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Case Report

Moschcowitz Syndrome – A Rare Conundrum with Acute Pancreatitis – Case Report and Narrative Review of Literature

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Abstract

Introduction: Moschcowitz syndrome or Thrombotic Thrombocytopenic Purpura (TTP) is a thrombogenic condition due to deficiency or dysfunction of A disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13 (ADAMTS13), which causes a myriad of clinical presentations. The association between acute pancreatitis and TTP is a conundrum as both can be etiology and effect of one another. We describe a clinical case and review the available literature to understand this conundrum better.
Case: A 52-year-old male was admitted to our setting with acute pancreatitis and on further evaluation was found to have deranged renal function with anemia and thrombocytopenia. He had multiple seizures during his stay requiring mechanical ventilation. Based on clinical findings a diagnosis of TTP was suspected which was confirmed on relevant investigations. His course and management were a challenge for the team.
Discussion: A thorough literature search was conducted to identify all published reports/case series on acute pancreatitis and TTP. Of 38 identified publications, 20 case reports were reviewed as a cohort of acute pancreatitis and TTP. All cases had acute pancreatitis before TTP, alcohol being the most common cause. Early diagnosis and initiation of plasma exchange improves prognosis.
Conclusion: Acute pancreatitis is a sinister trigger for TTP. Vigilance, suspicion, and early diagnosis are crucial to manage these cases. Early plasma exchange reduces mortality and hospital stay.

Keywords: thrombotic thrombocytopenic purpura, ADAMTS13 deficiency, acute pancreatitis, plasmapheresis

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1. Introduction

Moschcowitz syndrome was first described by Eli Moschcowitz in 1924, in a 16-year-old girl with anemia, bruises, microscopic hematuria, and disseminated microvascular thrombi (noted during autopsy). Moschcowitz syndrome or commonly known as thrombotic thrombocytopenic purpura (TTP) is a rare fatal multiorgan thrombogenic condition [1]. The classic pentad of microangiopathic hemolytic anemia (MAHA), thrombocytopenia, renal dysfunction, neurological symptoms, and fever may not be appreciated in all cases. The annual reported incidence is 6 per million. Pathologically it is related to deficiency or dysfunction of A disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13 (ADAMTS13). This leads to uncontrolled activity and accumulation of ultra-large von Willebrand factor (ULVWF) molecules, which cause disseminated microvascular thrombosis. It may be primary (congenital absence or dysfunction of ADAMTS13 – also known as Upshaw Schulmann syndrome), secondary (due to known triggering factors – pregnancy, vascular diseases, autoimmune conditions, cancer, drugs, infections, etc.) or idiopathic [2, 3].

The association between acute pancreatitis (AP) and TTP is a conundrum, since what causes what is still unknown. Hosler et al., [4] described the involvement of pancreas in 30 out of 51 cases of TTP, in a postmortem study. In contrast, Swisher et al., [5] noted 5 cases in their series with 16 previously reported cases where acute pancreatitis occurred, on an average, 3 days before initiation of TTP. Hence, the complex interlude between both these pathologies persists till date.

Here, we report a case of simultaneous occurrence of acute pancreatitis and TTP, and review the available case reports in English literature in a cohort study format in order to better understand the correlation between this “chicken and egg” conundrum.

2. Case Presentation

A 52-year-old male presented to emergency with severe abdominal pain and fever for 1 day without any history of vomiting, nausea, altered bowel, or any other systemic or local complaints. He denied any history of travel, animal contacts, drug intake, addictions or high-risk recreational activity, vaccinations, or binging on any high-fat diet. His blood counts showed low hemoglobin (Hb) and platelets (Figure **1**) on admission. His liver and renal function parameters were also deranged with mildly elevated aspartate transaminase (AST = 65.3 U/L), alanine transaminase (ALT = 73.2 U/L), mixed hyperbilirubinemia (total bilirubin 42 µmol/L and direct bilirubin 19.4 µmol/L) and raised creatinine (153 µmol/L) (Figure **1**). He had markedly elevated amylase (1016 U/L) and lipase (4182 U/L) with ultrasound and contrast-enhanced computed tomography abdomen suggestive of acute pancreatitis (AP) (Figure **2**) without any evidence of cholelithiasis or cholecystitis. He was shifted to the intensive care unit (ICU) where he was managed as per AP protocol with multiorgan dysfunction.

