Original Research Paper

Volume - 15 | Issue - 10 | October - 2025 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Hematology

ESSENTIAL THROMBOCYTHEMIA IN ADOLESCENCE: A RARE CASE WITH DIAGNOSTIC AND THERAPEUTIC CHALLENGES

Dr. K. Sai Chandra Rohith* Junior Resident, Department of General Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation. *Corresponding Author

Dr. Sai Surya Teja. B Assistant Professor, Department of General Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation.

Dr. Eswar.G Professor Emeritus, Department of General Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation.

KEYWORDS :

INTRODUCTION

Essential thrombocythemia (ET) is a chronic myeloproliferative neoplasm characterized by sustained thrombocytosis due to clonal proliferation of megakaryocytes. We present a case of a 13-year-old girl with chronic headache and splenomegaly, later diagnosed as ET based on bone marrow biopsy and followed longitudinally to demonstrate her response to therapy.

Case Presentation

A 13-year-old girl presented to the emergency room with complaints of *headache for 7 days and cough with expectoration for 6 days.* The headache was insidious in onset, gradually progressive, intermittent, localized to the forehead, aggravated by bending forward, and relieved with rest. It was not associated with nausea, vomiting, lacrimation, or visual disturbances. The cough was productive with white, non-foul smelling sputum, without diurnal or postural variation. There was no history of dyspnoea, chest pain, palpitations, abdominal pain, fever, or urinary complaints.

She had a *history of recurrent headaches for 2 years.* Menstrual cycles were regular since menarche at 11 years, with average flow and no dysmenorrhea. Family history was unremarkable. She followed a mixed diet, with decreased appetite over the past week.

Examination

On general examination, the patient was conscious, coherent, and oriented with no pallor, icterus, cyanosis, clubbing, lymphadenopathy, or oedema.

- **Vitals at admission**: BP 120/80 mmHg, PR 98/min, RR 18/min, SpO_2 98% (room air), Temp 97°F, GRBS 130 mg/dL.
- **Systemic examination**: Frontal sinus tenderness and Grade 2 splenomegaly were noted. Other systems were within normal limits.

Investigations

- **Laboratory parameters**: Complete blood picture revealed Hb 11.2 g/dL, TWBC 6.9 × 10^3/µL, and severe thrombocytosis (11.01 lakhs/µL). Peripheral smear confirmed thrombocytosis with large platelets, consistent with a myeloproliferative process.
- **Bone marrow aspiration and biopsy**: Revealed proliferation of large, hyper lobulated megakaryocytes, diagnostic of ET.
- **Imaging**: USG abdomen showed splenomegaly (14.5 cm) with a prominent splenic vein. MR venogram demonstrated pansinusitis but no intracranial abnormality.
- **Other work-up**: Normal serum electrolytes and chest X-ray.
- The diagnosis of ET follows the World Health Organization (WHO) 2016 criteria (Table 1)

Table 1. WHO Diagnostic Criteria for ET.

Diagnosis requires meeting all 4 major criteria or the first 3 major criteria and the minor criterion
Major Criteria
1. Platelet count ≥ 450 × 10^9/L 2. Bone marrow biopsy showing proliferation of megakaryocyte lineage that are large and mature with hyperlobulated nuclei, no significant increase of left shift in neutrophil granulopoiesis or erythropoiesis, and minor increase in reticulin fibers 3. Must not meet diagnostic criteria for BCR-ABL CML, PV, PMF, or other myeloid neoplasms 4. Presence of *JAK2, CALR,* or *MPL* gene mutation
Minor Criterion
1. Presence of a different clonal marker or the lack of evidence of reactive thrombocytosis

Note. CML = chronic myelogenous leukemia; PV = polycythemia vera; PMF = primary myelofibrosis.

