CASE COMMENTARY

Peutz-Jeghers Syndrome and Colon Cancer in a 10-Year-Old Girl: Implications for When and How to Start Screening?

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Abstract

The Peutz-Jeghers syndrome (PJS) is characterized by hamartomatous polyposis of the gastro-intestinal (GI) tract, with mucocutaneous pigmentation. We have experienced a case of a 10-year-old girl who presented with PJS, intussusception, colonic perforation and colonic adenocarcinoma. Finally, this case developed airway obstruction from the mediastinal mass. In order to prevent cancer and short bowel syndrome, aggressive screening is recommended.

Key Words: Peutz-Jeghers Syndrome - colon cancer - screening

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Introduction

Peutz-Jeghers syndrome (PJS) is a rare disorder , with an incidence of 1 in 29,000 to120,000 live births (Finan et al,1989, Lindor et al, 1998). The disease has an equal sex distribution and is characterized by intestinal polyps with mucocutaneous pigmentation spots of mouth, hands and feet (Lelli, 2006). Most patients have a characteristic clinical course of recurrent episodes of polyp induced bowel obstruction and bleeding. The risk of gastrointestinal and extra-gastrointestinal malignancies is significantly increased in PJS patients (Giardiello et al, 2000). The relative risk of dying from a gastrointestinal cancer is 13-fold elevated. 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 (Spigelman et al., 1989). We herein report a 10-year-old girl with PJS who early developed malignancy and present screening protocols for this inherited syndrome.

Case report

A 10-year-old girl, who appeared normal without any history of previous diseases, presented with intermittent abdominal pain 7 days before admission. The last 2 days she developed mucous bloody stool and started to vomit. From physical examination, left lower abdominal mass was detected. The computer tomography showed an abdominal mass compatible to intussusception. Emergency hydrostatic reduction with barium enema was performed and showed intussusception in the upper sigmoid colon. The reduction was not success. Then, the patient was took to the operating theater. During the operation, manual reduction was performed successfully. After the operation, the pigmentation on her lips, face and both hands was found. No family history of PJS or any other polyposis syndrome could be verified. Her parents were free of symptoms. In post operative phase, an investigation of the entire gastrointestinal tract was performed and showed multiple polyps in sigmoid colon, descending colon and ascending colon but there was no evidence of stomach or small bowel polyp. The largest polyps were biopsied under general anesthesia.

The result from histological report was colonic polyp with intestinal metaplasia and mild dysplasia. Further management were discussed and planned. The girl was discharged from hospital with good conditions and had an appointment for follow up. Before the appointed date, the girl developed progressive abdominal pain at left side with fever. Peritonitis was concluded from physical examination. Abdominal films showed no gut obstruction, no free air or free fluid in abdominal cavity. A second operation was performed. The operative finding was colonic mass, adhering to abdominal wall, with perforation at the antimesenteric side of the descending colon, and multiple polyposis. Colonic segmental resection and end-to-end anastomosis was performed. Pathological report was hamartoma confirming the clinical diagnosis of PJS and well differentiated adenocarcinoma invading muscular wall. Two in 27 regional lymp nodes were metastatic adenocarcinoma. The plan for subtotal colectomy was set up. But the unexpected event took place, airway obstruction was occurred because of the compression from mediastinal mass. She expired only at the age of 10 years and 8 months.

Discussion

PJS is inherited as an autosomal dominant condition

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Table 1. Screening Recommendations for PJS,(UGI = Upper Gastrointestinal, SHFT = Small bowel follow-through, U/S = Ultrasonography)

Site of cancer	Age to start screening	Duration to repeat diagnostic tests(yr)	Diagnostic tests
Colon	10	2	Colonoscopy
Proximal GI tract/small bowel	10	2	Upper endoscopy UGI-SBFT
Pancreas	30	1-2	Endoscopic U/S
Breast	20	2	Mammography
Uterus	20	1	Transvaginal U/S Endometrial biopsy
Cervix	20	1	Pap smear
Testicular	10	1	Physical examina tion, U/S if clinical indicated

characterized by hamartomatous gastrointestinal polyps and mucocutaneous pigmentation. Specific genetic factors other than STK11 have not yet been identified (Amos et al., 2004) On the other hand, not all patients with PJS have a mutation in this gene (Boardman et al., 2000).

