J Ped Surg Case Reports 3 (2015) 566–569

Contents lists available at ScienceDirect

Journal of Pediatric Surgery CASE REPORTS

journal homepage: www.jpscasereports.com

Altered mental status as a presentation of juvenile polyposis syndrome

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ARTICLE INFO

Article history:
Received 20 April 2015
Received in revised form
23 September 2015
Accepted 24 September 2015

Key words:
Gastrointestinal hemorrhage
Hypoalbuminemia
Juvenile polyposis syndrome
Protein losing enteropathy
Intracranial sinus thrombosis

ABSTRACT

Juvenile polyposis coli (JPC) is a rare hereditary disorder in which patients have multiple polyps in the gastrointestinal tract and present most commonly with hematochezia. We describe a 4-year-old with intermittent rectal prolapse presenting with altered mental status and headaches. JPC was diagnosed by the presence of multiple, pedunculated, colonic polyps on colonoscopy; his altered mental status resulted from cerebral venous sinus thrombosis. Although JPC is known to be associated with a protein losing enteropathy (PLE), this usually manifests as merely hypoalbuminemia and protein losses without major clinical sequelae. We present a rare complication of cerebral venous sinus thrombosis which highlights altered mental status as a rare presentation of JPC. To our knowledge, this is the first case report in the literature linking JPC, decreased protein S activity, a single mutation in the methylenetetrahydrofolate reductase gene and cerebral thrombosis.

Colorectal polyps are the most common tumors of the colon and rectum in childhood. A retrospective review of 487 children in China reveals hematochezia to be the most common presentation. 8.8% of the cohort presented with rectal prolapse. Interestingly, rectal polyps can be misdiagnosed as intermittent rectal prolapse, and solitary juvenile polyps (88.4%) were the most common cause. Moreover, 3% of these patients presented with juvenile polyposis syndrome (JPS) [1]. JPS is a rare, autosomal dominant hereditary disorder occurring in 1:16000–1:100,000 of the population [2]. It has been categorized into three subsets. One subset is juvenile polyposis of infancy, which occurs in the first two years of life with multiple polyps throughout the gastrointestinal tract. This is the most severe form and is associated with early death. These patients develop a protein losing enteropathy with severe diarrhea, cachexia, failure to thrive and hypoproteinemia. Generalized JPS and juvenile polyposis coli (JPC) are the two other subsets. These both occur later in the first two decades of life, but they can be differentiated by the distribution of the polyps. Generalized JPS presents with polyps throughout the gastrointestinal tract, while JPC is limited to the colon [3].

JPC can present with a variety of symptoms; although severe hematochezia is the most common, JPC can also present with anemia, persistent abdominal pain, tenesmus, diarrhea, hypoprotenemia, malnutrition, intestinal obstruction and rectal prolapse. As mentioned earlier, severe protein losing enteropathy (PLE) with hypoproteinemia, cachexia and failure to thrive may develop. These patients will often be found to have digital clubbing [3,4]. We describe a patient with a rare presentation of altered mental status secondary to his protein losing enteropathy.

1. Case presentation

A 4-year-old African American boy with a two-year history of constipation and asthma and a one-year history of intermittent headaches was being evaluated for suspected intermittent rectal prolapse. On presentation he was noted to have malnutrition with an albumin of 1.5 g/dl. He was in the 25th percentile for weight and possessed clubbing of his digits on physical examination. One day after his outpatient visit, he returned with recurrent emesis, dehydration and altered mental status with lethargy and headaches. A head CT demonstrated a dural venous sinus thrombosis of

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2213-5766/
http://dx.doi.org/10.1016/j.epsc.2015.09.014

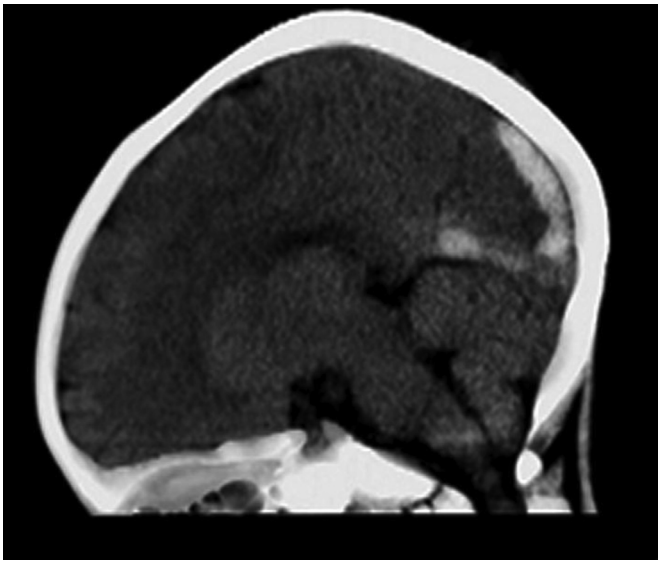

Fig. 1. MRV demonstrating absent flow in the vein of Galen, straight, superior sagittal and proximal transverse sinuses with prominent draining veins consistent with cerebral venous sinus thrombosis.

the sagittal and straight sinuses and the vein of Galen; this was later confirmed by MRI/MRV (Fig. 1). Further workup shown in Table 1 revealed protein S activity deficiency of 53% (normal range of 60–145%), believed to be secondary to malabsorption and a single methylenetetrahydrofolate reductase (MTHFR) mutation, A1298C, without a C677T mutation. This single A1298C mutation is not associated with elevated homocysteine levels, which are associated with thrombosis [2]. Indeed, our patient had a normal homocysteine level of 4.3 (0–15 umol/L). The remainder of the hypercoagulable workup was negative.