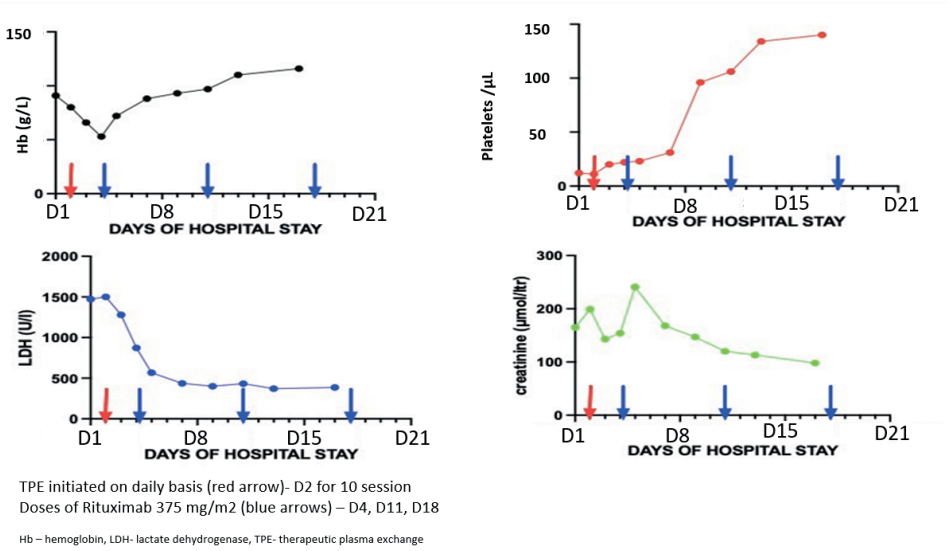

Figure 1: Course of lab parameters in hospital.

