Peutz-Jeghers Syndrome: A Case Report and Literature Review in Indonesia

Kaka Renaldi, Yudha Friatna***

*Division of Gastroenterology, Pancreatobiliary, and Gastrointestinal Endoscopy, Department of Internal Medicine, Cipto Mangunkusumo Hospital

**Department of Internal Medicine, Cipto Mangunkusumo Hospital

Corresponding Author:

Kaka Renaldi, MD. Division of Gastroenterology, Pancreatobiliary, and Gastrointestinal Endoscopy, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia Dr. Cipto Mangunkusumo Hospital. Jl Diponegoro 71, Jakarta 10430, Indonesia. Email:kakarenaldi@gmail.com

ABSTRACT

Background: *Peutz-Jeghers Syndrome (PJS) is a rare hereditary polyposis syndrome that is autosomal dominant and has the main characteristics of hamartoma polyps, mucocutaneous pigmentation, and increased susceptibility to malignancy.*

Case: *This case report presented a 19-year-old man referred from a secondary hospital with complaints of diarrhea for one month before hospital administration. The symptoms happened five times a day with residue in the stool. Mucus or bleeding was not found. Around ten days prior, the polyp came out from the anus, but the patient could pull it back by himself. Diarrhea had been recurring since 2014. The patient then underwent polypectomy (while still children) and until now has undergone polypectomy 11 times. Abdominal CT scan showed multiple polyps with varying morphology in the luminal mucosa of the duodenum, jejunum, ileum, descending colon, sigmoid colon, and rectum, in accordance with the presentation of Peutz-Jeghers syndrome. The colonoscopy examination found a Peutz-Jeghers appearance after a polypectomy with a hemoclip installed. The patient was diagnosed with Peutz-Jeghers Syndrome post polypectomy. The patient received a plan for post-operative complete blood count examinations and periodic colonoscopies.*

Conclusion: *PJS is an important diagnosis to consider in young patient with polyposis, even without mucocutaneous pigmentation.*

Keywords*: Peutz-Jeghers syndrome, polyposis, polypectomy*

ABSTRAK

Latar Belakang: *Sindrom Peutz-Jeghers (SPJ) adalah suatu sindrom polyposis langka yang bersifat autosomal dominan. Ciri khasnya adalah ditemukannya polip hamartoma, pigmentasi mukokutan, dan peningkatan risiko untuk mengalami kanker.*

Kasus: *Laporan kasus ini mendeskripsikan seorang pasien laki-laki berusia 19 tahun yang dirujuk dengan keluhan diare sejak satu bulan lalu. Frekuensinya adalah lima kali sehari dengan residu di tinja. Tidak ada mukus atau perdarahan. Sekitar sepuluh hari lalu, terdapat polip yang keluar dari anus, namun pasien bisa memasukkannya kembali sendiri. Diare terjadi berulang sejak tahun 2014. Pasien ada riwayat polipektomi sebanyak 11 kali sejak kecil. Hasil CT abdomen menunjukkan polip multipel dengan morfologi yang bervariasi di mukosa duodenum, jejunum, ileum, kolon desendens, kolon sigmoid, dan rektum, yang sesuai dengan sindrom Peutz-Jeghers. Pemeriksaan kolonoskopi menampilkan gambaran khas Peutz-Jeghers setelah polipektomi dan*

pemasangan hemoklip. Pasien kemudian didiagnosis dengan sindrom Peutz-Jeghers pasca polipektomi. Pasien direncanakan untuk menjalani pemeriksaan darah perifer lengkap pasca operasi dan kolonoskopi secara periodik.

