Peutz Jeghers Syndrome in 47 Years Old Woman (Histopathological Review) : Case Report

Danu Yuliarto[1], Prasetyadi Mawardi[2], Ambar Mudigdo[3]

[1]Recidency Program, [2]Associate Professor in Department of Dermatology and Venereology, Faculty of Medicine, Sebelas Maret University/ Dr. Moewardi General Hospital, Surakarta, Indonesia, [3]Professor in Department of Anatomical Pathology, Faculty of Medicine, Sebelas Maret University/ Dr. Moewardi General Hospital, Surakarta, Indonesia

Abstract

Background: Peutz-Jeghers syndrome (PJS) is an autosomal dominant inherited disorder, characterized by intestinal hamartoma polyps in association with distinct patterns of skin and mucosal macular melanin deposition. Patients with PJS have a 15-fold increased risk of developing bowel cancer compared to the general population.

Case: A 47-year-old woman complained of black patches appearing on the lower and upper lips. Several months ago, the patient said that black patches appeared on the gums and inner cheeks. Gastrointestinal complaints such as nausea or vomiting were previously denied. Dermatological examination in the oris et ginggiva et buccalis region showed multiple well-defined hyperpigmented macules. Histopathological examination found an increase of melanocytes in the stratum basale with rows of melanocytes. Patient had an endoscopy in the gastrointestinal tract and histopathological examination of the colonic mucosa, no abnormalities were found and no signs of malignancy were found on histopathological examination.

Conclusion: Result of histopathological examination showed an increase in the number of melanocytes in the stratum basale with lined melanocytes. Based on histopathological examination in this patient more leads to the diagnosis of PJS

Key words: *Peutz-jeghers Syndrome, Histopathology, Melanocytes*

Introduction

Peutz-Jeghers Syndrome (PJS) is an autosomal dominant inherited disorder characterized by intestinal hamartoma polyps in association with a distinct pattern of association of skin and mucosal macular melanin deposition.[1-9] This syndrome was described in 1921 by Jan Peutz (1886-1957) , a Dutch physician who noted the association between intestinal polyps and mucocutaneous macules in Dutch families. Harold Jeghers (1904-1990), an American physician, contributed with a definitive descriptive report of this syndrome, when he published "generalized intestinal polyposis and melanin spots of the oral mucosa, lips and fingers", in 1949, with McKusick and Katz. The eponymous Peutz-Jeghers syndrome was introduced by the radiologist Andre J. Bruwer in 1954.[3-5]

Forty-eight percent of patients with PJS develop cancer and die from cancer at 57 years old. Cancers that develop in the gastrointestinal tract of patients with PJS have a higher frequency than that occurring in the

Corresponding Author:
Dr. Danu Yuliarto
Medical Faculty of Sebelas Maret University, Surakarta, Indonesia/ Jl. Swadarma Raya no. 6 Rt 7 Rw 8, Ulujami, Pesanggrahan, Jakarta, Indonesia (Postal Code: 12250)
Email: danuyuliarto@yahoo.com

general population.[8] During the first 3 decades of life, anemia, anal bleeding, abdominal pain, obstruction or intussusception are common complications in patients with PJS.[13,14] Nearly 50% of patients experience intussusception during their lifetime, most often in the small intestine.[15] The median age at first diagnosis of cancer is 42.9 years, ± 10.2 years.[10-12]

Peutz-Jeghers syndrome should be diagnosed in patients as early as possible. Genetic counseling should also be provided. Many of the gastrointestinal lesions begin to develop early in life, even if the syndrome does not become clinically apparent until the second and third decades of life. Appropriate screening for colon cancer and extra intestinal cancer must be carried out.[12] This paper will report a case report with the results of anamnesis, physical examination, dermatological examination and histopathological picture of melanocytes lined up in the stratum basale. The purpose of this case report is to increase knowledge about diagnosis through histopathological examination of PJS.

Case

A 47-year-old woman from Sukoharjo came to the skin and genital polyclinic of the dr. Moewardi Regional General Hospital Surakarta on March 29th, 2016 with the main complaint of black spots appearing on her lips and gums.

The current history of the disease began about a year ago where the patient complained of black patches appearing on the lips. Initially, the complaint of spotting appeared only on the lower and upper lips, but several months ago the patient said black spots appeared on the gums and inner cheeks. There are no complaints of pain in the spot and never bleed.

