Peutz–Jeghers syndrome

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Key Points

1. Autosomal dominant inheritance and mutation of *STK11* gene.
2. Mucosal pigmentation and hamartomatous polyps in the gastrointestinal tract that may lead to complications such as intestinal bleeding, intussusception, and intestinal obstruction.
3. Because it is associated with the development of gastrointestinal tumor or extraintestinal tumor, regular screening is important.

Prevalence and Related Genes

PJS has an estimated prevalence of 1:5000 to 1:25,000 births [1], and may manifest with various clinical features. One family member may exhibit pigmentation, while the other family member may have pigmentation and polyps. PJS can be diagnosed by identifying mutations in *STK11 (serine/threonine-protein kinase 11; LKB1)* through genetic testing. The *STK11* gene is located on chromosome 19p13.3 and is known to suppress AMP activator protein kinase (AMPK) and the mTOR signaling pathway. However, the precise mechanism of action of *STK11* is unknown.

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Clinical Features

PJS can be diagnosed when positive family history, hyperpigmentation, small intestinal polyps, or more than two of these clinical features are exhibited [2, 3]. Hyperpigmentation occurs as spots on the mucous membranes of the lips, mouth, eyes, and ball, and may rarely occur on the fingers, toes, palms, soles of the feet, or intestinal mucosa. It is very rare that the disease becomes malignant and it may disappear in adolescence. The unique characteristic of the hamartomatous polyps caused by PJS is that the cellular components are normal, but the polyp structure is distorted [2].

Therefore, endoscopy cannot distinguish the polyps, but PJS can be diagnosed through histological confirmation. Polyps usually appear in the small bowel of patients aged 11–13 years. Double-balloon enteroscopy, capsule endoscopy, and magnetic resonance (MR) enterography may be helpful in the diagnosis of small intestinal polyps (Figs. 1, 2). Before 30 years of age, approximately 50% of the patients show symptoms of anemia, gastrointestinal bleeding, abdominal pain, intussusception, or ileus [4–5]. Intussusception is usually seen in the small bowel [6], but the association between intussusception and the *STK11* mutation is unclear [7] (Fig. 3).

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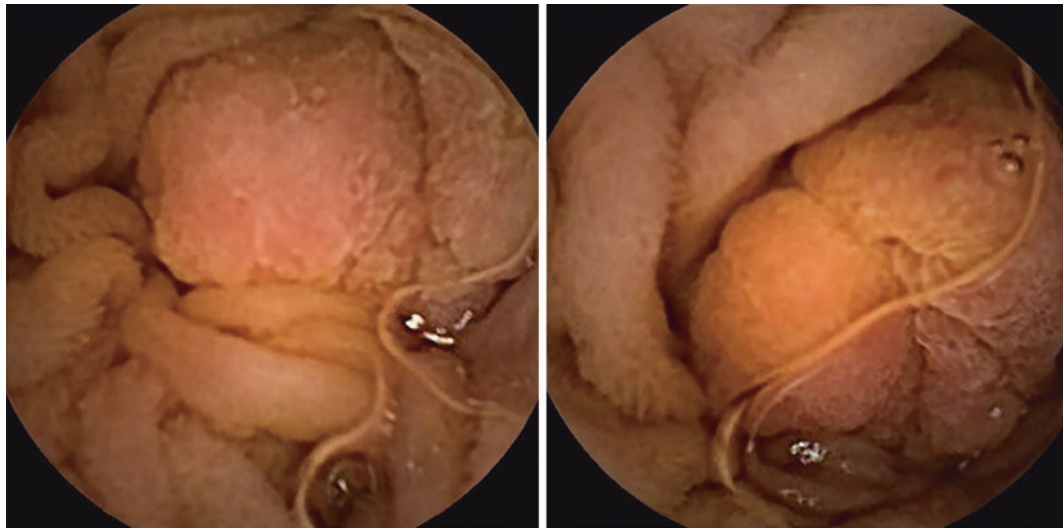

