction, and late myocardial enhancement on imaging. Electrocardiographic features commonly included low voltage QRS, atrial fibrillation, and first-degree AV block[3][4]. Misdiagnosis or delayed diagnosis remains common due to phenotypic overlap with hypertrophic or restrictive cardiomyopathies and other causes of heart failure[1][4]. Cardiac amyloidosis carries a poor prognosis with median survival without treatment is under two years for AL type, with better



outcomes for ATTR patients[1][6]. Heart transplantation is controversial, with variable post-transplant survival and risk of disease recurrence[2][1]. Early diagnosis and a multidisciplinary approach can greatly improve outcomes[1][6].

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Case Report

A RARE CASE OF DYKE-DAVIDOFF-MASSON SYNDROME IN AN ADOLESCENT FEMALE

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Abstract :

Dyke-Davidoff-Masson syndrome is a rare condition first described in 1933, with characteristic clinical and radiological features such as facial asymmetry, hemiplegia, seizures, mental retardation, cerebral hemiatrophy, and skull and frontal sinus abnormalities. We describe the clinical features, brain imaging and clinical course of a 17 years old patient with this syndrome.

Introduction :

Atrophy or hypoplasia of one cerebral hemisphere (hemiatrophy) is referred to as Dyke-Davidoff-Masson syndrome (DDMS), first described in 1933. This condition is typically brought on by an injury to the developing brain during prenatal or early childhood.[1] The clinical features are variable and depend on the extent of brain injury. More commonly they present with recurrent seizures, facial asymmetry, contralateral hemiplegia, mental retardation or learning disability, and speech and language disorders. Sensory loss and psychiatric manifestations like schizophrenia had been reported rarely.[2,3] The gold standard for the diagnosis of DDMS is computed tomography or magnetic resonance imaging. The underlying pathologic processes' nature and extent vary widely[1]. The radiological finding includes cerebral hemiatrophy, which is associated with ipsilateral lateral ventricle dilatation and prominent sulcal spaces while thalamus and brainstem atrophy can also be seen but are uncommon.[4]

Case Report :

A case of a 17-year-old female, presented to the hospital with multiple episodes of generalized tonic and clonic seizures since 2 days and altered sensorium since 1 day. Her father reported that she has been experiencing episodes of generalized tonic and clonic seizures with brief periods of loss of consciousness since her childhood and increased in frequency over 5 months. She had delayed developmental and intellectual impairment since childhood. No history of surgery, trauma, or significant illness in the past. There was no history of similar presentations in rest of her family members. On general examination, the patient was irritable. On neurological workup, power was 3/5 on the right side with decreased sensation and hypertonic right limb. We could also observe a mild facial tilt towards the right. Her blood counts, ESR, liver and renal function tests were within normal limits. The patient had no significant medical history in the past.

Magnetic resonance Imaging (MRI) was done, which revealed diffuse left cerebral hemiatrophy with encephalomalacia and gliotic changes, associated ex vacuo dilation of the lateral horn of the ipsilateral lateral ventricle. Mild thickening of the calvaria on the left side also seen. A diagnosis of Dyke-Davidoff-Masson Syndrome was made. Now she is under anti-epileptic medication.

Discussion:

Dyke, Davidoff, and Masson documented 9 patients with pneumato-encephalographic abnormalities on a skull radiograph who had hemiparesis, facial asymmetry, seizures, and mental retardation in 1933 [5]. The case presented here displayed the characteristic radiological and clinical findings that are consistent with a diagnosis of DDMS. The etiopathogenesis may result from acquired factors such as trauma, infection, vascular

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abnormalities, and intracranial haemorrhage during the perinatal period or shortly after ward, which cause hemi cerebral atrophy. Vascular insult during intrauterine life may cause hypoplasia of acerebralhe misphere. These variables, in turn, lead to a decrease in the production of brain-derived neurotrophic factors, which promotes cerebral atrophy [6].

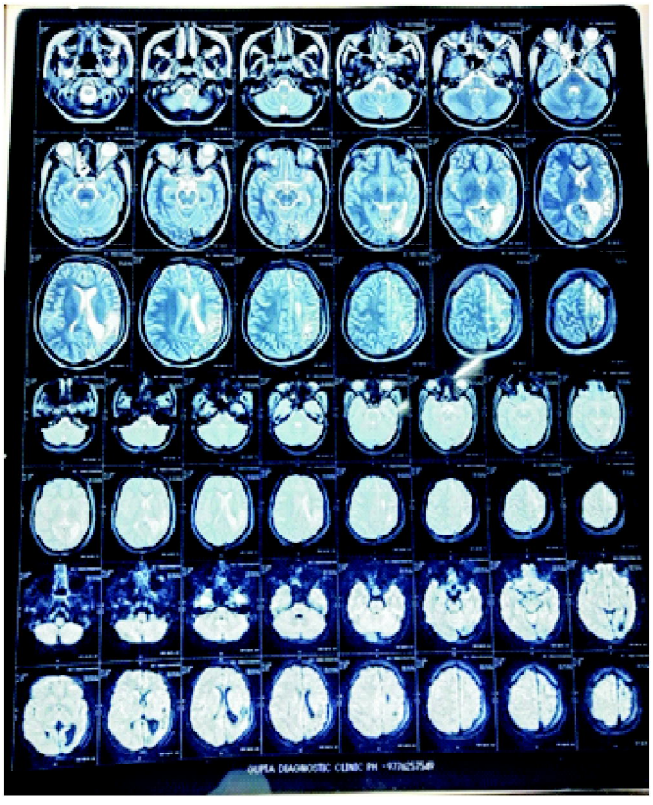

Figure 1 MRI of brain showing diffuse left cerebral hemiatrophy with encephalomalacia, associated ex-vacuo dilation of the lateral horn of the ipsilateral ventricle

The atrophic hemisphere's large sulci and encephalomalacia are signs of late-onset brain damage brought on by aberrant neuronal and glial growth or apoptosis during cortical development, indicating acquired causes. On the other hand, no noticeable sulci will be present if the brain injury occurs during embryogenesis when the creation of gyri and sulci is incomplete [7]. A precise diagnosis and the implementation of suitable management are made possible by imaging via CT and MRI, which is of great importance. Because they offer crosssectional images with tiny slices and post-processing capabilities, these 2 imaging modalities are useful. Cerebral hemiatrophy/ hypoplasia, hyper-pneumatization of the paranasal sinuses, and compensatory osseous hypertrophy are relevant imaging characteristics for DDMS. As the patient ages, these radiological traits will become increasingly noticeable[8].

This disorder has to be distinguished from Rasmussen encephalitis, Basal ganglia germinoma, Sturge-Weber syndrome, Silver-Russel syndrome, Linear nevus syndrome, and Fishman syndrome [9]. Rasmussen encephalitis is a persistent, immune-mediated condition that is hypothesized to develop as a result of viral infections. Intractable focal epilepsy and cognitive deficits in childhood are the typical symptoms. Unilateral hemisphere atrophy without apparent calvarial alterations is one of the imaging characteristics. Leptomeningeal angioma-related brain atrophy is represented by Sturge-Weber syndrome (encephalotrigeminal angiomatosis). The intracranial tram track calcification, the port-wine facial nevus, and the lack of midline displacement are the identifying characteristics. Whereas, poor growth, delayed bone age, clinodactyly, normal head circumference, normal IQ, the distinctive facial phenotype (triangular face, broad forehead, short pointed chin, and narrow-wide mouth), and hemihypertrophy are all characteristics of Silver-Russel syndrome.[9]

Rasmussen encephalitis is unlikely, as the patient had an ipsilateral thickened calvarium with a non-progressive pattern of seizure and neurologic deficit. The patient did not have skin lesions which are typically seen in Sturge-Weber syndrome which rules out this condition. In the presented case, the patient had no history of trauma, infection, or tumorto suggest an acquired variety of the syndrome. Since the majority of patients with this disorder present with refractory seizures, management focuses on controlling seizures with the proper anticonvulsants. Additionally, homebased occupational, speech and physical therapy are also important[6]. Patients with hemiplegia and uncontrollable, incapacitating seizures should consider hemispherectomy, which is successful in 85% of instances. Patients with hemiparesis that develops after age 2 or without recurring seizures may have a better prognosis [4].

