

Chest pain with increased troponin level; not always a cardiology issue

STAMATIS S. PAPADATOS¹, STAMATIS J. KARAKATSANIS², GEORGE DELIGIANNIS³, ELENI GATSA⁴

¹3rd Department of Internal Medicine, National and Kapodistrian University of Athens School of Medicine, Sotiria General Hospital, Athens, Greece

²Hematology Unit, 3rd Department of Internal Medicine, National and Kapodistrian University of Athens School of Medicine, Sotiria General Hospital, Athens, Greece

³Department of Cardiology, General Hospital of Karditsa, Thessaly, Greece

⁴Hematology Unit, General Hospital of Trikala, Thessaly, Greece

Thrombotic Thrombocytopenic Purpura (TTP) is a thrombotic microangiopathy syndrome resulting from decrease or absence of “a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13” (ADAMTS13). TTP has been characterized by the classical pentad of thrombocytopenia, hemolysis, fever, renal injury and neurological deficits, yet the patient may present with any atypical symptom related to microthrombi formation in the microcirculation. Here we present a rare case of a young patient with retrosternal chest pain and myocardial injury as the first manifestation of TTP.

Key words: Thrombotic Thrombocytopenic Purpura, Myocardial Injury, ADAMTS13, Microvascular Hemolysis.

INTRODUCTION

Chest pain is a common symptom accounting for about 40% of emergency hospital admissions. [1] As the management of a patient with chest pain depends on the accurate diagnosis, the main concern of the clinicians is to distinguish between the cardiac and non-cardiac chest pain. Acute coronary syndrome (ACS) is a common emergency especially in ages > 40 years old and in patients with classical risk factors for coronary heart disease; rapid response is the key to treatment. Yet, all chest pain patients do not experience a classical myocardial infarction (MI).

Herein we present a rare case of myocardial injury in a young male patient neither with positive family history nor any other risk factor for early-onset coronary heart disease.

CASE REPORT

A 25-year-old patient presented to the Emergency Department complaining about dizziness and retrosternal chest pain that had initiated

30 minutes before. His medical history was unremarkable. On clinical examination, blood pressure and respiratory rate were within normal range but his heart rate was 105 pulses per minute and his temperature was 37.8°C. An electrocardiogram (ECG) was performed and showed sinus tachycardia without specific ST-T changes (Figure 1) while the Chest X-Ray revealed no pathology. Typical routine blood tests were performed on admission. Further testing for benzo-diazepines and barbiturates were negative and arterial blood gases was within the normal range as well. Troponin test (cTnT) (Roche CARDIAC Trop T Sensitive test) was positive, > 50 ng/L (tested twice) yet an urgent transthoracic echocardiogram (echo) revealed no wall hypokinesis. Within the next few minutes the patient developed a remarkable alteration in mental status, including confusion and lethargy. An emergency head computerized tomography (CT) scan was performed but no brain pathology was diagnosed. A lumbar puncture would have been the next step in the management but the blood tests results revealed remarkable thrombocytopenia (PLTs 5.000/μL). Normocytic anemia with schistocytes was additionally confirmed by a peripheral blood smear (Figure 2).

Blood biochemistry tests were compatible with haemolysis (Table 1). The laboratory findings combined with the clinical presentation of the patient set the diagnosis of Thrombotic Thrombocytopenic Purpura (TTP). Methylprednisolone 1mg/kg was administered and two units of fresh frozen plasma were transfused before the patient was urgently transferred to the Hematology Department of a Third Grade Hospital for therapeutic plasma exchange. There, the diagnosis of TTP with severe ADAMTS13 deficiency was confirmed by measurement of ADAMTS13 activity and the patient was discharged after two months of continuous hospitalization and multiple plasmapheresis sessions without permanent neurological deficits or renal injury.