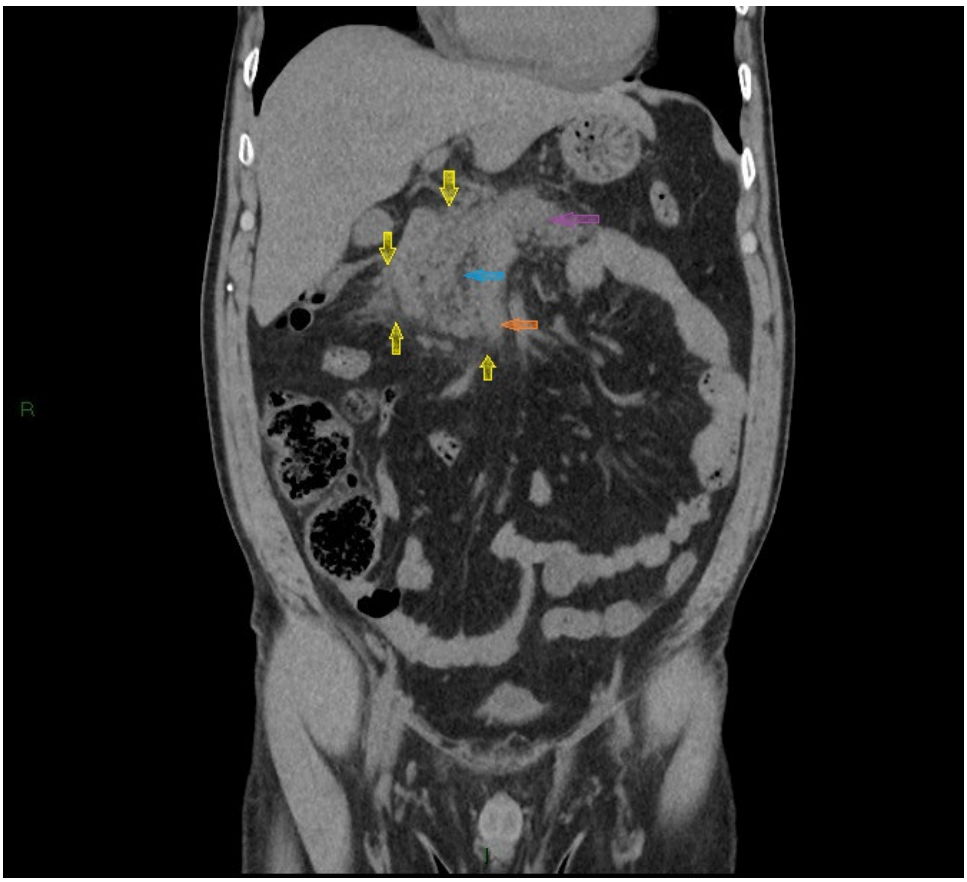

Figure 2: CT Abdomen (without contrast) coronal section showing peri pancreatic fat stranding suggestive of acute pancreatitis (yellow arrows). Uncinate process (orange arrow), head (blue arrow), and body (purple arrow) of pancreas are marked.

His course had a dramatic turn over the next 36 hours when he had multiple seizures with altered consciousness, for which he was intubated and mechanically ventilated. His platelet count at this hour were

11/µL, Hb 80 g/L with mean corpuscular volume (MCV) 83 fL, lactate dehydrogenase (LDH) 1472 U/L, creatinine 199 µmol/L, AST 56 U/L, ALT 68 U/L, international normalized ratio (INR) 1.14 and gamma-glutamyl transferase (GGT) 46 U/L. His peripheral smear clinched the diagnosis with reporting of schistocytes (Figure **3**) along with features of hemolytic anemia and thrombocytopenia. He had a raised reticulocyte index of 2.98% with a normal coagulation profile. Other pathological examinations, including blood and urine culture, procalcitonin, antinuclear antibody, direct Coomb's test, viral hepatitis serologies (Hepatitis B, Hepatitis C, and Human immunodeficiency virus), and echocardiography screening were negative.

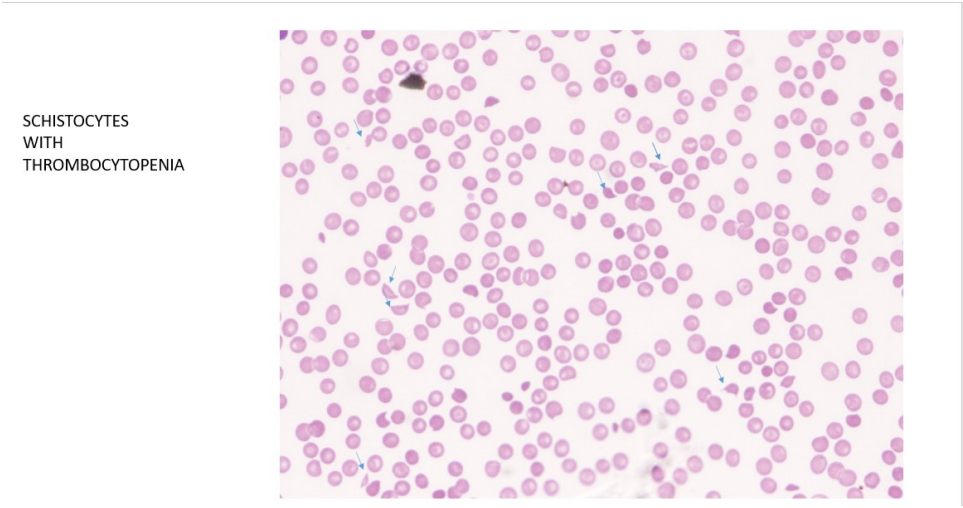

Figure 3: Light microscopy x100 magnification in oil immersion field stain showing schistocytes in peripheral blood (blue arrow) in between normal red blood cells. Platelets are not visible in the picture due to severe thrombocytopenia.

