Peutz-Jeghers syndrome. A case report.

M. Homan, Z. Dolenc Stražar and R. Orel

SUMMARY

Peutz-Jeghers syndrome (PJS) is an unusual hamartomatous polyposis of the gastro intestinal (GI) tract, with pigmentation around lips and macules on the buccal mucosa. The case of a 10-year-old girl who presented with intussusception is reported. A polyp was found to be the cause of an invagination. Histologically it was a hamartoma. PJS is a rare syndrome inherited in an autosomal dominant pattern. Most patients have recurrent episodes of polyp induced bowel intussusception which requires repeated laparotomies. In addition, these patients have an increased risk of malignant disease in gastrointestinal and also non-gastrointestinal sites. To prevent cancer and short bowel syndrome, aggressive screening is recommended. Upper and lower endoscopy should be performed every two years from 10 years of age. Extra-intestinal surveillance for cancers, including abdominal and pelvic ultrasound, as well as testicular and breast examinations once yearly should be introduced in the second decade of life.

Introduction

Peutz-Jeghers syndrome (PJS) (1,2) is a rare disorder characterized by typical pigmented perioral macules, pigmented spots in the buccal mucosa which are present in 90% of patients, and multiple, although rarely more than 20 hamartomatous polyps predominantly in the gastrointestinal (GI) tract (3). Polyps may occasionally be absent. Polyp sizes vary from a few mm to 6 or 7 cm. Most patients have a characteristic clinical course of recurrent episodes of polyp induced bowel obstruction and bleeding. The disease affects males and females equally.

In addition to polyposis, the risk of gastrointestinal and extra-gastrointestinal malignancies is significantly increased in PJS patients (4). The relative risk of dying from a gastrointestinal cancer is 13 times greater. The risk of any other malignancy (especially cancer of the reproductive organs and breast, and also of the pancreas and lung) is 9 times greater than in the general population (5). The Johns Hopkins University reported a 48% incidence of cancer, with 73% of tumors arising in the gastrointestinal tract (6).

A few years ago, two independent groups of inves-

KEY WORDS

Peutz-Jeghers syndrome, 10-year-old girl, case report, diagnosis, follow-up

tigators defined the mutated gene responsible for PJS (7,8). The gene was localized to chromosome 19p34-p36 and is known as STK 11, a serine-threonine kinase involved in growth control regulation (9,10,11). On the other hand, not all patients with PJS have a mutation in this gene (12). Mutations of chromosome 6q and 19q have been suggested in a few families.

Case report

A 10-year-old girl, who appeared normal and without any history of previous diseases, suddenly developed abdominal pain and started to vomit. Examinations showed an intussusception in the upper part of the small bowel. Intraoperatively, a small bowel polyp was found to be the cause of the intussusception. During the procedure the duodenum was manually disinvaginated, and the polyps were not removed. She was transferred to the University Pediatric Clinic in Ljubljana. No family history of PJS or any other polyposis syndrome could be verified and both parents are free of symptoms. Her mother first noted pigmented spots around lips when she was 5 years old (Figure 1). When we examined her, we noticed further pigmentation on the buccal mucosa.

An investigation of the entire gastrointestinal tract was performed. Several polyps of the stomach and duodenum were found endoscopically and largest polyps were biopsied. As a consequence of bleeding from the GI polyps she developed anemia. The polyps were later on removed endoscopically under general anaesthesia.

Macroscopically the largest duodenal polyp, measuring 1,5 x 1 x 0,8 cm, had cerebriform convolutions. The gastric polyps were smaller, between 0,3-0,5 cm in diameter.

Histologically, most of gastric polyps were of hyperplastic type, except for one, which had some branching muscle fibers and was most likely a hamartoma. The largest polyp in the duodenum had sparse arborization of muscularis mucosae covered with normal villi and was defined as a hamartoma, thus confirming the clinical diagnosis of PJS (Figure 2).

After the operation the girl was dismissed from hospital in good condition. She will be closely and regularly monitored.

