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Unmasking Advanced HIV Infection: A Case of Refractory Thrombocytopenia Misdiagnosed as Immune Thrombocytopenic Purpura

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A B S T R A C T

Thrombocytopenia is a frequent hematological abnormality in individuals with human immunodeficiency virus (HIV) infection and can be the initial presenting sign. Its clinical picture can closely mimic primary Immune Thrombocytopenic Purpura (ITP), leading to diagnostic delays and inappropriate management. This report highlights a case where an HIV diagnosis was revealed during the workup for refractory thrombocytopenia. A 39-year-old female presented with fatigue and gingival bleeding. She had a previous diagnosis of ITP and had been treated intermittently, but the thrombocytopenia repeatedly recurred. Physical examination was notable for oral candidiasis. Laboratory investigations confirmed severe thrombocytopenia with a platelet count of 4,000/µL. Subsequent serological testing was reactive for HIV, with a CD4 count of 136 cells/µL. The patient was managed for severe thrombocytopenia and opportunistic infection, with a plan to initiate antiretroviral therapy. In conclusion, this case underscores the critical importance of including HIV infection in the differential diagnosis for patients presenting with new-onset or refractory thrombocytopenia. Clinical clues, such as opportunistic infections, should prompt immediate HIV screening to ensure timely diagnosis and initiation of definitive therapy, thereby preventing misdiagnosis and improving patient outcomes.

1. Introduction

Thrombocytopenia, defined as a platelet count below 150,000/µL, is a common and clinically significant hematological disorder encountered in internal medicine.[1] While its etiologies are vast, a crucial distinction lies between primary and secondary causes. Primary immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by isolated thrombocytopenia resulting from antibody-mediated platelet destruction and impaired platelet production, diagnosed after the exclusion of other causes.[2] However, a significant proportion of thrombocytopenia cases are secondary to underlying systemic conditions, including infections, malignancies, and other autoimmune diseases.

Among the infectious etiologies, human immunodeficiency virus (HIV) infection is a prominent cause of secondary thrombocytopenia.[3] The incidence of thrombocytopenia in people living with HIV/AIDS (PLWHA) is reported to be between 5% and 30%, and it can manifest at any stage of the disease, often serving as the initial clinical indicator of the

underlying viral infection.[4] In the advanced stages of HIV, characterized by severe immunosuppression, the prevalence of thrombocytopenia can be as high as 40%. The clinical and laboratory presentation of HIV-associated thrombocytopenia can be indistinguishable from primary ITP, creating a significant diagnostic challenge.[5]

This mimicry poses a substantial risk of misdiagnosis. HIV infection is renowned for its diverse clinical presentations, frequently emulating other pathologies and thereby complicating the diagnostic process.[6] The challenge is so significant that studies have reported that nearly one in seven patients with an initial diagnosis of primary ITP is ultimately found to have been misdiagnosed.[7] A registry-based study highlighted that among patients initially diagnosed with primary ITP, 12.2% were later reclassified as having a different underlying condition after thorough follow-up and investigation.[8] Such diagnostic errors carry profound clinical implications, leading to the administration of potentially harmful and ineffective treatments (such as prolonged high-dose corticosteroids or splenectomy) while delaying the initiation of lifesaving antiretroviral therapy (ART).[9]

The novelty of this case report lies in its detailed illustration of a common yet critical diagnostic pitfall in clinical practice. While the association between HIV and thrombocytopenia is well-established, this report provides a step-by-step account of the clinical reasoning process, highlighting the pivotal role of a subtle physical finding (oral candidiasis) in correcting a previous misdiagnosis of refractory ITP.[10] Therefore, the aim of this manuscript is to underscore the indispensability of considering and actively screening for HIV in all patients with new-onset or treatment-refractory ITP. Through this detailed case, we seek to reinforce the diagnostic principle that failure to respond to standard therapy for a presumed primary disorder should trigger a comprehensive search for underlying secondary causes, particularly for an eminently treatable condition like HIV.

