



# **Ischemic Stroke in a Patient with Essential Thrombocythemia (ET) at St. Francis Regional Referral Hospital, Ifakara, Tanzania: A Case Report**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author AHM participated in the patient's management and in writing the case report. Authors JPM, WL and DR contributed to patient management. Authors MM and SJ participated in writing the case report. All authors read and approved the final manuscript.*

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**Case Report**

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## ABSTRACT

**Introduction:** Essential Thrombocythemia (ET) is a slow-progressing myeloproliferative neoplasm characterized by persistent thrombocytosis and an increased risk of thrombotic and hemorrhagic events, including ischemic stroke, myocardial infarction, and venous thromboembolism. Thrombotic complications remain the leading cause of morbidity, particularly in elderly patients.

**Case Presentation:** An 85-year-old male presented with sudden left-sided weakness, facial deviation, lower extremity numbness, and severe headache of one-day duration. He had a three-year history of ET, confirmed by bone marrow biopsy and JAK2 V617F mutation, and was on hydroxyurea 500 mg and low-dose aspirin. His medical history included well-controlled hypertension. On examination, he was conscious (GCS 11/15) with stable vitals, left-sided weakness (0/5), mouth deviation, and splenomegaly (18 cm below the costal margin).

A non-contrast CT scan revealed a right parietal lobe ischemic infarct and senile atrophy. Laboratory tests showed platelets  $988 \times 10^3$  per microliter, normal white blood cell count, and hemoglobin 10 g/dL. Hydroxyurea and aspirin doses were adjusted, physiotherapy initiated, and the patient stabilized for discharge with follow-up plans.

**Conclusion:** Despite cytoreductive and antiplatelet therapy, patients with ET remain at risk of thrombotic events. This case highlights the need for individualized management, close follow-up, and multidisciplinary care in elderly patients with ET to mitigate morbidity, and mortality from ischemic stroke.

**Keywords:** *Essential thrombocythemia; myeloproliferative neoplasm; ischemic stroke; JAK2 617F; cytoreductive therapy.*

## ABBREVIATIONS

CAR	: Calreticulin
CBC	: Complete Blood Count
CT	: Computer Tomography
ECG	: Echocardiogram
ECHO	: Electrocardiogram
ET	: Essential Thrombocythemia
GCS	: Glasgow Coma Scale
IRB	: Institutional Review Board
JAK2	: Janus Kinase 2
LMICs	: low and middle-income countries
MPL	: Myeloproliferative Leukemia
SFUCHAS	: St. Francis University of Health and Allied Sciences
WHO	: World Health Organization

## 1. INTRODUCTION

Essential Thrombocythemia is one of the chronic myeloproliferative neoplasms (MPNs) characterized by a persistent elevation of platelet counts, resulting from the abnormal proliferation of megakaryocytes in the bone marrow and excessive platelet production, it commonly presents with thrombosis and hemorrhage (Moniruzzaman et al., 2022).

It is a relatively rare condition, with an annual incidence of 0.2 to 2.5 new cases per 100,000 population (Moniruzzaman et al., 2022, Godfrey et al., 2022) The incidence increases with age, with a median age at diagnosis ranging from 60

to 70 years; however, approximately 20% of patients are younger than 41 years, with a higher ratio in females compared to males (Godfrey et al., 2022). The pathogenesis is commonly associated with driver mutations: approximately 60% of patients harbor the *JAK2 V617F* mutation, while *CALR* mutations are present in about 75% of *JAK2*-negative patients, accounting for roughly one-third of all cases (Beer & Green, 2009, Tefferi et al., 2024). Mutations in the *MPL* gene are detected in approximately 4% of patients with myeloproliferative neoplasms (Beer & Green, 2009, Tefferi et al., 2024, Brière, 2007). In the early stages, patients with Essential Thrombocythemia (ET) are often asymptomatic. As the disease progresses, they may develop

symptoms such as headache, dizziness, visual disturbances, splenomegaly, easy bruising, bleeding, and thrombotic complications (Godfrey et al., 2022, Yu et al., 2019, Yan et al., 2022). Thrombosis may present as ischemic stroke, myocardial infarction, superficial thrombophlebitis, deep vein thrombosis, or pulmonary embolism, while hemorrhagic events can also occur (Moniruzzaman et al., 2022, Yu et al., 2019, Arboix et al., 1995). Risk factors for thrombotic complications in ET include advanced age (>60 years), prior history of thrombosis, hypertension, diabetes mellitus, and tobacco use (Arboix et al., 1995, Richard et al., 2011).

