Case Study: An Unusual Cause of Right Upper Quadrant Pain

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Case Study

Background and Clinical Importance: Common causes of RUQ pain include hepatobiliary diseases, pancreatitis, and peptic ulcer disease, and occasionally myocardial ischemia or right lower lobe pneumonia. We report a case of a man who complained of abdominal pain who was found to have no disease within the abdominal or thoracic cavities. It is important to conduct a thorough evaluation of patients with abdominal pain so that uncommon life-threatening diseases are not missed.

Description and Methods: A 42-year-old man presented to clinic with worsening RUQ pain, constipation, and feeling unwell. No diarrhea, vomiting, or fever. No surgeries. Family history was unremarkable. The patient drinks 28 beers per week and smokes cigars and marijuana. PE revealed an uncomfortable-looking man who was alert and oriented. Vital signs: T 97.6 °F, P 105, R 14, BP 193/129, O2 98%. HEENT, neck, heart and lungs were normal. Abdomen was nontender without organomegaly. No rashes or edema. Neuro exam was physiologic.

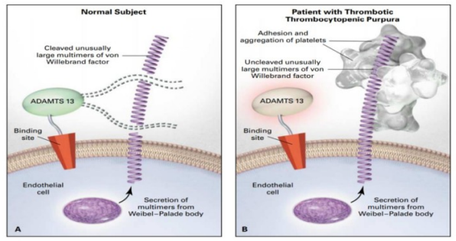
Results: He was transferred to the ED and placed on a nicardipine drip. WBC was 10.0 K (3.7-10.1) with 86% neutrophils, Hb 11.3 g/dL (13.4-16.8), Hct 31.4% (39.6-48.8), platelets 2 K (146-337). Peripheral smear 3+ schistocytes. Haptoglobin < 30 mg/dL (30-200). LDH 1746 U/L (100-190). INR 1 (0.9-1.1), PTT 30 s (24-34), D dimer > 3700 ng/mL (< 500). Na 133 mmol/L (135-145) K, Cl, CO2, glucose were normal. Ca 8.2 mg/dL (8.9-10.5). Creatinine 2.1 mg/dL (0.7-1.3), BUN 31mg/dL (7-25), eGFR 39 ml/min (>60). Total bili 11.2 mg/dL (< 1.5), direct bili 5.4 mg/dL (< 0.3), albumin 4 g/dL (3.5-5), alkaline phosphatase 74 U/L (32-126), ALT 23 U/L (10-52), AST 67 U/L (10-39), Venous pH 7.38 (7.32-7.43). Lactate 0.6 mmol/L (0.5-2.0). Creatine kinase 299 U/L (30-220). Troponins 4,000-8,000ng/dL (< 53). Urine was brown then bloody. U/A positive for protein, bilirubin, and blood, but no pyuria or bacteriuria. ECG, CXR unremarkable. Normal cardiac echo and coronary CT. No obstructive uropathy. MRI revealed a L thalamic lacunar infarct. He was thought to have thrombotic thrombocytopenic purpura (TTP) and treated empirically with IV methylprednisolone and plasma exchange.

Conclusions and Discussion: Confirmatory bloodwork revealed ADAMTS 13 activity 2% (>40) and IgG antibody against ADAMTS 13 20.8 U/ml (<12). Caplacizumab was begun. Within days, normalization was seen in platelets, LDH, haptoglobin, bilirubin, and renal function improved. TTP is a major cause of hemangiopathic hemolytic anemia in which widespread microthrombi lead to mechanical lysis of RBCs, consumption of platelets, and ischemia--which can cause stroke, TIAs, myocardial ischemia or infarction, and sometimes AKI. Yet 69% present with abdominal pain or other GI symptoms, and the median age is 40. TTP is caused by autoimmune blockade of the ADAMTS 13 enzyme, which limits the size of von Willibrand Factor (vWF) in blood vessels walls. If ADAMTS 13 is inhibited, vWF molecules are too long and cause widespread intravascular precipitation of fibrin meshwork. There are about 100 causes of acute abdominal pain, many of which are common, but it behooves clinicians to remember that sometimes "zebras" are seen.

Thrombotic Thrombocytopenic Purpura

Thrombotic thrombocytopenic purpura (TTP) is a form of microangiopathic hemolytic anemia and thrombocytopenia resulting from a **congenital or acquired deficiency of ADAMTS13**, an enzyme that cleaves von Willebrand factor (vWF).

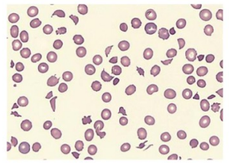
With decreased ADAMTS13 activity, multimers of vWF accumulate, causing platelet aggregation and eventual **thrombi formation**, which leads to ischemia and end-organ damage. The hemolytic anemia observed in this disorder is due to destruction of red blood cells as they pass through small vessels occluded by thrombi, producing the abnormal schistocyte structure. Thrombocytopenia is also present as platelets are consumed during thrombi formation.



