

Peutz-Jeghers syndrome without mucocutaneous pigmentation: a case report

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ABSTRACT

Peutz-Jeghers syndrome is a rare condition characterized by mucocutaneous pigmentation, polyposis and an increased cancer risk at a number of gastrointestinal and extra intestinal organs. We present a patient with a history of gastrointestinal bleeding with no mucocutaneous pigmentation. Upper and lower gastrointestinal endoscopy revealed multiple polyps located in the duodenum and colon. Histopathological evaluation of the polyps revealed hamartomatous polyps of Peutz-Jeghers syndrome.

Keywords: Hamartomatous polyps, Mucocutaneous pigmentations, Peutz-Jeghers syndrome.

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Introduction

Peutz-Jeghers syndrome (PJS) is an autosomal dominantly inherited rare syndrome characterized by mucocutaneous pigmentations, with intestinal and extraintestinal hamartomatous polyps. It is accepted to be a precancerous syndrome. The polyps can cause anemia and intestinal obstruction and intussusceptions (1).

Case report

We report a case of a 37 year old man who admitted to our hospital with complaint of occasionally painless rectal bleeding since 8 years ago which had exacerbated with no history of weight loss, abdominal pain, loss of appetite or anal pain. He had no significant past medical history or significant family history of GI malignancy. In physical

examination he did not had any pigmentation in mucocutaneous and any abnormal finding in abdomen and rectal examination.

Gastrointestinal endoscopy revealed multiple polyps located in the duodenum and less than 100 polyps in colon with aggregation in left colon and sigmoid with pathology of juvenile polyposis.

A barium enema he had mucosal lesions in keeping with polyps in sigmoid (figure 1). A laparotomy was performed and multiple giant polyps entire colon was found. Total abdominal proctocolectomy and J pouch ileoanal anastomosis and omentectomy was performed and a diverting ileostomy was inserted. Histopathological evaluations of the polyps revealed hamartomatous polyps in keeping with a diagnosis of Peutz Jeghers syndrome (figure 2).

Discussion

In 1921, the Dutch physician Peutz first described the combination of gastrointestinal polyps and

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mucocutaneous melanin spots in three young children. His observations in this family led to the definition of what is now known as Peutz–Jeghers syndrome—the American physician Jegher published 10 additional cases in 1944. The disease is inherited as an autosomal dominant gene with high penetrance and 20–63% of cases show inactivating mutations of the gene *STK11* (*LKB1*) (1).

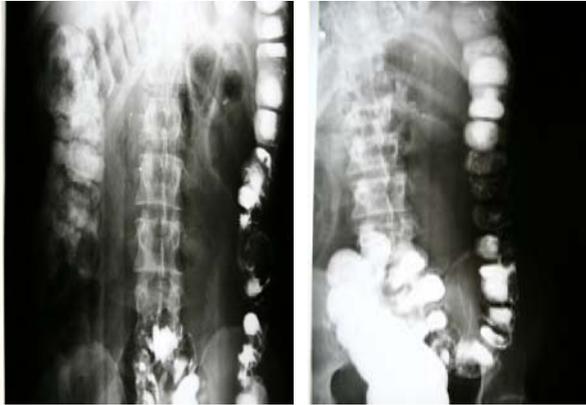


Figure 1. Barium enema showed mucosal lesions with polyps in sigmoid.

Family history is negative in up to 45% of index cases indicating a high incidence of *de novo* germline mutations (2). It is thus recommended that every first degree relative of the PJS patient should be screened for polyps. The incidence of cancer in first degree relatives of these patients has been found to be higher than the normal population (3).