This is the first time for the patient has experienced this type of complaint. No family member is sick like this. A history of taking drugs in the long term, a history of wounds, canker sores or previous skin diseases in the area was denied. There was no history of asthma, allergies to certain foods or drugs in the patient or family. Gastrointestinal complaints such as nausea or vomiting were not previously found.

Physical examination showed good general condition with vital signs still within normal limits. Dermatological examination of the oris *et* ginggiva *et* buccalis regions showed multiple well-defined hyperpigmented macules (**Figure 1**). This case was differentially diagnosed with PJS and Cronkhite-Canadian syndrome (CCS).

Subsequently, this patient underwent a skin biopsy in the oris region. After histopathological examination, the epidermis showed an increase in the number of melanocytes in the stratum basale with rows of melanocytes (**Figure 2**).

The patient is planned for consulted to the internal medicine department, then endoscopy is done by the internal medicine department. This patient received therapy in the form of cryotherapy for lesions on the lip mucosa from the skin.

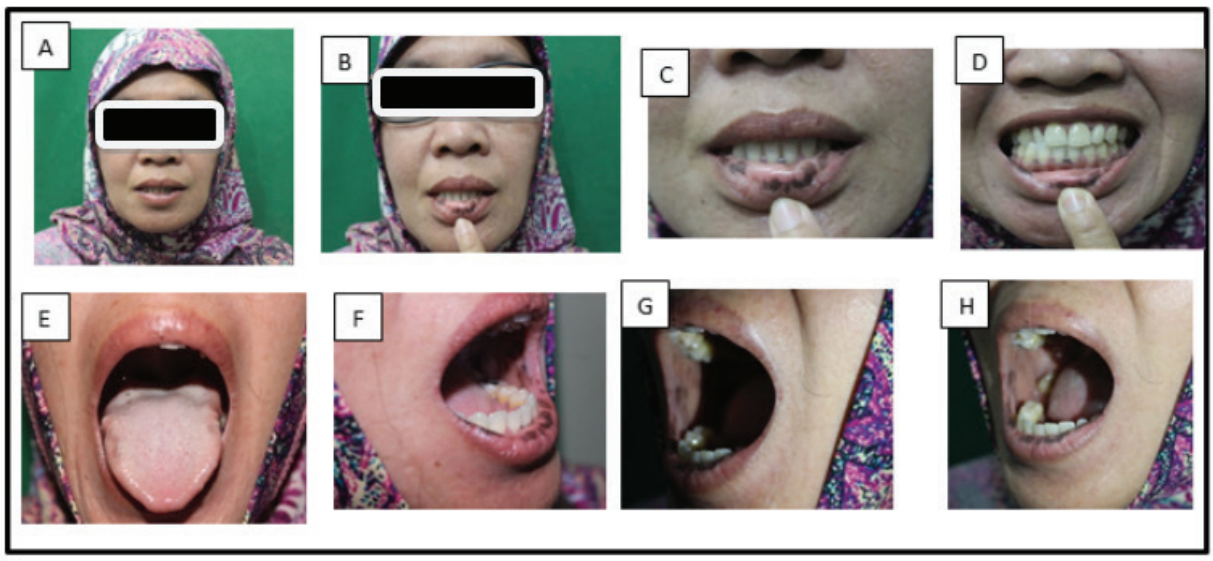

Figure 1. A-D The oris *et* gingival region shows multiple hyperpigmented macules with well-defined borders. E-H The region buccalis *dextra et sinistra* showed multiple hyperpigmented macules with well-defined borders.

