Early onset Peutz–Jeghers syndrome, the importance of appropriate diagnosis and follow-up

A case report

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Abstract

Rationale: Peutz–Jeghers syndrome (PJS) is currently defined as an inherited condition, also called a familial hamartomatous polyposis syndrome, characterized by the association between pigmented mucocutaneous lesions and hamartomatous polyps in the gastrointestinal tract, especially in the small bowel.

Patient concerns: We present the case of a 7-year-old male patients, diagnosed at the age of 3 years with PJS due to a surgical intervention for acute abdominal pain that revealed a rectal polyp associated with hyperpigmented maculae on the lips and oral mucosa. His family history revealed the same condition in his mother, who was diagnosed much later, at the age of 25 years.

Diagnoses: The upper and lower digestive endoscopy revealed multiple polyps of different sizes within the stomach, and 2 polyps at 5 cm from the anal orifice. The barium enterography revealed 3 polyps within the ileum.

Interventions: We administered blood transfusions and both recto-anal polyps were surgically removed.

Outcomes: The outcome was favorable and the patient was discharged with the recommendations for clinical assessment at least every 6 months, annual laboratory tests, but also follow-up of the detected polyps and screening by upper digestive endoscopy, barium enterography and colonoscopy every 2 years.

Lessons: Early onset of PJS presenting with polyps is quite rare since they require time for their development manifesting usually after the first decade of life. Close monitoring is essential for PJS in order to prevent potential complications and early detect the development of related malignancies.

Abbreviation: PJS = Peutz–Jeghers syndrome.

Keywords: diagnosis, follow-up, Peutz–Jeghers syndrome

1. Introduction

Connor and Hutchinson were the first that reported and illustrated Peutz–Jeghers syndrome (PJS) in a pair of identical twins who presented melanotic macules in 1895 and 1896, respectively.\cite{1,2} Nevertheless, the first publication of PJS belonged to Peutz approximately 35 years later, in 1921, defining the condition in a Dutch family as gastrointestinal familial polyposis associated with pigmentation.\cite{3} PJS is currently defined as an inherited condition, with autosomal dominant pattern of transmission, also called a familial hamartomatous polyposis syndrome, characterized by the association between pigmented mucocutaneous lesions and hamartomatous polyps in the gastrointestinal tract, especially in the small bowel.\cite{4} Thus, genetic determinism is essential in the development of PJS similar to other conditions.\cite{5} Hamartomatous polyposis syndromes carry a considerable predisposition to malignancy and they are rare conditions, representing <1% of all inherited gastrointestinal syndromes with increased risk for cancer.\cite{6} Except for PJS, these syndromes also include familial juvenile polyposis syndrome, phosphatase and tensin homolog gene hamartoma tumour syndromes, basal cell nevus syndrome, multiple endocrine neoplasia syndrome 2B, neurofibromatosis type 1, Cronkhite–Canada syndrome, and hereditary mixed polyposis syndrome.\cite{4} Despite the wide variability regarding the prevalence of PJS reported by different studies, most-likely it is of approximately 1 in 100,000 people.\cite{7} Even though it is well-documented that PJG is an inherited, autosomal dominant disorder, its penetrance varies even among the members of the same family. Thus, it is possible for certain members to express only mucocutaneous hyperpigmentation, while others may be found to manifest both hyperpigmentation and hamartomatous

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**Editor:** N/A.

This research was partially supported by the UEFISCDI grant: “The development of an innovative diagnostic guide of obese child through genetics, anthropometric, bioimpedance and ultrasound assessment”, project number: 8159/27.07.2017 - PN-III-P4-ID-PCE-2016-0766.

The authors have no conflicts of interest to disclose.

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Medicine (2019) 98:27.07(e16381)  
Received: 18 February 2019 / Received in final form: 7 May 2019 / Accepted: 13 June 2019  
http://dx.doi.org/10.1097/MD.0000000000016381
The incriminated gene in the etiology of PJS is STK11 or LKB1, which was suggested to act as a tumor suppressor gene. Mutations in this gene have been identified in 30% to 70% of sporadic cases of PJS and 70% of PJS patients with a positive family history.