***Simpulan:** Diagnosis PJS penting untuk dipertimbangkan pada pasien usia muda dengan poliposis, meskipun tidak ditemukan pigmentasi mukokutan.*

***Kata kunci**: Sindrom Peutz-Jeghers, poliposis, polipektomi*

INTRODUCTION

Peutz-Jeghers Syndrome (PJS) is a rare hereditary polyposis syndrome that is autosomal dominant and has the main characteristics of hamartoma polyps, mucocutaneous pigmentation, and increased susceptibility to malignancy. PJS syndrome is a rare disease, with an incidence of approximately 1 in 25 to 300 thousand individuals in the United States. The incidence in Indonesia is unknown.[1]

The LKB1 tumor suppressor gene mutations, the cause of PJS, can induce hamartomatous polyps at an early age, which leads to several consequences, such as acute intestinal blockage, anemia, and stomach pain. Certain cancers are more likely to develop in PJS patients (gastrointestinal, pancreatic, lung, breast, uterine, ovarian, and testicular tumors). PJS prevalence is estimated to range from 1 in 8300 to 1 in 280,000 people.[2]

Device-assisted enteroscopy (double-balloon enteroscopy, spiral enteroscopy, or single-balloon enteroscopy) has become the gold standard in reducing small-bowel polyp burden in PJS. Endoscopic resections in Peutz-Jeghers Syndrome should be performed with special care depending on the polyp size, intestinal anatomy, and motility, and may require different endoscopic techniques. Surveillance should lead to the prevention of complications and thus a reduction in mortality and morbidity of patients.[3]

Below, we present a case report about a young patient with rectal polyps and without mucocutaneous pigmentation. The patient had received multiple polypectomies since he was a child, but no diagnosis of PJS had been made. PJS is rarely diagnosed in Indonesia. This may represent either a low disease prevalence or underdiagnosis. Therefore, we present this case report to raise awareness of PJS in Indonesia.

CASE ILLUSTRATION

A 19-year-old man was referred from a secondary hospital to the internal polyclinic with complaints of diarrhea for one month before hospital administration. The symptoms happened five times a day with residue in the stool. Mucus or bleeding was not found. Around ten days prior, the polyp came out from the anus, but the patient could pull it back by himself. Diarrhea had been recurring since 2014. Thus, he underwent polypectomy (while still children) and until now has undergone polypectomy 11 times. He also complained of decreased appetite due to nausea but no abdominal pain or vomiting.

There were no symptoms when he came to the internal medicine clinic. The stool consistency was normalized, with a frequency of 2-3 times a day. The last time he had abdominal complaints was 2 weeks before entering the hospital. The polyp in the anus only appears when the patient is straining, but the lump can still be pushed back in with the finger. No blood or black stool, cough, fever, shortness of breath, or night sweats were found.

History of diabetes mellitus, hypertension, or tuberculosis was denied. In 2018, he underwent surgery for polyp removal. The patient admitted that he smoked approximately six cigarettes in a day but had stopped a year ago. The history of alcoholism was denied. History of malignancy, diabetes mellitus, hypertension, and heart disease in the family was also denied.

The physical examination found that the patient looked mildly ill, with normal vital signs and a BMI of 24.9 kg/m^2. No abnormalities were found on examination of the head, neck, lungs, heart, and abdomen. Laboratory investigations on 4/5/23 found Hb 10, Ht 35.8, Leukocytes 10,390, Platelets 336,000, PT/APTT <1.5X/<1.5x. Abdominal CT scan on 24/10/2022 showed multiple polyps with varying morphology in the luminal mucosa of the duodenum, jejunum, ileum, descending colon, sigmoid colon, and rectum, especially in the jejunum, varying in size (around 8-30 mm), in accordance with the presentation of Peutz-Jeghers Syndrome. There were no signs of passage or obstruction. There was deformity with sclerotic edges on the posterior aspect of the T11 vertebral body with the impression of butterfly vertebrae. On May 3, 2023, the colonoscopy examination found a Peutz-Jeghers appearance after a polypectomy with a hemoclip installed **(Figure 1).**

