Peutz–Jeghers Syndrome which Develops into Descending Sigmoid Colon Adenocarcinoma

Abdul Mughni 1, Albert Eko Hendrawijaya 1*, Meira Dewi Kusuma 2

1 Digestive Surgery Department, Faculty of Medicine, Diponegoro University / Dr. Kariadi General Hospital Center, Semarang, Indonesia
2 Anatomical Pathology Department, Faculty of Medicine, Diponegoro University / Dr. Kariadi General Hospital Center, Semarang, Indonesia

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ABSTRACT
Introduction: Peutz–Jeghers Syndrome (PJS) is an autosomal dominant hereditary condition mainly characterized by hamartomatous gastrointestinal (GI) polyps and mucocutaneous pigmentation [1,2]. The incidence of PJS is estimated to be between 1 in 50,000 to 1 in 200,000 live births [2]. PJS polyps tend to be large, stemmed, and have typical histological characteristics that show a wide band of smooth muscle fibers (often in tree-like configurations), chronic inflammation, edema, and fibrosis within the lamina propria and dilated glands [3]. Polyps are found 60-90% in the small bowel and 50-64% in the colon. They can also be found in extraintestinal sites such as the gallbladder, bronchi, bladder, and ureter. Patients often seek medical treatment because of complications arising from polyps (obstruction, bleeding, anemia, and abdominal pain due to obstruction or infarction). Mucocutaneous hyperpigmentation (melanin deposition) on the lips, buccal mucosa, vulva, fingers, and toes. PJS is also associated with an increased risk for colorectal or extraintestinal tumors.

Case Presentation: A 24-year-old female complained about a lump in her abdomen and constipation. The physical examination found hyperpigmentation on the lips and a hard and mobile mass on the left quadrant abdomen. We found a descending-sigmoid colon tumor with multiple polyps on all colon mucous and performed total colectomy and ileorectal anastomosis on the laparotomy operation. Two months later, Esophagogastroduodenoscopy revealed multiple polyps on Duodenum 1, II, and gaster. The colon tumor pathology result showed well-differentiated adenocarcinoma.

Conclusions: PJS can develop into malignant intestinal tumors that require surgery for resection of the tumor.

CASE REPORT

INTRODUCTION

Peutz-Jeghers syndrome (PJS) is an autosomal dominant hereditary condition mainly characterized by hamartomatous gastrointestinal (GI) polyps and mucocutaneous pigmentation [1,2]. The incidence of PJS is estimated to be between 1 in 50,000 to 1 in 200,000 live births [2]. PJS polyps tend to be large, stemmed, and have typical histological characteristics that show a wide band of smooth muscle fibers (often in tree-like configurations), chronic inflammation, edema, and fibrosis within the lamina propria and dilated glands [3]. Polyps are found 60-90% in the small bowel and 50-64% in the colon. They can also be found in extraintestinal sites such as the gallbladder, bronchi, bladder, and ureter. Patients often seek medical treatment because of complications arising from polyps (obstruction, bleeding, anemia, and abdominal pain due to obstruction or infarction). Mucocutaneous hyperpigmentation (melanin deposition) on the lips, buccal mucosa, nostrils, perianal area, fingers, and volar aspects of hands and feet appears in children but tends to fade in adulthood, notable in around 95% of the patients [1,2]. Besides being associated with an increased risk of colorectal cancer, PJS is also associated with an increased risk of colorectal, breast, pancreatic, ovarian, and gallbladder cancer [4–7]. According to a meta-analysis of 20 cohort studies, PJS is associated with malignancies. The risk of cancer varies between 37 to 93%, with colorectal cancer as the most common (93%), followed by breast, small bowel, gastric, and pancreatic cancer. Other studies support the results [8–10]. The majority of PJS cases occur due to pathogenic variants in the Serine/threonine kinase 11 gene (STK11) or Liver Kinase B1 (LKB1) gene. The germline mutation of that particular gene on chromosome 19p13 is considered the hereditary cause of PJS [11,12]. However, other genetic mutations may be involved because some PJS patients are estimated to have no detected STK11/LKB1 mutations [8]. It has been reported that the mutation can be found in 75–94% of PJS patients [13].

