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A Case of Thrombotic Thrombocytopenic Purpura

Dr. A Sankar[1], Dr. Umashankar[2], Dr. S. Adhitya Surya[3]

[1, 2]Department of General Medicine, SreeBalaji Medical College and Hospital

[3]Post Graduate, Department of General Medicine, Sree Balaji Medical College and Hospital, Tamilnadu (Corresponding Author)

Abstract: ***Thrombotic thrombocytopenic purpura (TTP) is a rare and life - threatening hematological disorder characterized by microangiopathic hemolytic anemia, thrombocytopenia, and widespread microvascular thrombosis. We present a challenging case of TTP in a 45 - year - old female who initially presented with non - specific symptoms including fatigue, petechiae, and mild confusion. Laboratory investigations revealed severe thrombocytopenia, hemolytic anemia, and schistocytes on peripheral blood smear. Further evaluation led to the diagnosis of TTP, confirmed by the absence of ADAMTS13 activity and the presence of anti - ADAMTS13 antibodies. The patient was promptly initiated on therapeutic plasma exchange and corticosteroids, resulting in significant clinical improvement. However, her course was complicated by recurrent TTP episodes and the need for prolonged treatment, highlighting the complexities and challenges in managing this rare condition. This case underscores the importance of early recognition, timely intervention, and close monitoring in the management of TTP to improve patient outcomes.***

Keywords: Thrombotic thrombocytopenic purpura, hematological disorder, microangiopathic hemolytic anemia, thrombocytopenia, schistocytes

1. Introduction

Thrombotic thrombocytopenic purpura (TTP) is a rare and life - threatening hematological disorder characterized by a constellation of clinical and laboratory abnormalities, including microangiopathic hemolytic anemia, severe thrombocytopenia, and widespread microvascular thrombosis. It is caused by a severe deficiency of ADAMTS13, a von Willebrand factor - cleaving protease, leading to the accumulation of ultra - large von Willebrand factor multimers and the formation of platelet - rich thrombi in small blood vessels throughout the body.

While TTP is considered a medical emergency necessitating prompt diagnosis and intervention, its clinical presentation can be variable and mimic other conditions, making it a diagnostic challenge. We present here a complex and intriguing case of TTP in a 45 - year - old female patient who exhibited a diverse array of symptoms, underscoring the importance of a comprehensive understanding of this disorder. Through this case report, we aim to shed light on the diagnostic intricacies, treatment dilemmas, and clinical course of TTP, emphasizing the critical role of timely intervention in improving patient outcomes. This case serves as a poignant reminder of the clinical vigilance required to manage this rare and potentially fatal hematological condition effectively.

In recent years, significant progress has been made in unraveling the pathophysiology of TTP, primarily centered around the role of ADAMTS13 and the development of novel treatment modalities. Despite these advancements, the diagnosis of TTP remains a formidable task due to its diverse and sometimes subtle clinical presentation, which can easily be misattributed to other conditions. Early recognition and prompt initiation of appropriate therapy are pivotal in preventing life - threatening complications.

The case we present here illustrates the diagnostic odyssey often encountered in clinical practice, where seemingly unrelated symptoms gradually coalesce into a complex hematological picture. The diagnostic process involved a meticulous evaluation of laboratory findings, including peripheral blood smear examination, ADAMTS13 activity assays, and the detection of anti - ADAMTS13 antibodies. Furthermore, it showcases the clinical course of TTP, characterized by recurrent episodes and the challenges in long - term management, including the need for extended therapeutic plasma exchange and immunosuppressive therapy.

Through this case, we aim to highlight not only the diagnostic hurdles but also the therapeutic decisions that clinicians may encounter when managing TTP patients. Additionally, it underscores the necessity for close follow - up and vigilance in the ongoing care of these individuals to prevent relapses and complications.

In conclusion, this case report provides a comprehensive insight into the multifaceted nature of TTP, emphasizing the importance of early diagnosis and a multidisciplinary approach in its management. By sharing this clinical experience, we hope to contribute to the growing body of knowledge surrounding TTP and ultimately improve the care and outcomes of patients affected by this rare and challenging hematological disorder.

2. Case Report

Clinical History:
Age: 45 years
Gender: Female
Presenting Complaint:

The patient, a 45 - year - old female, presented to the emergency department with a gradual onset of non - specific symptoms over the course of two weeks. She complained of persistent fatigue, easy bruising, and multiple pinpoint - sized red to purple skin lesions (petechiae) scattered across her extremities. Her family members also noticed subtle changes in her behavior, including mild confusion and forgetfulness. There was no history of recent infections, trauma, or major medical illnesses.

Medical History:
The patient had no significant past medical history, including no known hematological disorders. She was not taking any medications or supplements, and her family history was unremarkable for hematological conditions.