2. Case Presentation

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. All patient data have been anonymized to protect confidentiality. A 39-year-old female was referred to the Internal Medicine Polyclinic at Prof. Dr. I.G.N.G Ngoerah General Hospital for evaluation of thrombocytopenia. She presented with a one-week history of progressive fatigue and a two-day history of spontaneous gingival bleeding (Figure 1). She denied any other bleeding manifestations, such as petechiae, purpura, or melena. There was no history of chronic fever, persistent cough, chronic diarrhea, or significant weight loss. The patient denied any history of intravenous drug use, tattoos, or high-risk sexual behaviors.

Her past medical history was significant for recurrent thrombocytopenia, for which she was diagnosed with ITP at a regional hospital in November 2023. She had received treatment and required multiple platelet transfusions in the past but had been lost to follow-up for several months. Concurrently, the patient was a consultation from the cardiology service with a complex cardiac history; the working diagnosis was rheumatic heart failure, with several potential underlying etiologies under investigation, including congenital heart disease and various forms of pulmonary hypertension.

On presentation, the patient was conscious and alert (Glasgow Coma Scale E4V5M6). Her vital signs were stable: blood pressure was 120/75 mmHg, heart rate was 90 beats/minute, respiratory rate was 20 breaths/minute, and oxygen saturation was 98% on room air. The physical examination was significant for the presence of white, plaque-like lesions on the buccal mucosa and tongue, consistent with oral candidiasis (Figure 2 A&B). Cardiovascular examination revealed a grade III/VI pansystolic murmur at the left sternal border and a split S2 sound. There was no evidence of petechiae, ecchymoses, or purpura on the skin. There was no palpable

hepatosplenomegaly or lymphadenopathy.

Initial laboratory investigations revealed severe thrombocytopenia with a platelet count of 4,000/µL. The complete blood count also showed mild normocytic, normochromic anemia (Hemoglobin 11.8 g/dL) with a normal leukocyte count (Figure 3). A peripheral blood smear confirmed the severe reduction in platelet numbers, with the presence of some macrothrombocytes (large platelets). Red blood cell morphology showed mild abnormalities, but no schistocytes to suggest microangiopathic hemolytic anemia (Figure 4). Liver function tests showed mildly elevated transaminases (SGOT 64 U/L, SGPT 51 U/L). Renal function and coagulation profiles (APTT, PT, INR) were within normal limits. Electrolyte analysis revealed mild hypokalemia (K 3.38 mmol/L) (Figure 5).

Figure 1. Clinical summary on admission.

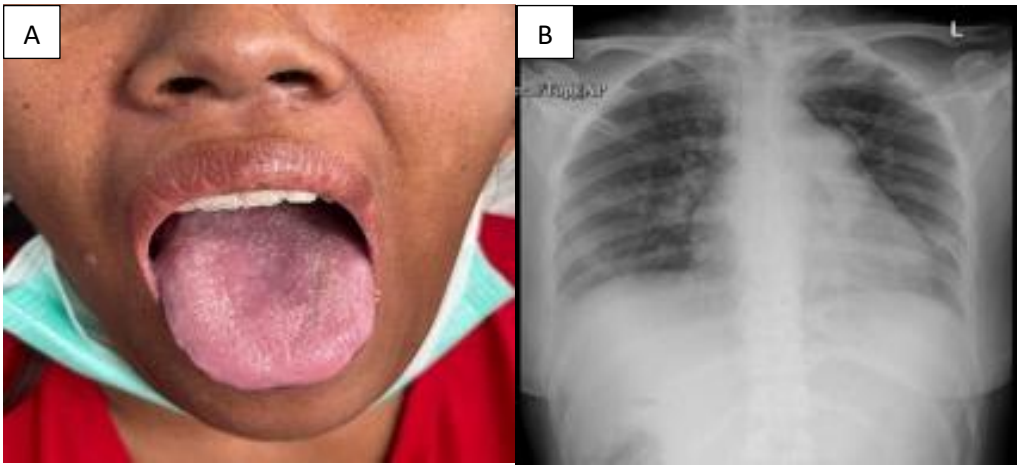

Figure 2. Clinical presentation and X-ray imaging of patients. (A) oral candidiasis; (B) chest X-ray imaging on admission.