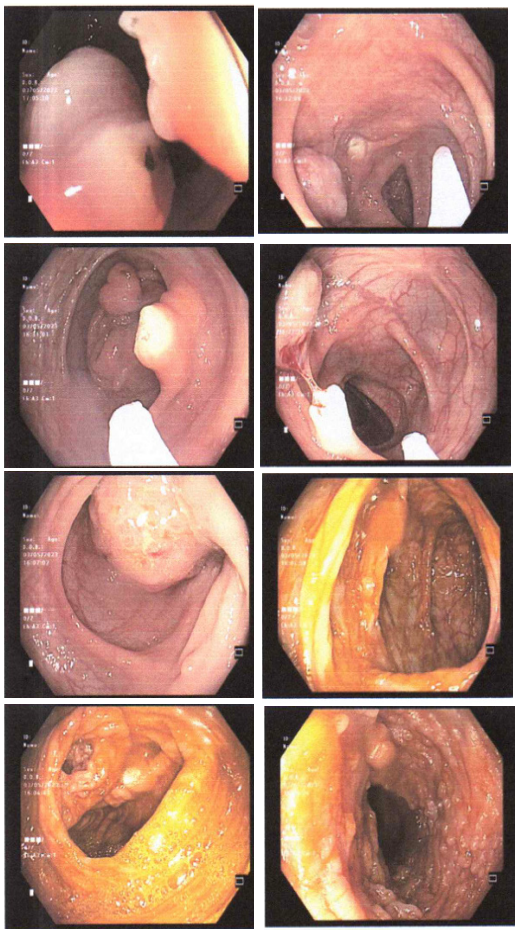

Figure 1. Colonoscopy imaging with the presentation of Peutz-Jeghers Syndrome post polypectomy

The patient was then diagnosed with Peutz-Jeghers Syndrome post-polypectomy. The patient then received a plan for post-operative complete blood count examinations and periodic colonoscopies.

DISCUSSION

In more than 90% of cases of PJS, the genetic abnormality occurs at the STK11/LKB1 gene locus. STK11 is a Tumor Suppressor Gene (TSG) that induces growth arrest in the G1 phase of the cell cycle. This function allows the epithelial cells of the small intestine to undergo cell regeneration cycles without the risk of malignancy. Mutations in this gene often cause polyps and cancer in PJS. [4–6]

Mucocutaneous pigmentation can be found in 95% of PJS cases and is often the main marker of PJS. These pigmented lesions are generally black or brown, round or oval, 1-5 mm in diameter, and the majority are located on the buccal mucosa and lips. Apart from the buccal mucosa and lips, these lesions can also be found around and in the mouth, eyes, nostrils (nostrils), perianal, and on the fingers and toes. These pigmentation spots usually appear for the first time during infancy or early childhood (toddlers), can also be found at birth or later, and tend to enlarge when entering adolescence. The spots may disappear as the patient ages, but the buccal mucosal patches will usually persist. However, in this case, no mucocutaneous pigmentation was observed in the patient's body.[7]

The main clinical manifestations of PJS syndrome are in the digestive tract, especially in the small intestine (generally the jejunum). Polyps can also appear in other parts, such as the large intestine, rectum, and stomach. In rare cases, polyps can be found outside the digestive tract (extraintestinal), such as in the gall bladder and ducts, bronchi, bladder, and ureters. [1,8]

PJS syndrome can be diagnosed if one of the following four conditions or conditions is fulfilled: 1) ≥2 PJ polyps confirmed histologically; 2) the presence of PJ polyps in patients with a first-degree family history of PJS; 3) prominent pigmented mucocutaneous lesions in patients with a family history of PJS syndrome, or 4) the presence of PJ polyps in patients with prominent mucocutaneous pigmented lesions.[9,10,11] The majority of PJS polyp growth begins in the first decade of life, but clinical manifestations usually only begin to appear when entering the second or third decade. These symptoms are often due to large polyps that can experience infarction, ulceration, or bleeding, causing obstruction and intussusception, usually in the small intestine.[1] In this case, the patient reported that polyps were found even in childhood, and the colonoscopy identified the specific characteristic of hamartoma polyps in the digestive tract (anal). Differential diagnosis to consider include other hamartomatous syndromes such as juvenile polyposis syndrome, PTEN hamartoma tumor syndrome, and hereditary mixed polyposis syndrome.[11]