Table 1
Hematology and biochemistry tests on admission

Total blood count and serum parameters		
Hematocrit (Hct)	%	20 (42-47)
Hemoglobin (Hgb)	g/dL	6.6 (13.5-16.5)
Reticulocytes	%	26.4 (0.5-2.5)
MCV	fL	97.6 (80-98)
MCH	pg	32.2 (27-33)
RDW	%	27.3 (9-11)
Platelets (PLT)	x103/ μ L	13 (150-450)
Urea (UR)	mg/dL	35 (20-40)
Creatinine (CR)	mg/dL	0.94 (0.5-1.1)
(Potassium) K	mmol/L	3.7 (3.3-5.2)
(Sodium) Na	mmol/L	140 (135-145)
Lactate Dehydrogenase (LDH)	IU/L	1455 (55-100)
Total Bilirubin (TBIL)	mg/dL	3.06 (0.2-1.2)
Indirect Bilirubin (IBIL)	mg/dL	2.31
D-Dimers	μ g/mL	1.87 (<0.5)
Fibrinogen (FIB)	mg/dL	207 (150-400)



Figure 1. The patient's ECG shows sinus tachycardia without ST abnormalities.

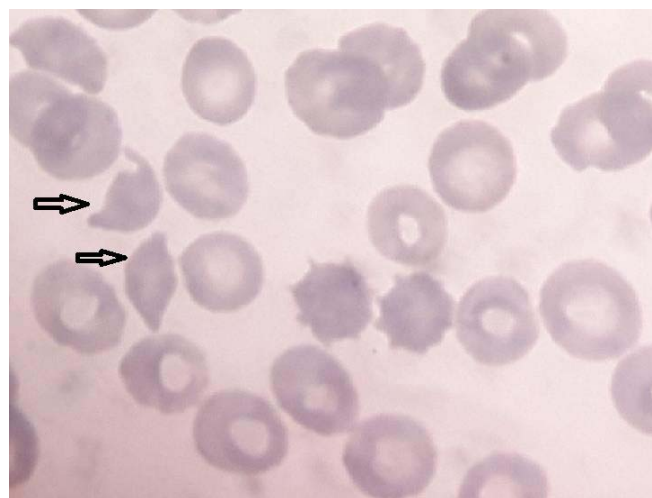


Figure 2. Peripheral blood smear of the patient. The presence of schistocytes (arrows) on a blood smear is the morphologic hallmark of the disease (May-Grunwald-Giemsa $\times 100$, photo enlarged).

DISCUSSION

Thrombotic microangiopathies (TMAs) are a family of pathological conditions characterized by diffuse microvascular occlusion by platelet thrombi and partial or complete obstruction of the vessel lumina, which result in thrombocytopenia, microangiopathic hemolytic anemia and ischemic end-organ damage. Endothelial injury is the key step leading to microcirculation thrombosis and this may be ignited by a variety of reasons, namely bacterial toxins, drugs, genetic or autoantibody-induced abnormal complement activation, procoagulants (e.g. antiphospholipid antibodies) or severe deficiency of anticoagulants (eg ADAMTS13 defects) [2]. A malignancy-associated form of TMAs has also been described and it is probably related to chemo-therapy, antibodies and immunotoxin therapy or is a manifestation of cancer itself [3].

The laboratory findings are similar in all TMAs. A complete blood count demonstrates anemia and thrombocytopenia; the biochemistry results show increased direct bilirubin and lactate dehydrogenase. The coagulation testing may reveal slightly elevated D-Dimer and red blood cell fragments are present in the peripheral smear. The history and the clinical presentation of the patient should give the initial direction in the diagnostic evaluation. The differential diagnosis of other microangiopathy is vital as it usually triggers treatment.

Table 2 summarizes the differential diagnosis between TTP, Idiopathic Thrombotic Purpura (ITP) and other hemolytic syndromes.