The clinical diagnosis of PJS is made when a person has at least two of the following: two or more types of PJS polyps in the gastrointestinal tract, mucocutaneous
hyperpigmentation (melanin deposition) of the mouth, lips, nose, eyes, genitalia, or fingers; or PJS family history. This is consistent with the American College of Gastroenterology statements regarding genetic testing and management of hereditary syndromes associated with colorectal cancer. Because PJS is rare, patients are referred to particular teams or centers with unique expertise [14].

Treatment involves Esophagogastroduodenoscopy (EGD) and colonoscopic removal of polyps (probably all those > 0.5 or 1 cm in diameter). Colectomy is sometimes necessary to control colonic polyps and should be considered if colonoscopic management is difficult and primarily if a neoplastic change is found in colonic polyps [14].

This case report described a case of PJS that developed into adenocarcinoma of descending sigmoid colon.

CASE PRESENTATION

A 24-year-old female complained about the presence of a mass in her abdomen and defecation difficulties for a month. On the physical examination, hyperpigmentation on the lips was observed (Figure 1). The lower left quadrant abdomen mass was palpated stiff and mobile. The MSCT abdominal scan with intravenous contrast showed intraluminal mass descending-sigmoid colon (3.14 cm x 10.96 cm) accompanied by pericolic tissue infiltration and some visceral peritoneum with multiple lymphadenopathies of the aorta, mesentery, and pericolic (Figure 2). Because the patient experienced bowel obstruction for three days, emergency laparotomy surgery was performed before colonoscopy examination. Intraoperatively, tumors were found in the descending-sigmoid colon accompanied by multiple polyps in the mucosa of the entire colon; thus, total colectomy with ileorectal anastomosis was performed (Figure 3). Tumor pathology descending–sigmoid mass results showed well-differentiated adenocarcinoma (pT2N0Mx) with hyperplastic polyps (Figure 4).

The two-month post-operative EGD examination showed multiple polyps on duodenum I, II, and gastric (Figure 5). Polyp pathology results showed hyperplastic gastric polyps accompanied by chronic gastritis. Based on the anamnesis, physical examination, and work-up, the patient was diagnosed with PJS. The patient met the diagnosis criteria of multiple gastrointestinal polyps with the malignant intestinal or extraintestinal tumors requiring tumor resection.
DISCUSSION

PJS is associated with hamartomatous polyps in all gastrointestinal tracts and hyperpigmentation (melanin deposition) in the skin [2]. The most common location of the Peutz–Jeghers polyp is in the upper gastrointestinal tract. Although most of these patients are relatively asymptomatic, some experience secondary abdominal pain because of impending obstruction due to polyps and others due to gastrointestinal bleeding or accompanied malignant intestinal tumor [1]. PJS has a moderate risk of developing gastrointestinal or extraintestinal malignancy [14].

In this patient, there were melanin deposits on the lips, mass in the left lower quadrant of the abdomen, multiple polyps in the gastric, duodenum, and all colon according to the signs and symptoms of PJS accompanied by adenocarcinoma colon descending-sigmoid tumor. Laparotomy operations were performed before a colonoscopy because the patient’s obstruction worsened. The presence of this malignant tumor is in accordance with the findings of previous clinicians that a malignant gastrointestinal tumor can accompany PJS [4-8]. The therapy needed is a surgical intervention to remove the polyp and malignant tumors [15].

It is widely accepted that PJS is associated with an increased risk of cancer, especially colorectal cancer. The risk of colorectal cancer may reach 39% among PJS patients. The cancer risk among PJS patients varies due to their geography, race, culture, and diet. The mechanism in which PJS develops into cancer is not fully understood. It has been proposed that cancer arises from dysplasia that takes place in the polyps. Some data support the role of somatic mutation or loss of heterozygosity of unaffected LKB1 allele. It is known that LKB1 mutation causes dysregulation of the mTOR (mammalian Target of Rapamycin) pathway which is vital in cellular regulation [15].

This was a rare case proving that PJS can develop into a malignancy. The fact should support that surveillance endoscopy may be needed to detect malignancy as early as possible.

CONCLUSIONS

PJS is the second most common hamartomatous polyp syndrome. Suspicions of the diagnosis leading to this syndrome is characterized by multiple gastrointestinal polyps accompanied by malignant intestinal or extraintestinal tumors that require surgery for resection of the tumor. The history, physical examination, and the use of reasonable and proper diagnostic procedures are expected to identify PJS with malignant tumors as early as possible.

DECLARATIONS

Competing of Interest
The authors declare no competing interest in this study.

Acknowledgment
Not applicable

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