To establish the extent of the disease and the need for clinical follow-up in an individual diagnosed with Peutz-Jeghers syndrome, the evaluations summarized in **Table 1** (if not performed as part of the evaluation that led to the diagnosis) are recommended.[11]

Following initial workup after the diagnosis, endoscopy, colonoscopy, and small bowel examination should be performed every 2-3 years to detect polyps and potential tumors. An annual mammogram is recommended for women. Testicular ultrasound can be done every two years for men. As PJS increases the risk of breast, uterine, and ovarian cancer, it is possible for affected women to undergo preventive mastectomy, hysterectomy, or salpingo-oophorectomy (surgical removal of the breasts, uterus, and fallopian

Table 1. Recommended Evaluations Following Initial Diagnosis in PJS[13]

System/Concern	Evaluation	Comment
Gastrointestinal polyps/cancer	• Colonoscopy • Upper endoscopy • Small-bowel exam by MRE or VCE	Beginning at age 8 yrs or earlier if symptomatic
Breast cancer (females)	Clinical breast exam	Beginning at age 18 yrs
	Breast MRI & mammogram	Beginning at age 30 yrs
Gynecologic cancer (females)	Exam for precocious puberty	Beginning at age 8 yrs
	• Pelvic exam for uterine & ovarian cancer (typically SCTAT) • Pap smear for cervical cancer (typically adenoma malignum)	Beginning at age 18-20 yrs
Testicular cancer (males)	• Testicular exam • Exam for feminizing changes in males • Testicular ultrasound exam if clinically indicated	Beginning at age 10 yrs
Pancreatic cancer	Pancreatic imaging w/endoscopic ultrasound or MRI/MRCP ideally performed at center of expertise	Beginning at age 30 yrs
Genetic counseling	By genetics professionals [1]	To inform patients & their families re nature, MOI, & implications of PJS in order to facilitate medical & personal decision making

MOI= mode of inheritance; MRCP = magnetic resonance cholangiopancreatography; MRE = magnetic resonance enterography; PJS = Peutz-Jeghers syndrome; SCTAT = sex cord tumors with annular tubules; VCE = video capsule endoscopy

tubes and ovaries, respectively). Polyps over 1 cm in size are removed with endoscopic techniques to avoid polyps-related complications such as bleeding and intussusception. These complications might require surgical interventions to be corrected. If a patient undergoes surgery, endoscopic removal of polyps (polypectomy) is performed at the same time as surgery to reduce the risk of recurrence of complications and surgery. In cases where dark-pigmented spots (melanocytic macules) have a greatly negative psychological impact on affected individuals, they can be partially removed with laser treatment.[12,13]

Patients with PJS have a risk of malignancy, both gastrointestinal and extra-gastrointestinal, even from a young age. As many as 48% of patients with PJS suffer from cancer, 73% of which are extra-gastrointestinal (breast, pancreas, thyroid, multiple myeloma, skin). Van Lier et al. stated that the relative risk of malignancy for PJS sufferers ranges from 4.8 to 18 times the general population, with a lifetime cumulative cancer risk of up to 93%. The relative risk of cancer incidence on average, is higher in female patients than in men.[14] The 2015 American College of Gastroenterology (ACG) guidelines stipulate the importance of data on a family history of malignancy, especially the age at diagnosis and the lineage of family members concerned with sufferers of PJS.[15] The most important history is from first- and second-degree relatives.[1,13] In this patient, there were no risk factors of malignancy history in the family. Still, the patient had a history of cigarette smoking, which can be a risk factor for malignancy. Therefore, the patient was planned to establish a routine colonoscopy to evaluate the potency of gastrointestinal polyps or malignancy.