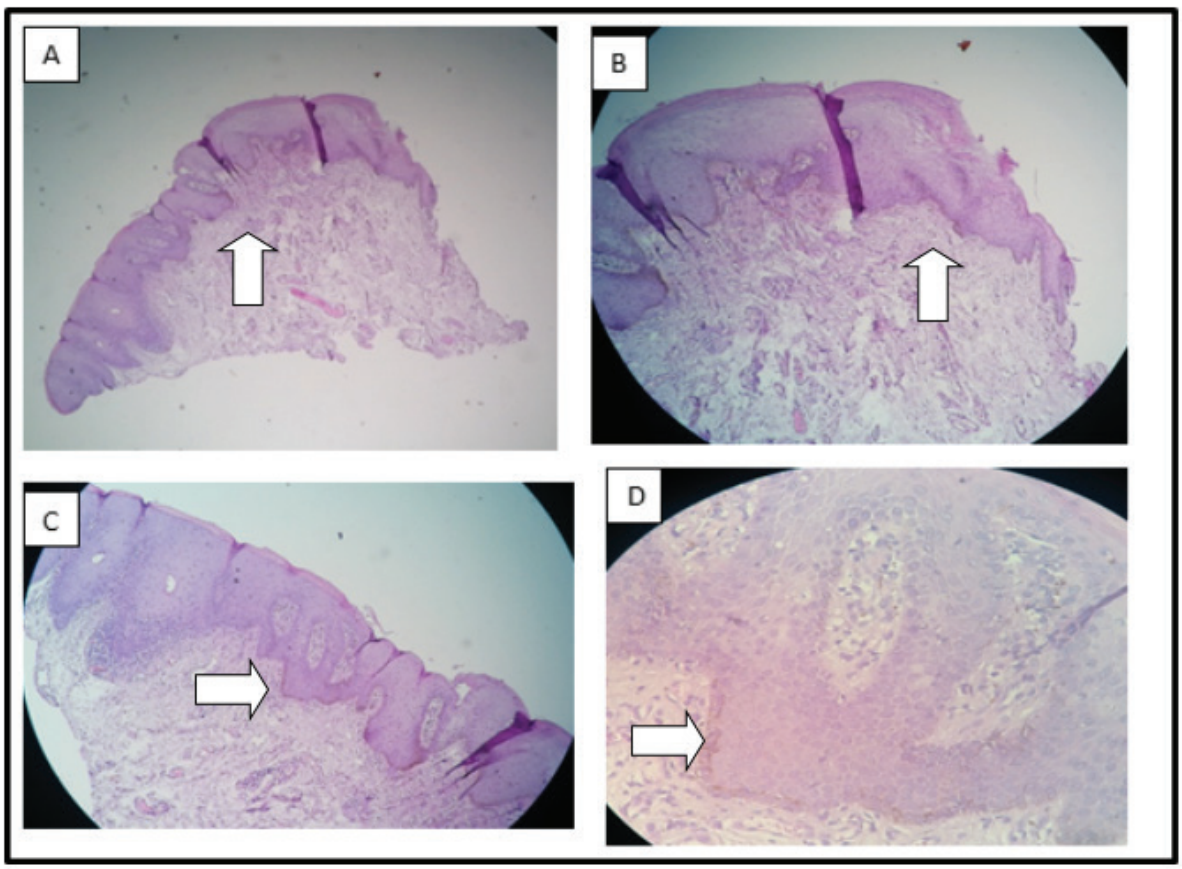

Figure 2. A-D. Melanin cells at the base are lined up. Melanin in the papillary dermis.

Discussion

Peutz-Jeghers syndrome consists of two main components, hamartomatous polyposis of the gastrointestinal tract and mucocutaneous pigmentation. The incidence of PJS is reported to be 1 in 150,000 to 200,000 people.[18] Initial manifestations of PJS are melanin spots, i.e. 1-5 mm hyperpigmented macules on the lips, buccal mucosa, periorbital area, nose, genitals and fingers, usually present in the first year of symptoms and represent mucocutaneous marker of this syndrome. This sign is most commonly seen on the mucous membranes of the lips and cheeks as well as the anal and intestinal mucosa, nose, periorbital area and hands and feet. In some observations there is pigmentation on the nails, however this finding is rare.[16] This case was differentially diagnosed with CCS. Cronkhite-Canada syndrome was first described by Cronkhite and Canada in 1995; so far, about 400 cases mainly of European or Asian descent with a mean age of 59 years have been reported. Cronkhite-Canadian syndrome is also characterized by intestinal polyposis and lentigo-like macules, usually on the face, extremities and palms. Pigmentation tends to be more diffuse than in PJS. Symptoms of CCS may vary, but classic symptoms are characterized by the presence of diffuse gastrointestinal tract polyposis, dystrophic changes in the nails, alopecia, skin hyperpigmentation, diarrhea and weight loss. Other symptoms such as hypogeusia and xerostomia have also been described in the literature.[21] On physical examination in this patient found black patches on the lips, patches on the upper and lower lips, black spots also appeared on the gums and inner cheeks, so in this case it is more suitable with a picture of PJS.

