sciendo Acta Marisiensis - Seria Medica 2023;69(2):135-137 DOI: 10.2478/amma-2023-0017

CASE REPORT

The importance of early diagnosis and surveillance in Peutz-Jeghers Syndrome: A case report

Marina-Georgia Balosin*

3rd Department of Gastroenterology, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Introduction: Peutz-Jeghers syndrome is a rare autosomal dominant inherited disorder characterized by hamartomatous intestinal polyps and mucocutaneous pigmentation. Most cases appear to be linked to the mutation of the STK11 gene. Patients are at a lifetime risk of gastrointestinal and non-gastrointestinal cancers. **Case Presentation**: The present study offers the case of this rare disorder in a young woman revealed by jejunal obstruction caused by intussusception. A 32-year-old woman was referred to the surgical department with symptoms suggestive of an obstructive syndrome. On examination, there were multiple perioral pigmented lesions. An urgent exploratory laparotomy revealed bowel obstruction caused by an intussusception with a large polyp. The patient suffered another similar episode 4 years before leading to the diagnosis of Peutz-Jeghers Syndrome, however she was under no surveillance. Patients with pigmented lesions and a family member suffering from the mentioned syndrome should perform endoscopy and genetic tests to diagnose early and avoid complications. **Conclusion**: Peutz-Jeghers Syndrome is difficult to treat due to its nonspecific symptomatology and late diagnosis. Life-threatening complications such as intussusception and various types of cancer are unanticipated. It is vital to diagnose and perform routine screening, which will make it possible to prolong the survival of many patients.

Keywords: hamartomatous polyps, anemia, intussusception, screening, family history

Received 20 December 2022 / Accepted 10 April 2023

Introduction

Peutz-Jeghers syndrome (PJS) is an autosomal dominant inherited polyposis syndrome, characterized by multiple hamartomatous polyps in the gastrointestinal tract, associated with mucocutaneous melanin lesions especially around the mouth [1] but also can be found oral, palmar, or plantar [2]. It is a rare condition, attributed to a mutation in STK11 gene (also called LKB1) on chromosome 19p13.3 [2]. STK11/LKB1 is a tumor suppressor gene, and its function is to provide instructions for making an enzyme called serine/threonine kinase 11 [3]. The purpose of this enzyme is to keep cells from growing and dividing uncontrolled [3]. Thus, the patients risk developing multiple types of cancer, such as gastrointestinal (GI), ovary, pulmonary, breast, uterine, or cervical [2]. The hamartomatous polyps may vary in size and location as they can be found in the stomach, small intestine, and large intestine. Histologically, they are characterized by a smooth muscle arborization within the lamina propria associated cystic gland dilatation [1]. Complications of gastrointestinal polyps include bleeding and abdominal pain due to intussusception, obstruction, or bowel infarction.

The incidence of PJS is estimated to be between 1 in 50,000–200,000 live births [4]. Although this syndrome was first described over a century ago, our understanding of it is still incomplete because of its rarity.

This report describes the case of a 32-year-old Caucasian female with family history of PJS presenting acutely due to intestinal obstruction with poor surveillance of her condition. This case further highlights the importance of recognizing patients at risk of developing PJS and prevention strategies in patients with PJS in order to avoid complications.

Case Presentation

A 32-year-old woman was referred to the surgical department in July 2010, with symptoms suggestive of an obstructive syndrome: intense diffuse abdominal pain, abdominal distension, vomiting, and constipation. On examination, there were multiple perioral pigmented lesions. An urgent exploratory laparotomy revealed small bowel obstruction caused by an intussusception with a large polyp.

The patient had a similar episode in 2006 when the diagnosis of PJS has been confirmed histopathologically, revealing hamartomatous polyps and other highly dysplastic polyps with segments of glandular and mucinous carcinoma. However, no surveillance of the condition has been done for 4 years following the diagnosis resulting in major complications.

Regarding the past medical history, the patient suffered five other surgical interventions, including three others linked to an obstructive phenomenon, appendicectomy, and extrauterine pregnancy. Moreover, it was discovered that the family history was associated as her grandparent died from unknown neoplasia, her father suffered from multiple intestinal obstructions and died from pulmonary neoplasm, and her brother was diagnosed with PJS.