The most distinctive clinical features are melanin pigmentation – brown to black 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, labial and rectum (Tovar et al.,1983; Entius et al., 1999). The pigment spots usually present at infancy and often fade at puberty. Multiple hamartomatous polyps in the gastrointestinal tract are the hallmark of PJS. Polyps are found predominantly in the small bowel but also in the stomach and colon. Complications induced by polyps include colicky abdominal pain, bleeding, and bowel obstruction due to intussusception. 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 (Fernandez Seara et al.,1995). Some patients do not present the full spectrum of the disease.

The diagnostic criteria for PJS 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 (Giardiello et al., 1989). Routine genetic testing and gene therapy for this disease are under investigation but are currently not available (McGarrity et al., 2000).

From this case study, colonic polyps 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 her family. But, according to literature, approximately 50% of cases are sporadic and represent new mutations, as is the case with our patient. These patients have a well established increased cancer risk and many of them die from malignancies at relatively young age (that is, fifth to sixth decadeof life) (Giardiello et al, 2000). This case was only 10 years old but developed colonic adenocarcinoma and airway obstruction from mediastinal mass which is the cause of death. This necessitates a greater awareness of the presentation and care of children with these conditions. Although gastrointestinal cancers develop in PJS, it remains unclear whether these neoplasms are related to the polyps and whether the polyps carry an inherent (pre)malignant potential or not. Individuals with PJS are at an increased risk of colorectal and small intestinal cancer, ductal breast cancer,lung, thyroid, pancreatic, uterine, Sertoli cell testicular, and ovarian sex cord tumors (Lim et al., 2004). Testicular cancer may occur in childhood and may present as gynecomastia.

Recommendations for treatment have changed over the past decade because it was found that there is the increasing of malignancy in PJS. Previous study showed that 30% of PJS clients by the age of ten years needed laparotomy because polyps were of significant size and caused symptoms (Hinds et al., 2004). In addition, polyps larger than 0.5 mm found at endoscopy should be removed. Laparotomy with intraoperative enteroscopy is recommended for removal all small bowel polyps grater than 15 mm in diameter. (Lelli,Jr.,2006) . The previous practice of radical intestinal resections should be avoided because the recurrent nature of the polyps and the ensuing short-bowel syndrome can occur. Almost half the patients underwent two or more laparotomies, which resulted 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. Any intestinal or extraintestinal tumors should be treated aggressively.

Early screening and detection for cancer were recommended to prevent morbility and mortaility. For examples, the management protocol proposed by Phillips and Spigelman (1994) included the following annual evaluations: (1) symptoms relate to polyps, (2) blood cell count to detect anemia cause by blood loos, (3) Breast and pelvic examinations with cervical smears and pelvic ultrasonography in girls, (4) testicular examination with ultrasonography in boys, and (5) pancreatic ultrasonography. McGrath DR (2001) found that screening strategies need to involve upper endoscopy, colonoscopy, and small bowel series in order to remove gastrointestinal polyps in patients aged 12 years and upwards. Esophagogastroduodenoscopy and colonoscopy were also recommended on a bimanual basis along with small intestine contrast studies (Hinds et al., 2004). Futhermore, magnetic resonance imaging (MRI) had shown promise as a surveillance modality for small intestinal screening (Kurugoglu et al., 2003). In addition, mammography was recommended at 25, 30, 35 and 38 years of age, biennially until 50 years of age, and then annually (Writzfeld et al., 2001). Due to the high estimated lifetime risk of malignancy in individuals with PJS and the result from this recent study, the author would like to suggest that screening surveillance protocols need to be aggressive considered such as gastrointestinal, genitourinary, and breast cancer surveillance as shown in Table 1.

Conclusion

Peutz-Jeghers syndrome should be suspected in any

child who presents with colicky pain or occult blood anemia and melanotic pigmented spots. The nature of polyp formation in PJS is unknown. Continuous surveillance through regular endoscopy, laboratory, radiologic investigation, referral for genetic counseling and surgery are crucial recommendation for taking care of this inherited condition in order to reduce risks of cancer and the number of laparotomies. Recent advances in genetic testing, genetic therapy, endoscopic and surgical techniques should be considered to improve management of patients with PJS.

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