Conclusion :

DDMS is a rare neurological disorder that leads to refractory seizures along with a spectrum of disabilities. Due to the rarity of this condition, it can be easily missed or underreported. A thorough history and imaging can give an early diagnosis and helps to differentiate the condition from other similarconditions. Primary focus of treatment is symptomatic care while in some circumstances surgery is the last resort.

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Case Report

PERIPHERAL NEUROPATHY ASSOCIATED WITH IMATINIB THERAPY FOR CHRONIC MYELOID LEUKAEMIA – A CASE REPORT

Dr. Jyotiprakasha Mallick[1], Dr. Ranjan Kumar Sen[2], Dr Saroj Kumar Tripathy[3]

Abstract :

Imatinib, a tyrosine kinase inhibitor, is widely used in the management of chronic myeloid leukaemia (CML). While most adverse effects are mild and reversible, late-onset neurotoxicity is exceedingly rare and often under-recognized. Among these, peripheral neuropathy is particularly uncommon. We report a rare case of peripheral neuropathy in a patient of CML who was on Imatinib therapy for around 3 years.

Keywords: Imatinib, Chronic Myeloid Leukaemia, Peripheral Neuropathy, Tyrosine Kinase Inhibitor, Neurotoxicity

Introduction :

Chronic myeloid leukaemia (CML) is a myeloproliferative neoplasm characterized by the Philadelphia chromosome t(9;22)(q34;q11), which results in the BCR–ABL fusion gene and uncontrolled tyrosine kinase activity. The introduction of imatinib mesylate revolutionized its management by transforming CML from a fatal disease to a chronic, controllable condition (1). Imatinib inhibits BCR–ABL along with c-KIT and platelet-derived growth factor receptor (PDGFR), thereby targeting key proliferative pathways.

Common side effects of imatinib include fluid retention, periorbital edema, gastrointestinal upset, muscle cramps, and rash (2). These effects typically occur early and diminish with continued therapy. Neurological complications are very uncommon, though isolated cases of optic neuritis, sensorineural hearing loss, and peripheral neuropathy have been reported (3–5). We present a patient in chronic-phase CML who developed peripheral neuropathy after three years of imatinib therapy, with near-complete recovery upon withdrawal and switch to nilotinib.

Case Report :

A 47-year-old female, a known case of chronic-phase chronic myeloid leukaemia (CML), presented to the Department of General Medicine, SCB Medical College & Hospital, Cuttack, with progressive numbness, tingling, and burning sensations in both upper and lower limbs for about two weeks. She complained of clumsiness while handling small objects, difficulty buttoning clothes, and a sense of unsteadiness on uneven ground. There was no limb weakness, facial deviation, diplopia, dysphagia, or sphincter disturbance. She denied fever, weight loss, or recent infection. The patient had been diagnosed with chronic-phase CML in 2021 following evaluation for persistent anemia and splenomegaly.

Her initial complete blood count revealed hemoglobin 7.3 g/dL, total leukocyte count 227 × 10^3/μL, and platelet count 226 × 10^3/μL. Differential count showed neutrophils 86.6 %, lymphocytes 4.2 %, monocytes 0.6 %, eosinophils 3.9 %, basophils 4.7 %, and immature granulocytes 30 %. Peripheral-smear morphology demonstrated marked leukocytosis with myelocytes, metamyelocytes, and basophilia. Molecular analysis confirmed BCR–ABL fusion transcript positivity, establishing the diagnosis of chronic-phase CML.

She was initiated on imatinib mesylate 400 mg once daily, the standard first-line tyrosine-kinase-inhibitor (TKI) regimen. Over the following six months she achieved complete haematologic remission, and by one year, major molecular response (BCR–ABL d" 0.01 %). She remained fully compliant with therapy and

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maintained regular follow-up. Minor adverse events—transient periorbital puffiness, pedal edema, and muscle cramps—resolved spontaneously. She had no history of diabetes mellitus, thyroid disease, alcohol consumption, or exposure to neurotoxic agents.

In August 2024, after approximately three years of continuous imatinib therapy, the patient experienced gradual onset of tingling and numbness in the fingertips and toes. Over the next fortnight these symptoms progressed proximally to involve palms and soles and were accompanied by imbalance while walking, particularly in dim light. She described difficulty in buttoning clothes and an unusual "cotton-wool" sensation over her hands and feet. There was no pain, weakness, or sphincter involvement. She had not started any new medication, and there was no history of toxin exposure or recent viral illness. On general examination she was conscious, cooperative, and afebrile. There was no pallor, icterus, cyanosis, clubbing, lymphadenopathy, edema or thyromegaly. Blood pressure was 120/80 mm Hg, pulse 82 beats/min and respiratory rate 16/min. The abdomen was soft, non-tender, and the spleen was not palpable, indicating continued remission. Cardiovascular and respiratory examinations were normal.

On neurological examination: Higher functions and cranial nerves were intact. Motor system evaluation showed normal tone and power (5/5) in all muscle groups. Deep-tendon reflexes were depressed globally (1+), and plantar responses were flexor. Sensory testing revealed loss of fine touch, pinprick, vibration, and joint-position sense in a glove-and-stocking distribution. Vibration sense was lost below the knees and wrists. Proprioception was impaired at the toes and fingers. Coordination testing showed sensory ataxia with unsteady heel-to-shin movements and difficulty performing tandem gait. There were no cerebellar signs or extrapyramidal features. Based on these findings, a symmetrical sensory neuropathy was suspected.

At the time of neuropathy, her complete blood count demonstrated: Hemoglobin 10.4 g/dL, Total leukocyte count 6.8 × 10^3/μL with normal differential, platelet count 1.9 × 10u /μL. The peripheral smear showed normocytic, normochromic red cells with no blasts or immature myeloid elements. These findings confirmed that the patient remained in complete haematologic remission and that neuropathy was unrelated to CML relapse.

Biochemical profile revealed: fasting glucose 87 mg/dL, serum urea 20 mg/dL, serum creatinine 1.0 mg/dL, uric acid 3.0 mg/dL, sodium 143 mEq/L, potassium 3.3 mEq/L, calcium 9.3 mg/dL, total protein 8.0 g/dL, albumin 3.2 g/dL, serum bilirubin (Total) 0.3 mg/dl, serum bilirubin (Direct) 0.1mg/dl, SGOT 31 IU/L, SGPT 28 IU/L, ALP 86 IU/L, total cholesterol 177 mg/dL, Serum Triglycerides 78mg/dl, HDL Cholesterol 31 mg/dL, LDL Cholesterol 112 mg/dL, and C-reactive protein 33.8 mg/L. The normal hepatic and renal parameters excluded metabolic causes of neuropathy.

Endocrine and nutritional assessment: T*f* 0.88ng/mL, T4 10.19 μg/dL, and TSH 1.6 μIU/mL indicated euthyroid status. Serum vitamin D was mildly low (27 ng/mL). Vitamin B, level exceeded 2000 pg/mL owing to previous supplementation, ruling out deficiency as an etiology. Serum ferritin 120 ng/mL. Serology: HIV, HBsAg, and anti-HCV tests were non-reactive. Antinuclear antibody and rheumatoid factor were negative. Collectively, these investigations ruled out diabetes, hypothyroidism, nutritional deficiency, chronic kidney or liver disease, autoimmune disorders, and infections.

A nerve-conduction study (NCS) performed on 29 August 2024 demonstrated bilateral axonal demyelinating sensory polyneuropathy. Motor conduction of median, ulnar, peroneal, and tibial nerves showed mildly reduced compound muscle action potential (CMAP) amplitudes with normal velocities. Sensory nerve action potentials (SNAPs) in bilateral median, ulnar, and sural nerves were absent (non-recordable), confirming severe sensory involvement. F-wave and H-reflex latencies were mildly prolonged. The overall interpretation was symmetrical axonal–demyelinating sensory polyneuropathy involving both upper and lower limbs. No myopathy, or radiculopathy was detected. These electrophysiological findings were in concordance with the clinical picture of distal sensory loss and ataxia.