The results of microscopic examination of the skin of patients with PJS who were biopsyed gave an abnormal picture of increased melanin deposition, there was basal hyperpigmentation in the pigmented macula. There is conflicting opinion as to whether an increased number of melanocytes, basal hyperpigmentation with or without increased melanocyte proliferation, that seen in CCS.[16] In this patient's biopsy, histopathological examination results in the epidermis showed an increase in the number of melanocytes in the stratum basale with rows of melanocytes. This is more likely with the histopathological picture in PJS, whereas in CCS when histopathological examination is carried out, hyperpigmentation results in the stratum basale without an increase in the number of melanocytes.

Autosomal dominant PJS is characterized by the association of gastrointestinal polyposis with the presence of pigmented macules, this syndrome has an increased risk of developing cancer at a relatively young age. There is genetic heterogeneity, although the majority of cases involve the serine/threonine kinase (STK11/LKB1) gene on chromosome 19p13.3. This gene encodes the protein LKB1 that regulates the p53 mutation pathway. Apoptosis in gene regions involved in substrate recognition is more often associated with malignancy than mutations in gene regions involved in ATP binding and catalysis. A case has been reported in association with primary melanoma of the rectum.[16,19] In the majority of cases, multiple polyps develop in the small intestine which may become malignant in 2-3% of patients.[20] According to Giardiello et al, endoscopic examination is a surveillance for cancer detection. The age range of finding colorectal cancer in PJS varies from 21-71 years, with an overall risk of 39%, the majority being in males. Hearle et al found that colorectal cancer was the most common cancer of the gastrointestinal tract. The risk of colorectal cancer is 3%, 5%, 15% and 39% at the age of 40, 50, 60 and 70 years. In this large series only one case of sigmoid cancer was detected during surveillance. Less common upper gastrointestinal cancer. Gastric cancer is much more common than oesophageal and the median age at diagnosis of cancer of the gastrointestinal tract is 30 years. Although very rare, upper gastrointestinal cancers have been reported during the first and second decades of life.[12,22] Upper GI colonoscopy and endoscopy are sometimes performed as early as 8 years of age. It is possible that polyps are detected, this should be repeated every 3 years. If no significant polyps are found on initial endoscopy, routine surveillance is repeated at age 18 or earlier depending on symptoms, then repeated every three years. We

recommend that after the age of 50 years the frequency of examinations increases to every 1–2 years because of the increased risk of malignancy at this age.[22] While the endoscopic appearance of CCS may vary, colonic polyps have been characterized by a "strawberry-like" appearance in one study.[21] The etiology of CCS is not well understood but several studies have shown an association with elevated antinuclear antibody (ANA) and IgG4 levels, there is also an association between CCS and hypothyroidism and various autoimmune diseases such as erythematous systemic lupus, rheumatoid arthritis, and scleroderma, all of which lead to autoimmune etiology.[16,19] In this patient, an endoscopy of the gastrointestinal tract and histopathological examination of the colonic mucosa was performed, from the two investigations, no abnormalities were found on gastrointestinal endoscopy and no signs of malignancy were found on histopathological examination of the colonic mucosa.

Although the mucocutaneous pigmentation seen in PJS may fade with age, it can be psychologically disturbing for the patient. The use of intense pulse light (IPL) with a 590nm cut-off filter was reported in one case where it led to cosmetic improvement of the lesions. Similar improvements also have been described with Q-switched ruby lasers and CO2-based lasers. In addition, in the study reported, cryotherapy was performed on 15 patients and gave satisfactory results. Cryotherapy has a mechanism of tissue destruction by rapid clotting. The lesion froze and produced necrotic tissue which then sloughed off spontaneously.[22] In this patient's case, cryotherapy was administered to the skin and genitals.

Conclusion

It has been reported a case of PJS in a 47-year-old woman with complaints of black spots appearing on the lips, the spots appearing only on the lower and upper lips, the complaints have been felt since one year ago, the spots do not increase. On dermatological examination in the oris *et* ginggiva *et* buccalis region, multiple hyperpigmented macules were clearly demarcated. After histopathological examination, the epidermis showed an increase in the number of melanocytes in the stratum basale with rows of melanocytes, this picture supports the diagnosis of PJS. No abnormalities were found on gastrointestinal endoscopy examination from the internal medicine department. Furthermore, this patient received therapy in the form of cryotherapy on the skin and genitals.

Acknowledgements: Nil

Ethical Clearance: This study did not use ethical clearance

Source of Funding: Self-funding. The authors received no financial support for the research, authorship, and publication of this article.

Conflict of Interest Statement: Nil.

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