The disease is stratified into four categories: very low-risk, low-risk, intermediate-risk, and high-risk (Accurso et al., 2019). Patients with intermediate- and high-risk disease are treated with cytoreductive therapy using hydroxyurea, along with antiplatelet agents, to reduce the risk of vascular complications (Yu et al., 2019, Accurso et al., 2019, Ergio et al., 1995, Griesshammer et al., 2001, Barbui et al., 2015).

Despite appropriate treatment, some patients with Essential Thrombocythemia (ET) may still experience serious thrombotic complication (Ergio et al., 1995). We report the case of an 85-year-old man with ET, maintained on long-term hydroxyurea and aspirin therapy, who presented with clinical features of ischemic stroke. This case highlights the persistent risk of thrombotic events in ET, emphasizing the importance of close monitoring and individualized management by underscoring the role of interdisciplinary collaboration in optimizing patient outcomes.

## 2. CASE PRESENTATION

An 85-year-old male presents at our facility with a history of sudden onset of left-sided extremity weakness, mouth deviation, numbness in the lower extremities, and severe headache for one day. There was no history of loss of consciousness, convulsions, vomiting, difficulty in breathing, fever, or head trauma. The patient was diagnosed with essential thrombocythemia three years ago at another center. The diagnosis of essential thrombocythemia had been confirmed by a bone marrow biopsy and the presence of the JAK2 V617F mutation. The patient was attending the hematology clinic and had been on treatment with hydroxyurea 500mg and low-dose aspirin. Also, he reported a history of hypertension, which was well controlled with

antihypertensives and regular follow-up in the cardiology clinic. On arrival, the patient was conscious with a Glasgow Coma Score (GCS) of 11/15 and stable vital signs. Neurological examination revealed left-sided extremity weakness, graded 0/5, and mouth deviation, with no other neurological pathological findings observed. Abdominal examination demonstrated splenomegaly measuring 18 cm below the costal margin.

Among other findings, a non-contrasted CT scan of the brain showed a right parietal lobe ischemic infarct and senile atrophy. The echocardiogram (ECHO) and electrocardiogram (ECG) were unremarkable. Laboratory investigations, including the coagulation profile, were within normal limits, except for the complete blood count, which showed an abnormal platelet count of  $988 \times 10^3$  per microliter, indicating marked thrombocytosis. The total white blood cell count was within the normal range, and the hemoglobin level was 10g/dL.

The hematology team was consulted, and adjustments were made to the patient's hydroxyurea dose, up to 1500mg once per day, and a low dose of aspirin 75mg once per day. Literature recommends increasing the dosage of low-dose aspirin to twice a day in high-risk patients. He was also commenced on physiotherapy, with significant neurological improvement observed after five days. The patient was discharged home in a stable condition with instructions to continue regular follow-up at the hematology clinic.

## 3. DISCUSSION

Essential thrombocythemia (ET) is a myeloproliferative neoplasm characterized by persistent elevation of platelets and increased risk of thrombotic complications, such as ischemic and hemorrhagic events, which remain the leading cause of morbidity and mortality (Accurso et al., 2019, Chen et al., 2021). Advanced age and cardiovascular comorbidities, such as hypertension, significantly increase the risk of thrombotic events, particularly ischemic stroke (Arboix et al., 1995, Richard et al., 2011, Ergio et al., 1995, Kim et al., 2023). In our case, the patient developed a thrombotic event despite receiving cytoreductive therapy with hydroxyurea and low-dose aspirin, highlighting the importance of close monitoring in high-risk patients due to the complex pathophysiology of essential thrombocythemia (Patel & DeRon, 2024).