Nerve	Site	Latency (ms)	Duration (ms)	Amplitude (mV)	NCV (m/s)
Rt Median	Wrist	3.36	13.04	14.7	—
	Elbow	7.15	12.56	13.4	52.4
Lt Median	Wrist	3.38	13.01	14.8	—
	Elbow	7.25	12.82	12.5	52.6
Rt Ulnar	Wrist	2.60	13.51	8.6	—
	Elbow	6.00	13.22	8.3	59.0
Lt Ulnar	Wrist	2.65	13.78	8.8	—

Nerve	Site	Latency (ms)	Duration (ms)	Amplitude (mV)	NCV (m/s)
Rt PTN	Ankle	4.80	13.52	11.8	—
	Knee	10.40	12.81	14.5	49.1
Lt PTN	Ankle	4.85	13.60	10.7	—
	Knee	10.46	12.96	12.4	49.0
Rt CPN	Ankle	3.92	12.09	3.9	—
	Knee	8.13	11.70	3.7	50.5
Lt CPN	Ankle	3.95	12.14	3.9	—
	Knee	8.10	11.85	3.8	50.6

Nerve	Site	Latency (ms)	Amplitude (μV)	NCV (m/s)
Rt Median	Wrist	5.2	6	36
Lt Median	Wrist	5.3	5	35
Rt Ulnar	Wrist	5.4	5	34
Lt Ulnar	Wrist	5.5	4	33
Rt Sural	Mid-Calf	5.8	4	32
Lt Sural	Mid-Calf	6.0	3	31

Table 3 showing sensory conduction studies inboth upper and lower limbs

Given the clear temporal relationship between long-term imatinib exposure and onset of neuropathy, and the absence of alternative causes, a diagnosis of imatinib-induced peripheral neuropathy was made. The patient was counseled about the suspected drug-related nature of her symptoms. After multidisciplinary discussion with the haematology team, imatinib therapy was discontinued.

Supportive treatment was instituted to promote neural recovery and relieve symptoms: Vitamin therapy: Pyridoxine 100 mg/day. Neuropathic pain control: Gabapentin 100 mg thrice daily, later tapered over six weeks. Physiotherapy: Balance and proprioceptive-training exercises under supervision. Dietary modification: Protein-rich, balanced diet and adequate hydration. Lifestyle advice along with avoidance of neurotoxic agents are given. Regular follow-up was arranged to monitor neurological improvement and haematologic stability.

Within three weeks of discontinuing imatinib, the patient noted a significant reduction in paresthesia and improved coordination. The "pins-and-needles" sensation in the fingertips diminished gradually, and her gait steadied. By the eighth week, she reported complete resolution of numbness and regained normal fine-motor function. Neurological examination at that stage demonstrated restored vibration and position sense, normal reflexes, and a steady tandem gait. A repeat NCS performed on 4 November 2024 revealed partial electrophysiological recovery. Sensory responses, which were previously absent, showed reappearance of low-amplitude SNAPs in the median (5–6 μV), ulnar (4–5 μV), and sural (3–4 μV) nerves bilaterally, with slowed conduction velocities (31–36 m/s). Motor conduction parameters remained within normal limits. These findings were consistent with early neural regeneration and remyelination, matching the patient's subjective improvement in coordination and reduction of paresthesias. Throughout this period, her CBC remained normal, indicating that discontinuation of imatinib did not precipitate disease progression.

After neurological recovery, a new tyrosine-kinase inhibitor was required to maintain remission. She was switched to nilotinib 300 mg twice daily, chosen for its similar efficacy and favorable toxicity profile. Baseline ECG, lipid profile, and liver-function tests were obtained before initiation. Nilotinib was well tolerated without recurrence of neuropathic symptoms. At six-month follow-up, she remained completely asymptomatic neurologically. Haematologic indices were stable (Hb 11.6 g/dL, TLC 7.1 × 10^3/μL, platelets 2.1 × 10u /μL), and quantitative BCR–ABL PCR continued to show major molecular response. No new adverse effects were reported.

The chronological sequence—normal blood counts and molecular remission preceding the onset of neuropathy, absence of other etiologies, and marked improvement after withdrawal—strongly supported a causal association with imatinib therapy. The clinical presentation and NCS pattern were consistent with previously reported cases of mixed axonal-demyelinating sensory neuropathy linked to long-term imatinib exposure. The reversibility of neuropathy after drug cessation, as observed in this patient, further supports a metabolic or functional rather than structural mechanism of injury. Importantly, switching to nilotinib—another selective BCR–ABL inhibitor with minimal PDGFR interference—allowed maintenance of remission without recurrence of neuropathic symptoms, reinforcing the drug-specific nature of the reaction.

Two months after discontinuing imatinib, the patient resumed all routine activities without limitation. At serial follow-ups over six months, a third NCS demonstrated complete electrophysiological normalization. Sensory latencies, amplitudes, and velocities had returned to normal (median SNAP amplitude 20–22 μV, sural 15–16 μV; conduction velocities 45–50 m/s).

Motor conduction studies of median, ulnar, tibial, and peroneal nerves were also normal. The interpretation confirmed complete recovery of peripheral nerve function.

Clinically, the patient was asymptomatic, with full restoration of vibration and position sense, normal reflexes, and steady gait.

She continued to remain asymptomatic, with normal gait and sensory examination. Laboratory monitoring confirmed stable counts and liver-function parameters, and molecular testing showed sustained remission on nilotinib therapy.

Discussion :

Peripheral neuropathy results from structural or functional damage to peripheral nerves and may manifest as numbness, tingling, or burning sensations. Common drug-induced causes include vincristine, cisplatin, and isoniazid. Tyrosine kinase inhibitors such as imatinib are rarely implicated (6).

The mechanism of imatinib-induced neuropathy remains speculative. One hypothesis implicates inhibition of PDGFR signaling in Schwann cells, which may impair axonal support and myelin maintenance(7). Another possibility involves mitochondrial dysfunction due to off-target kinase inhibition, leading to axonal degeneration(8).

Several authors have described reversible peripheral neuropathy with imatinib. Gajula et al. (4) reported the first such case in India, where a patient developed neuropathy after six months of therapy, which resolved after discontinuation and vitamin supplementation. Chakupurakal et al. (5) described a similar presentation in a patient treated for over five years, and Kavanagh et al. (6) reported a case of sensory neuropathy after ten years of imatinib use, both showing improvement on drug withdrawal.

Our patient's course was consistent with these reports: late onset after years of exposure, exclusion of other causes, and full recovery after cessation. The absence of relapse following nilotinib substitution further supports imatinib causality.

Nilotinib, a second-generation TKI, has demonstrated efficacy comparable to imatinib in chronic-phase CML, with a favorable toxicity profile (9). Studies such as the ENRICH trial have shown that switching to nilotinib alleviates chronic imatinib-related adverse effects while maintaining remission (10).

This case underscores the importance of recognizing rare neurotoxicities of imatinib. Early detection allows modification of therapy to prevent irreversible nerve injury. Given the increasing life expectancy of CML patients on TKIs, monitoring for late adverse effects is crucial.

Conclusion :

Imatinib-induced peripheral neuropathy is a rare but reversible adverse event. Clinicians should consider drug-induced neurotoxicity in patients on long-term imatinib presenting with new-onset sensory symptoms. Prompt discontinuation and substitution with nilotinib can lead to full recovery and continued CML remission. Awareness and reporting of such cases will strengthen pharmacovigilance and improve patient safety.

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Case Report

RIFAMPICIN RESISTANT SKIN TUBERCULOSIS AND HYPERSENSITIVE PNEUMONITIS: DILEMMA IN DIAGNOSIS & TREATMENT

Dr. Samir Sahu

Abstract :

Extrapulmonary TB is increasingly being reported in Odisha. Drug resistant TB is also being found in Odisha. Hypersensitive Pneumonitis after exposure to birds is the most common ILD found in India. We report a case of drug resistant (DR) Skin TB along with Hypersensitive Pneumonitis and the challenges faced in diagnosing and treatment of such a case.

Case Report :

A 30 year female developed cellulitis right leg in April 2022 which improved with Amoxiclav. She had history of disseminated TB in 2012 and had taken antitubercular treatment for 6 months and was cured.

