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CASE REPORT

Family with Peutz–Jeghers syndrome in Indonesia

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Abstract

Peutz–Jeghers syndrome (PJS) is a rare autosomal dominant disorder characterised by mucocutaneous pigmentation, gastrointestinal polyps and an increased risk of gastrointestinal and other cancers. We report an Indonesian woman, aged 28, with black spots on her lips who had multiple polyps extending from the stomach to the rectum. Her father and a son also had mucocutaneous lesions but they did not undergo gastrointestinal investigations. All three had mutations in the serine/threonine kinase 11 gene (*STK11*).

Introduction

Peutz–Jeghers syndrome (PJS) is a rare disorder with pigmented or melanotic macules on the lips or in the mouth and polyps in the gastrointestinal tract. There is also a high risk of malignancy, particularly gastrointestinal cancer. The disease is caused by mutations in a tumor suppressor gene, *STK11* or *LKB1*, that is located on chromosome 19p13.3[1–4]

Apart from the gastrointestinal tract, polyps can also occur in other organs such as the lungs, renal pelvis, urinary bladder, and nasopharynx. Not all these organs have an increased risk of cancer but there is a higher-than-expected risk in pancreas, lungs, breast, uterus, ovaries, and testes.[1,5]

Case report

A 28-year-old Indonesian woman presented with weight loss, 2 months after a jejunostomy for intussusception. She had black spots on her lips, which had begun to fade. Her father and a son also had similar black spots but those on the father had faded and were difficult to photograph. Those on the patient and her son are shown in Figure 1. Colonoscopy, upper GI endoscopy, and enteroscopy revealed multiple polyps in the colon, stomach, duodenum, and jejunum, as shown in Figure 2.

The shape of the polyps was highly variable and included pedunculated polyps, sessile polyps and polyps with up to four lobes. The size of the polyps varied from 3 mm to 15 mm. At histology, the polyps were lined by columnar cells and contained thickened smooth muscle, lymphocytes, histiocytes, blood vessels and stroma. The polyps were categorised as hamartomas.

All three family members had mutations in the *STK11* gene. However, neither the father nor the son had gastrointestinal investigations. The patient has been included in a regular surveillance program.

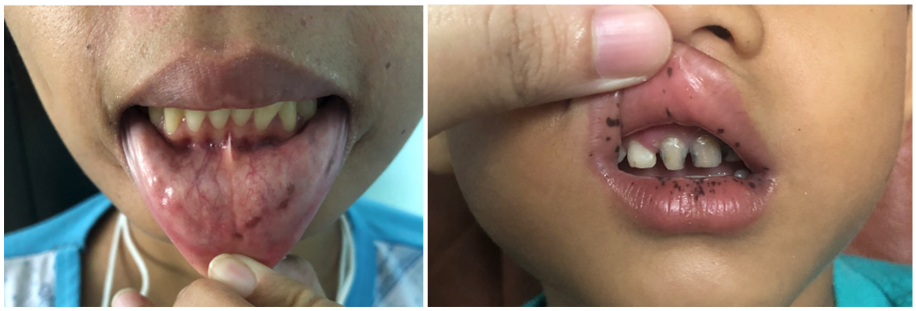

Figure 1 Black spots on the lips of the patient (left) and the patient's child (right).

