Intestinal intussusception due to a pyogenic granuloma

Zorica Stojsic[1], Dimitrije Brasanac[1], George Kokai[2], Dragana Vujovic[3], Dragana Zivanovic[4] Ivan Boricic[1], Dragoljub Bacetic[1]

[1]Institute of Pathology, University of Belgrade, and Departments of [3]Pediatric Surgery and [4]Pediatric Gastroenterology, University Children's Hospital, Belgrade, Serbia, and [2]Department of Histopathology, Royal Liverpool Children's NHS Trust – Alder Hey Hospital, Liverpool, United Kingdom

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Pyogenic granuloma (PG), also known as lobular capillary hemangioma, is a benign vascular tumor, most commonly arising on the skin and the oral mucosa. Gastrointestinal localization of PG, except for the oral cavity, is exceptionally rare. We describe a case of ileal PG occurring in a 13-year-old girl, presenting with intestinal obstruction.

Histological examination revealed proliferation of capillary-sized vessels, with prominent intravascular component, involving the entire thickness of the intestinal wall. Immunohistochemistry showed positivity for CD31, CD34 and von Willebrand factor, whereas immunostaining for glucose transporter-1 protein (GLUT1) and for human herpes virus 8 (HHV-8) was negative. We suggest that PG should be considered in the differential diagnosis of childhood gastrointestinal polypoid lesions.

Key words: child, intestinal obstruction, pyogenic granuloma, small bowel.

Pyogenic granuloma (PG) is a common benign vascular tumor that typically arises on the skin and mucosa of the oral cavity. The basic lesion is a lobular proliferation of capillary-sized vessels in a fibromyxoid stroma. Accordingly, PG has been designated as lobular capillary hemangioma[1,2]. The lesion may develop at any age, and both genders are affected equally. Granuloma gravidarum and subcutaneous and intravenous PG are rare variants of the tumor[1,3]. PGs are extremely rare in the gastrointestinal tract, except for the oral cavity. To the best of our knowledge, only 16 cases have been reported in the alimentary tract, all of them occurring in adults[4-7]. Here, we describe a new case of PG of the ileum in a 13-year-old girl, causing intestinal obstruction.

Case Report

A 13-year-old girl presented with a three-day history of vomiting, colicky abdominal pain and constipation. On clinical examination, the abdomen was diffusely distended and tender. Bowel sounds were absent. Laboratory findings showed white cell count of 14.7 x 10^9/L with 67.2% neutrophils. Biochemical analysis results were unremarkable and the patient was afebrile. Ultrasonographic examination of the abdomen revealed dilated loops of small intestine with fluid accumulation. Plain abdominal radiography showed multiple air-fluid levels (Fig. 1). The patient underwent an emergency laparotomy with the presumptive diagnosis of intestinal obstruction. Operative findings revealed ileo-ileal intussusception, 80 cm proximal to the ileocecal valve, and a large amount of brown-colored intraperitoneal fluid. The affected gangrenous loop of the small bowel was resected and a temporary terminal ileostomy was performed. The postoperative period was uneventful. After closure of the stoma, the patient remained in good general health, free of any symptoms.

Pathologic Findings

The resected specimen consisted of a segment of small bowel measuring 50 cm in length, with a 4x3x3 cm polypoid lesion in the lumen, which

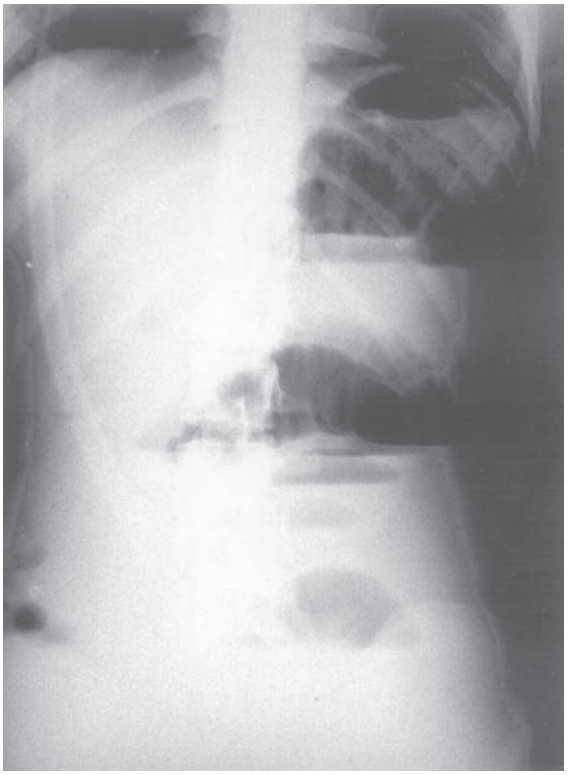

Fig. 1. Abdominal radiography shows multiple air-fluid levels in small bowel obstruction.

acted as a leading point for the intussusception (Fig. 2). The bowel wall displayed intensive congestion with a thin layer of fibrin on the serosal surface. On opening, the lumen contained blood-stained fluid.

