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Original Research Article

Peutz-Jeghers Syndrome with Huge Ileo-Ilial Intussusception: Case Report and Literature Review

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Abstract:
Peutz-Jeghers syndrome (PJS) is an inherited polyposis disorder distinguished by the presence of multiple hamartomatous polyps in the gastrointestinal tract. These polyps are specifically observed along the vermilion border of the lip and are associated with pigmentation of the mucosa. A germline mutation in the STK11 (LKB1) gene causes this autosomally dominant inheritance disorder. Mucocutaneous pigmentations most frequently impact the nosoal region, lips, perioral regions, buccal mucosa, eyes, extremities, palms, soles, and perianal areas. Although they can be found anywhere in the gastrointestinal tract, hamartomatous polyps are most commonly located in extraintestinal sites such as the bronchus, renal pelvis, and bladder. These polyps carry a low malignant risk. In light of the extensive range of carcinomas to which these patients are prone, it is advisable to implement stringent screening protocols. Patients with PJS must be closely monitored and followed up on in order to detect related malignancies early and prevent potential complications; this is due to the increased risk of intestinal and extraintestinal malignancies.

Keywords: Peutz-Jeghers Syndrome; Hamartomatous Polyps; Gastrointestinal Polyps; Mucocutaneous Pigmentation; STK11 Gene; LKB1 Protein.

Introduction

Peutz-Jeghers syndrome (PJS) is an inherited polyposis disorder distinguished by the presence of multiple hamartomatous polyps in the gastrointestinal tract. These polyps are specifically observed along the vermilion border of the lip and are associated with pigmentation of the mucosa. A germline mutation in the STK11 (LKB1) gene causes this autosomally dominant inheritance disorder. Mucocutaneous pigmentations most frequently impact the nosoal region, lips, perioral regions, buccal mucosa, eyes, extremities, palms, soles, and perianal areas. Although hamartomatous polyps are uncommon outside the gastrointestinal tract, they are particularly prevalent in the jejunum and extraintestinal sites such as the bronchus, renal pelvis, and bladder [1]. They carry a low malignant risk and can be detected anywhere in the gastrointestinal tract.

When one intestine segment telescopes into another, it results in intussusception. This affects the normal peristaltic movements of the bowel and can lead to obstruction and reduced blood flow. It can result in complications including bowel obstruction, ischemia, necrosis, and perforation if not treated promptly. In adults, intussusception is exceedingly uncommon, occurring in less than 1 in 1300 abdominal operations. The proportion of children affected compared to adults is approximately 20 to 1 [2]. The majority of the time, the clinical manifestation of adult intussusception is vague and variable. The most frequently observed primary symptom is nonspecific abdominal pain, which is shortly after intestinal obstruction or palpable mass [3].

In the below presented case study, we report a 19-year-old young male adult with small bowel obstruction due to ileoileal intussusception caused by a Puetz-Jeghers polyp.

Case Presentation

A 19-year-old young adult male presented at the emergency department of our hospital with intermittent pain, abdominal distention, and nausea, but no vomiting, and absence of flatulence and defecation. The patient had a previous history of intussusception two years ago for which he underwent small bowel resection. Detailed information was not available. While questioning the family history of the patient it was noted that the mother of the patient also had multiple pigmentation on the finger skin and lip mucosa. The physical examination of the patient revealed pigmentation of finger skin and lip mucosa,

decreased bowel movements, upper and lower abdominal tenderness, no rebound pain, there was a palpable mass in the lower right abdomen; because of the accompanying abdominal distension, tenderness, and guarding, its characteristics were unclear. The patient was hemodynamically stable and the oxygen saturation was above 96%. The routine blood test was remarkable for increased WBC count. The abdominal CT examination revealed an small intersection in the lower abdomen (Fig. 1). After the initial resuscitation, the patient underwent exploratory laparotomy. During the procedure, small bowel intussusception(ileo-illeal) was observed. The affected segment was about 75cm long (Fig. 2). About 40cm of the intestine was necrotized (Fig. 3). Finally, a small intestine resection line was made based on the ischemic necrotic intestinal segment, and side-to-side anastomosis of the proximal and distal small intestine using a linear cutting closure device was performed. The resected small intestine was examined and a palpable mass of size 3.6*2*1.5cm was observed (Fig. 4). The pathology specimen reported the mass to be puetz-jeghers polyp (Fig. 5). Postoperatively the patient recovered well and was dicharged from the hospital.