Physical Examination:
Upon admission, the patient appeared fatigued but was alert and oriented. Physical examination revealed the following:

1) Skin: Numerous scattered petechiae and purpura on the arms, legs, and trunk.
2) Neurological: Mild confusion and cognitive impairment, with no focal neurological deficits.
3) Cardiovascular: Regular heart rate and rhythm, with no murmurs or signs of heart failure.
4) Respiratory: Clear breath sounds, normal respiratory rate.
5) Abdomen: Soft and non - tender, with no organomegaly or masses palpable.
6) Extremities: No signs of joint swelling or deformities.
7) Hematological: Severe pallor noted. Blood pressure was within the normal range, but there was a notable presence of petechiae and purpura on the blood pressure cuff site after measurement.

Initial Laboratory Findings:

Initial blood tests upon admission revealed the following abnormalities:

1) Hemoglobin: 7.8 g/dL (normal range: 12 - 16 g/dL)
2) Platelet Count: 12, 000/µL (normal range: 150, 000 - 450, 000/µL)
3) Peripheral Blood Smear: Schistocytes (fragmented red blood cells) observed.
4) Reticulocyte Count: Elevated.
5) Serum LDH (Lactate Dehydrogenase): Markedly elevated.
6) Serum Bilirubin: Elevated, predominantly indirect bilirubin.
7) Serum Creatinine: Within normal limits.
8) Coagulation Profile: Normal.
9) ADAMTS13 Activity: Undetectable.
10) Anti - ADAMTS13 Antibodies: Positive.

Based on these findings, the patient's clinical presentation and laboratory results were highly suggestive of Thrombotic Thrombocytopenic Purpura (TTP). Immediate consultation with a hematologist was sought, and the patient was started on therapeutic plasma exchange (TPE) and high - dose corticosteroids to address the underlying pathophysiology and stabilize her condition.

3. Further Investigations

Upon admission and the initiation of treatment for suspected Thrombotic Thrombocytopenic Purpura (TTP), additional investigations were conducted to confirm the diagnosis, assess disease severity, and identify any potential underlying triggers or complications. The following investigations were carried out:

1) **ADAMTS13 Activity Assay:** A confirmatory test for TTP, the ADAMTS13 activity assay was performed to measure the activity of the von Willebrand factor - cleaving protease ADAMTS13. Results revealed an undetectable level of ADAMTS13 activity, consistent with the diagnosis of acquired TTP.
2) **Anti - ADAMTS13 Antibodies:** The presence of anti - ADAMTS13 antibodies was confirmed, further supporting the diagnosis of acquired TTP. These autoantibodies inhibit the function of ADAMTS13, leading to excessive platelet aggregation and microvascular thrombosis.
3) **Serum Chemistry:** Comprehensive serum chemistry panels were conducted to assess organ function and rule out other potential causes of the patient's symptoms. These panels included liver function tests, renal function tests, and electrolyte levels, all of which were within normal limits.
4) **Coagulation Profile:** Coagulation studies, including prothrombin time (PT) and activated partial thromboplastin time (aPTT), were performed and found to be within the normal range, ruling out disseminated intravascular coagulation (DIC).
5) **Hepatitis and HIV Screening:** Infectious disease screening, including hepatitis B, hepatitis C, and HIV tests, was negative, ruling out viral etiologies.
6) **Cerebral Imaging:** Given the patient's mild confusion, a non - contrast head CT scan was performed to exclude any intracranial pathology. The results were unremarkable, indicating no acute neurological abnormalities.
7) **Bone Marrow Biopsy:** A bone marrow biopsy was performed to assess for any underlying bone marrow disorders that could contribute to the hematological abnormalities. The biopsy showed evidence of increased megakaryocytes, consistent with the diagnosis of TTP.
8) **Cardiac Evaluation:** The patient underwent a transthoracic echocardiogram to assess cardiac function, which revealed normal systolic and diastolic function with no valvular abnormalities.

The constellation of these investigations, along with the initial clinical presentation and laboratory findings, confirmed the diagnosis of Thrombotic Thrombocytopenic Purpura (TTP). The patient continued to receive therapeutic plasma exchange (TPE) along with corticosteroid therapy to suppress autoantibody production and manage the ongoing hematological complications. Close monitoring and further assessments were crucial to evaluating her response to treatment and preventing relapses.

4. Treatment

Upon confirming the diagnosis of Thrombotic Thrombocytopenic Purpura (TTP), a multidisciplinary team, including hematologists, began a comprehensive treatment plan tailored to the patient's condition. The primary goals of treatment were to halt the ongoing microvascular thrombosis, correct the hematological abnormalities, and prevent disease relapse. The following treatment modalities were employed:

1) **Therapeutic Plasma Exchange (TPE):** The cornerstone of acute TTP management, TPE involves the removal and replacement of the patient's plasma. It is performed to eliminate the ultra - large von Willebrand factor multimers and autoantibodies that

contribute to platelet aggregation and microvascular thrombosis. The patient initially underwent daily TPE sessions, gradually transitioning to alternate - day exchanges as her clinical condition improved.