She complained of cough and a chest x-ray(CXR) on 1-Jun-2022 revealed bilateral infiltrates in the lungs. Gamma Inteferon was positive (1.219/0.983) on 6-Jun-2022. On 30-Jul-2022 she developed fever and an abscess on right knee. Pus culture did not grow any organism. The abscess turned into a chronic ulcer not healing with antibiotics. Due to chronic non healing ulcer, infiltrates on Chest X-Ray and fever a trial of antitubercular drugs (HREZ) was started on 3-Sep-2022. She had severe vomiting for which pyrazinamide was replaced by Levofloxacin (HRELfx). Wound started healing and she became afebrile.

After 2 months of HRELfx HRCT thorax (2-Nov-2022) showed bilateral consolidation (Organizing pneumonia). She was keeping birds in her house. Ulcer Biopsy showed necrotizing granuloma but MTB PCR was not detected. A diagnosis of Hypersensitive pneumonitis was made, antitubercular drugs were stopped and prednisolone was started.

After 2 months of steroid and stoppage of ATT fever increased, lung lesion increased, multiple abscesses developed. Steroids were stopped and ATT was restarted. Bronchoscopy was done on 13-Jan-2023. MTB PCR was not detected on BAL fluid examination. Aspergillus antigen Galactomanan was positive (3.55) on BAL. Suspecting Pulmonary Aspergillosis Voriconazole was started. Adding Voriconazole did not show any improvement in the lung lesion and it was stopped. On 30-Jan-2023 an ulcer developed on right great toe. Skin biopsy from the ulcer revealed Epitheloid granuloma. A repeat HRCT thorax done on 16-Feb-2023 was same as that done on 9-Jan-2023. Repeat Bronchoscopy was done on 20-Feb-2023. CBNAAT MTB was not detected from BAL fluid. CT guided Lung Biopsy was done on 22-Feb-2023 which revealed organizing pneumonia.

On 1-Mar-2023 an abscess developed on right thigh. Another abscess developed in the right calf on 18-Mar-2023. Pus from the fresh abscess revealed one be aded AFB and MTB pus culture was sent. Suspecting MDR TB on 25-Mar-2023 ATT regimen was escalated (HRELfxLzdClarAm). MTB culture sent in March 2023 was negative on 2-May-2023 and 16-May-2023. After 2 months she developed an ulcer on right great toe, ulcers in right thigh & right calf showed some signs of healing.

On 22-May-2023 an abscess developed in right foot and pus for CBNAAT for MTB was detected which was resistant to Rifampicin. Rifampicin resistance was detected after 2 months of suspecting drug resistant (DR) TB. All oral longer DR TB regimen was started

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on 23-May-2023(6Bdq, 20 LfxLzdCfzCs) (Bedaquiline, Levofloxacin, Linezolid, Clofazimine, Cycloserine).

After 2 months she developed severe peripheral neuritis which was treated with methylcobalamin, pregabalin and duolexitine. Linezolid was stopped and Delanamide was started. She developed bilateral foot drop due to peripheral neuritis. Cycloserine was not available for 1 month in August 2023 and she developed fever. Pus culture for MTB was sent on 9-Aug-2023 which was negative. On 20-Oct-2023wound healed, CXR showed bilateral opacities, spirometry was normal(FVC-82%).

On follow up on 3-Jun-2025 she had completed 20 months DRTB regimen (Bedaquiline, Levofloxacin, Cycloserine, Delanamid, Clofazimine). There was residual peripheral neuritis with bilateral foot drop which had improved from the previous state. There was a scar on the back of the right knee. She was complaining of shortness of breath on exertion. Spirometry (13-Jun-2025) revealed severe restriction (FVC-53%). HRCT thorax (8-Jul-2025) revealed bilateral fibrosis. Her Hypersensitive Pneumonitis had led to Fibrosing ILD. She was started on Nintedenib.

Discussion :

In summary a 37yr female with H/O TB in 2012, adequately treated presented with cellulitis right leg in April2022 progressing to abscess and skin ulcers. Developed respiratory symptoms and CT Thorax revealed features of Hypersensitive Pneumonitis in June 2022. When ulcers did not heal with antibiotics ATT (2HRELfx) was started in September 2022. Biopsy of Skin ulcer revealed necrotizing granuloma in November 2022 but sputum MTB PCR was negative. Fever reduced, ulcers healed partially but chest lesions increased. The diagnosis of cutaneous tuberculosis rests on the clinical presentation supported by a positive tuberculin test, granulomatous histopathology and regression following antitubercular therapy.[1] In our case IGRA was positive, histopathology revealed necrotizing granuloma and there was clinical improvement.

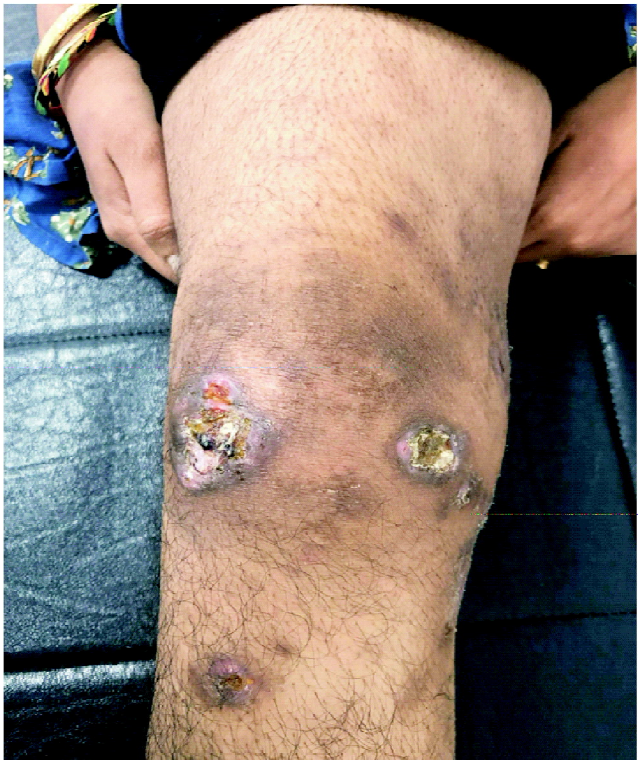
With birds in her house a suspicion of Hypersensitive Pneumonitis with Organizing Pneumonia was made.[4] ATT was stopped & Prednisolone started in November 2022. In January 2023 fever persisted, skin lesions increased. CT thorax showed no improvement. Steroids were stopped and ATT restarted (HRELfx). Bronchoscopy BAL fluid for MTB was negative, Aspergillosis antigen Galactomanan was positive therefore Voriconazole was added to ATT. In February 2023 sputum AFB and CBNAAT was negative, no granuloma on repeat skin biopsy and pus was negative for AFB and CBNAAT.Lung Biopsy revealed Organizing Pneumonia and AFB and CBNAAT was negative. Organizing Pneumonia has been reported in cases of Pulmonary TB.[5] But in our case repeated examinations from BAL fluid and lung biopsy did not reveal TB. Therefore the Hypersensitive Pneumonitis in this case was probably due to exposure to birds.[4] Due to suspected MDR Skin TB steroids and immunosuppressives were not started in this case.

On 18-Mar-2023 pus from a fresh abscess revealed one be aded AFB. MTB pus culture was sent and was negative on 2-May-2023 and 16-May-2023. Multidrug-resistant cutaneous tuberculosis cannot be ignored when there is poor response to standardanti-tubercular drugs in patients where no othercause is forthcoming.[1] This is what we encountered in our case. In skin TB isolation of organisms is difficult and molecular testsfor detection of resistance have low sensitivity.[2] Where there is strong suspicion of cutaneous tuberculosis and the patient does not respond to first-line antitubercular drugs, a trial of second-line drugs may be justified.[1] Suspecting MDR TB on 25-Mar-2023 ATT regimen was escalated (HRELfxLzdClarAm).

In spite of escalating ATT fresh abscess appeared. On 22-May-2023 CBNAAT MTB was detected with Rif resistance from pus from right foot abscess (very low). 6Bdq, 20 LfxLzdCfzCs was started on 23-May-2023.