Discussion

PJS is a rare disease. The incidence is 1 in 30000 to 120000 live births (13). It is inherited GI hamartomatous polyposis syndrome that is associated with mucocutaneus pigmentation. The most distinctive clinical features are melanin pigmentations – brown to black

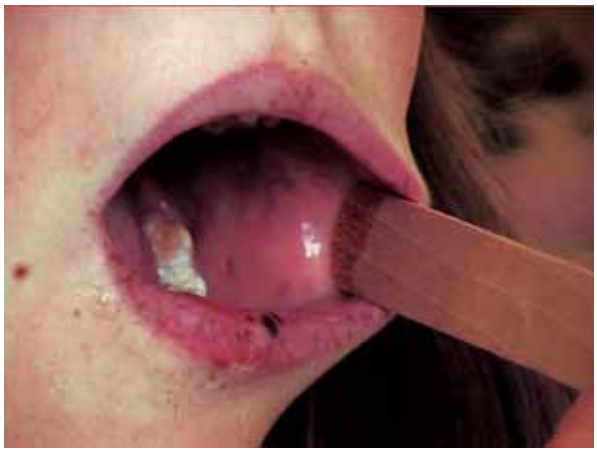

Figure 1. Brown macules on the lips and on oral mucosa.

spots in the lips and buccal mucosa. Pigmentations can also be present in other parts of the body, such as fingers, toes, hands, feet and the mucosa of the nose, conjunctiva and rectum. Some patients do not present the full spectrum of the disease. Giardello et al. proposed diagnostic criteria for PJS (14). The definition requires histopathological confirmation of hamartomatous gastrointestinal polyps and two of the following features: small bowel polyposis, positive family history and pigmented skin or mucosal brown macules. In our case study polyps in the small bowel and stomach were found during the operation, some of them were histologically confirmed as hamartomas and the girl has typical muco-cutaneus hyperpigmentations. We were not able to find any relatives with PJS in the girl's family. But, according to literature, approximately 50% of cases are sporadic and represent new mutations, as is the case with our patient.

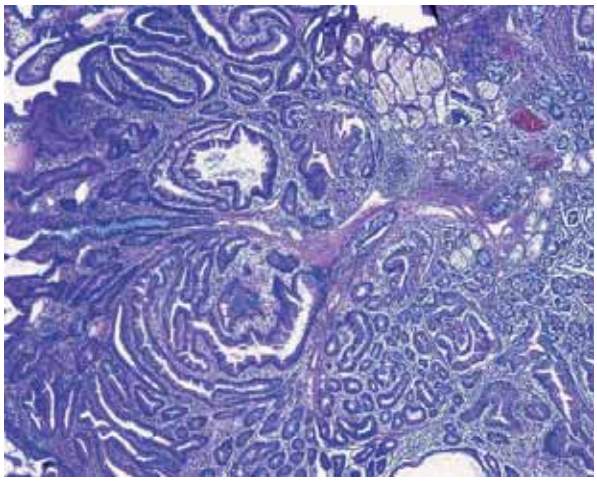

Figure 2. Histopathology: a large polyp displaying a tree-like structure of musculature covered with normal mucosa. HE x 200.

Multiple hamartomatous polyps in the gastrointestinal tract are the hallmark of PJS. Mostly gastrointestinal polyps are found in the small intestine. They can also be found in the stomach and large intestine.

Complications induced by polyps include colicky abdominal pain, bleeding, and bowel obstruction due to intussuception. The time when abdominal symptoms commence can vary. They may present as early as the first year of life or at the age of 40 years (15). By the age of ten years, 30% of patients with PJS already required a laparotomy (16). Individuals with certain type of mutation (missense mutations) of STK 11 had a later onset of PJS symptoms (17). If the polyps are symptomatic or are of significant size (greater than 1,5 cm in diameter) a laparotomy with enteroscopy is recommended.

Almost half the patients underwent two or more laparotomies, which resulted in a sizable percentage of patients suffering from short bowel syndrome as a consequence of the repeated bowel resections. Recently, intraoperative endoscopy and endoscopic polypectomy, rather than segmental resection of the bowel, have been recommended. Periodic endoscopic screenings are advocated every 2 years (16). The new mouth to anus (M2A) capsule endoscopy will probably become the most useful screening tool in the near future.

Conclusion

Patients with PJS should be regularly and closely monitored, because of the increased risk of cancer and to reduce the number of laparotomies. Recent advances in genetic testing and capsule endoscopy should result in improved management of patients with PJS.

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AUTHORS' ADDRESSES

Matjaž Homan MD, MSc, University Pediatric Clinic, Vrazov trg 1, 1000 Ljubljana, corresponding author. e-mail: matjaz.homan@guest.arnes.si
Zvezdana Dolenc Stražar MD, Institute of Pathology, Medical Faculty, Korytkova 2, 1000 Ljubljana
Rok Orel MD, University Pediatric Clinic, Vrazov trg 1, 1000 Ljubljana