Hematoxylin-eosin (HE) and immunohistochemical staining were performed on formalin-fixed, paraffin-embedded tissue. For immunohistochemical examination, sections were pretreated in a microwave oven and incubated with primary antibodies against CD31 (Clone JC/70A; dilution 1:25; DAKO, Glostrup, Denmark), CD34 (QBEnd/10; 1:50; DAKO), von Willebrand factor (F8/86; 1:25; DAKO), glucose transporter-1 protein (GLUT1) (1:25; Labvision Neo Markers, Fremont, CA) and human herpes virus 8 (HHV-8) (13B10; 1:50; Cell Marque, Hot Springs, AZ). Immunohistochemistry was performed using DAKO EnVision kit, with diaminobenzidine as the chromogen and Mayer's hematoxylin for the counterstain.

Microscopic examination revealed a protuberant growth of capillary-sized vessels, lined by a single layer of bland endothelial cells, in a distinctive lobular arrangement. The vascular channels were intensely congested with massive and extensive sludging of erythrocytes.

The lesion involved the entire thickness of the bowel wall. The superficial portion of the tumor and the overlying intestinal mucosa showed hemorrhagic infarction with ulceration. In addition, foci of intravascular proliferation of angiomatous tissue were present. One large vein, running from the submucosa to the mesentery and a few smaller veins in the submucosa contained proliferation of minute capillaries and scarce larger vessels with muscular wall, set in the cellular stroma (Fig. 3). Immunohistochemistry showed positive reaction for CD31, CD34 and von Willebrand factor in endothelial cells of the proliferating vessels. Intense GLUT1 immunoreactivity was observed in erythrocytes

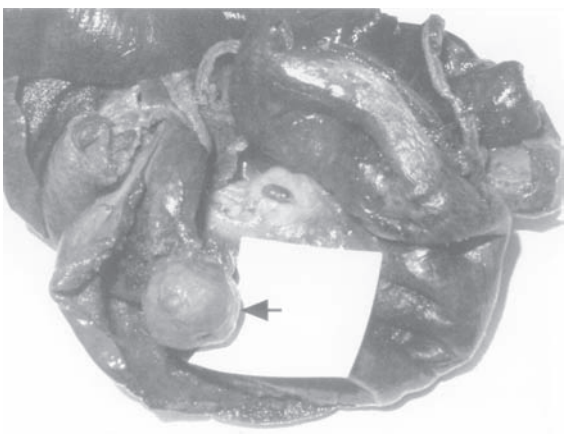

Fig. 2. Pyogenic granuloma (arrow) of the ileum as a leading point for intestinal intussusception. The intestinal wall is hemorrhagic and covered with fibrinous exudate.

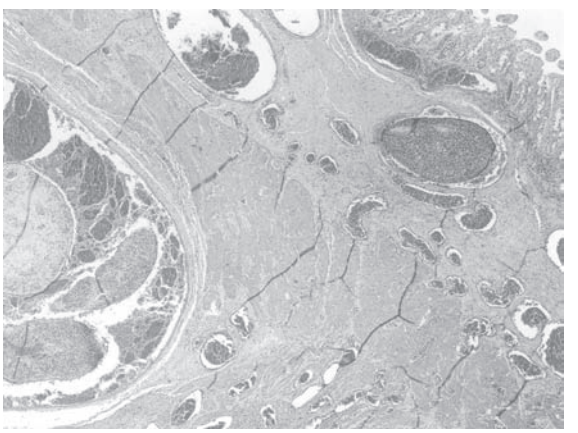

Fig. 3. Intravenous component of pyogenic granuloma within bowel wall (hematoxylin and eosin, original magnification x40).

as well as in the endothelium of all types of the lesional and native vessels: capillaries, veins, arteries and arterioles (Fig. 4). HHV-8 immunostaining was negative.

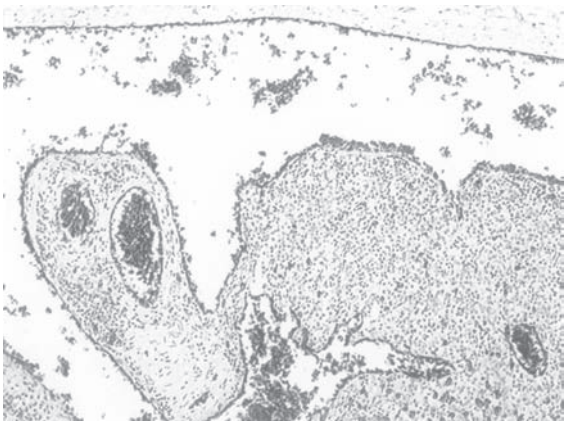

Fig. 4. False GLUT1 immunopositivity in the endothelium of the native vein containing PG, which normally should not be stained with GLUT1 (streptavidin-biotin, original magnification x100).