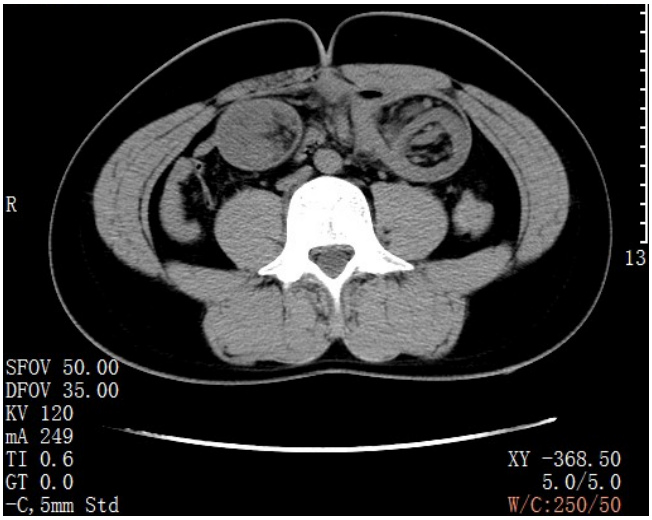

Figure 1: Abdoinal CT

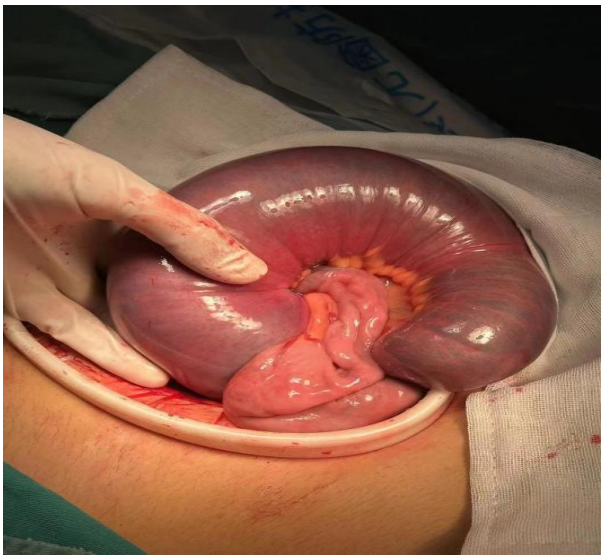

Figure 2: Small bowel intussecption

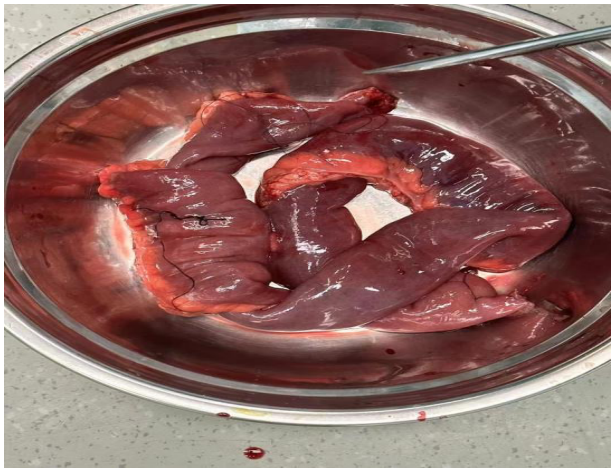

Figure 3: Necrtotized part of small intestine

Figure 4: Polyp seen on the resected specimen

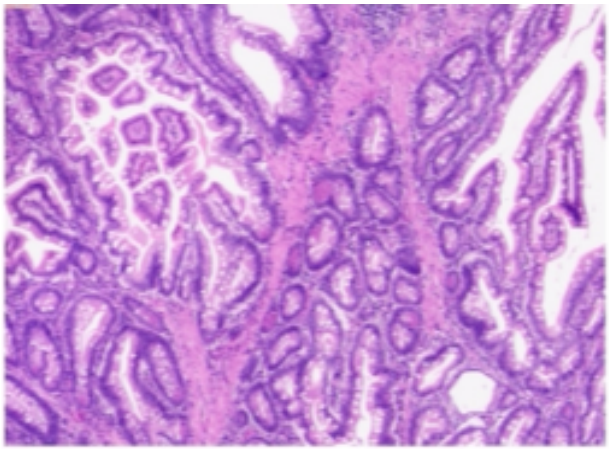

Figure 5: Puetz-Jeghers syndrome polyp

Discussion

The earliest description of Peutz-Jeghers syndrome was given by Dr. J. T. Connor in the year 1895[4]. And later on in the year 1921, a Dutch physician Johannes Peutz described a case of a family with autosomal dominant inheritance gastrointestinal polyps and pigmentation of skin and mucous membrane [5]. Later on in the year 1949, a paper published by Dr. H. Jegher reported 10 cases with pigmentation of the oral mucosa, lips, and digits and intestinal polyps along with a review of relevant literature, stating it as a syndrome of diagnostic significance [6]. Although pigmented macules may develop later in life, they often appear in early childhood and may even be present at birth. These pigmented macules are typically found around the mouth, nose, lower lip, buccal mucosa, perianal

area, hands, and feet. The prevalence rate for Peutz-Jeghers syndrome ranges from 1 in 8,300 to 1 in 280,000 individuals [7].

1997 marked the identification of the Peutz-Jeghers syndrome locus on chromosome 19 p 13.3. The identification of the gene mutation (STK11/LKB1) located on chromosome 19p13.3, which encodes a protein consisting of 433 amino acids, occurred one year later [8-9]. The tumor suppressor function of STK11/LKB1 is achieved through the regulation of cell division, polarity, and the coupling of cell growth and division to cellular energy levels [10]. As of now, the mutation rate of the LKB1/STK11 gene as detected by multiplex ligation-dependent probe amplification (MLPA) and direct sequencing technology is between 80% and 94% [11].

Although most prevalent in the small intestine (jejunum, ileum, and duodenum, in that order of prevalence), gastrointestinal hamartomatous polyps can also manifest in the large intestine, stomach, extraintestinal sites such as the renal pelvis, bronchus, gall bladder, nasal passages, urinary bladder, and ureters [12]. The epithelial component of the polyp has a frond-like elongation. It is possible to see cystic gland dilatation spreading into the muscularis propria or submucosa. The