Furthermore, the laboratory results showed normochromic normocytic anemia linked to an iron deficiency with a hemoglobin of 10,5g/dl and protein malnutrition due to the short bowel syndrome post-surgical resection. As for imaging, abdominal ultrasonography was performed, which showed intussusception of the bowel, a hepatic he-

* Correspondence to: Marina Georgia Balosin
E-mail: marina.balosin@yahoo.com

mangioma, and Computer Tomography (CT) showed a benign pulmonary tumor located in the left inferior lobe.

Later in October 2010, the patient was presented to the gastroenterology department for obscure gastrointestinal bleeding. CT enteroclysis had shown several jejunal polyps. A spiral endoscopy procedure was performed. Multiple pedunculated and sessile polyps of varying sizes in the small bowel were detected beyond the ligament of Treitz, some with superficial erosions, and friable (Figure 1). A hot snare polypectomy was performed for several lesions (Figure 2). Four polyps were removed from the proximal jejunum (Figure 3), two of which were PJS polyps with high-grade dysplasia and in situ carcinoma, emphasizing the risk of gastrointestinal cancer.

The Regional Gastroenterology and Hepatology Institute has managed the patient from 2010. In present, she is treated endoscopically every two years with polypectomy. Polyps larger than 15-20mm must be resected within elective polypectomy to prevent obstruction and intussusception. Smaller polyps should be resected as well if they are symptomatic. Consecutive to a routine endoscopy surveillance and polypectomies for the last 13 years the physicians were able to prevent complications.

Another essential and frequent complication is the bleeding from polyps which can be manifested by anemia, melena, or rectorrhagia. Occult hemorrhages can be revealed by a complete blood count and a hemoccult test every year. Also, the anemia is managed with iron supplements.

As for routine screening for non-GI cancer, the most important for a female patient is the breast and gynecologic exam every year. The breast exam consists of MRI, mammography, and ultrasonography. Moreover, the gynecologic exam should include PAP and HPV tests and screening for ovarian and uterine cancer [2].

Discussions

Most cases of PJS are revealed at a young age, either by acute intestinal obstruction or anemia. The present study offers the case of this rare disorder in a young woman revealed by jejunal obstruction caused by intussusception. The clinical picture suggests the diagnosis of Peutz-Jeghers syndrome. Mucocutaneous pigmented lesions represent the first clue of the diagnosis, as they occur in approximately 95% of patients with PJS [5]. Patients with perioral or buccal pigmentation and/or ≥ 2 GI hamartomatous polyps or a family history of Peutz-Jeghers syndrome should be evaluated for this syndrome, including testing for *STK11* mutations [6].

PJS might be sporadic or inherited, and clinical manifestations are impressively heterogeneous in both forms. The family history of PJS was detected in the present case suggesting a link with the *STK11* gene. Approximately 60-78% of individuals with PJS have an affected relative [7]. The risk of passing the abnormal gene from an affected parent to an offspring is 50% for each pregnancy. The risk is the same for males and females [7]. Other genetic abnor-