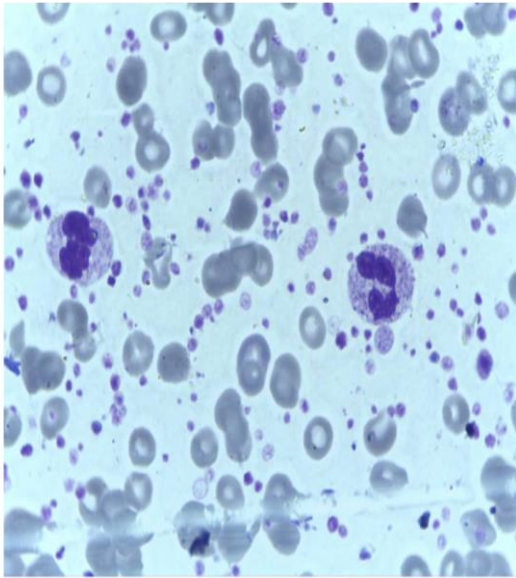


Fig. 1a.

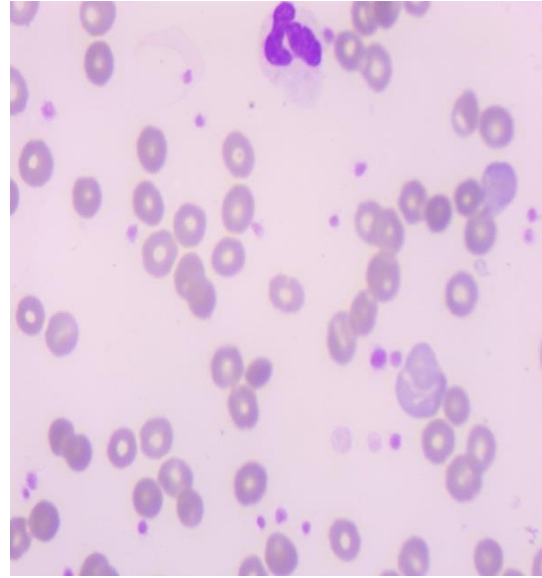


Fig. 1b.

**Fig. 1a and 1b. Blood film microscopy findings under 100x magnification were notable for an increased platelet count and the presence of mature segmented neutrophils during admission, and 1b, which showed improvement one month after discharge**

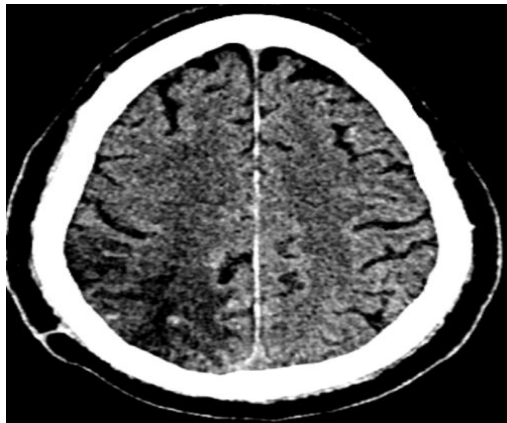


Fig. 2a.



Fig. 2b.

**Fig. 2a and 2b. A non-contrast CT scan of the brain reveals hypodensity in the right parietal lobe, consistent with an ischemic infarct, and senile atrophy in the posterior lobe**

The diagnosis of essential thrombocythemia requires the following criteria according to the WHO classification: persistent thrombocytosis (platelets  $\geq 450 \times 10^9/L$ ), presence of clonal markers such as JAK2, CALR, or MPL mutations, absence of other chronic myeloproliferative neoplasms such as chronic myeloid leukemia, primary myelofibrosis, polycythemia vera, myelodysplastic syndrome, and other causes of thrombocytosis (Tefferi et al., 2024). These criteria signify accurate diagnosis and correct risk stratification, which is important in preventing thrombotic complications