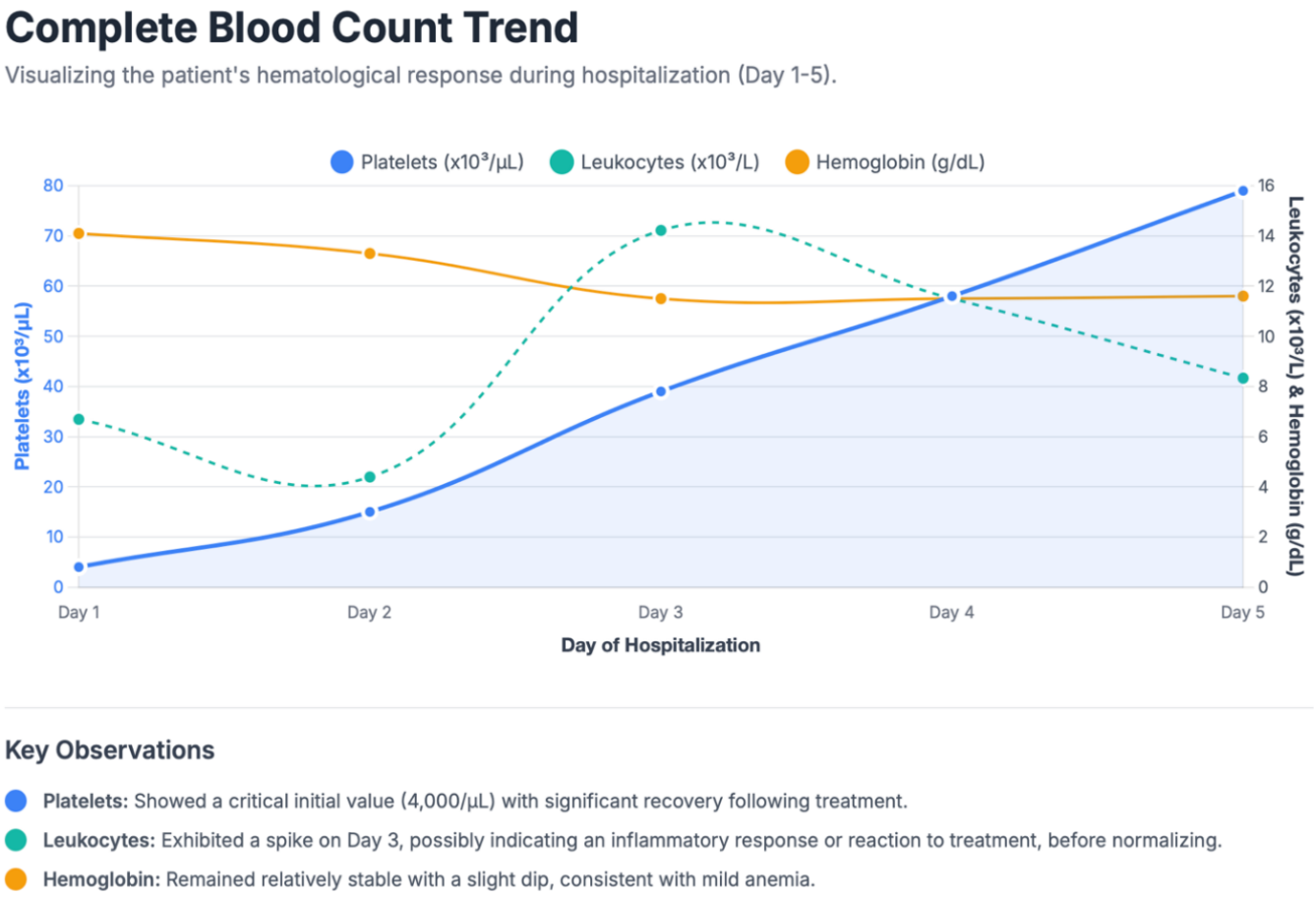

Figure 3. Complete blood count trend.

