Elective proctocolectomy to facilitate treatment of Cerebral Venous Thrombosis (CVT) in Ulcerative Colitis (UC) complicated by gastrointestinal hemorrhage: A case report

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Abstract

Ulcerative colitis (UC) is an autoimmune inflammatory bowel disease affecting the rectum and lower gastrointestinal tract. Cerebral venous thrombosis (CVT) is a relatively rare complication of UC with risk estimated to be 1.3% to 7.5%. Anticoagulation is the primary treatment of CVT. Unfractionated heparin or low molecular weight heparin (LMWH) are used as first line therapy, and patients often require long term anticoagulation. Here we report a case of a 71-year-old female with a known diagnosis of UC who developed CVT complicated by severe gastrointestinal bleeding that was unresponsive to angiographic embolization. The patient ultimately required proctocolectomy to facilitate continued anticoagulation. To our knowledge, this is the first reported case of urgent proctocolectomy to allow a patient with UC and CVT to receive therapeutic anticoagulation.

Keywords: ulcerative colitis, cerebral venous thrombosis, urgent proctocolectomy

Introduction

Ulcerative colitis (UC) is an autoimmune inflammatory bowel disease affecting anywhere from 37.5 to 238 per 100000 people in North America, with increasing incidences in developed countries [1]. This type of inflammatory bowel disease (IBD) is characterized by diffuse inflammation of the rectal and colonic mucosa, resulting in bloody diarrhea, abdominal pain and tenesmus [2]. Cerebral venous thrombosis (CVT) is a relatively rare complication of UC, occurring between 1.3% to 7.5%. [3,4] CVT typically presents with a variety of neurological symptoms ranging from headaches, focal neurological deficits and seizures, to coma and is thought to develop from platelet activation, activation of coagulation factors and abnormal fibrinolysis [3,5,6]. Interestingly, approximately 2% of all CVTs occur in patients with underlying IBD, including UC [7] and factors which increase the risk in this population that include anemia, thrombocytopenia, increased levels of Factor VII/VIII, and deficiency of Anti-thrombin III, Protein C and Protein S [5].

Standard initial treatment of UC includes 5-aminosalicylic acid (5-ASA) preparations, often followed by long term immunosuppressant agents or corticosteroids in refractory cases. However, 5-ASA treatment fails to induce remission in more than 50% of patients, necessitating a possible colectomy [8]. Nearly 16% of UC patients will need colectomy in the first 10 years of diagnosis [9], which itself can be complicated by venous thromboembolism (VTE) [10]. Importantly, although colectomy for the treatment of chronic UC is commonly utilized, we present a unique case of colectomy as a means to continue anticoagulation in the setting of CVT.

Case Report

A 71-year-old female with a known diagnosis of UC presented to the Emergency Department with a one-week history of bloody diarrhea, decreased oral intake, and progressive confusion. She had right hemiparesis over the preceding evening and a stroke evaluation was initiated. Non-contrasted head CT revealed a subcortical left fronto-parietal ischemic infarction [Figure 1]. As the duration of the ischemic infarction was unknown, she did not receive any intravenous thrombolytic therapy.

Shortly after admission, the patient’s neurological examination declined with new sensory deficits in the R arm and worsening of right hemiparesis. A second head CT revealed a left parietal intraparenchymal hemorrhage [Figure 2].

Due to the atypical location of the hemorrhage, an MRI brain with gadolinium and MRV were obtained which revealed CVT...
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Involving the left transverse sinus, left sigmoid sinus, extending into the left internal jugular vein (Figure 3). The patient was started on IV heparin at 12 units/kg/hr. Packed red blood cells were transfused intermittently with a goal hemoglobin greater than 7.5.

As the patient’s encephalopathy was worse than that which could be explained by her neuroimaging, a continuous EEG monitoring (cEEG) was ordered. cEEG revealed low voltage 1 Hz sharp waves originating from the left centrotemporal head region, which evolved into higher voltage 1-2 Hz spike and wave discharges involving the left hemisphere (Figure 4). Twelve such episodes were captured on cEEG without any clinical correlate, and the patient was diagnosed with non-convulsive status epilepticus.

IV lorazepam was given followed by levetiracetam and lacosamide which terminated the seizures. Over the next few hours the neurological examination continued to improve and the patient was able to follow commands. However, the patient continued to require frequent blood transfusions to treat her acute blood loss anemia in the setting of continued anticoagulation therapy with IV heparin for the CVTs.