branching muscle core that penetrates the superficial epithelial layer is arguably the most distinctive feature. Symptomatic polyps in the gastrointestinal tract affect approximately one-third of patients by the age of ten and one-half of patients by the age of twenty. Typical clinical manifestations include intussusception, obstruction, or hemorrhage [13].

Individuals diagnosed with PJS have been identified as having an elevated susceptibility to both gastrointestinal and extraintestinal malignancies. A meta-analysis found that patients with PJS had a 93% chance of developing cancer of any site between the ages of 15 and 64. Patients are most susceptible to developing pancreatic cancer (36%), breast cancer (54%), colon cancer (39%), gastric cancer (29%), and ovarian cancer (21%), in that order [14]. The incidences of cancer in 412 Chinese individuals with PJS were analyzed in a retrospective study published in 2022; 109 (26.46%) of these individuals developed 113 malignancies at a median age of 40 years [15]. The diagnosis for the Peutz-Jeghers syndrome can be made based on the diagnostic criteria and categories described by Yamamoto H,et al.[16].

The diagnostic crieteria is as follows:

A. Symptoms: pigmented maculae on lips , mouth and fingertips of size 1-5mm.

B. Examination finding: Endoscopy showing hamartomatous polyps in GI tract except the esophagus and pathologically diagnosed as Peutz-Jeghers polyps.

C. Distinguishing this condition from others such as tuberous sclerosis, causal adenomatous polyposis, Cronkhite-Canada syndrome, hereditary mixed polyposis syndrome, juvenile polyposis syndrome, Cowden syndrome/PTEN hamartomatous syndrome, and Laugier-Hunziker-Baran syndrome involves distinguishing between these conditions.

D. Genetic testing for germline pathogenic variant in STK11 gene.

The diagnostic categories are as follows:

1. Symptoms, Examination findings(endoscopy and pathology) are fulfilled and the differential diagnosis are excluded.

2. the presense of symptoms in an individual who has a family history of Peutz-Jeghers syndrome in close relation and the differential diagnosis are excluded.

3. The endoscopy is positive for the presence of hamartomatous polyps and pathology reveals Peutz-Jeghers polyps.

4. The endoscopy is positive and the multiple lesions are proven to be Peutz-Jeghers polyps and the differential diagnosis are excluded.