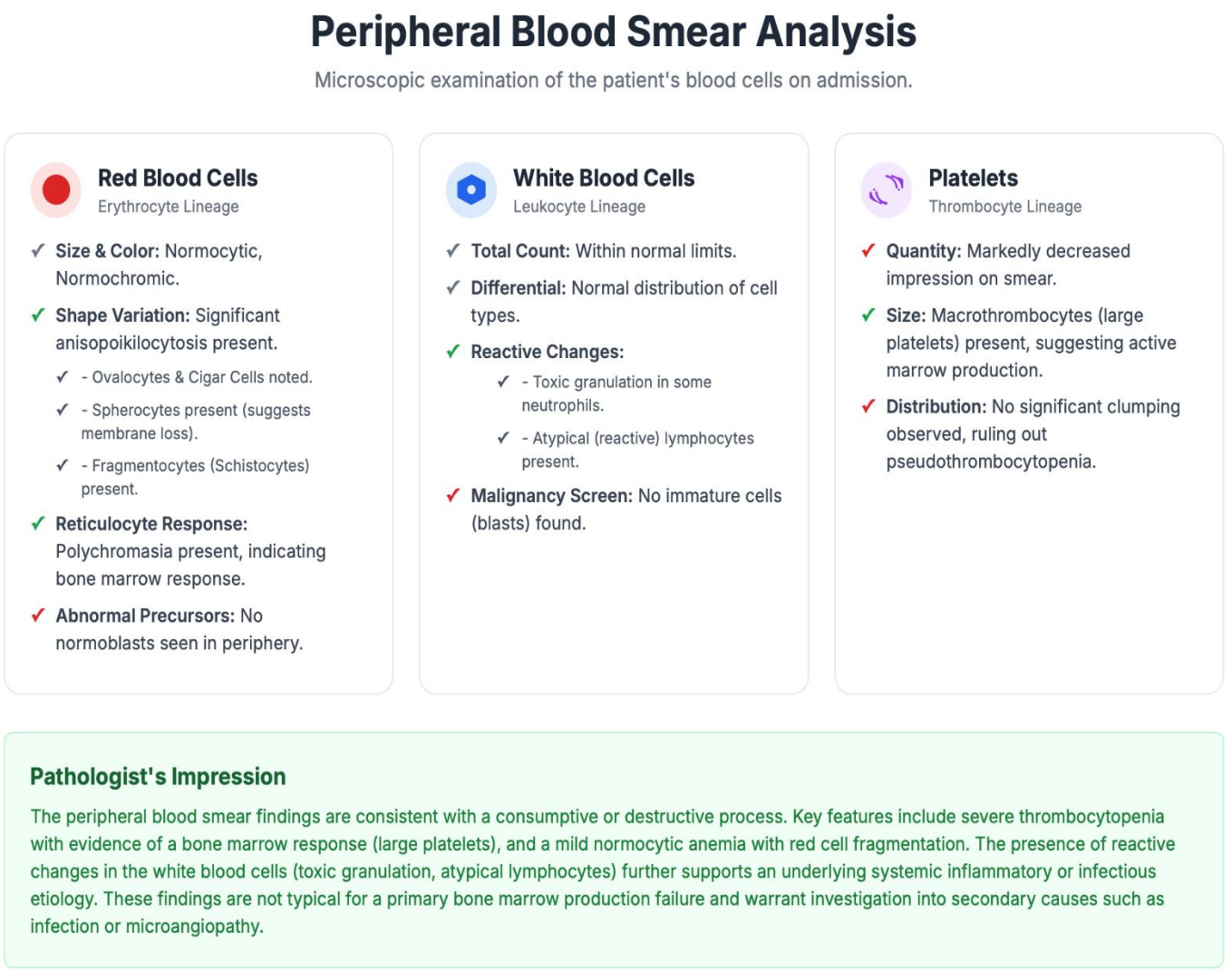

Figure 4. Peripheral blood smear analysis.