Commonly, the polyps from PJS require time for their growth, and the patients usually became symptomatic after the first decade of life. These polyps most frequently affect the small bowel, but they commonly occur also in the colon and stomach, and their sizes vary between 0.1 and 5 cm in diameter. On the other hand, mucocutaneous pigmentation usually occurs during infancy and fades later in life, commonly during late adolescence. These lesions are a result of the presence of pigment-laden macrophages in the dermis, are dark brown or blue-brown, and their sizes vary between 1 and 5 mm. Melanotic pigmented macules are usually located on the vermillion border of the lips (94%), the oral mucosa (66%), hands (74%), and feet (62%), but they can also appear in the periocular, perianal and genital area. The diagnosis of PJS can be established based on the association between the presence of hamartomatous polyp(s) and at least 2 of the following criteria: a positive family of this condition, labial melanin deposits and small bowel polyposis. Due to the increased susceptibility of malignancy in patients with PJS, follow-up and malignancy screening is of major importance. Among the optimal methods used in this purpose, we recall barium enterography, computed tomography with oral contrast, magnetic resonance imaging with enteroclysis, capsule endoscopy, colonoscopy, and upper endoscopy. Other possible malignancies that can occur in PJS patients must also be screened using abdominal ultrasound, chest X-ray, mammography, testicular examination, carbohydrate antigen (CA-19-9), cancer antigen (CA125). Nevertheless, these methods should be chose depending on the specific patient’s manifestations, available resources, psychosocial conditions, and personal preferences. The aim of this case report is to underline the importance of early diagnosis and appropriate follow-up in children with PJS.

The informed written consent was obtained from the patient’s mother prior to the publication of this case report.

2. Case report

2.1. Presenting concerns

We present the case of a 7-year-old male patient, diagnosed at the age of 3 years with PJS due to a surgical intervention for acute abdominal pain that revealed a rectal polyp associated with hyperpigmented macule on the lips and oral mucosa. His family history revealed the same condition in his mother, who was diagnosed much later, at the age of 25 years. We mention that since the diagnosis, the patient was not appropriately monitored due to several factors related to the patient’s compliance and available resources. We must also mention that during this entire period he presented chronic rectal bleeding.

2.2. Clinical findings

The clinical exam at the time of admission revealed influenced general status, severe pallor of the skin and mucosa, multiple pigmented macule on the lips and oral mucosa (Fig. 1), abdominal pain, abdominal scar post-laparotomy, rectal bleeding, and anal extrusion of polyp during defecation.

2.3. Diagnostic focus and assessment

The laboratory tests performed at the time of admission revealed severe anemia (Hb 6.3 g/dL, MCV 53.8 fl, MEH 13.8 pg, Htc 24.5%). Based on all history and his general status, we decided to administer blood transfusion. The abdominal ultrasound did not reveal any pathological findings. We performed an upper digestive endoscopy, which showed multiple polyps of different sizes within the stomach, the biggest one of approximately 10 mm (Figs. 2 and 3). We also performed a colonoscopy and we identified 2 polyps of different sizes at approximately 5 cm from the anal orifice (Fig. 4), and we recommended their excision due to the troublesome anal extrusion of the bigger polyp. The small bowel was assessed using barium enterography, which revealed 3 polyps within the ileum, the biggest one of approximately 10 mm.
2.4. Therapeutic focus and assessment

Based on the previous findings, the patient was referred to the surgeon, and both recto-anal polyps were excised, with a favorable evolution. The histopathological exam of the gastric poly and both recto-anal polyps did not reveal any signs of dysplasia, showing specific hamartomatous polyps.

2.5. Follow-up and outcome

We decided to discharge the patient with the recommendations for clinical assessment at least every 6 months, annual laboratory tests, but also follow-up of the detected polyps and screening by upper digestive endoscopy, barium enterography and colonoscopy every 2 years.

3. Discussions

The diagnosis of PJS is usually established around a similar age in men and women, 23 years and 26 years, respectively.[9] Nevertheless, in our case the diagnosis was established much earlier, at the age of 3 years, but his mother was diagnosed at the age of 25 years similar to most of the PJS patients reported in the literature. The most frequent complaints of patients with PJS are intestinal intussusception (43%), abdominal pain (23%), blood in the stool (14%), polyp anal extrusion (7%), while in the remaining 13% of the patients, the diagnosis is established due to the presence of pigmented mucocutaneous lesions.[12] Our patients presented intestinal intussusception at the age of 3 years. Despite the fact that polyp anal extrusion is a relatively rare complaint in patients with PJS, he was admitted in our clinic at the age of 8 years presenting polyp anal extrusion during defecation. Moreover, since the age of 2 years until the age of 8 years, he complained of recurrent abdominal pain, and he expressed blood in his stool resulting in a severe chronic anemia. Specific mucocutaneous lesions are present in 95% of the patients diagnosed with PJS, their malignant degeneration is extremely rare, and they can disappear during adolescence.[14] Our patient presented multiple, intense pigmentations on the lips and oral mucosa. Nevertheless, data from the literature revealed also cases where no mucocutaneous changes were noticed, as in the case of a 44-year-old male patients reported by Loureiro et al, resulting in an increased difficulty of establishing the diagnosis of PJS.[13] Even though, Peutz–Jeghers polyps most frequently affect the small bowel, colon and stomach, they were also described in the lungs, nares, renal pelvis, and urinary bladder.[14] In PJS, polyps are reported to present the following locations and frequencies: small bowel and colon (equal frequency, 64%), stomach (49%), and rectum (32%).[9] Our patient presented polyps within the stomach, small bowel and at 5 cm from the anal orifice. Usually, the median age for the first presentation due to the presence of polyps is between 11 and 13 years, but approximately one half of the patients will have expressed complaints by the age of 20 years.[15] Nevertheless, our patient was diagnosed with PJS due to the presence of polyp at only 3 years of age. Moreover, the most common complications that can occur during the first 5 decades of life in these patients are: abdominal pain, rectal bleeding, anemia, bowel obstruction or intussusception.[15] Nevertheless, gastrointestinal bleeding with subsequent anemia may be encountered in other gastrointestinal disorders.[16–22] In our case, despite the small age, of only 7 years, the patient experienced all the previously mentioned complications. Intussusception was reported in other cases of PJS, but in older patients.[23,24] Gastric outlet obstruction due to a giant gastric poly is another rare, but possible complication in patients with PJS.[24] In our case, we also identified a big gastric polyp that might lead in time to this complication requiring close monitoring. The most commonly affected gastrointestinal part by PJS polyps is the small bowel, more than 90% of the patients presenting polyps in the small bowel during their lifetime. Within the small bowel, the incidence is the highest in the jejunum, progressively decreasing in the ileum and duodenum.[15] Nevertheless, in our case we identified polyps within the ileum.