In extrapulmonary forms like cutaneous tuberculosis, which are essentially paucibacillary, isolation of organisms in culture is difficult and hence demonstration of drug resistance becomes difficult.[1] This highlights the difficulty in detecting paucibacillary DR TB. Skin lesions improved. In July 2023 Linezolid was stopped due to increase in peripheral neuritis and foot drop and Delanamid added. MTB culture was negative in Aug 2023. By 3-Jun-2025 she had completed 20 months DRTB regimen. Delamanid and Bedaquiline were extended beyond 6 months. There was residual

peripheral neuritis with bilateral foot drop. This highlights the severe side effects of DR TB regimens. All skin lesions had healed with residual scars. She was complaining of shortness of breath on exertion. Spirometry (13-Jun-2025) revealed severe restriction (FVC-53%). HRCT thorax (8-Jul-2025) revealed bilateral fibrosis. Her Hypersensitive Pneumonitis had led to Fibrosing ILD.[4]



Conclusion :

In this case of Rifampicin resistant Skin TB AFB was detected after 11 months and Rifampicin resistance was detected after 1 year in spite of repeated (five) examinations from multiple sites (skin, pus, BAL and lung tissue). She developed severe peripheral neuritis and foot drop to the DR TB regimen. Linezolid was replaced by Delamanid. Delamanid and Bedaquiline were extended beyond six months. Pulmonary lesions were due to Hypersensitive Pneumonitis and not due to tuberculosis. Immunosuppressants were not given along with MDR treatment with the fear of failure of MDR regimen. Hypersensitive Pneumonitis progressed to Fibrosing ILD.

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Case Report

DENGUE HAEMORRHAGIC FEVER ASSOCIATED HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS : A RARE CASE REPORT

Dr. Biplabi Biswa Kesari Mohanty, Dr. Abhilash Patnaik, Dr. Smita Priyadarshini, Dr. AK Budhia, Dr BL Parija

Introduction :

Haemophagocytic lymphohistiocytosis (HLH), also known as hemophagocytic syndrome, is an uncommon systemic inflammatory clinical syndrome associated with numerous conditions [1]. HLH may be inherited (primary) or secondary to severe infections, malignancies, or rheumatologic conditions [2]. HLH is sporadically seen in clinical practice and is a rare complication of dengue characterized by persistent fever, pancytopenia, hepatosplenomegaly, and increased serum ferritin level. The overlap in clinical features makes diagnosing HLH in a dengue patient difficult, necessitating a bone marrow examination [3]. HLH is associated with significant mortality and morbidity even with appropriate treatment, and the outcome is further poor if the diagnosis is delayed or left untreated [4]. Therefore, a high clinical suspicion is paramount in diagnosing HLH, especially in an atypical presentation of a possible medical condition [2]. Here we present a case of HLH in an adolescent, which occurred secondary to dengue hemorrhagic fever, which was successfully treated and recovered.

Case Presentation :

A 31years old female, Housewife from Khurda, Odisha presented with Fever, Generalized Myalgia and skin rashes lasting 7days before admission to Hitech Medical College & Hospital, Bhubaneswar. Initially she was treated in a government Hospital for 3 days and diagnosed a case of Dengue Fever. Initial examination reveals Moderate Pallor, Petechial Rashes over Left Breast and Hemorrhagic Spots over left Conjunctiva .Blood pressure was under normal range, Tachycardia, Oxygen Saturation was 97% in room air. Systemic Examination reveals no abnormal respiratory, Cardiac and CNS Findings. Abdominal Examination reveals Mild Splenomegaly.

Initial laboratory tests showed Total Leukocyte Count (7240/uL), Hemoglobin- 8.1 gm%, Thrombocytopenia (22,000/mL) and elevated levels of alanine aminotransferase (ALT, 71 IU/L) and aspartate transaminase (AST,143.4IU/L) Dengue NS1 - Positive. PT INR (1.05) were within the normal range. The Patient was diagnosed as a case of Dengue Hemorrhagic Fever and managed conservatively and 02 units of RDP transfused initially.

Parameters and points in the HScore

Parameter	No. of points (criteria for scoring)
Known underlying immunosuppression*	0 (no); or 18 (yes)
Temperature (°C)	0 (<38.4), 33 (38.4–39.4), or 49 (>39.4)
Organomegaly	0 (no); 23 (hepatomegaly or splenomegaly), or 38 (hepatomegaly and splenomegaly)
No. of cytopenias†	0 (1 lineage), 24 (2 lineages), or 34 (3 lineages)
Ferritin (µg/L)	0 (<2000), 35 (2000–6000), or 50 (>6000)
Triglycerides (mmol/L)	0 (<1.5), 44 (1.5–4), or 64 (>4)
Fibrinogen (g/L)	0 (>2.5) or 30 (≤2.5)
Aspartate aminotransferase (U/L)	0 (<30) or 19 (>30)
Hemophagocytosis on bone marrow aspirate	0 (no); or 35 (yes)

*HIV positive or receiving long-term immunosuppressive therapy (ie, glucocorticoids, cyclosporine A, azathioprine)

†Defined as a hemoglobin level of 9.2 g/L and/or a leukocyte count ≤5 × 10⁹/L and/or a platelet count ≤110 × 10⁹/L.

Diagnostic Criterion for HLH

The diagnosis of HLH requires either a molecular diagnosis consistent with HLH or fulfilling 5 of the 8 clinical, laboratory, and histopathological criteria listed below.

1. Fever
2. Splenomegaly
3. Cytopenia (in at least 2 of the 3 cell lineages)
   a. Hemoglobin level <9 g/dL
   b. Platelet counts <100 × 10⁹/L
   c. Neutrophils count <1.0 × 10⁹/L
4. Hypertriglyceridemia and/or hypofibrinogenemia
5. Low or absent NK-cell activity
6. Ferritin level ≥500 µg/L
7. Soluble CD25 level ≥2400 U/ml
8. Hemophagocytosis in bone marrow, spleen, or lymph nodes

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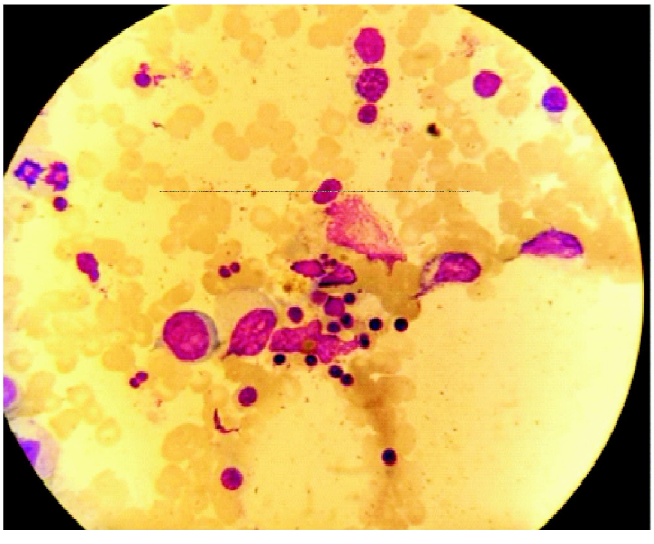
On Day 3 of Hospitalization, fever persisted and patient looks lethargic. Platelet Count was initially increased post platelet transfusion but again decreased and Hemoglobin level dropped to 6.8 gm%. With suspicion for secondary HLH after dengue infection, diagnostic tests were performed. Reports revealed High Triglyceride Count (367.8 mg/dl) and High Serum Ferritin (749.5 ng/ml). Bone marrow examination revealed features of an increased hemophagocytic activity and diagnostic criteria of HLH were met: fever, splenomegaly, cytopenia, hypertriglyceridaemia (fasting TG 367.8 mg/dL), hyperferritinaemia (ferritin 749.5 ng/mL) and hemophagocytosis in bone marrow study. She was immediately started with IV prednisolone 500mg OD for 7 days and the patient experienced excellent recovery. The fever settled within 24h after starting intravenous prednisolone doubling platelet count and white cell count. She was discharged after a 10 days of hospital stay with oral dexamethasone 10 mg per body surface area (16 mg) for the first 2 weeks, gradually tailed of over 8 weeks as per HLH-2004 protocol and completely recovered while reviewing in the hospital after 8 weeks.