The presence of oral candidiasis, a classic opportunistic infection, immediately raised the index of suspicion for an underlying cellular immunodeficiency. This prompted a crucial shift in the diagnostic paradigm away from primary autoimmunity. Subsequent serological testing was performed, which returned a reactive result for anti-HIV antibodies. Further immunological evaluation revealed a CD4 absolute count of 136 cells/µL (CD4% 10.51), confirming a state of advanced immunodeficiency. Screening for co-infections with Hepatitis B (HBsAg) and Hepatitis C (Anti-HCV) were non-reactive. A chest X-ray was unremarkable, and a molecular test (TCM Sputum) for *Mycobacterium tuberculosis* was not detected, ruling out active pulmonary tuberculosis. An electrocardiogram (ECG) showed sinus rhythm with right axis deviation and right ventricular hypertrophy, consistent with her underlying cardiac condition.

Ancillary Laboratory Results

A comprehensive summary of biochemical, immunological, and microbiological findings on admission.

Parameter	Result	Reference Range	Units
Coagulation Profile			
Activated Partial Thromboplastin Time (APTT)	29.9	24.0 - 36.0	seconds
Prothrombin Time (PT)	11.9	10.8 - 14.4	seconds
International Normalized Ratio (INR)	1.12	1 - 1.5	
Liver & Renal Function			
Serum Glutamic Oxaloacetic Transaminase (SGOT)	**64.00**	< 39.00	U/L
Serum Glutamic Pyruvic Transaminase (SGPT)	**51.00**	< 48.00	U/L
Ureum	7.04	8.4 - 25.7	mg/dL
Creatinine	0.93	0.72 - 1.25	mg/dL
Electrolytes			
Sodium (Na)	137	135 - 145	mmol/L
Potassium (K)	**3.38**	3.6 - 5.5	mmol/L
Chloride (Cl)	**111**	98 - 108	mmol/L
Serology & Immunology (Key Diagnostic Findings)			
Anti-HIV	**Reactive**	Non-Reactive	
CD4 Absolute Count	**136**	(Normal: 500-1500)	cells/µL
Anti-HCV	Non-Reactive	Non-Reactive	
HBsAg	Non-Reactive	Non-Reactive	
Microbiology			
TCM Sputum (for M. tuberculosis)	Not Detected	Not Detected	

Figure 5. Summary of biochemical, immunological, and microbiological findings on admission.

Based on these findings, the patient was diagnosed with HIV Infection, WHO Clinical Stage III, pre-ART, with associated severe thrombocytopenia and oral candidiasis. The previous diagnosis of ITP was revised to HIV-associated thrombocytopenia. Her other diagnoses included the pre-existing complex heart disease and hypokalemia, likely due to low intake.

Figure 6. Timeline treatment and follow-up of patients.

The patient was admitted for management. She received intravenous fluids and nutritional support. For the severe thrombocytopenia with active bleeding, she was treated with daily apheresis platelet transfusions to maintain a platelet count above 20,000/µL and high-dose intravenous methylprednisolone (125 mg every 12 hours) as a bridging therapy to rapidly reduce immune-mediated platelet destruction. Her oral candidiasis was treated with oral nystatin suspension, and prophylaxis for *Pneumocystis jirovecii* pneumonia (PJP) was initiated with oral cotrimoxazole (960 mg daily) due to her CD4 count being below 200 cells/µL. She also continued her prescribed cardiac medications, including bisoprolol, beraprost, and sildenafil (figure 6).