Based on clinical pentad (MAHA, thrombocytopenia, renal dysfunction, fever, and seizure) with presence of schistocytes (Figure **3**), his clinical diagnosis was TTP hence he was immediately initiated on plasmapheresis along with intravenous glucocorticoid pulses. Magnetic resonance imaging (MRI) of the brain showed cerebral edema with suspicion of posterior reversible encephalopathy syndrome (PRES). The diagnosis was confirmed by low ADAMTS13 activity (< 2%) with raised antibody titer against ADAMTS13.

He received 10 sessions of therapeutic plasma exchange (TPE) along with a pulse of intravenous methylprednisolone 1 gm for 3 days followed by oral prednisolone equivalent of 1 mg/kg/day. He also received intravenous rituximab 375 mg/m2 weekly for 3 doses because of inadequate response to primary treatment. Post 7th session of TPE and rituximab 1st dose, his platelets and Hb started improving. He was eventually discharged on day 20 post-admission with normal Hb, platelets, creatinine, and LDH levels (Figure **1**). Post-discharge, the patient followed up at a center of excellence in his home country and a call was made to him 2 months later where he updated that he was on steroid tapering and was doing well with no further recurrences either of AP or TTP.

3. Discussion

A literature search was conducted on PUBMED central for reported cases of acute pancreatitis and TTP. A total of 66 search items were identified between 1969 and 2023. Singh et al., [6] in 2003 and Swisher et al., [2] in 2007 did a literature review along with reporting of their respective cases. Hence, this literature review was conducted from 2007 to 2023 dated forward to Swisher et al's. publication. We identified 38 publications in the PUBMED search, of which 11 were excluded – 3 were not in English literature, 3 were TTP secondary to other causes (2 due to infections and 1 secondary to a drug) and 5 were publications unrelated to the objective of this literature review.

A total of 20 case reports [7-25] were finally identified and reviewed as a cohort of TTP triggered by AP due to various causes. The mean age was 38 years (± 17.19), with 12 males and 8 females. All the described cases had onset of acute pancreatitis prior to TTP, with simultaneous occurrence of both in 3 cases [18, 19, 21] (similar to index case). Most cases had onset of TTP on day 2 or 3 of acute pancreatitis; however, two cases [9, 17] have described the occurrence of TTP up to 3-4 weeks after AP. Thus, we can assume the risk period to be within the onset of AP to 4 weeks after, where constant surveillance and high vigilance are needed by the clinical team to detect TTP at the earliest onset of hemolytic anemia, thrombocytopenia, or rising creatinine.

Alcohol was the most common cause of AP [8, 10, 11, 15, 16, 25] (6 cases) followed by post-endoscopic retrograde cholangiopancreatography [19, 22, 23] (4 cases), gallstone [13, 14, 20] (3 cases), fatty meal [7], autoimmune pancreatitis [21] (1 case each) and idiopathic [9, 12, 17, 18, 24] (5 cases). All cases had anemia on the onset of TTP with a mean Hb of 7.4 gm/dl and raised lactate dehydrogenase (LDH) (mean 2152 U/L). Similarly low platelets with mean 30,550 µL were common to all except one [17]. On the contrary, renal failure (mean creatinine 3.3 mg/dl) was present in 80% and the least commonly described clinical features were fever (50%) and neurological symptoms (35%). The presence of schistocytes in peripheral blood smear hints the diagnosis in almost all cases. Only 8 cases [10, 11, 14, 15, 16, 17, 19, 21] reported ADAMTS levels, except for one [14] who had low levels, 3 reported [10, 15, 17] recovery post treatment. Antibody to ADAMTS was done in only 4 cases [14, 15, 17, 21], of which 2 reported positive [17, 21]. PLASMIC score, a screening tool, for suspected TTP, was reported in only 1 case [11]. Hence, clinical features and the presence of schistocytes seem to be the most relevant for early diagnosis of TTP, post AP.