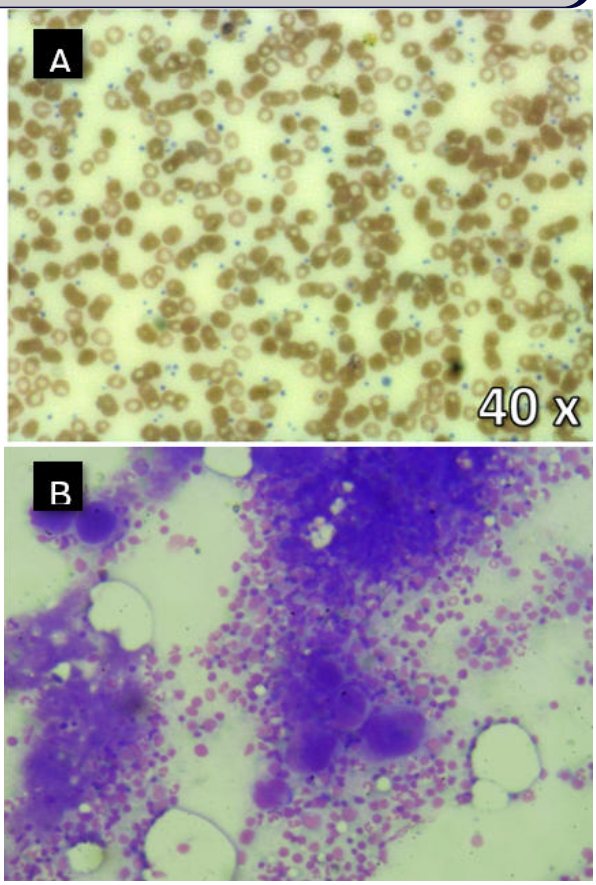

Figure-1: A) At 40x magnification, the peripheral blood smear reveals marked thrombocytosis, with platelets present in large numbers, often appearing in prominent clumps or aggregates. Within this increased platelet population, significant anisocytosis is observed, including numerous abnormally large or giant platelets (megathrombocytes) of bizarre, irregular shapes. The red blood cells appear largely unremarkable and are normocytic and normochromic, though some scattered, nonspecific morphologic changes may be present. The white blood cell count appears within the normal range, without significant dysplasia or a prominent left shift. B) The bone marrow trephine biopsy reveals a mildly hypercellular marrow with marked hyperplasia of the megakaryocytic lineage. These megakaryocytes are typically increased in number, often clustering loosely, and display distinct features, including enlarged, mature forms with highly lobulated, "staghorn" nuclei, while severe dysplasia is minimal or absent. Notably, the erythroid and granulocytic lineages are typically normally represented and mature without significant proliferation or left-shift. Furthermore, a key finding is the minimal to absent reticulin fibrosis, which helps distinguish ET from prefibrotic myelofibrosis, and blasts constitute less than 5% of the total cellularity.

Table 2. Bone Marrow Aspiration And Peripheral Smear Findings At First Admission

Parameter	Findings	Remarks
Cellularity	Normocellular	Preserved marrow cellularity
Erythroid Series	Normal in number with megaloblastic maturation	No dysplastic changes
Myeloid Series (overall)	Normal in number and maturation	Differential count shown below
– Myeloblasts	2	Within expected limits
– Promyelocytes	4	–
– Myelocytes	6	–
– Metamyelocytes	18	Mildly increased
– Band forms	19	Increased
– Neutrophils	23	Adequate mature forms
– Eosinophils	3	–
– Basophils	1	–
Megakaryocytic Series	Increased in number and size with enlarged hyperlobated forms	Classical for ET morphology
Myeloid : Erythroid Ratio	3:1	Within expected range
Peripheral Smear – RBCs	Normocytic, normochromic	–
Peripheral Smear – WBCs	Normal in number and morphology	–
Peripheral Smear – Platelets	Markedly increased in number	Correlates with marrow megakaryocytic hyperplasia
Hemoparasites	Absent	–
Overall Impression	Normocytic normochromic anemia with severe thrombocytosis; marrow features consistent with Essential Thrombocythemia	Confirms diagnosis

Treatment And Hospital Course

The patient was initially managed symptomatically with **antibiotics (Cefpodoxime), antihistamines, analgesics, and supportive therapy**. Following confirmation of ET, she was started on **Ecosprin 75 mg OD** and advised regular follow-up. She remained hemodynamically stable during hospitalization and was discharged with instructions for **JAK2 mutation analysis and haematology consultation**.