Table 2
Differential Diagnosis between TTP and other hemolytic syndromes. (HUS: Hemolytic-uremic syndrome, DIC: Disseminated intravascular coagulation)

	TTP	HUS	DIC
Neurological Involvement	+++	+/-	+/-
Renal Involvement	+	+++	+/-
Liver Involvement	+/-	+/-	+/-
Hemolysis	+++	++	+
Schistocytes	++	++	++
Thrombocytopenia	+++	++	++
Prothrombin Time (PT)	↔/↑	↔	↑↑↑
Partial Thromboplastin Time (PTT)	↔/↑	↔	↑↑↑
Fibrinogen	↔	↔	↓
Fibrin Degradation	↔	↔	↑↑↑
D-Dimers	↔	↔	↑↑↑

TTP is characterized by the “classic pentad” fever, thrombocytopenia, microangiopathic hemolytic anemia, renal dysfunction and neurologic symptoms but this is seen only in 1/3 of the patients [4]. The

symptoms are of acute or subacute onset; the neurologic abnormalities are usually prominent and may vary from comma, seizures and stroke to confusion or headache [5]. The 30-year-old patient that we confronted presented with dizziness, followed by acute neurological deterioration which rapidly (less than 3 hours) resulted in dysphasia, confusion and disorientation.

Cardiac involvement is not included in the diagnostic criteria of TTP; yet coronary heart thrombosis has been established in many autopsy studies [6]. Despite the fact that acute myocardial infarction (AMI) is reported to be the most common cardiac manifestation of TTP [12], TTP presenting primarily with cardiac symptoms has rarely been reported [7]. It is suggested that small vessel occlusion by platelet thrombi results in hypoxia which is aggravated by the anemia – induced elevated oxygen demands of the heart. This pathophysiologic mechanism may result in myocardial ischemia or acute myocardial injury [8]. Since TTP is a disease of microvessels, it is not surprising that there are reports of TTP and acute myocardial infarction with angiographically normal coronary arteries [9].

Apart from ischemia, involvement of the cardiac conduction system is thought to be a cause of sudden death in patients with TTP [10]. Increased troponin I is associated with fatal outcome in acquired thrombotic thrombocytopenic purpura [11] and cardiac troponin-I level on admission is proposed to be a reliable marker of cardiac involvement in patients with acquired TTP, allowing the identification of patients with a more aggressive presentation and a higher risk for death and refractoriness [12]. The chest pain in the presented patient was the leading symptom and along with the elevated troponin levels was suggestive for cardiac involvement.

The inability to dynamically monitor Tn levels, due to the urgent relocation of the patient to a special hematology department, could not contribute to the firm diagnosis of myocardial ischemia. A Coronary Computed Tomography Angiography (CCTA) could probably improve the diagnostic accuracy if an occlusion of a larger coronary vessel is suspected; nonetheless the experience of CCTA is limited in our center. Management of such cardiac complications is a real challenge. Antiplatelet agents are contraindicated when thrombocytopenia is severe (PLTs < 50 × 10⁹/L); furthermore there are reports that Clopidogrel might be a trigger for TTP itself [13]. Finally, cardiac catheterization is discouraged due to the possible coexisting renal

injury and the severe thrombocytopenia [14]. Plasma exchange is the most important acute intervention and it should be immediately initiated [15] as it remains the therapy of [4]. Our patient was transferred to a special hematology department in less than 3 hours from his admission.

Adjuvant intravenous steroid therapy takes place in TTP treatment especially in patients in whom the etiology is unclear [4].

CONCLUSION

In conclusion, TTP is a rare and potentially fatal disorder which may present atypically with early cardiac involvement. It is very important to integrate the clinical and laboratory data, set the diagnosis and approach the patient in a multi-disciplinary way.

Conflict of interest: None declared.

Purpura trombotică trombocitopenică (TTP) este o microangiopatie datorată scăderii nivelurilor sau chiar absenței moleculei ADAMTS13 ("a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13"). TTP este caracterizată de pentada clasică reprezentată de trombocitopenie, hemoliză, febră, insuficiență renală și deficite neurologice. Totuși pacienții pot avea manifestări atipice datorate formării cheagurilor în cadrul microcirculației. Prezentăm cazul unui pacient tânăr cu durere retrosternală și leziune miocardică ca primă formă de manifestare a TTP.

Correspondence to: Stamatis S Papadatos, M.D, 3rd Department of Internal Medicine, National and Kapodistrian University of Athens School of Medicine, Sotiria General Hospital, 152 Mesogeion Ave, Athens, Greece; Tel.: +306973750882
E-mail: stamspap@gmail.com

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