Her clinical condition improved during hospitalization. The gingival bleeding resolved, and her platelet count gradually increased to 79,000/µL by the day of discharge. She was discharged with a plan for outpatient follow-up in the HIV clinic to initiate definitive lifelong antiretroviral therapy (ART) with a fixed-dose combination of Tenofovir, Lamivudine, and Dolutegravir (TLD) after completing a two-week course of cotrimoxazole to ensure tolerance.

3. Discussion

This case provides a compelling illustration of the diagnostic complexities arising from the hematological manifestations of HIV infection.[9] The patient's journey from a diagnosis of refractory ITP to the ultimate discovery of advanced HIV disease highlights critical learning points in clinical reasoning, pathophysiology, and management. Thrombocytopenia is one of the most common hematological complications of HIV, second only to anemia.[10] Its prevalence is significantly higher in ART-naïve individuals compared to those on effective treatment and increases with disease progression. In patients with advanced immunosuppression (CD4 count <200 cells/µL), the prevalence of thrombocytopenia is markedly higher, a finding consistent with our patient's CD4 count of 136 cells/µL. Some studies suggest a higher prevalence in females, potentially due to a combination of biological susceptibility and socioeconomic factors, which aligns with the demographic of our patient.[11] The median age of presentation is often in the fourth decade of life, again consistent with our 39-year-old patient. The clinical spectrum can range from asymptomatic, incidental findings to severe, life-threatening hemorrhage, with bleeding manifestations reported in around 3.2% of cases. Our patient's presentation with gingival bleeding at a platelet count of 4,000/µL falls into the category of severe, symptomatic thrombocytopenia.

The mechanism underlying thrombocytopenia in HIV is multifactorial and complex, involving a confluence of processes that both increase platelet destruction and decrease platelet production.[11] Immune-mediated platelet destruction is the most well-understood mechanism and the reason for the significant overlap with primary ITP. The process is driven by a profound dysregulation of the immune system.[12] The HIV virus, particularly its envelope proteins like gp120 and core proteins like p24, shares structural similarities with platelet surface glycoproteins, such as GPIIb/IIIa and GPIb/IX. This molecular mimicry can lead to the production of autoantibodies that cross-react with platelets, tagging them for destruction.[12] These anti-platelet antibodies are detectable even in early, asymptomatic stages of HIV, indicating that immune dysregulation begins long before overt immunodeficiency develops. Circulating immune complexes, composed of HIV antigens and anti-HIV antibodies, can bind non-specifically to the FcγRIIa receptors on platelets.[13] These opsonized platelets are then rapidly cleared from circulation by the reticuloendothelial system, primarily in the spleen and liver. This accelerated clearance dramatically shortens the platelet lifespan.

HIV infection also directly impairs the bone marrow's ability to produce platelets.[13] HIV can directly infect megakaryocytes, the precursor cells of

platelets. This infection can lead to abnormal development (dysplasia), increased programmed cell death (apoptosis), and overall ineffective thrombopoiesis, resulting in a reduced output of mature platelets from the marrow. The chronic inflammatory state induced by HIV can disrupt the production and signaling of key hematopoietic growth factors, including thrombopoietin (TPO), which is the primary regulator of platelet production.[13] This dual-pronged assault on both platelet survival and production explains the often severe and persistent nature of thrombocytopenia seen in untreated HIV infection.

The central challenge highlighted by this case is the differentiation between primary ITP and HIV-associated secondary thrombocytopenia. The diagnostic algorithm for ITP is one of exclusion.[14] When a patient presents with isolated thrombocytopenia, clinicians often presumptively diagnose ITP after ruling out more obvious causes. However, this case demonstrates the peril of this approach without a comprehensive screen for secondary etiologies.