No significant cardiac abnormalities were uncovered. Family history was negative as was cystic fibrosis genetic testing. A positive calprotectin of >1250 ug/g (normal range of 0–120 ug/g) demonstrated signs of an inflammatory process without infection. Esophagogastroduodenoscopy revealed hemorrhagic gastritis and erosive esophagitis, but no polyps. Capsule endoscopy also found no polyps in the remaining small bowel. A flexible sigmoidoscopy uncovered more than 20 pedunculated and sessile polyps ranging from 2 to 25 mms with submucosal hemorrhage in the recto-sigmoid junction (Fig. 2).

Table 1
Hypercoaguable panel of patient with JPC.

Hypercoaguable workup		
Name	Level	Range
Pre-colectomy		
Homocysteine	4.3	0–15 umol/L
Anticardiolipin IgA	<9	0–12
Anticardiolipin IgM	<9	0–14
Anticardiolipin IgM	<9	0–11
AT III Activity	131	75–135%
Factor V Leiden mutation	Negative	
Factor V activity	98	60–140%
Factor II DNA mutation	Negative	
Protein S activity	51	67–136%
Post-colectomy		
Protein S total	123	58–150
Protein S free	91	56–124%
Protein C activity	110	74–151%
Protein C level	106	70–140%
Vitamin B12	653	180–914 pg/mL

The patient was found to have protein losing enteropathy with a stool content of α-1 antitrypsin of >1.33 (0.00–0.62). Initially, the patient was treated medically with total parental nutrition, albumin infusion and octreotide for 7 days. His mental status and lethargy improved four days after starting anticoagulation. Despite stopping his anticoagulation therapy, he continued to have hematochezia and was unable to remain off anticoagulation due to worsening headaches and clot burden; his symptoms resolved within three days of restarting his anticoagulation therapy. Two weeks later, following successful anticoagulation therapy for his sinus thrombosis with decreasing thrombus density on a head CT, he underwent an urgent subtotal colectomy with end ileostomy (Fig. 3A). The definitive pull-through procedure was not done at this initial surgery due to his poor nutritional status, which could not be reversed by total parenteral nutrition with his colon in-situ.

Histological analyses confirmed the diagnosis of JPC (Fig. 3B). MRI two months later demonstrated complete resolution of his cerebral venous sinus thrombosis. Further hypercoagulable workup revealed a normal protein S and C levels. Following his colectomy, the patient was taken off total parental nutrition with a calorie count demonstrating his ability to maintain adequate enteral nutrition. The patient represented 6 months later with a normal nutritional status; at which time, he underwent a Soave endorectal ileoanal pull-through procedure with ileostomy closure.

He has since undergone annual endoscopic evaluations without evidence of recurrent polyps, as well as annual radiographic imaging of the brain without evidence of a recurrent dural venous sinus thrombosis. Three years after his initial surgery, the patient is doing well, with a normal appetite, three to five bowel movements per day, and normal weight gain and development without clinical or radiographic neurological sequel.

2. Discussion

Protein losing enteropathy is uncommon in JPC; rather, it is usually found in juvenile polyposis of infancy. Our patient presented with a rare complication of protein losing enteropathy in JPC, symptomatic cerebral venous sinus thrombosis related to protein S deficiency. Protein losing enteropathy is caused by protein leakage through the gastrointestinal mucosa resulting in decreased serum protein levels. Protein losing enteropathy is either a result of lymphatic dilation with rupture and leakage of protein-rich lymphatic fluid; venous hypertension impairing mesenteric flow or pathology causing increased cell permeability, loss of villi or mucosal erosions. Known causes include primary intestinal lymphagectesia (PIL) due to congenital lymphatic malformation, venous hypertension due to congestive heart failure, pericarditis, status post a Fontan procedure, lymphoma and mucosal erosions in infectious gastroenteritis or inflammatory bowel disease [5].

Hypoproteinemia in protein losing enteropathy typically impacts proteins with a slow turnover rate like albumin, immunoglobulin and fibrinogen. There is a compensatory increase in hepatic production; however, up to 60% of the enteric albumin pool is lost causing decreased oncotic pressures with resulting edema, ascites, pleural and pericardial effusion [5]. Although protein losing enteropathy results in hypoalbuminemia and causes edema, other protein losses rarely have shown to be of clinical significance.

Exceptions to this include patients with primary intestinal lymphagectesia and patients with depletion of clotting factors, as in