

PEUTZ-JEGHERS SYNDROME: ASSOCIATION WITH CANCER AND SURGICAL MANAGEMENT

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Peutz-Jeghers syndrome (P-JS) is a rare autosomal dominant disorder, which is characterized by hamartomatous polyposis of the gastrointestinal tract and melanotic pigmented spots.¹ The pigmented spots appear as flat cutaneous lesions, which are located mainly in the perioral area, especially in the mucous membrane of the oral cavity and lips. They can also be seen in the skin of fingers and toes. The lesions tend to gradually increase in intensity towards, and during, puberty, but slowly start to fade away later in adult life, and may even disappear in some cases.

The polyps can be found anywhere in the gastrointestinal tract, except in the mouth. They are most commonly found in the small intestine, especially in the jejunum,² but can also occur in the stomach and occasionally in the esophagus, duodenum and colon. They are hamartomas of smooth muscle that extend into the lamina propria, and are usually broad based and of variable sizes. The polyps can present with some complications, most commonly chronic rather than acute bleeding and intestinal obstruction due to intussusception or intraluminal obstruction by large polyps. The risk of polyps undergoing malignant transformation is only 2%-3%.³ Common bile duct obstruction that was related to polyposis in P-JS has also been reported.^{4,5} It is believed that polyps in the duodenum can distort duodenal and ductal anatomy and subsequently lead to duodenal and ampullary obstruction.^{5,6} This review looks into the association of P-JS with cancer, and the role of surgery in patients with this rare syndrome.

Association of Peutz-Jeghers Syndrome with Cancer

The association of P-JS with cancer remains a controversial issue. Dozois et al. found no associated cancer risk,⁷ and there was no evidence of an associated decrease in survival rates in a study by Linos et al.,⁸ however, two large studies involving 103 patients later confirmed a high relative risk for both intestinal and extra-intestinal malignancy.^{9,10} Furthermore, P-JS was also

associated with decrease in survival rates,^{10,11} with the risk of death from cancer approaching 40% by the age of 40 years.¹⁰ In the North American study, 15 of the 31 patients investigated (48%) developed cancers. Of these, 10 were nongastrointestinal cancers, four were gastrointestinal, and one was multiple myeloma.⁹ In the European study, 16 of the 72 patients (22%) developed malignant tumors, of which 9 were gastrointestinal and 7 were nongastrointestinal tumors.¹⁰

More recently, Boardman et al. identified 34 patients with P-JS from the Mayo Clinic records from 1945-1996. Of these, 26 noncutaneous cancer developed in 18 of the 34 patients, of which 10 were gastrointestinal and 16 were extra-intestinal.¹² They concluded that P-JS is associated with an increased risk for cancer, particularly that of breast and gynecological organs. Gynecological tumors seem to have a genuine association with P-JS, especially sex cord tumors and adenoma malignum of the cervix.¹³ Feminizing Sertoli cell tumor of the testis also occurs in this syndrome.¹⁴ A wider variety of malignant tumors, such as bilateral breast cancer and pancreatic cancer, is increasingly being reported in association with P-JS.^{10,15-17}

Although some malignant tumors may also arise *de novo*, the transformation of some hamartomas to dysplastic polyps and cancer raises the possibility of a hamartoma-adenoma-cancer sequence.^{9,10} Whether other extra-intestinal neoplasms, such as pancreatic cancer, bilateral breast cancer,¹⁶ and gynecological tumors have true association with P-JS or a mere coincidental existence remains unknown.¹⁷

The author recently encountered a young female patient with P-JS presenting with duodenal and common bile duct obstruction due to a large polyp in the second part of the duodenum, which looked radiologically and endoscopically malignant. Partial duodenectomy revealed a large completely benign hamartoma.⁶ Based on evidence from reviewed literature, this author believes that the risk of cancer in patients with P-JS is high and, therefore, a high index of suspicion should be maintained in such cases. The author also believes that any patient with P-JS should undergo a well-structured cancer screening program and follow-up protocol similar to that designed by St. Mark's Polyposis Registry.¹⁷ This involves yearly hemoglobin, pelvic and abdominal ultrasound tests (testis in males with feminising features), two-yearly upper and lower endoscopy, two-yearly small bowel x-rays (less frequent if successive examinations are clear), three-yearly cervical

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smear and mammography (at ages 25, 30, 35, and 40, then two yearly until 50, then yearly thereafter).¹⁷

Surgery in Peutz-Jeghers Syndrome

P-JS patients often have a history of multiple laparotomies for various polyp-related complications, e.g., bleeding, intestinal obstruction, etc. At laparotomy, intussusception is usually reduced and polyps acting as leading points are excised. Polypectomy is usually performed via multiple enterotomies, and as many polyps as possible should be removed to minimize the risk of future obstruction or bleeding that may necessitate another laparotomy. Large broad-base polyps may be treated by limited small bowel resection. Preoperatively, once polyps are detected endoscopically, attempts should be made to snare them by upper and lower endoscopies, which should be performed every two years, as advised by St. Mark's Polyposis Surveillance.¹⁷

Endoscopic polypectomy of jejunal polyps can also be performed¹⁸ and is well tolerated. Endoscopic perioperative panpolypectomy can also be carried out at the time of laparotomy, and only bulky, broad-based and invaginating polyps are removed by an enterotomy or a resection.^{19,20} This combined endoscopic and operative approach can preserve bowel integrity and reduce the amount of bowel to be resected, and hence avoid subsequent short bowel syndrome. However, this method is tedious, time-consuming, and necessitates close collaboration between endoscopist and surgeon.²⁰

The use of laparoscopy in diagnosis and reduction of intussusception has recently been reported.²¹ Laparoscopic small bowel resection can also be conducted safely and effectively, thereby eliminating the need for laparotomy, with its attendant postoperative complications. This new minimally invasive modality can be offered to patients with "virgin" abdomen, and can be repeated for the management of future episodes of complications, but its use becomes limited and more hazardous in patients with previous history of multiple laparotomies.

Conclusion

Patients with P-JS seem to be at an increased risk of intestinal and extra-intestinal cancers. Therefore, a high index of suspicion should be maintained in the management of affected patients. Cancer screening programs for the early detection of cancer and a follow-up protocol similar to that of the St. Mark's Polyposis Registry should be devised for such patients. Polyp-related complications often require surgery that may entail small bowel resections in patients with previous history of multiple laparotomies. Repeated resections may lead to short bowel syndrome. However, the use of intraoperative endoscopic snaring is emerging to minimize the length of bowel needing resection. Also, the increasing use of laparoscopy and

intraoperative enteroscopy in surgical treatment of polyp-related complications will certainly reduce the morbidity associated with repeated laparotomies.

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