Table 3. Laboratory Parameters

Parameter	Admission	Discharge (Day 7)	Follow-up (20/5/2025)	Follow-up (17/6/2025)	Follow-up (25/08/2025)
Hb (gm %)	11.2 {11.9–15}	11.5	12.0	12.0	11.5
TWBC ($\times 10^3/\mu L$)	6.9	6.8	6.5	9.8	6.40
N/L/E/M (%)	52/39/4/5/0	53/38/4/5/0	55/37/3/5/0	66/25/4/5/0	62/30/3/5/0
Platelets (/µL)	11,01,000	8,50,000	7,20,000	12,03,000	6,34,000
MCV (fL)	83	84	85	79.6	83
MCHC (g/dL)	28	30	31	33.2	33.8
PCV (%)	31.3	32.0	34.0	36.1	34
ESR (mm/hr)	8	10	10	40	30
Peripheral Smear	Thrombocytosis with large platelets	Platelets raised, normal RBC & WBC morphology	Platelets elevated, morphology normal	Platelets elevated, morphology normal	Platelets elevated, morphology normal
Impression	Normocytic normochromic anemia with severe thrombocytosis	Normocytic normochromic anemia with resolving thrombocytosis	Near-normal hemogram with persistent thrombocytosis (ET)	Near-normal hemogram with persistent thrombocytosis (ET)	Normocytic normochromic anemia with resolving thrombocytosis

Outcome And Follow-up

- **May 2025**: At her first follow-up, she admitted to poor compliance with medications. USG abdomen showed persistent splenomegaly (14.4 cm). She was counselled for strict adherence to **Ecosprin 75 mg OD** and close monitoring. Her platelet count remained elevated at 7.2 lakhs/µL.
- **June 2025**: Despite adherence to aspirin, repeat CBP revealed **persistently high platelet counts (10.2 lakhs/µL)**. In line with international guidelines for ET, which recommend **cytoreduction for platelet counts >1000 × 10^9/L** due to risk of acquired von Willebrand syndrome and bleeding, she was initiated on **Hydroxyurea 500 mg once daily**, while continuing **Ecosprin 75 mg OD, Vitamin B12, folic acid, and micronutrient supplementation (zinc, selenium)**.
- **August 2025**: On follow-up after 2 months of Hydroxyurea therapy, her platelet counts showed a significant reduction to **6.34 lakhs/µL**, confirming therapeutic response. She remained clinically stable, with no new symptoms.

DISCUSSION:

The present case illustrates the diagnostic and therapeutic challenges of **Essential Thrombocythemia (ET)** in a paediatric patient. ET is a rare clonal myeloproliferative neoplasm (MPN) characterized by sustained thrombocytosis, megakaryocytic hyperplasia in the bone marrow, and frequent mutations in **JAK2, CALR, or MPL genes**. Although it typically presents in the sixth decade of life, occasional cases in adolescents highlight its wide clinical spectrum (1–3).

Clinical Correlation

Our patient presented with *headache and splenomegaly*, manifestations consistent with ET. Headaches are attributed to *microvascular disturbances* caused by platelet activation and abnormal platelet–endothelial interactions, while splenomegaly reflects *extramedullary haematopoiesis* (1,4). Importantly, haemorrhagic manifestations were absent, which is not uncommon in paediatric ET where vascular complications are generally less frequent compared with adults (2).

Diagnostic Considerations

Diagnosis of ET requires adherence to the **2022 WHO/ICC criteria**, which mandate: (i) platelet count ≥450 × 10^9/L, (ii) bone marrow showing proliferation of large hyperlobulated megakaryocytes, (iii) exclusion of other myeloid neoplasms (polycythaemia vera, prefibrotic myelofibrosis, chronic myeloid leukaemia, MDS/MPN overlap), and (iv) presence of a driver mutation (5,6). In this case, bone marrow biopsy confirmed ET morphology, while JAK2 V617F mutation analysis was advised. Reactive thrombocytosis, a far more common cause in children, was excluded based on persistent thrombocytosis, splenomegaly, and marrow features (7).

Molecular And Prognostic Insights

Molecular profiling is central to risk assessment. **JAK2 V617F** is found in ~50–60% of ET, **CALR mutations** in 20–30%, and **MPL mutations** in ~5%. About 10–15% remain "triple-negative" (1,2,5). JAK2 mutations confer a higher risk of thrombosis, whereas CALR mutations are often associated with higher platelet counts but lower vascular risk (2,8). In paediatric ET, CALR mutations appear more frequent, often conferring a more indolent phenotype (9). Transformation risks include **myelofibrosis (5–10% at 15 years)** and **AML (<5%)**, though these are rare in younger patients (1,6).