As recommended by diagnostic guidelines, a diagnosis of ITP that is refractory to first-line therapies (corticosteroids or IVIG) should immediately trigger a broader investigation.[15] This workup should include screening for underlying infections like HIV, Hepatitis C, and *Helicobacter pylori*, as well as other autoimmune conditions. Our patient had been previously treated for ITP but had recurrent episodes, marking her condition as refractory or persistent and warranting this secondary workup long before her current presentation. The presence of a clinical "red flag"—the oral candidiasis—was the ultimate clue that pointed toward immunodeficiency and should serve as a powerful reminder to clinicians to always conduct a thorough physical examination for signs of underlying systemic disease.[16]

The management of our patient was twofold: acute stabilization and long-term definitive therapy. The use of platelet transfusions and high-dose corticosteroids was a necessary bridging strategy. Transfusions were critical to raise the platelet count above the threshold for spontaneous hemorrhage, especially given her active bleeding.[16] Corticosteroids, while not treating the underlying HIV, act as a potent immunosuppressant, temporarily reducing the antibody-mediated platelet destruction and providing a rapid, albeit transient, increase in platelet count. This approach buys time and ensures patient safety while preparing for definitive treatment. The cornerstone and definitive treatment for HIV-associated thrombocytopenia is effective antiretroviral therapy (ART).[17] By suppressing HIV replication, ART addresses the root cause of the pathology. It reduces the viral load, decreases the antigenic stimulus for autoantibody production, allows for the restoration of immune function, and alleviates the direct suppressive effects of the virus on the bone marrow. Studies have consistently shown that with viral suppression, platelet counts significantly improve, often normalizing completely. The planned TLD regimen is the globally recommended first-line therapy, known for its high efficacy, durability, and favorable safety profile.[18] The initiation of PJP prophylaxis with cotrimoxazole was also a critical step, adhering to the standard of care for patients with CD4 counts below 200 cells/μL to prevent life-threatening opportunistic infections.

Severe thrombocytopenia (platelet count ≤50,000/μL) in PLWHA is not merely a number; it is an independent predictor of disease progression and increased mortality. It is associated with a higher risk of bleeding, a poorer response to therapy, and a decreased quality of life.[19] However, this poor prognosis can be significantly altered by the early and effective initiation of ART. By treating the underlying HIV, the prognosis related to the thrombocytopenia is dramatically improved. This underscores the urgency of arriving at the correct diagnosis.

This report, while instructive, has several inherent limitations. Firstly, as a single case report, the observations are not generalizable and serve primarily to generate hypotheses and reinforce existing clinical knowledge. Secondly, the report lacks long-term follow-up data. The central argument—that HIV was the definitive cause of the patient's thrombocytopenia—would be most powerfully confirmed by documenting a sustained normalization of her platelet count following the successful initiation of ART.[20] This data was not available at the time of writing. Thirdly, the patient had a significant and complex cardiac comorbidity. While HIV is the most probable driver of her hematological issues, the potential confounding influence of chronic systemic inflammation from her heart condition cannot be entirely excluded. Lastly, the diagnostic process relied on the patient's self-reported denial of traditional HIV risk factors. It is a clinical reality that patients may be unaware of their risk, such as being unaware of a partner's status, or may be hesitant to disclose sensitive information, which reinforces the principle that testing should be guided by clinical indicators rather than perceived risk profiles.[20]

4. Conclusion

This case of a 39-year-old female with advanced HIV infection unmasked by an evaluation for refractory thrombocytopenia serves as a critical diagnostic lesson. It powerfully demonstrates that HIV-associated thrombocytopenia can perfectly mimic primary ITP, leading to potential misdiagnosis and a delay in essential, life-saving treatment. Clinicians must maintain a high index of suspicion for HIV in any patient presenting with new-onset or treatment-refractory thrombocytopenia, regardless of the patient's stated risk factors. A thorough physical examination for subtle signs of immunodeficiency, such as oral candidiasis, and a low threshold for HIV screening are paramount. The correct diagnosis is the crucial first step toward initiating definitive antiretroviral therapy, which not only resolves the hematological complication but also fundamentally alters the patient's overall prognosis.

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