

Introduction

- Hemolytic uremic syndrome (HUS) is clinically diagnosed from the triad of microangiopathic hemolytic anemia, thrombocytopenia, and renal injury.
- So-called "typical" HUS (Shiga toxin or ST-HUS) is most often caused by Shiga toxin-producing *E. coli* O157:H7 infection¹.
- HUS as a complication of *Clostridioides difficile* infection (CDI) is rare, with only 11 cases reported in adults.
- We present a case of a patient presenting with the classic triad of HUS, which was found to be due to non-complement mediated typical HUS from CDI.

Case Presentation

- A 43-year-old female with a past medical history of non-alcoholic steatohepatitis (NASH) cirrhosis was found unconscious with a 3-day history of loose bloody bowel movements, diaphoresis, and chills.
- Initial blood pressure was 186/97 mmHg and pulse of 110. Lactate dehydrogenase was 1223 U/L, creatinine 6.5 mg/dL, haptoglobin <10 mg/dL, platelets 98 K/uL, and there were schistocytes on peripheral blood smear.
- ADAMTS13 protease level came back normal at 0.95 IU/mL and inhibitor level undetectable at <0.4 BEU, suggesting the diagnosis of HUS. The patient's complement levels were normal (C3=119 mg/dL, C4=26 mg/dL). Renal biopsy showed thrombotic microangiopathy without fibrosis. Stool pathogen panel was negative for Shiga toxin but positive for *C.diff*. The patient was started on oral vancomycin.
- After complement-mediated HUS serum and plasma panel labs and genetic susceptibility panel labs returned negative for complement-mediated HUS, the leading diagnosis was so-called "typical" HUS.
- Thrombocytopenia and anemia improved dramatically after only a few sessions of plasmapheresis. After vancomycin treatment, the patient's symptoms completely resolved.

Discussion

- Our patient presented with the classic triad of thrombocytopenia, hemolytic anemia and renal failure with a renal biopsy showing thrombotic microangiopathy, confirming the diagnosis of HUS.
- A unique aspect of the case was typical HUS in an adult that was caused by an organism *not* commonly associated with HUS.
- It is unknown how CDI can trigger HUS in the absence of Shiga toxin. One theory is that like Shiga toxin, the toxins A and B of *C.diff* can induce apoptosis of the colonic cell membrane and release cytokines into circulation inducing a pro-inflammatory and hypercoagulable state^{1,3,4}.

Conclusion

- Our case was the only one to confirm the diagnosis of HUS by renal biopsy with further classification of "typical" HUS with negative advanced complement and genetic studies
- *C.diff* is a rare cause of HUS. Proper treatment can lead to complete resolution without recurrence.

