IS IT MORE THAN AN INFECTION?

Photos are for illustration purposes only.

Infections like COVID may be a trigger for atypical-HUS, a rare disease[1,2]

Thrombotic microangiopathy (TMA) can be associated with various triggers, like infections, that may accelerate the activation of the complement system[1]

Patients with infectious diseases can present with TMA[1]

Persistence of TMA, despite treatment of an ongoing infection like COVID, may suggest atypical-HUS, a rare disease[a,3,4]

[a]The incidence of atypical-HUS is estimated to range from 0.35 to 2 per million.[5,6]

Is it more than COVID?

This is José's story[7]

Adapted from an actual patient case. To ensure privacy, patient has been de-identified.

Initial Presentation

- José is a 35-year-old male who tested positive for COVID
- Patient displayed no symptoms of respiratory tract infection
- He visited his primary care physician due to persistent vomiting, diarrhea, and loss of taste; he was prescribed rest and increased fluid intake
- After worsening GI distress, he went to the emergency room (ER)
- In the ER, patient was alert, responsive, afebrile with normal blood pressure; he was in acute distress from vomiting and diarrhea
- His medical history was unremarkable

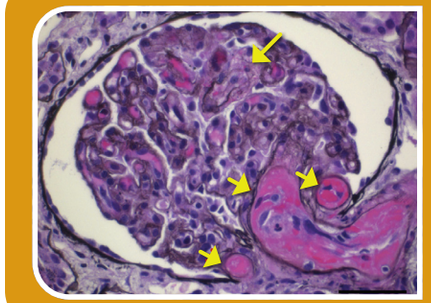
INITIAL SELECT LAB VALUES	
Hemoglobin (g/dL) (reference range: 14-18 g/dL)[8]	5.5
Platelet count (x 10^9/L) (reference range: 150-350 x 10^9/L)[8]	28
LDH (U/L) (reference range: 100-200 U/L)[8]	2066
Serum creatinine (mg/dL) (reference range: 0.6-1.2 mg/dL)[8]	5.6
Schistocytes on blood smear	Yes

Clinical Progression

- During the first days of admission, José received 5 packed **red blood cell transfusions** due to ongoing hemolysis
- The detection of **schistocytes** on a peripheral blood smear confirmed TMA
- An **urgent ADAMTS13 test** was ordered

Diagnosis

- A **renal biopsy** was performed on day 9 after admission confirming a TMA
- The **diagnosis of atypical-HUS** was made after exclusion of ADAMTS13 deficiency



Renal biopsy specimen from patient. Representative micrograph of thrombotic microangiopathy revealing several glomerular thrombi (arrowheads). Mesangiolysis with fibrillar appearance of mesangial tissue containing red blood cell fragments can also be seen (arrow).[7]

Management

- Patient was started on appropriate clinical **management for atypical-HUS**

Does your patient with COVID also have TMA?

- TMA can be caused by infections and/or by one of several disorders, including atypical-HUS[9-11]
- Potential types of infection that may cause TMA include HIV, sepsis, COVID, and influenza A[2,3,7,10]

WHEN SHOULD YOU SUSPECT ATYPICAL-HUS IN A PATIENT WITH A CONFIRMED COVID INFECTION?[7]

Platelet count	<150,000/µl or ≥25% decreased from baseline
Microangiopathic hemolysis	Schistocytes, elevated lactate dehydrogenase (LDH), decreased haptoglobin, decreased hemoglobin and hematocrit
Organ involvement	Renal impairment including high blood pressure and/or neurological symptoms (e.g., confusion, seizures) and/or gastrointestinal symptoms (diarrhea, abdominal pain, gastroenteritis)
Rule out TTP and STEC-HUS[1]	ADAMTS13 activity >10% Shiga toxin–producing *E. coli* (STEC) negative

Ideally draw ADAMTS13 activity test prior to initiating plasma exchange/plasma infusion (PE/PI)[1]

When treating COVID and a patient presents with persistent TMA, consider a differential diagnosis for atypical-HUS[7,9-11]

Differential diagnosis for TMAs: atypical-HUS, TTP, and STEC-HUS

Clinical signs indicating TMAs[1]

Thrombocytopenia	AND	Microangiopathic Hemolysis
Platelet count <150 x 10^9/L or >25% decrease from baseline		Schistocytes and/or Elevated LDH and/or Decreased haptoglobin and/or Decreased hemoglobin

Plus 1 or more of the following

Common Symptoms

Neurological Symptoms

Confusion and/or
Seizures and/or
Stroke and/or
Other cerebral abnormalities

Renal Impairment

Elevated creatinine level and/or
Decreased eGFR and/or
Elevated blood pressure and/or
Abnormal urinalysis results

GI Symptoms

Diarrhea ± blood and/or
Nausea/vomiting and/or
Abdominal pain and/or
Gastroenteritis/pancreatitis

Other Symptoms

CV Symptoms

MI and/or
Hypertension and/or
Arterial stenosis and/or
Peripheral gangrene

Pulmonary Symptoms

Dyspnea and/or
Pulmonary hemorrhage and/or
Pulmonary edema

Visual Symptoms

Pain and blurred vision and/or
Retinal vessel occlusion and/or
Ocular hemorrhage

Evaluate ADAMTS13 activity and Shiga toxin/EHEC test[a,1]

While ADAMTS13 results are awaited, a platelet count >30 x 10^9/L and/or SCr >1.7 to 2.3 mg/dL almost eliminates a diagnosis of severe ADAMTS13 deficiency (TTP)

≤5%[b] ADAMTS13 activity	>5% ADAMTS13 activity	Shiga toxin/ EHEC positive
TTP	Atypical-HUS	STEC-HUS

[a]Shiga-toxin/EHEC test is warranted in history/presence of GI. [b]Range found in published data is <5%-10%.

ADAMTS13, a disintegrin and metalloproteinase with thrombospondin type 1 motif member 13; CV, cardiovascular; eGFR, estimated glomerular filtration rate; EHEC, enterohemorrhagic *Escherichia coli;* HUS, hemolytic uremic syndrome; LDH, lactate dehydrogenase; MI, myocardial infarction; SCr, serum creatinine; STEC, Shiga toxin–producing *E. coli;* TMAs, thrombotic microangiopathies; TTP, thrombotic thrombocytopenic purpura.

Infections like COVID may be a trigger for atypical-HUS, a rare disease[1,2]

Several case reports of COVID-associated TMA and atypical-HUS in patients aged 16 months to 69 years have been published in hematology, oncology, and nephrology peer-reviewed medical journals[2,7,12-13]

When treating COVID and a patient presents with persistent TMA, consider a differential diagnosis for atypical-HUS[9-11]

Contact Alexion

For more information on atypical-HUS, connect with a live representative by calling 833-551-2539 or emailing alexionconnectteam@alexion.com.

References:

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