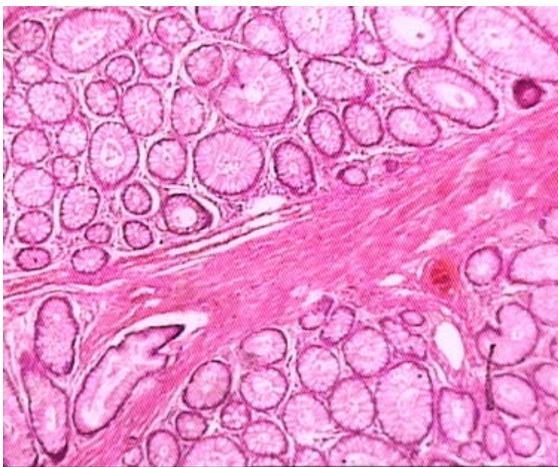


Figure 2. Histopathological evaluations of the polyps revealed hamartomatous polyps

PJS is a rare familial disorder, with an incidence of 1 in 12-30,000 live births (4) and occurs with an estimated frequency of 1/8300 to 1/280,000 individuals (5) and has a male to female ratio of 1:1. The average age at the time of diagnosis is 23 years in men, and 26 years in women (6). PJS presents with characteristic flat, pigmented, freckle-like cutaneous lesions mainly on the lower lip, perioral area, buccal mucosa, periorbital area and eyelids (4). These lesions are benign and not thought to have malignant potential (5). Our patient did not have any pigmentation in mucocutaneous area (figure 3).



Figure 3. No pigmentation was seen in mucocutaneous area

PJS is characterized by hamartomas of the stomach, small intestine (most commonly within the jejunum), colon and rectum. Less commonly, polyposis may also occur within the lung, urinary tract and nasal passages. Previously the hamartomas were not thought to be pre-malignant lesions. More recent research however has recognized that hamartomas in PJS do in fact have malignant potential (1) and in a few polyps, adenomatous change and foci of adenocarcinomas are present (7).

The World Health Organisation clinico-pathological criteria for diagnosing this rare disorder are:

1. Three or more polyps, which show histological features consistent with PJS.
2. A family history of PJS with any number of PJPs.
3. A family history of PJS with characteristic mucocutaneous pigmentation.
4. Characteristic mucocutaneous pigmentation with any number of PJPs (4).

The most frequent complications of PJS are intussusception and bleeding because of ulceration or infarction of the polyps, which often require multiple laparotomies (7). Enteric intussusception in adults is very rare and more than 90% of cases are associated with a pathological leading point. Ileo-ileal intussusception was the most common type. About 90% of cases presented with abdominal pain, while 40% exhibited signs of proximal small bowel obstruction. Rare presentations were diarrhea, bleeding and anaemia. Abdominal CT scan was shown to be the most effective diagnostic instrument (4).

The median age for onset of gastrointestinal symptoms is 13 years of age, and approximately 50% will have experienced symptoms by age 20. In contrast to the other hamartomatous syndromes in which polyps occur most commonly in the colon, PJS-related polyps occur most frequently in the small intestine. Up to 30% will develop polyps in the colon, and approximately 25% will develop gastric polyps. Individuals with PJS have an increased risk for numerous malignancies (5). The overall incidence of cancer among PJS patients has been estimated to be 15-fold higher than that in the general population (8).

Routine endoscopic surveillance of the small and large intestines, with polypectomy, are standard recommendations. Terauchi, Snowberger, and Demarco note that since 2000, capsule endoscopy has revealed images previously only available by radiological imaging or by biopsy specimens. Polypectomies may be performed concurrently with double-balloon endoscopy, a procedure utilizing sequentially inflated and deflated balloons, allowing the endoscope to advance deep into the small bowel.

According to McGarrity and Amos, with advancing age, the risk of intestinal cancer increases in patients with PJS. Indeed, the malignant transformation of previously benign polyps has been referred to as the "hamartoma-adenoma-carcinoma sequence." Patients with PJS are also at risk for extraintestinal malignancies, including cancers of the breast, lung, ovary, uterus, cervix, testicle, and pancreas (9). The greatest specific cancer risk is female breast cancer (45–54%) (5).

In particular, intestinal polyps can cause iron deficiency anemia due to gastrointestinal bleeding and can result in intestinal intussusception and obstruction because of their huge size. This may result in the need for repeated surgical interventions, although the diagnosis and therapy of intestinal polyps with endoscopy now possible (3).

Jejunal polyps can reach up to 100 in number and result in multiple operations which can cause short gut syndrome. The mean age for surgery is generally about 21.4 years and our patient was 37 years old. It has been recommended that pre- and intraoperative endoscopic examination be performed to prevent multiple operations and cancer development (3).