Classically, TTP is characterized by a **pentad of fever, hemolytic anemia, thrombocytopenia, renal dysfunction, and neurologic dysfunction.** Neurological symptoms are commonly seen on patient presentation and those associated with TTP include headache, confusion, vertigo, focal neurologic deficits, and seizures.

Laboratory evaluation that suggests a diagnosis of TTP includes:

- **Anemia**
- **Thrombocytopenia**
- Evidence of hemolysis:
  - **Schistocytes** on peripheral smear
  - Increased unconjugated bilirubin
  - Increased LDH
  - Increased reticulocyte count
  - Decreased haptoglobin
- Evidence of acute kidney injury



More specific lab work to help confirm the diagnosis of TTP include measuring ADAMTS13 activity, ADAMTS13 inhibitor, and antibodies against ADAMTS13**. An ADAMTS13 activity level less that 10% is highly indicative of TTP.**

TTP is considered a **hematological emergency**, as microthrombi in the small vessels can lead to multiorgan failure and the mortality rate of untreated TTP is about 90%. **Immediate plasma exchange is necessary for treatment** to remove ultra large vWF-platelet complexes and autoantibodies against ADAMTS13, as well as replace ADAMTS13 by infusing fresh frozen plasma. **High-dose corticosteroids** are used in conjunction with plasma exchanges. Therapeutic response is measured by clinical response and monitoring labs.

Other treatments of TTP used in conjunction with plasma exchanges include splenectomy, cyclosporine, cyclophosphamide, vincristine, rituximab, and caplacizumab.

"Thrombotic thrombocytopenic purpura and its diagnosis"

Journal of Thrombosis and Haemostasis, 2005
A. Veyradier, D. Meyer

This review article discusses the difficulties providers face diagnosing TTP and how they must rely on several clinical and biological symptoms to exclude other differential diagnoses and provide urgent treatment to patients.

An acute episode of TTP is difficult to diagnose based on the variety of non-specific symptoms that are associated with the disease, as seen below.

Table 1 Main clinical and standard biological features of TTP

Clinical/biological features	Approximate prevalence (%)
Presenting symptoms	
Headache, confusion	60
Digestive symptoms (nausea, vomiting, diarrhea, abdominal pain)	50
Weakness, fever	20
Bleeding symptoms (purpura, ecchymosis, menorrhagia)	20
Neurologic abnormalities	
Mild (headache, confusion)	25
Severe (coma, focal abnormalities, seizures)	50
Renal abnormalities	
Mild (proteinuria, renal insufficiency)	40
Severe (acute renal insufficiency)	5
Hematologic abnormalities	
Platelet count <20 giga L^{-1}	95
Hemoglobin <8 g L^{-1}	80

Per this review, about 50% of patients with TTP present with digestive symptoms, including abdominal pain, nausea, vomiting, and diarrhea, like the patient in the case study. This demonstrates the importance on not solely depending on the classic pentad of TTP symptoms and only considering neurological symptoms to point to a diagnosis. Keeping TTP on your differential diagnosis list in abdominal pain symptoms is important to prevent mortality from a missed diagnosis.

"Thrombotic thrombocytopenic purpura (TTP) presenting as pancreatitis"

The Journal of Emergency Medicine, 2003
A. Muniz, R. Barbee

This case report describes a 20-year-old male who presented with two days of epigastric pain, nausea, and vomiting.

Due to the history of vomiting and an elevated lipase on lab evaluation, the patient was presumed to have pancreatitis, and evaluation could have stopped there.

This report describes how the classic pentad is seen in less than half of TTP cases and clinical presentation can be varied, especially in early stages of the disease. This was the case of the reported patient, who developed more classic features of the pentad of TTP after his initial presentation, which included periods of confusion and lethargy. Lab evaluation confirmed the presence of anemia with increased LDH and thrombocytopenia, and immediate plasma exchange was performed. Throughout his hospital stay, a drop in his hemoglobin was observed and mild renal dysfunction was evident. He continued daily plasma exchanges until his condition stabilized.

This case reinforces the importance of maintaining a high index of suspicion for TTP, even in the absence of the complete clinical pentad, and underscores the need for timely diagnosis and intervention.

Conclusions & Recommendations

It is essential to maintain a broad differential diagnosis when evaluating patients with abdominal pain, as serious conditions like thrombotic thrombocytopenic purpura (TTP) may present atypically. As highlighted, TTP does not always manifest with the classic pentad of symptoms commonly emphasized in medical training, and failure to promptly recognize and treat this condition can lead to high mortality.
Developing strong clinical reasoning skills—including a thorough assessment of patient history, accurate interpretation of diagnostic tests, and consideration of rare but critical diagnoses—is vital for healthcare providers. These competencies enable timely identification and management of potentially life-threatening conditions, ultimately improving patient outcomes

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