Pancreatitis and Myocardial Infarction as Complications of Thrombotic Thrombocytopenic Purpura: A Case Report

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October 14, 2024

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Key Clinical Message:

Thrombotic thrombocytopenic purpura (TTP) can present with serious complications like pancreatitis and myocardial infarction. Early recognition and treatment with plasma exchange are critical to improving patient outcomes**.**

Abstract:

Thrombotic thrombocytopenic purpura (TTP) is a rare disease with a mortality rate of 90% if not treated promptly. Due to limited clinical experience and sometimes atypical presentation, early detection of TTP is not always easy. The pathophysiological mechanisms underlying TTP can accelerate thrombus formation and vascular occlusion, potentially leading to ischemic damage in various organs, including the heart and pancreas. Considering that the complications caused by these disorders can be life-threatening, the simultaneous manifestation of acute pancreatitis (AP), TTP, and heart damage in the patient may cause a significant risk of mortality if not treated in time and adequately. We report a case involving a 43-year-old patient who presented with symptoms of myocardial infarction (MI) and acute pancreatitis (AP) secondary to thrombotic thrombocytopenic purpura (TTP). The patient was diagnosed based on clinical manifestations, laboratory findings, and imaging studies. Immediate intervention included plasma exchange and supportive care, which led to the stabilization of the patient's condition. This case emphasizes the importance of increased vigilance for AP symptoms and cardiac complications in patients with TTP presenting with atypical symptoms. Early diagnosis and prompt treatment are critical in reducing the risk of mortality associated with these severe complications.

Keywords: Acute Pancreatitis(AP); Thrombotic Thrombocytopenic Purpura(TTP); Myocardial Infarction(MI)

1 | INTRODUCTION

Thrombotic Thrombocytopenic Purpura (TTP) is a potentially life-threatening condition characterized by severe thrombocytopenia and microangiopathic hemolytic anemia. The primary pathophysiological mechanism is considered to be reduced ADAMTS13 activity, which can be due to inherited gene mutations (hereditary TTP) or the formation of inhibitory autoantibodies (acquired TTP)1(). ADAMTS13 is a von Willebrand factor (VWF)-cleaving protease that prevents the accumulation of ultra-large VWF molecules by cleaving them into smaller fragments. In the absence of ADAMTS13, ultra-large VWF molecules accumulate within vessels, forming platelet-rich microthrombi. Consequently, diminished blood supply to tissues can result in multi-organ damage23(,). Given the systemic nature of TTP, it can lead to complications in

various organs, though some manifestations are exceedingly rare1(). Acute pancreatitis (AP) and myocardial infarction (MI) represent rare complications of TTP. Understanding the broader context of AP and MI helps underscore their clinical relevance in TTP patients. The annual incidence rate of AP ranges between 4.9 and 35 per 100,000 individuals, with mortality rates of 1.5% and 30% in mild and severe cases, respectively4-6(). Hence, early diagnosis and intervention are vital in managing these patients. AP can be attributed to several etiologies, including obstruction of the pancreatic duct due to gallstones (38%), alcohol consumption (36%), and hypertriglyceridemia (up to 4%)7(). In rare instances, pancreatitis can develop secondary to Thrombotic Thrombocytopenic Purpura/Hemolytic Uremic Syndrome (TTP/HUS). Approximately 2% of patients with TTP/HUS develop acute pancreatitis89(,). This phenomenon is hypothesized to occur due to the necrosis of pancreatic cells, which results from the blockage of pancreatic arterioles by platelet-rich thrombi. However, the etiology remains elusive10(). The occurrence of myocardial infarction (MI) as an initial presentation of thrombotic thrombocytopenic purpura (TTP) is uncommon, largely due to the formation of microthrombi within the cardiac vessels. The precise incidence of myocardial infarction (MI) resulting from TTP remains uncertain; however, studies report the prevalence of TTP-related cardiovascular complications to range between 9.5% and 77%11(). Nevertheless, the occurrence of myocardial infarction as an initial symptom of thrombotic thrombocytopenic purpura is exceedingly uncommon. We present a rare case of a 43-year-old man with acute pancreatitis and myocardial infarction (MI) as the initial presentation of TTP.

| Case history and physical examinations:

A 43-year-old man with no medical history went to the Emergency Department two days before being admitted to the hospital with the main complaint of severe abdominal pain in the epigastric area with radiation to the back, nausea, vomiting, cold sweat, and headaches. The patient had no history of alcohol or drug use. On examination, the patient was conscious and his vital signs were stable. The conjunctiva was pale, and the sclera showed evidence of icterus. Tenderness was observed in the epigastrium. Other examinations had normal results.