Therapeutic plasma exchange (TPE) was given in all cases. The mean sessions of TPE required was 10. All cases recovered post TPE, except two [9, 21]. Two cases [19, 21] also mentioned using rituximab, due to poor response to primary treatment, of which 1 case [19] used eculizumab as well. 9 cases were discharged and 1 died [19] even after best efforts. Recurrence of AP was mentioned in 3 reports, post TTP recovery [7, 10, 17].

A review by Thachil [26] on the immunopathogenesis of AP and its association with TTP has stated endothelial dysfunction as the primary inciting event common to both. Inflammatory cascade triggered

by pancreatic tissue damage releases a plethora of cytokines into the bloodstream, which then cause endothelial damage and release ULVWF. ULVWF rapidly consumes ADAMTS13 leading to a relative paucity of same and excess of ULVWF, which triggers disseminated microvascular thrombosis and organ damage. Whether AP triggers TTP or is a sequela to it, is still a matter of debate. ADAMTS levels may not be very low in patients with AP triggered TTP. Hence, the role of other agents like nitric oxide, complement cascade activation, vascular endothelial growth factor, endothelial-derived proteins etc., has also been implicated in inciting TTP post AP.

Management of TTP [27] is based on early recognition by a high clinical index of suspicion or using the PLASMIC score. Once the probability of TTP is high (PLASMIC score $\geq$ 6), urgent TPE is indicated with/without high-dose corticosteroids. Other agents like rituximab or eculizumab may be used in refractory cases. Caplacizumab [28] is an anti-vWf, that inhibits the interaction between vWf multimers and platelets and is a new agent approved for TTP. As noticed from the literature review, response to early TPE and steroids is generally favorable in TTP post AP. Post-recovery patients need follow-up at an expert center and monitoring of ADAMTS levels so that therapy can be initiated at the earliest signs of relapse of TTP.

4. Conclusion

Our index case developed TTP simultaneously with AP (cause unknown) and over 2 days had the pentad manifestations of TTP MAHA, renal failure, fever, thrombocytopenia, and neurological involvement in the form of seizures. From the literature review of published cases over the past 16 years, it is noted that anemia with raised LDH and thrombocytopenia post AP should prompt to ask for schistocytes on peripheral blood smear. If possible, ADAMTS level and antibody should be tested. Use of PLASMIC score in patients with multiorgan dysfunction post AP can help to initiate TPE in high risk of TTP without ADAMTS testing. Moschowitz syndrome aka TTP is not so uncommon phenomenon post AP, and it can be an event or trigger to the same. Early diagnosis and management are key to prevent mortality in this syndrome.

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Statement of Ethics

The above study involving human participants were planned, conducted, and reported in accordance with the World Medical Association (WMA) Declaration of Helsinki.

Ethical Approval

Approved for publishing of the case report by the Ethical Committee, Lifecare Hospital, Musaffah, Abu Dhabi on July 26, 2024, Approval number MOM/COM/ETHICS/260724/002.

Patient Informed Consent Statement

Written informed consent was obtained from the patient to publish their case and any accompanied images.

Disclosure Statement

Affirm that there is no financial disclosure, non-financial relationship, and activities.

Conflict of Interest

The authors declare that there is no conflict of interest.

Artificial Intelligence (AI) Disclosure Statement

AI-unassisted work.

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None.

Author Contribution

Baiju Faizal Puthenkote and Debashish Mishra were involved in patient management as well as drafting and finalizing the manuscript. All other authors were involved in the active management of the case. Sahithi Surapaneni and Yogesh Yadav helped with laboratory investigations and imaging, respectively. All authors were involved in reviewing, proofreading, and final drafting of the manuscript.

Data Sharing Statement

Data sets are not available publicly because of legal/security/privacy/policy reasons. However, it is available by request from the correspondence author.

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