(Tefferi et al., 2024, Accurso et al., 2019, Arber et al., 2016). These criteria signify an accurate diagnosis and correct risk stratification, which is important in preventing thrombotic events (Accurso et al., 2019, Arber et al., 2016). The pathogenesis of ischemic stroke in ET involves multiple mechanisms, including endothelial dysfunction, platelet overactivation, and prothrombotic states associated with the JAK2 V617F mutation (Arber et al., 2016, Kristiansen et al., 2025). Our patient had additional risk factors, including advanced age, elevated platelet counts, splenomegaly, and long-standing

hypertension. Studies have shown that ischemic stroke is one of the most common thrombotic presentations in ET (Yan et al., 2022, Chen et al., 2021. Accurso et al., 2020)

Ischemic stroke can result in long-term neurological deficits, including hemiparesis, speech impairment, cognitive dysfunction, and reduced quality of life (Rost et al., 2022). Survivors of ET-associated stroke may also face increased dependency, psychological sequelae, and a higher risk of recurrent vascular events, emphasizing the need for vigilant secondary prevention strategies (Rost et al., 2022). Stroke recurrence in ET is influenced by several factors, including older age, cardiovascular comorbidities (e.g., hypertension, diabetes), high platelet counts, JAK2 mutation positivity, prior thrombotic events, and suboptimal control of hematologic parameters (Arboix et al., 1995, Richard et al., 2011). Treatment adherence, choice of cytoreductive therapy, and adequate antiplatelet prophylaxis are also critical (Le Calloch et al., 2018, De Stefano et al., 2018, Jones et al., 2022). Understanding these risk factors can help clinicians tailor management strategies, balance the risks of thrombosis and hemorrhage, and optimize long-term outcomes (Tefferi et al., 2024, Arboix et al., 1995, Griesshammer et al., 2001).

Cytoreductive therapy with hydroxyurea aims to lower platelet counts and reduce the risk of thrombosis, while aspirin provides antiplatelet effects. In cases where patients remain at risk despite these therapies, alternative cytoreductive agents, such as anagrelide or interferon- $\alpha$ , may be considered (Griesshammer et al., 2001, Chen et al., 2021, Birgegård et al., 2018). On the other hand, treatment failure may still occur due to disease-related factors (persistent prothrombotic state despite platelet control), therapy-related factors (hydroxyurea resistance or aspirin non-responsiveness), or patient-related factors (advanced age, comorbidities, poor adherence) (Barbui et al., 2015). These challenges lead to important management dilemmas, particularly in balancing the risk of thrombosis with the potential for hemorrhage, especially when platelet counts are extremely elevated (Tefferi et al., 2024, Birgegård et al., 2018). The choice of cytoreductive therapy is also complicated in settings where access to second-line agents is limited (Tefferi et al., 2024, Birgegård et al., 2018).

This case highlights the importance of considering neurological complications in

patients with essential thrombocythemia (ET), even in those receiving appropriate treatment. Timely recognition of stroke presentations, prompt diagnosis, and multidisciplinary management are crucial for optimizing patient outcomes. Furthermore, close collaboration between hematologists, neurologists, and other clinicians is crucial for optimizing patient outcomes. Regular follow-up enables reassessment of thrombotic risk, adjustment of therapy, and early detection of complications, ultimately improving patient prognosis.

#### 4. CONCLUSION

This case highlights the persistent thrombotic risk in patients with Essential Thrombocythemia (ET), even under appropriate cytoreductive and antiplatelet therapy. Advanced age, cardiovascular comorbidities, elevated platelet counts, and JAK2 mutation positivity increase both the risk of initial thrombotic events and stroke recurrence. Timely recognition of ischemic stroke, adherence to WHO diagnostic criteria, and individualized management strategies are essential for optimizing outcomes. Multidisciplinary care, vigilant monitoring, and consideration of alternative therapies are crucial for high-risk patients to prevent complications and improve long-term prognosis. This report also emphasizes the importance of documenting such cases from low- and middle-income countries (LMICs) to strengthen the global understanding of ET complications.

#### DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

#### CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

#### ETHICAL APPROVAL.

Ethical approval for this case report was obtained from St. Francis University College of Health and Allied Sciences Institutional Review Board (SFUCHAS IRB). Informed consent and assent were obtained from the patient and the next of kin, respectively, for publication of this case report.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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