Discussion :

This report describes a case of a 31 years old female with dengue fever who progressed to the critical phase of the infection (Dengue hemorrhagic Fever). Even after the critical phase, the patient had a continuous moderate to high-grade fever, persistent thrombocytopenia, a gradual drop in hemoglobin levels, and splenomegaly. The diagnosis of HLH was made based on increased ferritin and triglyceride levels and confirmed with a bone marrow biopsy. This case is unique in several aspects. This patient's age at the time of diagnosis is relatively older than most reported cases, where HLH has been more commonly observed in children under the age of 10 [5]. At the same time, the patient had a successful response to intravenous Prednisolone therapy followed by an 8-week tapering regimen. This treatment approach differs from some of the other cases reported in the literature, where different immunosuppressive agents and/or hemopoietic stem cell transplants were used [6]. Therefore, this case highlights the effectiveness of Prednisolone in managing HLH associated with dengue infection and adds to the existing knowledge on the management of this rare and potentially fatal complication of dengue fever.

HLH is a rare, potentially fatal hyperinflammatory and haemophagocytic syndrome causing severe hypercytokinemia with excessive activation of lymphocytes and macrophages associated with numerous conditions [2, 7]. The disease is seen in all ages and has no predilection for race or sex [8]. There are two main types of HLH; primary or familial HLH associated with genetic predisposition and secondary or sporadic HLH associated with other medical conditions, including infective, autoimmune, and malignant conditions [5]. Nevertheless, the classification of genetic and acquired is more appropriate for HLH than the primary and secondary [1]. Acquired (secondary) HLH can occur in all age groups, although there are no published data on its incidence or age distribution [9].

HLH is an uncommon manifestation in dengue, and the diagnosis of HLH is difficult in dengue due to the overlap of the clinical features [3, 10]. Dengue fever is caused by the Dengue virus, which belongs to the family Flaviviridae, genus Flavivirus, and is transmitted to humans by Aedes mosquitoes, mainly Aedes aegypti [11]. The clinical spectrum of dengue viral infection includes undifferentiated fever, dengue fever (DF), dengue hemorrhagic fever (DHF), and expanded dengue syndrome or isolated organopathy[12]. Our patient demonstrated classic symptoms of DF such as fever, severe frontal headache with retro-orbital pain,

arthralgia, and myalgia, where the NS1 antigen positivity confirmed the diagnosis, facilitating further management. Persistent fever following dengue infection may occur due to sepsis and expanded dengue syndrome, including HLH [14–16]. HLH is an unusual hematological manifestation of expanded dengue syndrome, whereas other manifestations include disseminated intravascular coagulopathy and cytopenias[13]. The initial symptoms of HLH are nonspecific and may overlap with other inflammatory or hematopoietic diseases, and the diagnosis of HLH is based on the diagnostic criteria as revised for HLH-2004 [5, 18]. According to HLH-2004, there are two main criteria; Criterion1 and 2. The diagnosis of HLH can be established if Criterion1 or 2 is fulfilled. Criterion 1 included a molecular diagnosis consistent with HLH. Criterion 2 included fulfilling five of the eight criteria. Our patient developed continuous fever, thrombocytopenia, anemia, and mild splenomegaly. Her serum ferritin and triglyceride levels were high, fulfilling the criteria for diagnosing HLH. However, since cytopenias can occur in uncomplicated dengue infection, bone marrow examination is justifiable to confirm the diagnosis of HLH and exclude other possibilities like hematological malignancies [19]. Our patient's bone marrow examination revealed significant haemophagocytic activity, which confirmed the diagnosis of HLH, and the treatments were started promptly. Corticosteroids are the first choice to suppress hypercytokinemia. The first-line option is dexamethasone; since dexamethasone crosses the blood–brain barrier better than prednisolone, suppresses the central nervous system inflammation more effectively [9]. The 2004 treatment protocol developed at the second international meeting of the Histiocyte Society recommends an 8-week induction therapy with corticosteroids, etoposide, and cyclosporine A [1, 17]. In patients with milder forms of HLH, corticosteroids with or without immunoglobulins may be sufficient to control hyperinflammation; however, initially, mild cases can deteriorate rapidly within a short time [9]. The treatment of dengue-induced HLH by intravenous immunoglobulin G is associated with a favorable outcome [20]. HLH in dengue patients responds well to the conventional treatment of HLH [10]. Primary HLH has a near 100% fatality without adequate treatment. However, in a few international studies (HLH- 94/HLH-2004), survival has increased from ~0 to 60% with HLH-directed treatment, including dexamethasone and cytotoxic drugs [22]. Secondary HLH is a rapidly fatal disease. Most patients die of bacterial or fungal infections due to prolonged neutropenia, multi organ failure, orcerebral dysfunction. [8] Therefore, prompt treatment initiation is essential for patients' survival. The clinical course of HLH may be very aggressive. Sometimes initial treatment may be necessary to prevent early fatalities, even though the diagnostic workup has not been completed [17, 19]. After diagnosing HLH, our patient was started with intravenous prednisolone and gradually tailed off over 8 weeks converting to oral dexamethasone.

Conclusion :

This case report aims to generate awareness about dengue induced HLH and the importance of a high clinical suspicion for early detection thereby facilitating successful treatment. Dengue affects thousands of people worldwide every year and hence may be life saving to detect HLH in patients suffering from dengue. The diagnosis is usually challenging, as it can be easily mistaken with other clinical situations, such as sepsis or other systemic inflammatory response syndromes (SIRS). BothHLH- 2004 Trial Guidelines and HScore may be used simultaneously for an increased probability in successfully diagnosing a case of HLH through Clinical features and routine laboratory tests. This case report adds to the limited adult cases of dengue-associated hemophagocytic syndrome and stresses the need to work up patients with Dengue Hemorrhagic Fever for possibility of HLH

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Case Report

ORGANOPHOSPHOROUS INDUCED DELAYED NEUROPATHY : A RARE CASE REPORT

Dr. Nikesh Kumar Pradhan[1], Dr Sagnika Tripathy[2]

Abstract :

Organophosphate-induced delayed neuropathy (OPIDN) is a rare but well-documented neurological complication that occurs after ingestion of large amounts of organophosphorus compounds. It typically appears after a latent period of 1–3 weeks following the acute cholinergic phase. The clinical features include distal paraesthesia, tingling, and numbness in a glove-and-stocking pattern, followed by symmetrical, flaccid motor weakness that begins distally in the lower limbs and gradually ascends to involve the upper limbs. In severe cases, proximal muscles may also be affected.

We report a case of a 22-year-old male who developed progressive weakness in all four limbs approximately 20 days after ingesting a large quantity of 50% chlorpyrifos + 5% cypermethrin. Electrodiagnostic evaluation, including electromyography (EMG), nerve conduction study (NCS) revealed severe motor axonal polyneuropathy involving both upper and lower limbs. These findings were consistent with organophosphate-induced delayed neuropathy (OPIDN).

Introduction :

Organophosphates (OPs) are highly potent inhibitors of the cholinesterase enzyme, leading to the accumulation of acetylcholine and subsequent overstimulation of cholinergic receptors. Toxicity may occur through ingestion, inhalation, or cutaneous exposure.

Organophosphorus poisoning generally progresses through three distinct phases: the acute cholinergic crisis, the intermediate syndrome, and organophosphate-induced delayed neuropathy (OPIDN). In this context, we present a case of a patient who initially manifested acute cholinergic symptoms following OP intoxication, received appropriate hospital management, was discharged in an asymptomatic state, and subsequently developed subacute, predominantly motor, peripheral neuropathy.

