

# The Use of Epsilon Aminocaproic Acid in a Case of Massive Hemorrhage from Cytomegalovirus Colitis in a Patient with Multiple Myeloma Treated with Bortezomib

by Steven D. Deas, Marc D. Hopkins, Louis M. Varner

**Epsilon aminocaproic acid blocks fibrinolysis by binding competitively to plasminogen and preventing binding to fibrin. It has been primarily used following thoracic surgery as an adjunctive therapy to help treat persistent post-operative bleeding. We report a 56-year-old patient who developed lower gastrointestinal bleeding from presumed cytomegalovirus colitis after treatment with bortezomib and required transfusion of multiple blood products. After he was determined to not be a candidate for colectomy because of high surgical risk, he was treated with epsilon aminocaproic acid, which led to hemostasis and prevented any further transfusion requirement. This is the first reported case of the use of epsilon aminocaproic acid for the treatment of bleeding from a lower gastrointestinal source.**

## INTRODUCTION

**E**psilon aminocaproic acid (EACA) blocks fibrinolysis by binding competitively to plasminogen and preventing binding to fibrin. It has been primarily used following thoracic surgery as an adjunctive therapy to help treat persistent post-operative bleeding.<sup>1</sup> We report a patient with lower gastrointestinal bleeding from cytomegalovirus (CMV) colitis who was treated successfully with EACA.

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## Case Report

A 56-year-old African American man presented to our medical center with a single episode of hematochezia associated with diffuse, cramping abdominal pain. The patient, who had been diagnosed with multiple myeloma several months before, had received two rounds of bortezomib and dexamethasone induction chemotherapy, and was hemodialysis dependent because of myeloma cast nephropathy. In addition to chemotherapy, he had received a single dose of radiation therapy to a lumbar vertebral lesion.

The patient's medical history was otherwise significant for diabetes mellitus, hypertension and hypothyroidism. He was on insulin and antihypertensive

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medications as well as acyclovir and fluconazole for infectious prophylaxis while on chemotherapy. He reported no drug allergies. Though he had a history of heavy alcohol use over a period of decades, he quit drinking after he was diagnosed with myeloma. He denied tobacco or illicit drug use.

On presentation, he was tachycardic but normotensive and his physical exam was remarkable only for the presence of bright red blood in the rectal vault. He was noted to have a hemoglobin level of 7.5g/dL (from a baseline of 10g/dL). His leukocyte count was 10,700 with a neutrophilic predominance and his platelet count was 241,000. He had a normal coagulation profile, blood urea nitrogen and transaminase levels. His alkaline phosphatase was mildly elevated, but stable over time.

After admission to the medical ward, he had several more episodes of hematochezia, which required transfusion of two units of packed red blood cells. Colonoscopy on the following day revealed discontinuous areas of non-bleeding ulcerated mucosa at the splenic flexure, the transverse colon and the ascending colon. The ulcers appeared superficial and irregular with normal intervening mucosa.

The differential diagnosis for hematochezia with ulcerated mucosa included infectious and ischemic colitis as well as inflammatory bowel disease. He had no history of previous bleeding or abdominal pain to suggest undiagnosed inflammatory bowel disease, and though he was on hemodialysis, had no significant hypotension to suggest ischemic colitis. He had received a single treatment of radiation therapy to a lumbar spine lesion in recent weeks, but the pattern of his disease was not consistent with radiation-induced injury to the gastrointestinal tract. *Clostridium difficile* toxin evaluation was negative. Therefore, due to the endoscopic appearance of the lesions, as well as his immunocompromised state, viral etiology was suspected.

Multiple biopsies were obtained and revealed marked acute and chronic inflammation with granulation tissue. Within the granulation tissue were a number of cells with atypical cytologic features including nuclear pleomorphism, irregular nuclear contours and nuclear hyperchromasia. Rare cells showed putative intranuclear inclusions. Though immunohistochemical studies for cytomegalovirus failed to highlight biopsied tissue, the lesions were highly suspicious for cytomegalovirus

(CMV) colitis and the patient was found to be CMV IgG positive. He was treated empirically with intravenous gancyclovir. CMV colitis often develops as a result of reactivation during immune suppression, but interestingly has never before been reported as an adverse effect of bortezomib therapy.

There was no active bleeding at the time of colonoscopy, however the patient developed repeated episodes of hematochezia the following day and ultimately required transfer to the intensive care unit and multiple transfusions of blood and blood products. Transfusion requirement eventually came to a total of fifteen units of packed red blood cells as well as multiple units of fresh frozen plasma and platelets. The surgical consultant felt that total colectomy carried a high risk in this patient with multiple co-morbid conditions and recommended supportive care and continued treatment with gancyclovir, while reserving colectomy as a last therapeutic option.

In an effort to limit blood product transfusions, he was treated with epsilon aminocaproic acid (EACA) which was dosed intravenously at 4 grams every twelve hours. On days of dialysis, it was dosed following the hemodialysis session. Following the initiation of EACA therapy, there were no further episodes of hematochezia for the remainder of his hospital course. EACA was discontinued and the patient was monitored for three days prior to discharge.

On the night after discharge, he experienced recurrent rectal bleeding and was readmitted. EACA was restarted and hematochezia improved. Repeat colonoscopy showed non-bleeding ulcerated mucosa throughout the entire colon which was improved from prior endoscopy as well as an actively bleeding ulceration in the proximal ascending colon with a bleeding vessel which was endoscopically treated with an injection of epinephrine and hemostatic clipping. Bleeding did not recur and he was discharged home.

### DISCUSSION

Epsilon aminocaproic acid binds competitively to plasminogen, blocking the binding of plasminogen to fibrin and subsequent conversion to plasmin, effectively inhibiting fibrinolysis. Adverse effects reported with EACA use include thrombosis, myalgia and myopathy and intrarenal obstruction from ureteral clots or glomerular capillary thrombosis. It is contraindicated for use in patients with disseminated intravascular

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coagulation or an active intravascular thrombosis.

In a recent Cochrane review of 16 trials in a total of 1035 surgical patients, it has been shown to reduce the need for allogeneic blood transfusions in the perioperative period, especially during cardiac surgery. In cardiac surgery, there also appeared to be a significant decrease in perioperative blood loss. While there was no significant improvement in mortality, there was no significant increase in rate of occurrence of myocardial infarction, stroke, or thromboembolism.<sup>2</sup> EACA has also been used successfully in the treatment of hemorrhage following complicated dental extractions,<sup>3</sup> in patients with aneurysmal subarachnoid hemorrhage,<sup>5</sup> recurrent epistaxis due to hereditary hemorrhagic telangiectasia,<sup>5</sup> and in traumatic hyphema.<sup>6</sup>

The use of oral EACA in radiation-induced hemorrhagic gastritis has been described in a single case report,<sup>8</sup> but until now there are no reported cases describing the use of EACA in hemorrhage from a lower gastrointestinal source. In patients with diffuse hemorrhagic colitis, in which endoscopic therapy is not adequate and surgery is not a preferred option, treatment with EACA may be an additional treatment strategy to reduce the need for the transfusion of blood and blood products. Further study is needed to determine the true efficacy and safety of EACA in gastrointestinal hemorrhage. ■

**The opinions or assertions herein are the private views of the authors and are not to be construed as reflecting the views of the United States Air Force or the Department of Defense.**

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