References

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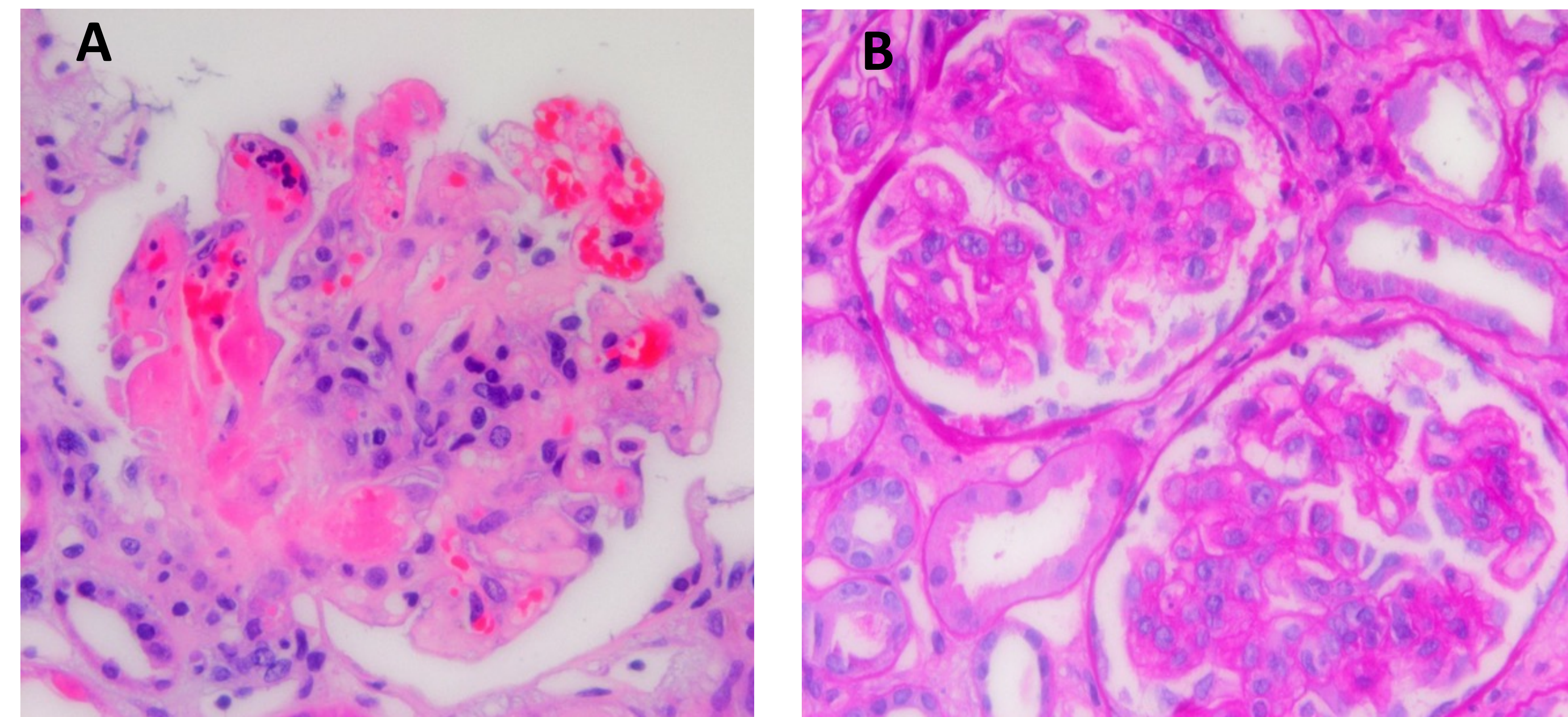


Figure 1. Kidney biopsy showed: (A) fibrin thrombi and neutrophils within the capillary loops of the glomeruli. RBC fragmentation is evident within capillary loops and the mesangium. (B) Mesangiolytic and endothelial cell swelling.

Case	Age	Sex	Diarrhea	Confusion	Dialysis	Plasmapheresis	Pharmaceutical Intervention
Mogyorosi 1997	51	Female	Non bloody	Yes	No	No	Oral and rectal vancomycin
Mbonu, 2003	46	Female	Bloody non	No	Yes	Yes	Oral metronidazole
Kalmanovich 2012	73	Female	bloody	no	Yes	No	IV metronidazole and steroids
Keshkar-Jahromi, 2012	62	Female	Non bloody	Yes	Yes	yes	Intravenous metronidazole and steroids
Alvarado 2014	29	Female	bloody non	no	No	No	Oral vancomycin and steroids
Alvarado 2014	52	Female	bloody	yes	No	yes	Oral metronidazole IV metronidazole, Oral vancomycin, eculizumab
Alvarado 2014	63	Female	bloody non	yes	No	yes	Plasmapheresis, Oral vancomycin, IV metronidazole, eculizumab
Inglis 2018	46	Male	bloody	no	Yes	yes	IV metronidazole, Oral vancomycin, eculizumab
Khurshid 2020	60	Female	bloody	No	Yes	yes	IV metronidazole, Oral vancomycin, eculizumab
Wadehra 2021	65	Male	Non bloody	No	Yes	No	Oral vancomycin, steroids
Moulton 2021	21	Female	Bloody	Yes	Yes	No	IV metronidazole, oral vancomycin, eculizumab and surgery

Table 1. A review of the medical literature revealed 11 previously reported cases of hemolytic uremic syndrome caused by CDI.