

A Rare Case of a Juvenile Polyp of Patient with Peutz-Jeghers Syndrome, Complicated with Intussusception of the Small Intestine

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Abstract

We report a rare case of Peutz-Jeghers syndrome (PJS) in a 35-year-old female. The patient was diagnosed with PJS when she was 11 years old. She has remained under observation since then. We strongly believe that PJS is a very rare diagnosis. However, it can have serious complications such as the intussusception we observed in our patient. Her condition (recurrent abdominal pain and vomiting) in childhood required further diagnostic procedures. Although the diagnosis of PJS was made, among many resected polyps, one of them appeared to be a juvenile polyp. The diagnosis was confirmed in the histopathology report, which was incredibly unique. Genetic testing revealed LKB1/STK11 gene mutation. Clinicians should be aware of the malignant potential in the course of PJS. Hence, these patients require tailor-made management, long-term follow-up, and our particular attention.

Keywords

cancer, colonic polyp, gastrointestinal polyps, hamartoma polyp, Peutz-Jeghers syndrome

INTRODUCTION

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant inherited disorder that always requires early diagnosis. It is characterized by the presence of hamartomatous polyps in the gastrointestinal tract, typically found in the small intestine and colon.^[1] The PJS patients have an increased risk of malignancy compared with the general population.^[2] Thus, they require a long-term follow-up to assess the diagnosis, treatment of malignant changes and other severe complications secondary to Peutz-Jeghers syndrome. Considering the recent advances in treatment, early management of PJS individuals is essential to avoid an unnecessary surgical emergency.

CASE REPORT

Herein, we present a case of a 35-year-old female who was admitted to the Department of Gastroenterology in July 2020, with Peutz-Jeghers syndrome recognized in 1996. The physical examination revealed no abnormalities, and the patient denied any ailments. Her medical history started when she was 10 years old. She had exhibited recurrent abdominal pain and vomiting during her childhood. However, no mucocutaneous pigmentation was observed. Nevertheless, she did not have a history of PJS in a close relative, her condition required further diagnostic procedures.

Intussusception of small intestine

In December 1995, our patient underwent a resection of her small bowels due to an intussusception of the small intestine

and its necrosis. During the surgery, two meters of the small intestine were found to be full of multiple polyps. Upper GI endoscopy showed many polyps of the antrum and the duodenum. Two months later, our patient underwent her first colonoscopy. Eleven polyps from the sigmoid colon and the rectum were removed. Five months later, 8 large intestinal polyps were resected endoscopically. Next, after 7 months, 30 polyps were found in the stomach, one of which was removed. During the next years, 23, 18, 12, 11, 14, 4, and 4 gastrointestinal polyps were removed in iterative colonoscopy procedures, consecutively.

Another surgery

It is a well-documented fact that patients with Peutz-Jeghers syndrome are at a high risk of developing both gastrointestinal and extraintestinal malignancies. Hence, our patient had a computed tomography (CT) scan of the abdomen. The CT scan indicated the presence of 60-mm focal changes in the left lumbar abdominal region. When she was 19 years old, in January 2005, on account of suspicion of a small intestine tumor, she underwent another resection of the small intestine localized 100 cm distally to the ligament of Treitz with intraoperative polypectomy of 51 polyps. The postoperative histopathology report excluded malignancy. Thus, the focal changes appeared to be a Peutz-Jeghers-type polyp that is defined as a hamartomatous polyp with the pathological features of Peutz-Jeghers syndrome but lacking the pigmentation and heritability.^[3]

In March 2006, our patient underwent a uterine curettage due to a benign hydatidiform mole. In August, 2007, seven Peutz-Jeghers polyps were removed. One year later, enteroscopy was performed during which another 7 hamartoma polyps were found 150 cm distally to the stomach and were excised.

Additionally, two years later in March, July, and October, while undergoing enteroscopy, 20 polyps, with diameters ranging from 1 cm to 5 cm, were removed; 10 polyps with 1-3 cm in diameter; and several dozens more, respectively. Interestingly, histopathology report showed a fragment of a juvenile polyp of the small intestine, and the rest of the detected polyps were described as Peutz-Jeghers polyps. This discovery of the juvenile polyp in our patient's small intestine did not

affect her model of screening. Moreover, one juvenile polyp does not fulfill the criteria of juvenile polyposis syndrome (JPS). However, it is a unique finding.

When she was 29 years old, due to her plans of getting pregnant in the nearest future, she underwent enteroclysis. The patient underwent polypectomy 14 times from 2010 to 2020. During the last hospitalization, our patient presented no oral or anal mucocutaneous pigmentations. The laboratory test results showed no abnormal values: haemoglobin level was 12.0 g/dL, red blood cell (RBC) count $4.32 \times 10^6/\mu\text{l}$, mean corpuscular volume (MCV) count 84.1 fL, platelets $284 \times 10^3/\mu\text{l}$, the international normalized ratio (INR) was 1.1, the sodium level was 139 mmol/L, the potassium level - 4.2 mol/L, the renal function test was normal, the inflammatory markers, such as serum C-reactive protein (CRP) was 2.611 mg/L. Ultrasonography of the abdomen revealed no pathology. Twenty-five polyps were resected endoscopically from the sigmoid colon and rectum (**Fig. 1**). The histopathology report was suggestive of Peutz-Jeghers polyps. The patient underwent genetic testing, which was positive for a germline mutation (frameshift deletion in exon 1) in the *STK11/LKB1* gene, confirming the diagnosis of Peutz-Jeghers syndrome. Genomic DNA was extracted from peripheral blood. She remains under observation and she is scheduled for a follow-up with an upper GI endoscopy in October this year. Additionally, our patient's sister was recommended to perform a colonoscopy.