The small bowel, outside the polypoid lesion, showed hemorrhage affecting the entire thickness of the wall with foci of mucosal necrosis.

Discussion

In the past, PG was regarded as a reactive lesion secondary to trauma with superimposed infection. Weiss and Goldblum[3] consider the lesion a granulation tissue-type hemangioma. Nowadays, it has been widely accepted that PG is a true angiomatous neoplasm, not simply a florid proliferation of granulation tissue[1,2].

According to the distinctive lobular arrangement of the lesional capillaries, the lobular capillary hemangioma has been introduced as the designation for PG[1,2].

Pyogenic granuloma usually occurs on the skin and the mucosa of the oral cavity. When present on the skin, the most frequently involved sites are the lips, face and fingers[2]. In the oral cavity, PG commonly involves gingiva, tongue and cheeks[3]. Sporadic cases of PG affecting the genital area have been observed as well[8,9].

Only a few cases of PG in the alimentary tract, other than those in the oral cavity, have been reported. A gastrointestinal counterpart of the skin PG has been proposed[7] because of the same macroscopic and histological features. According to Kusakabe[4], only 13 cases of PG arising in the alimentary tract were published until 2005. Since then, three additional cases of PG, located in the esophagus, ileum and colon, respectively, have been reported[5,6]. Gonzales-Vela[6] identified 25 cases of intestinal PG in the English literature, but the authors disputed the majority of them, yielding only one well-documented case of PG in the colon[7]. In total, 16 cases of PG in the gastrointestinal tract, other than the oral cavity, have been reported: four occurred in the esophagus, six in the ileum, three in the colon, and one each in the stomach, duodenum and jejunum[4-7]. The present case is the seventh reported in the ileum.

All the gastrointestinal PG cases reported thus far occurred in adult patients[5]. We believe our case to be the first pediatric PG arising in the gastrointestinal tract, apart from those in the oral cavity.

Gastrointestinal bleeding was the most common clinical symptom in cases with gastrointestinal PG[4-7] and none of the reported intestinal PGs caused intestinal obstruction. Our case was also the largest PG among the reported alimentary tract PGs, measuring 40 mm in diameter. The size of the previously reported gastrointestinal PGs was usually less than 20 mm, and only a few of them measured 30 mm[4-7].

Intravenous PG is a rare variant of the tumor, presenting predominantly on the neck and the upper extremity[3,10,11]. The tumor arises from the wall of the vein and protrudes deeply into the lumen. In the alimentary tract, only one case of intravenous PG, located in the jejunum, was published, in a small series of Yao et al.[7]. To the best of our knowledge, the current case is the second reported gastrointestinal PG with the intravenous PG component.

Major differential diagnoses of PG include inflammatory polyp, well-differentiated angiosarcoma, Kaposi's sarcoma, and juvenile capillary hemangioma[1-3,6]. Inflammatory polyps are usually multiple, occurring in association with chronic intestinal diseases. Histologically, they lack the lobular pattern. Angiosarcoma is differentiated from PG by infiltrative growth, irregular vascular spaces and cellular atypia. Similarly, Kaposi's sarcoma is not well circumscribed and it contains, at least focally, cellular zones of spindle cells and slit-like vascular spaces. This tumor was additionally excluded by negative HHV-8

immunostaining. Although never reported in the alimentary tract, juvenile capillary hemangioma and congenital hemangiomas should be included in differential diagnosis due to their lobular growth. The diagnosis of juvenile capillary hemangioma is based on the immunopositivity for GLUT1, the erythrocyte-type glucose transporter protein[12]. GLUT1 is exclusively expressed in juvenile capillary hemangiomas, but not in congenital hemangiomas, vascular malformations, pyogenic granulomas, and granulation tissue[12-14]. In extracutaneous infantile hemangiomas, GLUT1 immunoexpression is variable, being also positive[15], or absent/reduced[16]. GLUT1 is specifically expressed in the endothelium of capillaries of the lesion, but not in the arteries and arterioles or native blood vessels[12]. Accordingly, we regard the GLUT1 immunoreaction as false-positive since we found the positive reaction in endothelial cells of both the arteries and veins within the lesion itself, and of those outside of the lesion. We assume that this false immunopositivity could be caused by very marked congestion and sludging of erythrocytes developed during intestinal intussusception. Noninvoluting congenital hemangioma and a similar lesion, congenital nonprogressive hemangioma, have the lobular and occasional intravascular growth pattern and GLUT1 immunonegativity in common with PG[13,17,18]. These tumors differ from PG in that they exhibit intra- and extralobular fibrosis, stromal hemosiderin deposits, focal thrombosis and sclerosis of capillary lobules[13,18], features that were absent in our presented case.

In conclusion, we report herein the first documented case of pediatric PG of the gastrointestinal tract causing small intestinal intussusception. We suggest that PG should be considered in the differential diagnosis of gastrointestinal polypoid lesions in children.

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