1.2 | Investigations, diagnosis and treatment

Laboratory tests revealed the following results: hemoglobin: 6.7 g/dL; MCV: 88 fL; platelets: 13,000/L; total bilirubin: 5.3 mg/dL with indirect bilirubin: 3.2 mg/dL; LDH: 3981 U/L; retic percentage: 3%; International Normalized Ratio (INR): 1.3; creatinine: 1.3 mg/dL; cardiac troponin I level: 410 ng/mL; amylase: 390 U/L; and lipase: 510 U/L. Test results for direct and indirect Coombs tests were negative. The patient's peripheral blood smear showed the presence of schistocytes(Figure 1). ADAMTS-13 activity level was 0% with elevated inhibitor titer and negative anti-nuclear antibody level. The patient's electrocardiogram showed normal sinus rhythm without ST segment changes, and echocardiography showed normal findings. A diagnosis of TTP was made, and plasma exchange was rapidly initiated based on a plasma score of 7 (severe). Methylprednisolone 1000 mg per day intravenously was prescribed for three days. Due to increased serum amylase and lipase levels, a computed tomography (CT) scan of the abdomen was performed, which showed a swollen pancreas with fatty fibers around it (Figure 2). An abdominal ultrasound showed the absence of radiolucent stones. Subsequent laboratory tests ruled out hypercalcemia, and hypertriglyceridemia as potential causes of pancreatitis. A CT scan of the brain was normal. Based on the patient's symptoms, cardiac troponin I level was measured again, which was 1100 ng/ml. A consultation with a cardiologist revealed that a non-ST-segment elevation myocardial infarction had occurred. After three plasma exchanges, the patient's platelet count reached 52,000/L, and Tab Aspirin(ASA) and heparin were started at a therapeutic dose. After the seventh session of plasma exchange, the patient's platelets reached more than 150,000/uL, and after the eighth session, it was 190,000/uL. At the time of discharge, it was 205,000/uL. The patient's LDH also decreased to 446 U/L. Finally, after eight sessions of plasma exchange and three days of methylprednisolone and serum therapy, all the patient's symptoms were resolved, and the patient was discharged with Clopidogrel, ASA, Atorvastatin, and oral Prednisolone 50 mg. The dose of prednisolone was gradually reduced

over four weeks.

1.3 | Outcome and follow-up

During follow-up periods at one month and six months, the patient showed no signs of disease recurrence, and heart function remained normal.

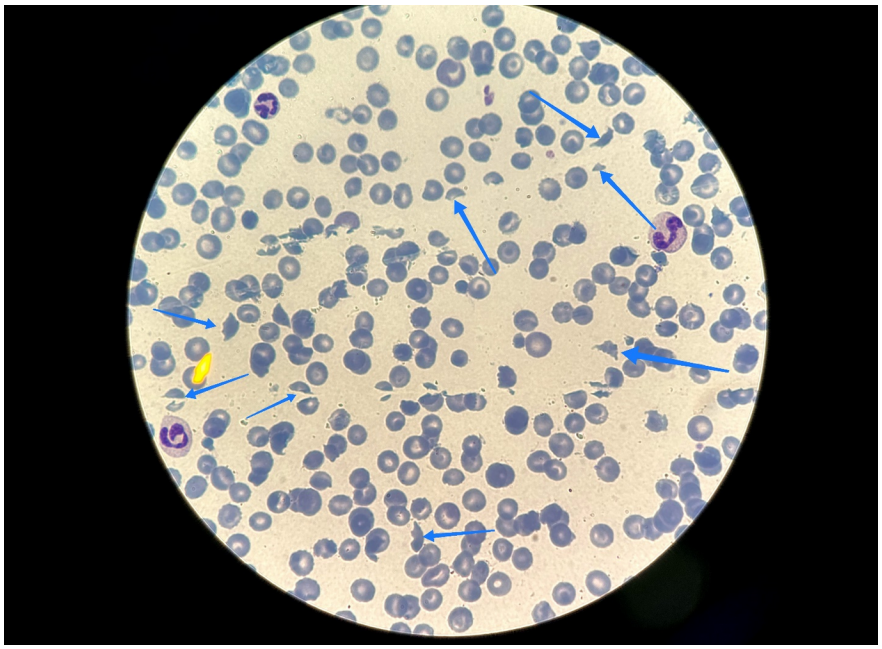

Figure 1: The Schistocytes (blue arrows) were found in peripheral blood smear (H&E staining with 100X magnification)