A study performed on 14 unrelated PJS patients revealed an even higher median age of the first symptoms, of approximately 19 years, varying between 2 and 72 years.[26] Thus, the age of the smallest patient included in the previously mentioned study is similar to our patient’s, though it is clear that most of the patients included in the study were older, above the age of 10 years. Only 3 patients were below the age of 10 years at the time of diagnosis, one was 2 years old, the second was 3 years old, while the third was 8 years old.[26] The same study revealed a positive family history in 6 cases underlining the fact that multiple PJS patients do not have any family members diagnosed with the same condition.[26] In our case, the patient’s mother was diagnosed
with PJS, but at a much older age, 25 years. The most frequent complications encountered in the study mentioned above were anemia and polypl-related bowel intussusception as in our patient. Extraintestinal polyps were also reported in patients with PJS, with different locations.\(^\text{[4–7]}\) In our case, we found no extraintestinal polyps.

It is a well-documented fact that patients with PJS present a high risk for both gastrointestinal and extraintestinal malignancies involving pancreas, lung, testis, breast, uterus, ovary and cervix.\(^\text{[6]}\) Therefore, appropriate and close monitoring of these patients is essential in order to detect both polyps, which can lead to intussusception, and any of the possible malignancies mentioned above. Appropriate monitoring depends mainly on the relationship between physician, patient and family that relies mostly on physician’s communication skills.\(^\text{[28]}\) Moreover, due to the high risk for malignancies, it would be ideal if this condition could be included in screening programs similar to other conditions.\(^\text{[29,30]}\)

Our patient was not appropriately monitored could be included in screening programs similar to other cases involving pancreas, lung, testis, breast, uterus, ovary and cervix.\(^\text{[6]}\) Therefore, appropriate and close monitoring of these patients is essential in order to detect both polyps, which can lead to intussusception, and any of the possible malignancies mentioned above. Appropriate monitoring depends mainly on the relationship between physician, patient and family that relies mostly on physician’s communication skills.\(^\text{[28]}\) Moreover, due to the high risk for malignancies, it would be ideal if this condition could be included in screening programs similar to other conditions.\(^\text{[29,30]}\) Our patient was not appropriately monitored because since the age of 3 years and until the age of 7 years he never underwent any supplementary investigations. This fact led to severe anemia due to chronic rectal bleeding associated with anal polyp extrusion during defecation. The treatment in these patients includes both supportive measures and surgical intervention. The supportive measures consist in blood transfusions for patients with severe anemia or anagliesis if needed, whereas the surgical treatment consists in polyp removal in case of troublesome symptoms or in case of malignancy features identified during the histopathological exam of their biopsies. Thus, the prognosis of these patients depends on the patient’s age at the time of diagnosis, the patient’s symptoms, the number of polyps, and especially their associated risk for malignancy transformation. In our case we used upper and lower digestive endoscopy for polyp screening along with polyp biopsy for potential malignancy features. Our patient’s prognosis is unpredictable based on the early onset of the disease with multiple gastric and ileum polyps that led to severe anemia. Nevertheless, further complications might be prevented in case of appropriate follow-up.

Despite its rarity, PJS expresses a particular clinical relevance due to its increased risk for both intestinal and extraintestinal malignancies. Early onset of PJS presenting with polypl is quite rare since they require time for their development manifesting usually after the first decade of life. Close monitoring is essential in PJS patients for the prevention of potential complications and early detection of related malignancies.

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