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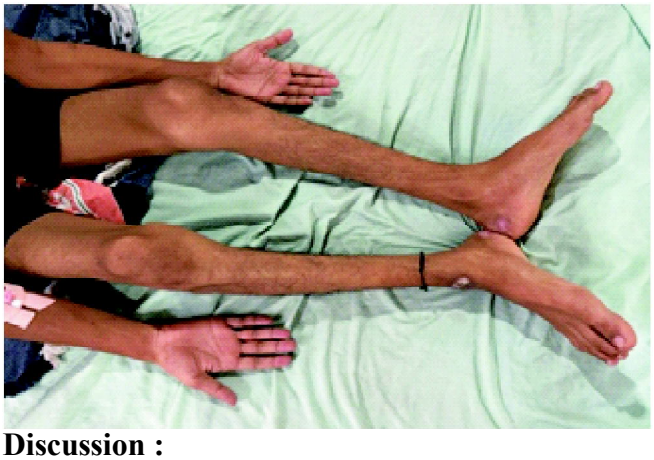
Case Report :

A 22-year-old male ingested a large amount of an organophosphate insecticide containing 50% chlorpyrifos and 5% cypermethrin. He presented to the emergency department with features of cholinergic crisis, including excessive salivation, lacrimation, pinpoint pupils, and shortness of breath, following a clear history of ingestion.An atropine infusion was initiated after a bolus dose; however, after supportive management including atropine, pralidoxime, and antibiotics. Over the next 96 hours, his condition gradually improved. He was discharged on the 8th day of admission in an asymptomatic state.After approximately 20 days, he developed progressive weakness in the lower limbs involving distal muscles . He was readmitted, and within two days, the weakness had ascended to involve the upper limbs.

Neurological examination revealed distal motor deficits in lower limbs and upper limbs with a muscle power of 1/5 and 3/5 respectively along with significant atrophy of lower limb and upper limb muscles shown in the picture below . Deep tendon reflexes were normal in the upper limbs and lower limbs bilaterally but ankle jerk was absent bilaterally and plantar responses were nonresponsive . Cranial nerves were intact. Pain and temperature sensations, touch, pressure, vibration, and joint position senses remained intact.A nerve conduction study demonstrated severe axonal motor neuropathy involving both upper and lower limbs, MRI spine revealed no significant abnormality. All these findings were consistent with organophosphate-induced delayed neuropathy(OPIDN).



Discussion :

Organophosphorous poisoining can have 3 types of manifestations. These are as follows Type I – Acute cholinergic crisis: Occurs within hours to a day; features salivation, sweating, diarrhea, vomiting, muscle fasciculations, and brady/tachycardia. Severe cases may develop coma or convulsions. Treated with atropine.

Type II – Intermediate syndrome: Appears 24–96 h post-exposure in 20–50% of patients. Characterized by proximal limb and neck weakness, cranial nerve palsies, and respiratory involvement, lasting 5–18 days.

Type III – Delayed neuropathy (OPIDN): Onset 10 days to 3 weeks after exposure. Features distal motor weakness, foot/wrist drop, paraesthesia, absent ankle reflexes, sometimes progressing to proximal muscles. Primarily motor nerves are affected.

Organophosphate-induced delayed neuropathy (OPIDN) results from inhibition of neuropathy target esterase (NTE), an enzyme involved in phospholipid metabolism and axonal membrane maintenance. Its inhibition leads to axonopathy, disturbed axonal transport, and membrane instability. Although NTE is present in many tissues, including non-neural ones, its exact biological role remains unclear, and NTE inhibition alone does not always predict neurotoxicity. Disruption of endoplasmic reticulum phospholipid homeostasis is also believed to contribute to OPIDN pathogenesis. The neuropathy predominantly affects motor function, initially involving distal lower limb muscles and later spreading to the upper limbs. Sensory symptoms are usually mild.

Electrodiagnostic findings typically demonstrate axonal motor neuropathy with evidence of denervation, while CSF studies are usually normal. Differential diagnoses include Guillain–Barré syndrome and acute disseminated encephalomyelitis.

There is no specific treatment for OPIDN. Supportive care, including physiotherapy and symptomatic management with drugs like amitriptyline, carbamazepine, or capsaicin, may help. Prognosis depends on the compound type, dose, delay in treatment, and neurological involvement. Cases with pyramidal or extrapyramidal tract damage often have a poor outcome, with residual spastic or flaccid paraparesis. Hence, patients should be monitored for 4–6 weeks post-intoxication for delayed neurological manifestations.

Conclusion :

Organophosphate-induced delayed neuropathy (OPIDN) is a rare but serious complication of organophosphate poisoning. The exact reason why it develops in certain individuals while sparing others remains unclear. Hence, all patients with organophosphate poisoning should receive comprehensive management and be counselled about potential delayed neurological sequelae. They should be advised to report early if they develop weakness or sensory symptoms, as timely recognition and supportive interventions, including physiotherapy, may help limit disability, although no definitive cure currently exists.

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Case Report

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS : A RARE PRESENTATION OF SYSTEMIC SCLEROSIS

Dr. Prajna Paramita Nayak[1], Dr. Sourav Shristi[2]

Introduction :

Systemic Sclerosis (SSc) is a disease of complex pathogenesis and variable clinical presentations. Microvasculopathy is an early and primary pathogenic event which can present with different clinical symptoms related to skin and various organs.[1] Though most common renal involvement of Systemic Sclerosis is scleroderma renal crisis, they can present with MPGN rarely.[2] They may involve chronic endothelial injury with subsequent immune complex deposition in the glomeruli, or may represent an overlap syndrome with lupus or mixed connective tissue disease[3]. However, in cases with no other autoimmune markers, the occurrence of MPGN appears to be a direct renal manifestation of SSc itself.

Case Report :

A 48years old female,known case of Hypertension since 10 years, Diabetes since 7years, Hypothyroidism since 5years presented with facial puffiness since 16 days.Then she developed swelling of feet after 6 days. On examination patient was concious oriented, her blood pressure was 172/100mm Hg, pulse rate of 82/minute, JVP was not raised. There was periorbital edema, mild pallor and bilateral pitting pedal edema. Laboratory investigation revealed Hb of 10.2g/dl, serum urea of 26mg/dl, creatinine of 1.4mg/dl,total protein of 5.87g/dl,serum albumin of 3.15g/dl,TSH of 9.59microiu/dl,Free T4 of6.93microgram/dl, urine routine microscopy revealed 3+ proteinuria and 8-10 PRBCs. On further evaluation spot urine protein was 833.8mg/dl, UACR was 18.3. On renal biopsy 7 glomeruli were seen which showed endo capillary proliferative glomerulonephritis. Immunofloroscence of the specimen was positive for IgG, C3, C1q on capillary loops and mesangium. Hence diagnosis of MPGN was made and patient was treated with cyclophosphamide. On further evaluation his autoimmune panel was positive for antinuclear antibodies (ANA) and Scl 70(topoisomerase l) and negative for anti double-stranded-DNA(ds DNA) and c-ANCA, p-ANCA. So our final diagnosis of Systemic Sclerosis with MPGN was made.

Discussion :

This case highlights the need for clinicians to consider glomerulonephritis, particularly MPGN, as a differential diagnosis in SSc patients presenting with proteinuria or renal dysfunction. Early renal biopsy remains crucial for accurate diagnosis and guiding therapy. Furthermore, understanding the underlying immunopathological mechanisms may help in identifying patients at risk and developing more targeted therapeutic approaches.

Therapeutically, management of MPGN in the context of SSc remains challenging. Immunosuppressive therapy, including corticosteroids and agents such as mycophenolate mofetil or cyclophosphamide, has shown variable success.[4, 5] However, corticosteroid should be used cautiously in systemic sclerosis due to the potential risk of precipitating scleroderma renal crisis. In this case, the patient showed improvement with a combination of immunosuppression and renin–angiotensin system blockade.