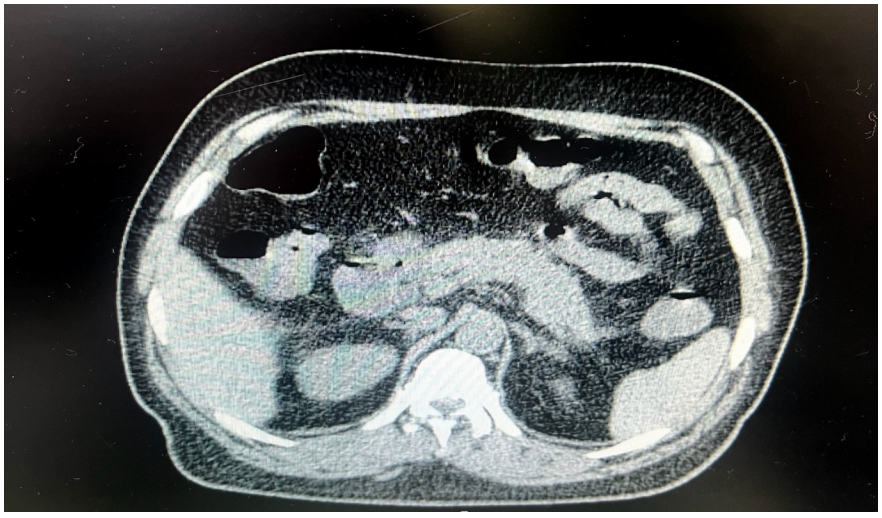

Figure 2: Abdomen Computed Tomography (CT) Scan; Pancreatic swelling and surrounding fat stranding

2 | DISCUSSION

TTP is a rare autoimmune disorder that results in small clots forming throughout the body. A deficiency of the von Willebrand factor (vWF)-cleaving protease, ADAMTS13 (activity <10%), leads to very large vWF multimers in the circulation, resulting in microvascular thrombosis. These microclots can occlude blood vessels, leading to tissue damage and organ dysfunction due to extensive microangiopathic hemolytic anemia caused by coagulation cascade activation. Thrombotic thrombocytopenia-induced myocardial infarction is a rare and potentially life-threatening condition that can occur as a complication of thrombotic thrombocytopenic purpura (TTP)12(). Previous studies have shown that TTP can also lead to pancreatitis in 1.7% to 2.0% of cases. Abnormal vWF multimers cause hyaline microthrombi in pancreatic small vessels, leading to ischemia and inflammatory changes. This case report describes the occurrence of both acute pancreatitis and myocardial infarction as potential manifestations of TTP-related microvascular injury13(). In 2024, Wang et al. reported a 44-year-old man diagnosed with acute pancreatitis as a rare manifestation of TTP, who presented with initial symptoms of abdominal pain14(). Harvey Olsen reported a case involving a 49-year-old male with TTP-induced acute pancreatitis (AP), who exhibited symptoms of abdominal pain and bleeding gums. Histological evaluation of the patient's pancreatic parenchyma revealed focal hemorrhages, fat necrosis, and round cell infiltration. Additionally, the presence of the pancreatic enzyme elastase was noted in the pancreatic tissue, aligning with the characteristics of AP10(). A separate review by Antes EH documented histological alterations in 63 TTP patients with confirmed AP. Of the nine individuals diagnosed with AP, five exhibited necrosis and two displayed hemorrhages in the pancreatic tissue, corroborating the aforementioned mechanism. Furthermore, an animal study demonstrated that thrombosis in pancreatic veins induced acute necrotizing hemorrhagic pancreatitis in dogs15(). Swisher et al. detailed the cases of five patients who initially presented with acute pancreatitis and later exhibited signs of TTP (including thrombocytopenia, anemia, elevated LDH, and the presence of schistocytes in blood smears) within a span of one to thirteen days16().