Despite numerous blood transfusions and as the acute rectal bleeding was not abating, a CT angiogram of the abdomen and pelvis was completed and noted active contrast extravasation in the distal transverse colon. To further identify the location of the bleeding nidus, a superior mesenteric angiogram was also done which revealed active contrast extravasation from the middle colic artery supplying a loop of bowel in the distal transverse colon. The patient received coil embolization across the bleeding vessel. No active extravasation was noted at the end of the procedure. While the gastrointestinal blood loss was slowed, the patient continued to have lower GI bleeding into the following day and concern for mesenteric ischemia which warranted surgical intervention if continued anticoagulation for the patient’s CVTs due to the high clot burden was going to continue. The patient was taken for elective total proctocolectomy with end ileostomy. Pathological exam of the resected specimen revealed chronic active colitis with pseudopolyps, transmural inflammation, perforation, and serositis consistent with chronic UC. Her anemia ultimately stabilized on postoperative day one and heparin held due to thrombocytopenia. Two days later dabigatran was initiated for chronic anticoagulation in the setting of a static neurologic exam. The choice of dabigatran was based on its lower risk of GI bleeding in comparison to warfarin and the fact that it was the only direct oral anticoagulant with a reversal agent at the time. Unfortunately, the prominent right hemiparesis did not resolve. The patient was discharged to a skilled nursing facility. In neurological follow up, the patient was at home and

Figure 1. Initial CT scan of the head (without contrast). The axial image demonstrates hypodensity involving the white matter of the left frontal lobe (arrow), suggestive of ischemic stroke.

Figure 2. Second CT scan of the head (without contrast). The axial image reveals an acute intracerebral hemorrhage involving the left parietal lobe.

Figure 3. Magnetic Resonance Venogram (MRV) of the brain. Note the decreased flow through the left transverse sinus (red arrows), left sigmoid sinus (blue arrows) and absent flow through left internal jugular vein (white arrow). Normal flow through the right internal jugular vein is indicated by a green arrow for reference.
ambulating with a walker with residual, but somewhat resolved right hemiparesis.

**Discussion**

Here we present a unique case of UC complicated by CVT, which required surgical resection of the colon to facilitate anticoagulation and successful treatment of CVT. Anticoagulation treatment for CVT resulted in prominent GI bleeding and resultant acute blood loss anemia requiring numerous blood transfusions. Selective embolization of the middle colic branch artery at the level of the distal transverse colon was unable to provide adequate hemostasis. The patient was then taken for an elective proctocolectomy with end ileostomy and anticoagulation was resumed on the following day. The patient ultimately improved neurologically and did not have any further bleeding. To our knowledge, this is the first reported case of elective proctocolectomy to allow a patient with UC and CVT to receive long term anticoagulation.

Systemic thromboembolic complications can occur in up to 6% of patients with IBD, and are associated with significant morbidity [11]. The risk of venous thromboembolism in IBD is three-fold higher than that of the general population [12], as endothelial activation and impaired inhibition of coagulation are thought to cause alterations in plasma and mucosal hemostasis. Simultaneously, release of acute phase reactants and activation of the coagulation cascade, occurring secondary to inflammatory changes associated with IBD, lead to a pro-coagulant state. Despite having similar etiologies, CVT is more common in UC than Crohn’s disease [13].

As CVT is a rare entity associated with IBD and UC, but given the likelihood of severe morbidity, CVT must be considered in the UC patient. IBD patients with severe refractory headaches, visual disturbances or papilledema should be evaluated for CVT. In addition, IBD patients with seizures should be evaluated, as seizures have been reported in up to 40% of these patients [14].

Neuroimaging plays a pivotal role in diagnosis of CVT. While a non-contrasted CT scan of head is used initially to rule out other pathology such as structural lesions or intracranial bleeding [6], the gold standard for diagnosing CVT is CT venogram or Magnetic Resonance Venogram (MRV). On head CT, hyperdensity of cortical veins or dural venous sinuses are suggestive of acute CVT. MRV is usually preferred over CT venography as MRI is more sensitive at any stage of thrombosis; however, findings on MRI are dependent on the duration of time from thrombosis formation. Early signs of CVT on non-contrast MRI are the combination of absent flow voids and altered signal intensity within the dural sinuses [15].

Anticoagulation is the primary treatment of CVT. Unfractionated heparin or low molecular weight heparin (LMWH) are used as first line therapy, and patients often require long term anticoagulation, often upward of 6 months. Anticoagulation for CVT can pose a therapeutic challenge among patients presenting with ICH, which occurs secondary to venous hypertension. Anticoagulation decreases the propagation of thrombus, and thus is indicated even among patients with ICH [16-19].

The literature reports a variety of cases of CVT in IBD patients that were managed medically (Table 1). One study reported a 11-year-old boy with a three-month history of UC, who developed pseudotumor cerebri secondary to superior sagittal sinus thrombosis; the patient was treated with Heparin for 7-10 days, bridged to Warfarin for 6 months and survived.
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Table 1. CVT case reports and series.