CONCLUSION

Peutz-Jeghers Syndrome (PJS) is a rare hereditary disease characterized by the main clinical manifestations of mucocutaneous pigmentation and gastrointestinal polyps. Until now, PJS therapy has only been to remove polyps in the patient's digestive tract by endoscopic and laparotomy methods. People with PJS have a high risk of getting cancer or malignancy, so they need regular screening.

REFERENCES

1. Mahendra C. Peutz-Jeghers syndrome. *CDK*. 2021;48(12):700-703.
2. Kolhe S, Munjewar P, Pathade A. Case report on management and complication of Peutz Jegher Syndrome. *J Pharm Negat Results*. 2022;13(7):1165-1169. doi:10.47750/pnr.2022.13.S07.166
3. Klimkowski S, Ibrahim M, Rovira JJI, et al. Peutz–jeghers syndrome and the role of imaging: Pathophysiology, diagnosis, and associated cancers. *Cancers (Basel)*. 2021;13(20):1-14. doi:10.3390/cancers13205121
4. Buu A, Cagir B. Peutz-Jeghers Syndrome [Internet]. USA: Medscape; 2018 [updated 2024; cited 12 Mar 2024]. Available from: https://emedicine.medscape.com/article/182006-overview.
5. Achatz MI, Porter CC, Brugieres L, et al. Cancer screening recommendations and clinical management of inherited gastrointestinal cancer syndromes in childhood. *Clin Cancer Res*. 2017;23(13):e107-e114. doi:10.1158/1078-0432.CCR-17-0790
6. Jiang YL, Zhao ZY, Li BR, et al. The altered activity of P53 signaling pathway by STK11 gene mutations and its cancer phenotype in Peutz-Jeghers syndrome. *BMC Med Genet*. 2018;19(1):1-10. doi:10.1186/s12881-018-0626-5
7. Raihan A, Kumaran MS. Exogenous ochronosis in an elderly Indian male: A case report. *Pigment Int*. 2019;6(1):34-36. doi:10.4103/Pigmentinternational.Pigmentinternational
8. Tacheci I, Kopacova M, Bures J. Peutz-Jeghers syndrome. *Curr Opin Gastroenterol*. 2021;37(3):245-254. doi:10.1097/MOG.0000000000000718
9. Daniell J, Plazzer JP, Perera A, Macrae F. An exploration of genotype-phenotype link between Peutz-Jeghers syndrome and STK11: a review. *Fam Cancer*. 2018;17(3):421-427. doi:10.1007/s10689-017-0037-3
10. Boland CR, Idos GE, Durno C, et al. Diagnosis and management of cancer risk in the gastrointestinal hamartomatous polyposis syndromes: Recommendations from the US multi-society task force on colorectal cancer. *Am J Gastroenterol*. 2022;117(6):846-864. doi:10.14309/ajg.0000000000001755
11. Wagner A, Aretz S, Auranen A, et al. The management of Peutz-Jeghers Syndrome: European hereditary tumour group (EHTG) guideline. *J Clin Med*. 2021;10(3):473. Published 2021 Jan 27. doi:10.3390/jcm10030473
12. Laveille E. Peutz-Jeghers Syndrome. Published online 2018.
13. Wu M, Krishnamurthy K. Peutz-Jeghers Syndrome [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [updated 2023 Jul 17; cited 12 Mar 2024]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535357/
14. van Lier MG, Wagner A, Mathus-Vliegen EM, Kuipers EJ, Steyerberg EW, van Leerdam ME. High cancer risk in Peutz-Jeghers syndrome: a systematic review and surveillance recommendations. *Am J Gastroenterol*. 2010;105(6):1258-1265. doi:10.1038/ajg.2009.725
15. Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol.* 2015;110(2):223-263. doi:10.1038/ajg.2014.435