DISCUSSION

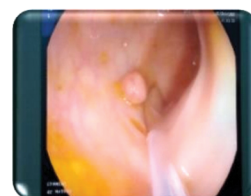
Peutz-Jeghers syndrome was first reported by Peutz in 1921 and described in 1949 by Jeghers.^[4] The etiology of Peutz-Jeghers syndrome remains unknown. The clinical symptoms are non-specific such as anemia, nausea, abdominal pain, and intestinal intussusception. Typical melanin spots on lips, buccal mucosa, and digits might be observed in PJS patients. According to the World Health Organization (WHO), diagnosis of PJS requires some specific criteria to be considered: three or more histologically confirmed Peutz-Jeghers polyps or any number of Peutz-Jeghers polyps with family history of Peutz-Jeghers syndrome or characteristic mucocutaneous pigmentation with a family history



a. Peutz-Jeghers-type polyp of large intestine (1)



b. Peutz-Jeghers-type polyp of large intestine (2)



c. Peutz-Jeghers-type polyp of large intestine (3)

Figure 1. Endoscopic photos from colonoscopy performed in PJS patient showing three (1, 2, 3) Peutz-Jeghers-type polyps of large intestine (a-c).

of Peutz-Jeghers syndrome or any number of Peutz-Jeghers polyps and characteristic mucocutaneous pigmentation.^[5]

The diagnosis of PJS is characteristic for childhood or early adulthood. The male-to-female ratio for PJS is almost 1:1. Pigmentations are typically observed in childhood while they may even disappear in adulthood.^[6] Our patient has not presented any pigmentation since she remains under our observation. Therefore, this case falls under the first category of WHO criteria for PJS diagnosis. Polyps in the outcome of Peutz-Jeghers syndrome can occur anywhere in the gastrointestinal tract, as well as in the nostrils, urinary bladder, or lungs.^[7] Typically, the Peutz-Jeghers polyps measure from 1 to 50 mm. Other than intussusception, complications that can be observed in patients with PJS are hemorrhage, occlusion, gastrointestinal necrosis, perforation, and more in PJS individuals.^[1] The majority of individuals with Peutz-Jeghers syndrome have been found to have germline mutation of the serine/threonine kinase-11 (LKB1/STK11) gene, located on chromosome 19p13.3.^[2] Even though LKB1 mutation is claimed to be a tumor suppressor gene, nowadays, it is also considered as a tumorigenesis promoting gene. LKB1 is responsible for inducing pathways that reduce oxidative stress. Since LKB1 gene signaling is believed to be necessary to reduce cancer cells invasion, therefore, any mutation in this gene is possible to cause proliferation of cancer cells.^[8] The possible risk for developing any cancer in the course of Peutz-Jeghers syndrome at the age of 30 is up to 5%, at the age of 40 the risk is almost 21%, and in the sixties it is almost 60%.^[2]

What is peculiar about our patient is that one of the histopathology reports (in 2009) detected one juvenile polyp. However, a juvenile polyposis syndrome diagnosis requires the presence of either juvenile polyps or family history of JPS.^[9] Furthermore, JPS can be diagnosed only in the absence of other hamartomatous polyposis syndromes, including PJS what excludes our patient as a JPS patient.^[10] Polyps of juvenile type are mostly detected in childhood but are very rare in adulthood.^[11] Thus, juvenile polyps may often be misdiagnosed as inflammatory polyps.^[12]

Our patient could be considered as a case of hereditary mixed polyposis syndrome (HMPS). HMPS is a rare autosomal dominant disease characterized by the appearance of different polyps, such as hyperplastic polyps, tubular adenomas, serrated adenomas, and hamartomatous polyps.^[13] Although standard clinical diagnostic criteria for HMPS have yet to be firmly established, HMPS differs from JPS in that only a few typical juvenile polyps are documented. If typical juvenile polyps are present in HMPS, they are often associated with mixed components. HMPS patients are rarely diagnosed before the third decade of their life. However, this diagnosis would require further investigation.^[13]

We report the unique case of a patient with PJS. Our patient underwent two surgical procedures in the course

of the disease as we mentioned above. Furthermore, in 2009, the histopathology report confirmed the coexistence of Peutz-Jeghers polyps and a juvenile polyp. Since then, there was no histopathology report that would show the presence of juvenile polyps. However, detecting one juvenile polyp does not have any influence on the screening pathway of our patient. Furthermore, it is unique because to our knowledge, it is very rare to recognize both types of polyps in one patient. Our patient remains under observation and she is expected for the next hospitalization in the appointed term.

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Редкий случай ювенильного полипа у больного с синдромом Пейтца-Егерса, осложнившегося инвагинацией тонкой кишки

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Резюме

Мы сообщаем о редком случае синдрома Пейтца-Егерса (СПЕ) у 35-летней женщины. Пациентке был поставлен диагноз СПЕ, когда ей было 11 лет. С тех пор она находится под наблюдением. Мы твёрдо убеждены, что СПЕ— очень редкий диагноз. Однако это может привести к серьёзным осложнениям, таким как инвагинация, которую мы наблюдали у нашего пациента. Её состояние (периодические боли в животе и рвота) в детском возрасте требовало дополнительных диагностических мероприятий. Хотя был поставлен диагноз СПЕ, среди многих резецированных полипов один из них оказался ювенильным полипом. Диагноз был подтверждён гистопатологическим отчётом, который был невероятно уникальным. Генетическое тестирование выявило мутацию гена LKB1/STK11. Клиницисты должны быть осведомлены о злокачественном потенциале при СПЕ. Следовательно, эти пациенты требуют индивидуального лечения, длительного наблюдения и особого внимания.

Ключевые слова

рак, полип толстой кишки, полипы желудочно-кишечного тракта, полип гамартумы, синдром Пейтца-Егерса