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Years with UC</th>
<th>Presenting Signs/Symptoms</th>
<th>Medical Management</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cruz</td>
<td>29</td>
<td>6</td>
<td>Seizure and 2-week Headache</td>
<td>Heparin bridged to Warfarin for 6 months</td>
<td>Partial recovery</td>
</tr>
<tr>
<td>Cruz</td>
<td>26</td>
<td>10</td>
<td>CVT discovered on MRI post operatively after craniotomy for ICH</td>
<td>Aspirin and Enoxaparin</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>Cruz</td>
<td>32</td>
<td>1</td>
<td>Headache, encephalopathy, papilledema</td>
<td>Heparin</td>
<td>Survival without complications</td>
</tr>
<tr>
<td>Agarwal</td>
<td>39</td>
<td>10</td>
<td>Headaches was most frequent symptom</td>
<td>25 were treated with LMWH or Heparin</td>
<td>Partial recovery</td>
</tr>
<tr>
<td>Katsanos (65 patients)</td>
<td>-</td>
<td>n/a</td>
<td>Headaches was most frequent symptom</td>
<td>19 recovered completely, 1 recovered partially, 2 died from sepsis</td>
<td>Survival without complications</td>
</tr>
<tr>
<td>Defilippis (6 patients)</td>
<td>-</td>
<td>n/a</td>
<td>Long term anticoagulation</td>
<td>4 recovered 2 died (one from progressive brain infarction, one from bowel perforation</td>
<td></td>
</tr>
<tr>
<td>Diakou</td>
<td>17</td>
<td>1.5</td>
<td>Headache, encephalopathy, papilledema</td>
<td>Heparin bridged to Warfarin</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>Cognat (8 patients)</td>
<td>-</td>
<td>n/a</td>
<td>Headache, encephalopathy, papilledema</td>
<td>Heparin or LMWH</td>
<td>Complete recovery in 7, partial recovery in 1</td>
</tr>
</tbody>
</table>

Grey boxes indicate that the information was not present in the report.

without complications [20]. A small case series reports: a 29-year-old woman with a six year history of UC treated with intravascular thrombolysis followed by oral anticoagulation, a 26-year-old woman with a 10-year history of UC, generalized seizure and a 2-week headache, confirmed to be CVT, treated with intravenous heparin bridged to warfarin therapy for 6 months, and a 32-year-old woman with a one year history of UC, presented with right hemiparesis and dysphasia and was found to have a large left tempo parietal hemorrhage which required urgent craniotomy. Subsequent MRI showed left transverse sinus thrombosis, and she was treated with aspirin and enoxaparin [21]. In a survey, a 39 year old male with a 10 year history of UC presented with diarrhea and a 1 week history of headache. After diagnosis of cerebral venous thrombosis was confirmed, he was treated with heparin, resulting in resolution of the thrombus [22]. Katsanos et al reviewed 65 case reports of IBD complicated with CVT. Forty-two were affected by UC and 21 were affected by Crohn disease (CD). Twenty five patients were treated with heparin or LMWH. The study reported that 19 patients recovered completely and 2 patients died from sepsis.

Two patients developed heparin induced thrombocytopenia but none received colectomy [5]. Defilippis et al reported 6 patients with IBD (four with UC, two with CD) who developed CVT. All patients were treated with long term anticoagulation. Four patients recovered and two died. One death was secondary to bowel perforation three weeks after presentation and the second death was due to progressive brain infarction [19]. Diakou et al. [23]reported a 17-year-old boy with a 1.5-year history of UC who developed CVT. The patient was treated with heparin and bridged to warfarin with a complete recovery. In a case series by Cognat et al, eight patients with inflammatory bowel disease (two with UC, six with CD) developed CVT. All patients were treated with heparin or low-molecular-weight-heparin. Seven patients achieved full recovery with one patient achieving partial recovery [7].

Here we report an older female with chronic UC that, upon medical management of CVT, developed GI bleeding following initiation of anticoagulation. After failing to control bleeding with coil embolization, the patient received an elective colectomy followed by resumption of anticoagulation, resulting in resolution of the CVT.

Conclusion

To the best of our knowledge, this is the first case of UC complicated by CVT in literature, wherein the patient required proctocolectomy followed by anticoagulation, resulting in a good outcome. Our case further highlights the challenging situation in patients with UC and CVT as treatment with anticoagulation alone may not be feasible and thus elective proctocolectomy should be considered to allow the patient to receive anticoagulation to reduce neuromorbidity.

References


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