5. Genetic testing if positive for pathogenic germline mutations.

For the patients who fulfill some of the kdiagnostic criteria but do not meet the diagnostic categories, in such individuals genetic testing should be done.

Once the diagnosis for PJS is established, timely surveillance and endoscopic resections of polyps should be done to avoid the n complications. The European Hereditary Tumour Group (EHTG) Guideline recommends oesophago-gastroduodenoscopy and colonoscopy shpold be done at 8years of age and if the polyps are detected then every 1 to 3 years surveillance should be performed[17]. In addition to computed tomography enterography and small bowel capsule endoscopy, the surveillance methods consist of balloon-assisted endoscopy and small bowel series magnetic resonance enterography. On the other hand, surveillance for the risk of the development of extragastrointestinal cancers should also be done. It has been proven that PJS patients have an increased risk of developing cancer of any site [14]. The guidelines [16,17] recommend gastrointestinal surveillance from the age of 8 years, breast surveillance starts with self-checking and the age of 18 years, and breast MRI imaging starting at 25 years of age followed by mammography after 50 years of age. Gynecological surveillance starts from the age of 18 years irrespective of family history for gynecological cancer. It is recommended to start Pancratic surveillance through MRCP or EUS at the age of 30 years. The patients during the course of PJS are highly surgical due to the size of polyps that

can cause intussusception, bowel obstruction, bleeding in the gastrointestinal tract, etc, and also the increased lifetime risk of malignancy. These could lead to multiple emergency laparotomies and also increase the risk of short bowel syndrome, so efforts should be made to avoid surgical treatment. The guidelines recommend that after the diagnosis endoscopic treatment is initiated for surveillance and also to prevent the complications such as intussusception and bowel obstruction. In case polyps larger than 1 to 1.5 cm are found polypectomy should be performed using balloon-assisted endoscopy [16,17]. While laparotomy should be indicated when the endoscopic treatment is not possible or in an emergency setting. When surgery is indicated, it is recommended that polypectomy is performed through enterotomy. And in cases of emergency due to bowel obstruction or intussusception excessive intestinal resection should be avoided to prevent the short gut syndrome.

In our case, the patient came to the emergency department with the complaint of intermittent abdominal pain and was diagnosed with bowel obstruction secondary to intussusception. It was noted that the patient previously underwent small bowel resection for the same. Intussusception occurs when one segment of the intestine telescopes into another. This affects the normal peristaltic movements of the bowel and can lead to obstruction and reduced blood flow. It can result in complications including bowel obstruction, ischemia, necrosis, and perforation if not treated promptly. The most common etiology of intussusception in adults is a pathological lead point. The aggregated rates of malignant and benign tumors and idiopathic etiologies in adults were 32.9%, 37.4%, and 15.1%, respectively, according to one study. The respective pooled rates for enteric, ileocolic, and colonic site locations were 29.1%, 19.9%, and 49.5%. The respective pooled rates of malignant tumors observed in enteric, ileocolic, and colonic intussusception were as follows: 22.5%, 36.9%, and 46.5% [18]. CT is widely regarded as the optimal diagnostic tool for intussusception, as evidenced by its 83.3% sensitivity in some studies. However, this figure remains debatable and necessitates the following factors be taken into account: (1) the prevalence of an underlying disease and the necessity for surgical intervention; (2) the presence of malignant disease and the extent of surgical treatment required; (3) the anatomic location and extent of intussusception; and (4) the existence of comorbid inflammation, edema, or bowel ischemia [19]. Intussusception in adults is usually caused by a lead point hence it necessitates surgical intervention. The cause, size, and site of intussusception and viability of the intestine determine the choice of surgical approach.

In our patient small intestine resection with side-to-side anastomosis of the proximal and distal small intestine using a linear cutting closure device was performed because, during the laparoscopic procedure, it was observed that the small bowel segment was necrotized.

Conclusion

PJS is a rare inherited polyposis condition that has a serious effect on the patients. The patients suffering from PJS often suffer from complications, with the most frequent being bowel obstruction and intussusception and they also have an increased risk of cancer development. This leads to increased requirements for timely surveillance and management of gastrointestinal polyps and also the surveillance of extra gastrointestinal organs to avoid the development of severe complications.

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