Successful treatment of cytokine storm in Shiga-toxin producing E. coli dysentery

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Background and Significance

Most cases of severe Shiga-toxin producing E. coli (STEC) dysentery typically do not present with fever (1). Our case involves a patient found to have Shiga-toxin 1 presence in the stool, who presented with high fever and rapid rise in pro-inflammatory biomarkers. Our patient was given steroid therapy with resolution of fever and improvement in clinical condition. This report explores the hypothesis that shiga-toxin mediated rise in pro-inflammatory cytokines in some cases lead to cytokine storm, which can be treated successfully with steroid therapy.

Hospital Course

This is a unique case of a 38-year-old Caucasian female with no significant medical history who presented to the hospital with complaint of 3 days of abdominal pain, nausea/vomiting, dark red formed stool, and fever (highest body temperature 102°F) at home before arrival). She reported eating meatloaf with her daughter two days before symptom onset, and daughter was reported to be ill as well. Upon initial exam, was hypotensive and tachycardic with lactate of 4.2 mmol/L. Stool guaiac test was positive. Significant lab values include creatinine 3.39 mg/dL (baseline normal), hemoglobin of 11.9 g/dL and platelet count of 50 k/mm^3. CT abdomen and pelvis showed no evidence of enterocolitis. Patient was admitted for severe sepsis with hypotension due to possible gastrointestinal source and started on broad spectrum antibiotics.

Initial blood cultures, respiratory viral panel, hepatitis panel, and HIV testing were all negative. Patient again developed high fevers on day 3 of admission. Stool sample given on day 3 of admission when cultured detected Shiga-toxin 1, leading to diagnosis of Shiga-toxin producing E. coli dysentery. Antibiotics were stopped at this point as they are not indicated in the treatment of STEC, and patient was continued on IV fluid resuscitation and blood product transfusion. The patient's fever curve continued to worsen, reaching body temperature of 102.9°F on day 4 of admission. The persistence of fever, along with elevation of pro-inflammatory biomarkers (lactate dehydrogenase (LDH), D-dimer, ferritin, C-reactive protein (CRP)) and evidence of multiple organ dysfunction on presentation (elevated liver enzymes, increased creatinine, elevated lactate) led to the suggestion of the immune response to the bacterial infection escalating into possible cytokine storm. IV methylprednisolone was started on day 4 of admission, which resulted in resolution of fever and significant improvement in overall condition. On day 6, patient was discharged in stable condition.

Graphics

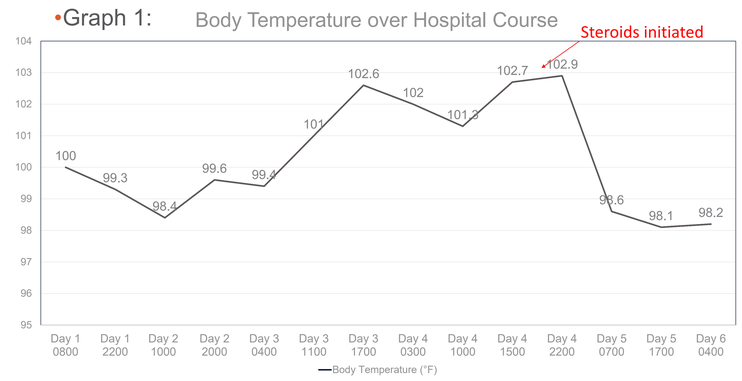

Table 1: Lab value trends during hospitalization

Lab Test	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Leukocytes (k/mm^3)	6.9	7.3	8.8	7.9	6.1	9.3
Platelet count (k/mm^3)	50	40	35	39	63	160
Creatinine (mg/dL)	3.39	2.50	1.64	1.43	1.00	0.90
Ferritin (ng/mL)	4216				1249	657
Lactate dehydrogenase (unit/L)	661	715			514	432
D-dimer (ng/mL)		55271		18774	5158	3202
C-reactive protein (mg/dL)		26.9			6.02	2.74
Aspartate transaminase (unit/L)	145	120	126	120	115	52
Alanine transaminase (unit/L)	81	58	50	52	61	44

Discussion

- "Cytokine storm" – systemic inflammatory syndrome that can arise in association with acute bacterial, iatrogenic, or autoimmune illness.
  - Thought to be an immune response which loses its negative feedback mechanism ("feed-forward" effect) allowing for an exponential rise in cytokinemia and hyperferritinemia, leading to multi-organ failure (2).
- Studies have shown that both shiga-toxins 1 and 2 are able to cause secretion of pro-inflammatory cytokines from monocytes and macrophages at the vascular endothelium in vitro (3).
- Significant elevation in multiple inflammatory biomarkers, as well as evidence of hepatic and renal injury (Table 1) led to the suggestion that the patient's natural immune response to the bacterial infection became that of a cytokine storm, for which steroid therapy was successful.

Limitations

Other diagnoses which can include steroids in their treatment protocol were not fully ruled out, which includes hemolytic-uremic syndrome (HUS) and hemophagocytic lymphohistiocytosis (HLH). Some but not all diagnostic criteria for HUS or HLH was appropriately met during stay (4). Unfortunately, the patient was unable to be reached after discharge to inquire about outpatient follow up testing such as bone marrow biopsy or gene testing.

Conclusion

Our case outlines an atypical presentation of STEC dysentery – presenting with fever as evidence of systemic inflammation. The outcome of this case suggests clinicians to recognize the possibility of cytokine storm in the setting of STEC dysentery, and in this scenario to consider utilization of steroid therapy.

References

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