Fig. 1 Hamartomatous polyps in capsule endoscopy

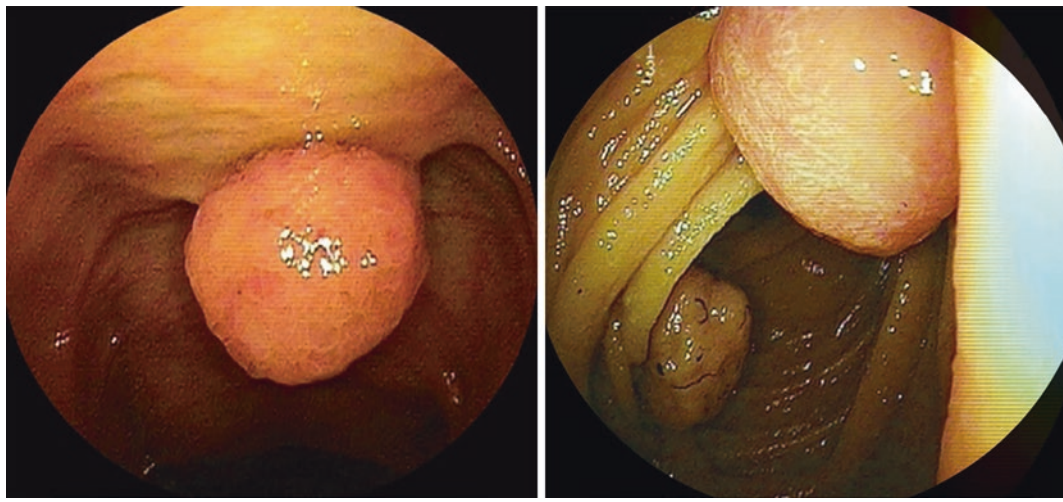

Fig. 2 Hamartomatous polyps in double-balloon endoscopy

Extraintestinal Tumor

PJS is associated with the development of extraintestinal tumors as well as breast cancer, lung cancer, pancreatic cancer, uterine cancer, and ovarian cancer due to a specific gene mutation. Therefore, screening for multiple polyps of the gastrointestinal tract as well as screening for cancer are required regularly [8].

Testicular screening in males is required every year until 12 years of age. If an abnormality of the testis is reported, testicular ultrasound should be performed. Women should complete a breast self-examination every month from the age of 18 years; a breast cancer screening should be performed every year between the ages of 25 and 50 years. Pap smears and liquid cytology should be performed every 3 years after 25 years of age. At 8 years of age, the first esophagogastroduodenoscopy and colonoscopy are necessary. If polyps are observed, they should be examined regularly every 3 years until 50 years of age. If polyps are not observed, the patients should be examined annually until 18 years of age and every 3 years between 18 and 50 years of age.

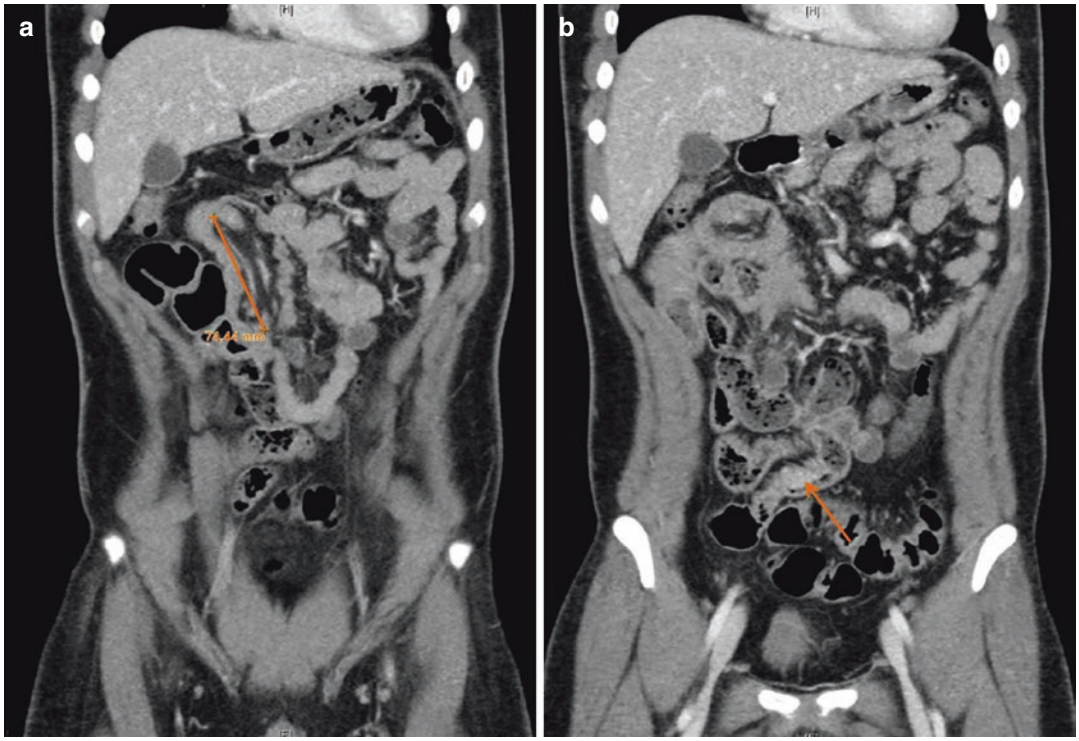

Fig. 3 Small bowel intussusception in abdominal computed tomography. (**a**) Intussusception is noted to be at least 15 cm in length in the small bowel (arrow). (**b**) Multiple polyps are observed in the small bowel

Summary

PJS is inherited through an autosomal dominant *STK11 (LKB1)* gene mutation that may result in hyperpigmentation and hamartomatous polyps. Before 30 years of age, approximately 50% of patients experience anemia, gastrointestinal bleeding, abdominal pain, intussusception, or ileus. Regular cancer screening is needed because it is associated with the development of breast cancer, lung cancer, pancreatic cancer, uterine cancer, and ovarian cancer as well as gastrointestinal and extraintestinal malignancy.

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