MI due to TTP is extremely rare as the presenting event of TTP. In 2023, Mohamed et al. reported a 45-year-old woman who presented with symptoms of fever, myalgia, diffuse arthralgia, and decreased urination three days after the diagnosis of Non-ST-Segment Elevation Myocardial Infarction and undergoing percutaneous coronary intervention (PCI). Attention to laboratory tests and a low ADAMTS13 level with a high inhibitory titer led to the diagnosis of TTP11(). Also, in 2022, Geeth et al. reported a 68-year-old woman who presented with an initial complaint of chest pain along with mental changes and fatigue, and a platelet count of 30,000/uL, with a non-ST elevation myocardial infarction as an unusual presentation of TTP. She was treated with plasmapheresis and steroids17(). Șalaru et al.18(), Ghodsi et al.19(), Takimoto et al.20(), and Dahal et al.21() also reported myocardial infarction as a rare and early manifestation of TTP. In this report, at the same time as the diagnosis of TTP and AP for the patient, Non-ST-Segment Elevation Myocardial Infarction was also discussed. Cardiac complications caused by TTP have a high mortality rate, and early diagnosis and management of this disease are very important11(). Studies have shown that TTP patients with high levels of positive cardiac biomarkers are at higher risk for severe complications and mortality. Troponin levels greater than 0.25 ng/mL are associated with a threefold increased risk of mortality in TTP patients22(). In this report, the troponin level was first 410 ng/mL and then 1100 ng/mL. Management of myocardial infarction in TTP patients can be challenging due to low platelet counts. Standard recommendations suggest a cardiac workup with clinical examination, Electrocardiogram(EKG), echocardiography, and serum evaluation of cardiac enzymes. In TTP patients with myocardial damage, immediate plasmapheresis is necessary to prevent further cardiac damage and mortality. Additionally, due to the increased risk of fatal arrhythmia, continuous heart monitoring is necessary for these patients11(). Here we report a 43-year-old man with acute pancreatitis and myocardial infarction (MI) as potential manifestations of TTP-related microvascular injury. This case report describes the occurrence of both acute pancreatitis and myocardial infarction as complications of TTP, emphasizing the critical importance of early diagnosis and intervention in the management of this disorder. It also provides insight into the challenges of diagnosing and treating TTP with unusual presentations such as pancreatitis and myocardial infarction. The complexity of managing TTP, especially when it is associated with multiorgan involvement, underscores the need for physicians to be vigilant in caring for such complications.

3 | IN CONCLUSION

This case report highlights the rare but serious complications of pancreatitis and myocardial infarction (MI) caused by thrombotic thrombocytopenic purpura (TTP). TTP is a life-threatening hematologic disorder characterized by extensive thrombosis, presenting a unique challenge in clinical management when complicated by pancreatitis and MI. Early diagnosis and aggressive treatment, including plasma exchange and immunosuppression, are critical to patient survival. This case emphasizes the importance of recognizing the potential for multiorgan involvement in TTP, advocating for comprehensive surveillance and interdisciplinary care to improve outcomes in patients with such complex presentations.

AUTHOR CONTRIBUTIONS

Farid Poursadegh: Conceptualization, Project administration, Supervision, Validation, Visualization

Mohsen Seddigh-Shamsi: Investigation, Methodology, Project administration, Resources, Validation, Visualization

Motahhareh Karimoddini: Conceptualization, Data curation, Investigation, Methodology, Resources, Software, Writing - original draft, Writing - review & editing

Najme Mohajer: Data curation, Investigation, Project administration, Visualization

CONFLICT OF INTEREST STATEMENT

I declare that there are no conflicts of interest related to the publication of this manuscript. As the corresponding author and representative of all co-authors, I confirm that the details furnished in this disclosure are accurate and comprehensive, to the best of my knowledge and belief.

DATA AVAILABILITY STATEMENT

The dataset supporting the conclusions of this research can be obtained upon request directed to the corresponding author. Public access to the data is restricted due to concerns regarding privacy and ethical considerations.

CONSENT

"I provide my written authorization for the use of my clinical data in publications, with the understanding that this information will be utilized solely for educational purposes aimed at healthcare professionals."

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