The primary renal involvement in systemic sclerosis patient is scleroderma renal crisis due to thrombotic microangiopathic process but other rare presentations can also be possible.[6] At the same time

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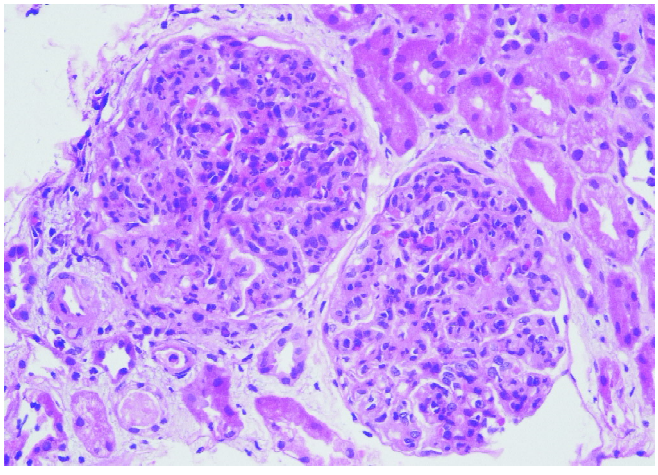

Fig 1 Endo capillary proliferative glomerulonephritis in renal biopsy

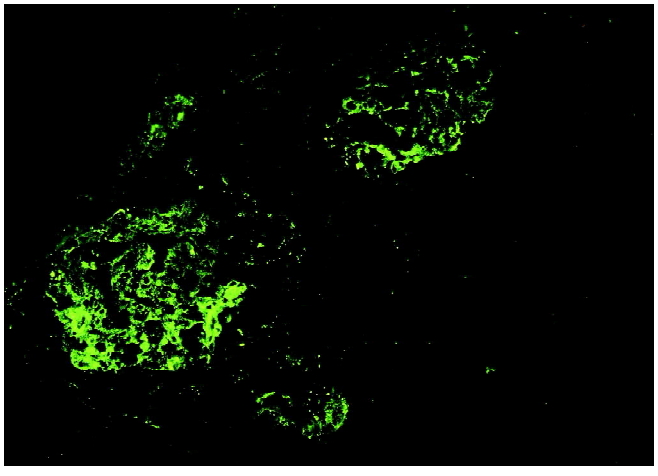

Fig 2 Immunofloroscence showing positive for IgG,C3,C1q on capillary loops and mesangium.

patients presenting with renal pathologies like MPGN should be investigated for the proper cause and treated accordingly .

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Pictorial CME

DECODING GRANULOMATOSIS WITH POLYANGIITIS: VISUAL CLUES TO DIAGNOSIS AND MANAGEMENT

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A 32 years female without any prior co-morbidity presented with complaints of epistaxis, petechiae, left eye proptosis, bilateral tympanic membrane perforation with bilateral active ear discharge with left sided lower motor facial palsy. There was bilateral sinus tenderness on investigation there was anemia (Hb -8.7 gm/dl) with neutrophilic leukocytosis (WBC-13, 040/mm^3) Thrombocytosis (Platelets-7.58 lakhs/mm^3) with ESR 99mm/1st hr and CRP -236 mg/dl. Chest X-ray and HRCT Thorax suggestive of a cavitary lesion in right lung.Sputum for AFB and CBNAT was negative. C-ANCA was significantly high (198.1AU/ml). Nasal mucosal biopsy findings suggestive of Granulomatosis with polyangitis. Injection Methylprednisolone (Pulse Therapy) and Cyclophosphamide (EUVAS Protocol). Initially there was clinical improvementbut after 3rd dose of cyclophosphamide patient's symptoms deteriorated with increased productive cough associated with hemoptysis. IV antibiotics were started but there was no significant improvement. Injection Rituximab (375 mg/m^2) once weekly was started and after 2nd dose there was significant improvement in clinical as well as biochemical parameters.

Discussion :

Granulomatosis with Polyangiitis (GPA), formerly known as Wegener's granulomatosis, is a necrotizing granulomatous vasculitis that primarily involves small- to medium-sized vessels, classically affecting the upper and lower respiratory tracts and kidneys. The disease may present with a wide clinical spectrum ranging from localized sinonasal disease to life-threatening systemic vasculitis. ENT manifestations such as epistaxis, otitis media, hearing loss, and facial nerve palsy are often early but nonspecific presentations, frequently leading to diagnostic delay.

In this case, the patient presented with multiple ENT manifestations, including epistaxis, tympanic membrane perforation, otorrhea, and facial nerve palsy, along with pulmonary cavitation. These findings, in conjunction with markedly elevated inflammatory markers and strongly positive C-ANCA titers, pointed toward GPA, which was further confirmed by nasal mucosal biopsy. Pulmonary involvement in GPA often manifests as nodules, cavitary lesions, or alveolar hemorrhage, reflecting the underlying necrotizing vasculitis.

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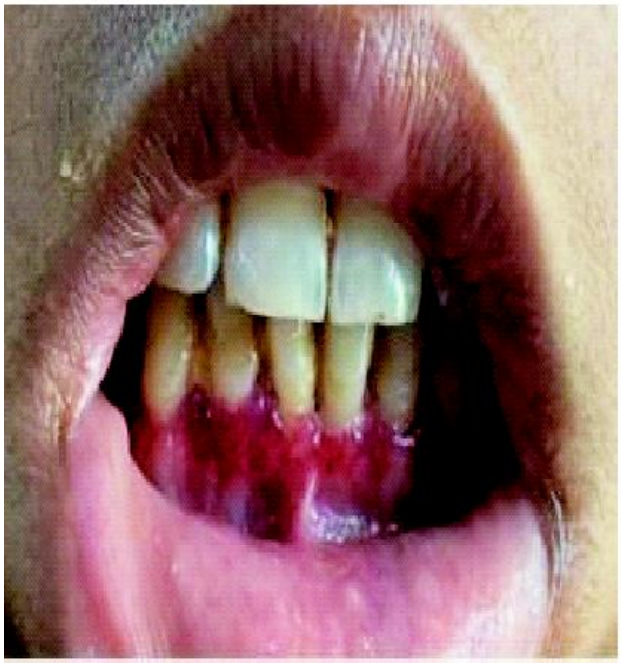
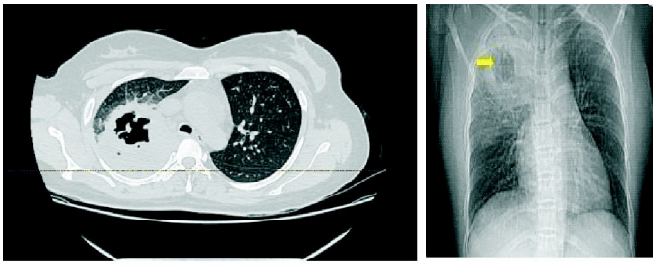
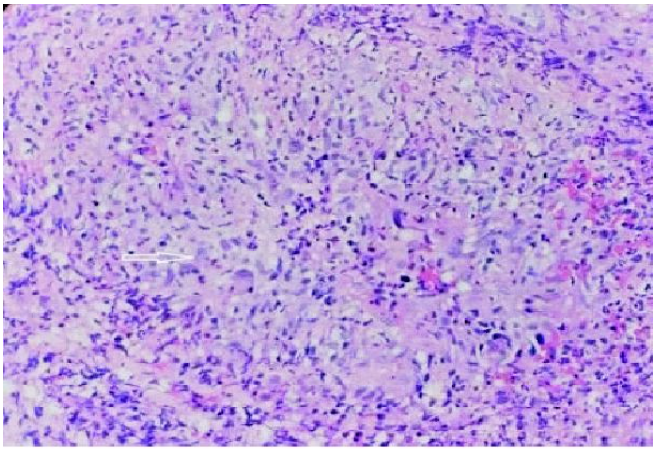


Cyclophosphamide combined with corticosteroids remains the conventional induction therapy for GPA as per the **EUVAS (European Vasculitis Study Group)** protocol. However, in refractory or relapsing cases, **rituximab**, an anti-CD20 monoclonal antibody, has emerged as an effective alternative. In this patient, worsening pulmonary symptoms and hemoptysis following cyclophosphamide therapy suggested treatment resistance, which responded favorably to rituximab, demonstrating its efficacy in refractory GPA.



Early recognition of GPA, particularly when presenting with ENT and pulmonary involvement, is crucial to prevent irreversible organ damage. Timely transition to targeted biologic therapy such as rituximab can significantly improve patient outcomes in cases unresponsive to conventional therapy.



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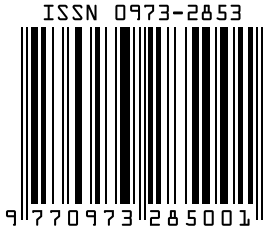
ISSN 0973-2853



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