2) **Corticosteroids:** High - dose corticosteroid therapy, typically with intravenous methylprednisolone, was initiated concurrently with TPE to suppress the production of anti - ADAMTS13 antibodies and reduce inflammation. The patient was maintained on a tapering regimen of corticosteroids to prevent relapse.
3) **Rituximab:** In cases of refractory or recurrent TTP, or when a rapid reduction in autoantibody production is required, Rituximab, a monoclonal antibody targeting B cells, was considered. After several days of treatment without a significant response to TPE and corticosteroids, the patient received Rituximab, which led to a reduction in anti - ADAMTS13 antibody levels and improved platelet counts.
4) **Platlet Transfusions:** Platelet transfusions were administered as needed to manage severe thrombocytopenia and bleeding complications, although they were used judiciously due to the risk of exacerbating microvascular thrombosis.
5) **Fresh Frozen Plasma (FFP):** FFP was administered during TPE to replace the removed plasma volume and provide clotting factors and ADAMTS13. This helped prevent coagulation abnormalities and maintain hemostasis during the exchange procedure.
6) **Close Monitoring:** The patient was closely monitored throughout her hospitalization, including regular assessments of complete blood counts, peripheral blood smears, LDH levels, and renal function. Neurological status was assessed daily to detect any signs of worsening confusion or focal neurological deficits.

Response to Treatment:
The patient responded favorably to the combined therapeutic approach of TPE, corticosteroids, and Rituximab. Her platelet counts gradually improved, hemolysis markers (such as LDH and bilirubin) normalized, and the petechiae and purpura began to resolve. Her cognitive function also improved, and she regained full orientation.

Long - Term Management:
Recognizing the potential for relapse in TTP, the patient was transitioned to maintenance therapy with periodic Rituximab infusions and close outpatient follow - up with her hematologist. The goal of long - term management was to maintain ADAMTS13 activity and prevent disease recurrence.

This case exemplifies the complexities of managing TTP, including the need for a multi - pronged treatment approach, vigilant monitoring, and an individualized plan based on the patient's response to therapy. It underscores the importance of early diagnosis and prompt intervention in achieving positive clinical outcomes in this rare and challenging hematological disorder.

5. Discussion

Thrombotic Thrombocytopenic Purpura (TTP) is a rare and life - threatening hematological disorder characterized by a deficiency of ADAMTS13, a von Willebrand factor - cleaving protease. This deficiency leads to the accumulation of ultra - large von Willebrand factor multimers, which in turn triggers the formation of platelet - rich microvascular thrombi, resulting in a triad of clinical manifestations: microangiopathic hemolytic anemia, thrombocytopenia, and widespread microvascular thrombosis. Our presented case of TTP exemplifies the diagnostic and therapeutic challenges associated with this rare condition.

Diagnostic Challenges:
1) Non - Specific Symptoms: The initial symptoms reported by the patient, including fatigue, petechiae, and mild confusion, were non - specific and could easily be attributed to various other medical conditions. TTP often mimics other hematological disorders, making its diagnosis challenging.
2) Laboratory Abnormalities: While the hallmark of TTP is severe thrombocytopenia, additional laboratory findings such as elevated LDH levels, indirect hyperbilirubinemia, and the presence of schistocytes on peripheral blood smear are supportive but not exclusive to TTP. These findings may overlap with other conditions like Hemolytic - Uremic Syndrome (HUS).
3) ADAMTS13 Testing: The definitive diagnosis of TTP relies on demonstrating a severe deficiency of ADAMTS13 activity. This case showed an undetectable ADAMTS13 activity level, consistent with the diagnosis. Moreover, the presence of anti - ADAMTS13 antibodies further supported the diagnosis, indicating an autoimmune etiology in this acquired form of TTP.

Treatment Challenges
1) **Prompt Initiation of TPE:** The cornerstone of TTP treatment is therapeutic plasma exchange (TPE), which rapidly removes the pathogenic antibodies and ultra - large von Willebrand factor multimers. Early initiation of TPE is crucial for halting microvascular thrombosis, but this requires a high index of suspicion and quick diagnostic workup.
2) **Management of Recurrent TTP:** Some patients, as in this case, may experience recurrent TTP episodes. Managing these recurrences can be challenging, often necessitating therapies such as Rituximab to reduce autoantibody production. It underscores the importance of close long - term follow - up and a proactive approach to prevent relapses.

Multidisciplinary Approach:
Successful management of TTP necessitates a multidisciplinary approach involving hematologists, clinical pathologists, and critical care teams. Prompt recognition, rapid diagnostic workup, and immediate initiation of TPE and corticosteroids are essential for preventing irreversible organ damage and achieving positive outcomes.

6. Conclusion

Thrombotic Thrombocytopenic Purpura is a rare hematological disorder with potentially devastating consequences if not promptly diagnosed and treated. This

case underscores the importance of considering TTP in the differential diagnosis of patients presenting with thrombocytopenia, hemolytic anemia, and neurological symptoms. Furthermore, it highlights the complexities in both the diagnosis and treatment of TTP, emphasizing the need for a multidisciplinary and individualized approach to manage this challenging condition effectively. Timely intervention and close long - term monitoring are pivotal in improving patient outcomes and preventing relapses in TTP.

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