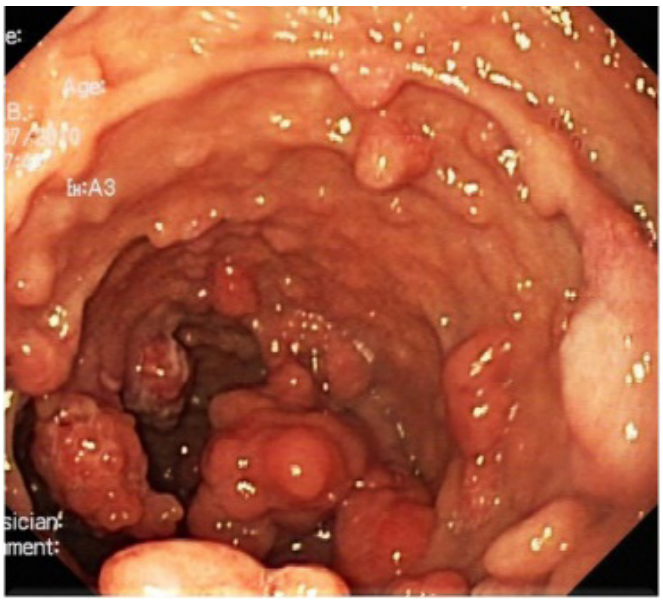

Fig. 1. Aspect of jejunal polyps before polypectomy

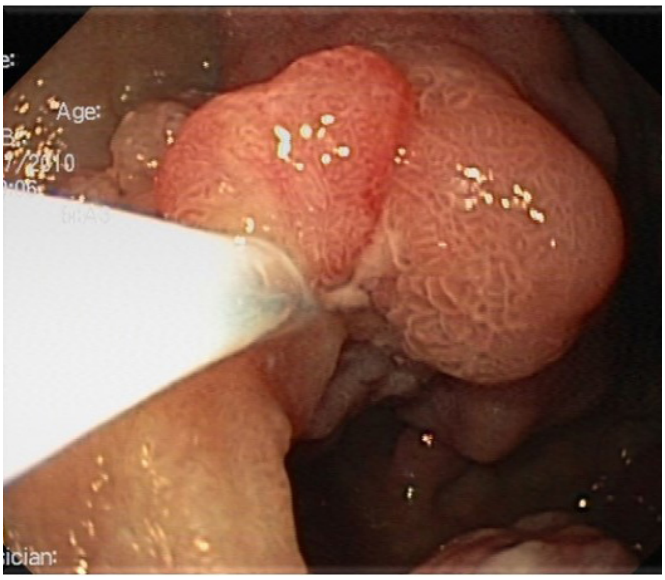

Fig. 2. Snare polypectomy

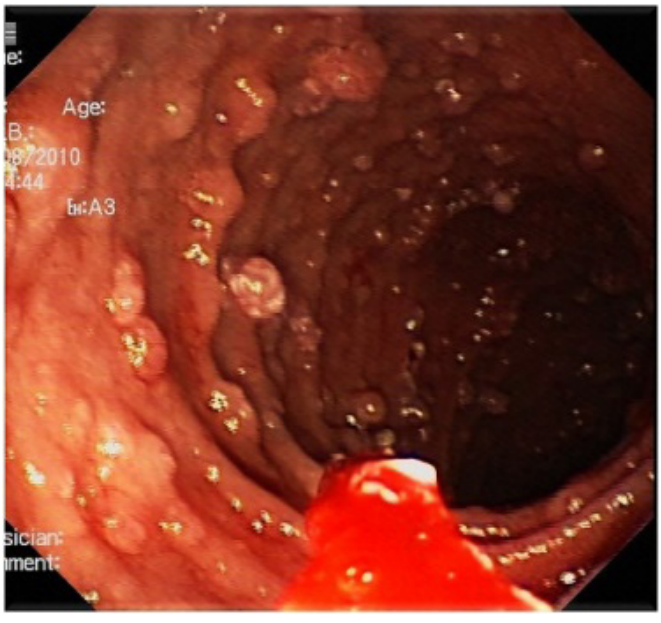

Fig. 3. Aspect of the jejunum after polyp removal

malities have been identified, including over-expression of COX-2, mutations in 19q13 gene, in 6p11 gene, and in the MYH11 gene [6].

The *STK11* gene produces a protein that is involved in the regulation of cell division and programmed cell death (apoptosis). It also interacts with p53, a major tumor suppression protein. Pathogenic mutations in *STK11* lead to either cessation or dysfunction of protein production by the gene and uncontrolled cell growth, which can lead to the development of benign polyps (hamartomas) and cancer [7].

Predisposition to cancer in multiple organs constitutes an essential feature of this condition [6]. Ishida H et al. have demonstrated that the most frequent site of the malignant tumor after the gastrointestinal tract (colorectum, small intestine including the duodenum, and stomach), was the breast, followed by gynecological organs (uterus and ovary), pancreas, and lung [8].

The dark pigmented spots (melanocytic macules) are thought to be caused by inflammation and blockage of melanin migration from cells where it is produced (melanocytes) to cells forming the outermost layer of the skin (keratinocytes) [7]. The pigmentation is frequent in patients and might be the first clinical sign encountered by a physician [4]. It is imperative to diagnose PSJ as soon as possible especially at a young age and in patients with de novo mutations with no family history as to avoid multiple laparotomies, bowel resections and small bowel syndrome subsequently.