Surgical excision of lesions may be required in:

- Endoscopic polypectomy for diagnosis and control of symptoms.
- Laparotomy and resection are reserved for repeated intussusception or persistent intestinal bleeding (10).

Because the entire length of the GI tract may be affected, surgery is reserved for symptoms such as obstruction or bleeding or for patients in whom polyps develop adenomatous features (11).

Currently large bowel surveillance is recommended at 2–3-year intervals beginning in adulthood. The intervention should visualize the entire colon by either colonoscopy or flexible sigmoidoscopy together with barium enema. To address the gastric cancer risk, surveillance guidelines recommend upper GI endoscopy at 2–3 year intervals.

Extraintestinal surveillance should include: yearly ultrasound examination of the reproductive organs (ovaries and Testis); mammography every 2–3 years from age 25, then yearly after age 50 and an annual cervical smear (Table 1) (1, 6).

Table 1. Management of Peutz-Jeghers Syndrome.

1. Upper endoscopy every 2 years starting at 10 to 15 years of age
 2. Enteroscopy/small bowel x-ray (small bowel follow-through or enteroclysis) every 2 years starting at 10 to 15 years of age
 3. Colonoscopy every 3 years starting at 15 to 20 years of age
 4. Removal of all polyps found >1 to 1.5 cm (by endoscopy methods or at laparotomy with intraoperative endoscopy)
 5. Endoscopic ultrasound or MRCP every 1 to 2 years starting at 30 years of age
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Intestinal polyps also can cause iron deficiency anemia by producing overt or occult bleeding into the gastrointestinal lumen. Less than 100 hamartomatous polyps in the rectum and duodenum were detected by histopathologic evaluation in our patient. Extraintestinal polyps are rarely found. They may be located in the respiratory system, urogenital system and gallbladder. There is controversy regarding the benefit of prophylactic polypectomy. Malignant transformation of small polyps is very rare but regular follow-up should occur. In our patient, no extraintestinal polyps were found and there were no gallbladder or urogenital polyps on ultrasonographic examination. During histopathologic evaluation, cancer can be mistakenly diagnosed if dysplastic epithelium is located in the submucosa and muscularis mucosa. It is thought that intestinal cancers seen in PJS patients may originate in the polyp's epithelium, and it is therefore essential that every polyp is excised and examined. Difficulty in reaching small intestinal polyps with an endoscope is a problem in PJS polyp surveillance programs. Although it has been found that there is a high cancer risk in PJS patients according to John Hopkin's hospital

polyposis registry (12), no cancer was found in our patient's polyps.

Breast cancer may be seen in younger patients and may be located in both breasts, but breast examination was normal in our patient. Cancer may also be seen in the pancreas (adenocarcinoma and cystadenocarcinoma), gallbladder and biliary tree and there is an increased association with carcinoid syndrome and malignant melanoma. Abdominal tomography, ultrasonographic evaluation and alphafetoprotein and carcinoembriogenic antigen levels were normal in our patient. Ovarian cysts and tumors are found in 5-12% of patients, with cervical adenocarcinomas and ovarian tumors being the two most common and sertoli cell tumor being the rarest. Ovarian tumors are generally sporadic and benign, although one malignant case has been reported. Testicular sex cord tumors can cause earlier bone maturation and prepubertal gynecomastia in 10% of patients. All patients with gynecomastia should therefore be screened for testicular tumor. Testicular ultrasonography and biopsy are necessary for diagnosis bilateral mucinous ovarian tumors are also common. The patient was advised to attend follow-up every two years. Tuberos sclerosis is a frequent neurologic problem in PJS patients and it is characterized by hamartomatous polyp, mental retardation, and epilepsy and adenoma cebaceum. This was not present in our patient and his neurological examination was normal (3).

Conclusion

In conclusion, it is recommended that any patient presenting with rectal bleeding should be investigated for poplys and Peutz-Jeghers syndrome. In addition, patients in whom this syndrome is diagnosed should be evaluated for cancer and family screening should be considered.

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