Risk Stratification

Several validated models guide prognosis. The **revised IPSET-thrombosis** stratifies risk based on age, thrombosis history, and JAK2 mutation (10). More recent models such as **MIPSS-ET** and the **triple-A (Age, ANC, ALC) model** integrate molecular and haematologic parameters for refined survival estimates (1,11). Our patient, being young, mutation-status pending, and without thrombosis, was initially placed in the **very low-risk category**.

Management Implications

Therapeutic goals in ET are to prevent vascular events while minimizing treatment toxicity. **Low-dose aspirin** remains the mainstay in patients with vasomotor symptoms or JAK2 mutations, provided platelet counts are <1000–1500 × 10^9/L to avoid bleeding from **acquired von Willebrand syndrome** (2,12). In our case, initiation of **Ecosprin 75 mg once daily** was appropriate as first-line therapy.

However, on follow-up in **June 2025**, platelet counts remained **persistently elevated at >10 lakhs/µL**, despite aspirin. International guidelines—including **NCCN, BSH, ELN, and WHO/ICC-based recommendations**—specify that **cytoreductive therapy is warranted** in patients with extreme thrombocytosis (>1000 × 10^9/L), due to increased risk of haemorrhage from acquired von Willebrand syndrome and thrombotic events (1,2,6,12). Accordingly, **Hydroxyurea 500 mg once daily** was added in combination with aspirin, along with vitamin B12, folic acid, and micronutrient supplementation.

On reassessment in **August 2025**, platelet counts had reduced significantly to **6.34 lakhs/µL**, aligning with the expected response to cytoreductive therapy. This demonstrates the efficacy of Hydroxyurea and validates its use in this patient, even in the paediatric setting, when persistent extreme thrombocytosis poses a substantial clinical risk and interferon-α is not the immediate choice.

CONCLUSION

This case highlights the importance of integrating **clinical features, marrow morphology, and molecular testing** to diagnose ET in children. While aspirin alone was initially justified, persistent thrombocytosis above 10 lakhs/µL necessitated escalation to **Hydroxyurea**, fully in line with international guidelines. The favourable platelet response following cytoreduction confirms the appropriateness of this strategy. Long-term follow-up remains crucial to monitor for vascular events, therapy-related toxicities, and disease evolution.

REFERENCES

1. Tefferi A, Vannucchi AM, Barbui T. Essential thrombocythemia: 2024 update on diagnosis, risk stratification, and management. *Am J Hematol*. 2024;99(4):697-718.
2. Godfrey AL, Green AC, Harrison CN. Essential thrombocythemia: challenges in clinical practice and future prospects. *Blood*. 2023;141(16):1943-51.
3. Hoffman R, Benz EJ, Silberstein LE, Heslop HE, Weitz J, Anastasi J, et al. *Hematology: Basic Principles and Practice*. 8th ed. Philadelphia: Elsevier; 2022.
4. McKenzie SB, Williams JL. *Clinical Laboratory Hematology*. 4th ed. Pearson; 2019.
5. Arber DA, Orazi A, Hasserjian R, et al. International Consensus Classification of myeloid neoplasms and acute leukemias: integrating morphologic, clinical, and genomic data. *Blood*. 2022;140(11):1200-28.
6. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. 5th ed. Lyon: IARC; 2022.
7. Kaushansky K, Lichtman MA, Prchal JT, Levi M, Press OW, Burns LJ, et al. *Williams Hematology*. 10th ed. New York: McGraw-Hill; 2021.
8. Barbui T, Finazzi G, Falanga A. Myeloproliferative neoplasms and thrombosis. *Blood*. 2013;122(13):2176-84.
9. Randi ML, Putti MC, Scapin M, Pacquola E, Zanesco L, Girolami A. Pediatric essential thrombocythemia: clinical and biologic features of 20 cases. *Blood*. 1998;92(7):2629-32.
10. Barbui T, Finazzi G, Carobbio A, Thiele J, Passamonti F, Rumi E, et al. Development and validation of an International Prognostic Score of thrombosis in World Health Organization–essential thrombocythemia (IPSET-thrombosis). *Blood*. 2012;120(26):5128-33.
11. Tefferi A, et al. Mutation-enhanced International Prognostic Scoring System for essential thrombocythemia (MIPSS-ET). *Leukemia*. 2021;35(11):3212-20.
12. Harrison CN, Campbell PJ, Buck G, Wheatley K, East CL, Bareford D, et al. Hydroxyurea compared with anagrelide in high-risk essential thrombocythemia. *N Engl J Med*. 2005;353(1):33-45.