European Society of Gastointestinal Endoscopy recommends a baseline esophagogastroduodenoscopy and colonoscopy at the age of 8 years in asymptomatic individuals with Peutz–Jeghers syndrome [2]. The interval for screening endoscopy is between 1–3 years based on phenotype for esophagogastroduodenoscopy and colonoscopy [2].

This case emphasizes the importance of patient education, routine surveillance, and tertiary prevention strategies to avoid complications in individuals diagnosed with PJS as well as the identification and screening of other family members that might have the same condition.

Conclusion

PJS is a pathology challenging to treat due to the nonspecific symptomatology and late diagnosis. Rare, life-threatening complications of PJS, such as intussusception, bleeding, and various types of cancer, are unanticipated. Thus, it is of utmost importance to diagnose PJS as soon as possible and perform routine screening, which will make it possible to prolong the survival of many patients. The key aspect of clinical diagnosis in PJS is the perioral mucocutaneous pigmentation encountered in most patients.

Author contribution

MGB (Conceptualization, Data Curation, Formal Analysis, Investigation, Writing-original draft, Writing-review and edit)

Conflict of interest

None to declare.

References

1. Derqaoui S, Antonio B V, Jahid A, Echarrab E M, Bernoussi Z, Znati K. Peutz Jeghers syndrome revealed by intestinal intussuception: A case report and a review of the literature [Internet]. Archives of Clinical and Medical Case Reports. Fortune Journals; 2020 [cited 2022Dec19]. Available from: https://www.fortunejournals.com/articles/peutz-jeghers-syndrome-revealed-by-intestinal-intussuception-a-case-report-and-a-review-of-the-literature.html
2. van Leerdam ME, Roos VH, van Hooft JE, Dekker E, Jover R, Kaminski MF, et al. Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) guideline [Internet]. Endoscopy. U.S. National Library of Medicine; 2019 [cited 2022Dec10]. Available from: https://pubmed.ncbi.nlm.nih.gov/31342472/
3. Hemminki A, Markie D, Tomlinson I, Avizienyte E, Roth S, Loukola A, et al. A serine/threonine kinase gene defective in Peutz-Jeghers syndrome [Internet]. Nature. U.S. National Library of Medicine; 1998 [cited 2022Dec19]. Available from: https://pubmed.ncbi.nlm.nih.gov/9428765/
4. Homan M, Dolenc Strazar Z, Orel R. R. Peutz-JEGHERS syndrome. A case report [Internet]. Acta dermatovenerologica Alpina, Pannonica, et Adriatica. U.S. National Library of Medicine; 2005 [cited 2022Dec19]. Available from: https://pubmed.ncbi.nlm.nih.gov/15818443/
5. Beggs AD, Latchford AR, Vasen HF, Moslein G, Alonso A, Aretz S, et al. Peutz-Jeghers Syndrome: A systematic review and recommendations for Management [Internet]. Gut. U.S. National Library of Medicine; 2010 [cited 2022Dec19]. Available from: https://pubmed.ncbi.nlm.nih.gov/20581245/
6. Syngal S,Brand RE, Church JM, Giardiello FM, Hampel HL, Burt RW. ACG clinical guideline: Genetic Testing and management of hereditary gastrointestinal cancer syndromes [Internet]. The American journal of gastroenterology. U.S. National Library of Medicine; 2015 [cited 2022Dec19]. Available from: https://pubmed.ncbi.nlm.nih.gov/25645574/
7. Etienne Leveille and Thomas J. McGarrity. Peutz Jeghers syndrome [Internet]. NORD (National Organization for Rare Disorders). 2018 [cited 2022Dec19]. Available from: https://rarediseases.org/rare-diseases/peutz-jeghers-syndrome/
8. Ishida H, Tajima Y, Gonda T, Kumamoto K, Ishibashi K, Iwama T. Update on our investigation of malignant tumors associated with Peutz-JEGHERS syndrome in Japan [Internet]. Surgery today. U.S. National Library of Medicine; 2016 [cited 2022Dec19]. Available from: https://pubmed.ncbi.nlm.nih.gov/26746637/