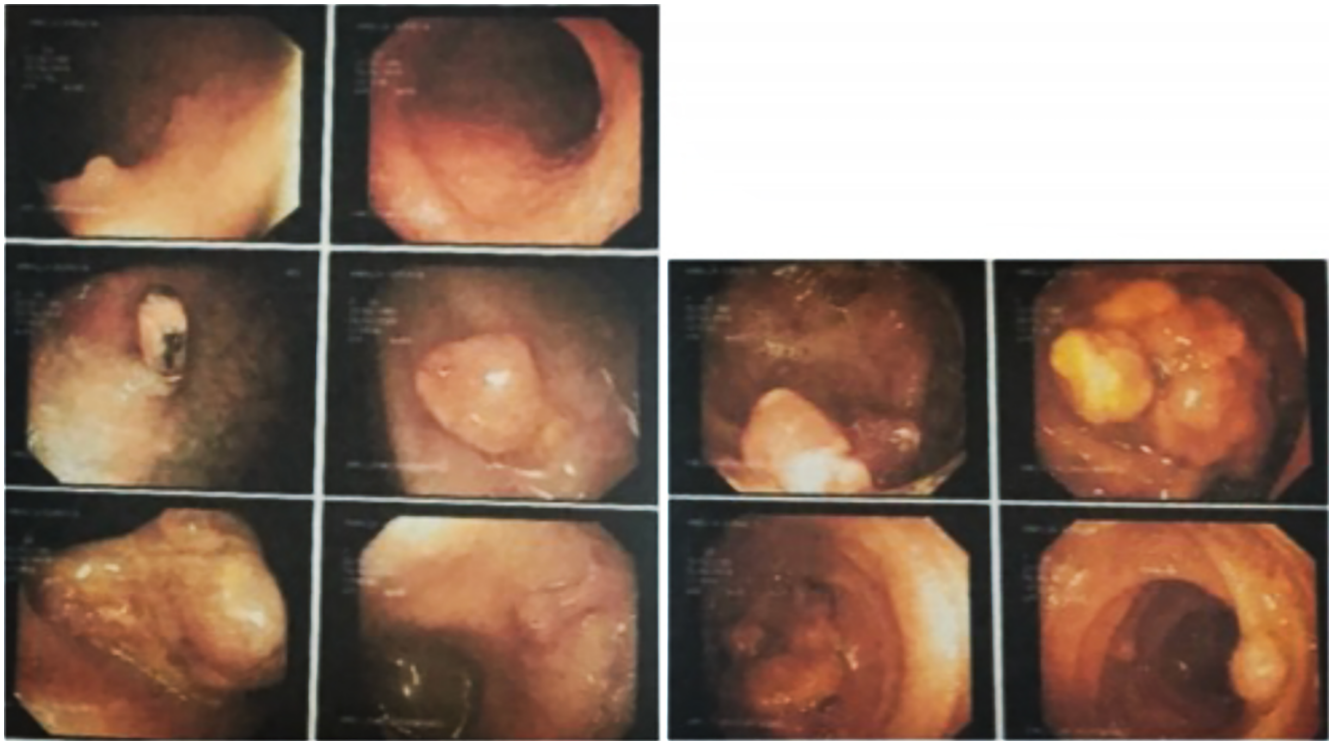

Figure 2 Polyps of various shapes and sizes in the stomach, small bowel and colon.

Discussion

The incidence of PJS in Europe was estimated between 1 in 50 000 and 1 in 200 000 individuals, while in Indonesia there exist still no epidemiological data for PJS. The prevalence is estimated to be in the range of about 1 in 8300 to 1 in 280 000 people.[1,6,7] Even within families, the manifestations of PJS can be highly variable ranging from pigmented mucocutaneous lesions as the only manifestation to pigmented lesions with multiple polyps. In some patients, the recognition of pigmented mucocutaneous lesions can be challenging as pigmentation often fades with advancing age and can be less obvious in people with darker skin.[1–6]

The small bowel is the most common site for hamartomatous polyps followed by the colon and stomach. Polyps are also the most common cause for symptoms including obstructive symptoms, bleeding, anaemia, and intussusception. The characteristics of polyps that are more likely to evolve into cancer is still unknown.

There is some variation in guidelines for the diagnosis of PJS (Table 1). Capsule endoscopy is now the procedure of choice for screening for small bowel polyps. In patients fulfilling the diagnostic criteria for PJS, a heterozygous pathogenetic variant in the *STK11* gene is found in over 90% of patients.[5] However, not all guidelines include genetic testing in the diagnostic criteria as some genetic variants are of uncertain significance and

Table 1 Diagnostic criteria for Peutz–Jeghers syndrome

Guidelines	Diagnostic Criteria
ACG Clinical Guideline 2015[10]	1. Perioral or buccal pigmentation and/or 2. Two or more histologically GI hamartomatous polyp(s) or 3. Family history of PJS
ESGE Guideline 2019[11]	1. ≥2 histologically confirmed Peutz–Jeghers polyps 2. Any Peutz–Jeghers polyps with a family history of PJS 3. The presence of characteristic mucocutaneous pigmentations in an individual with a family history of PJS 4. Any Peutz–Jeghers polyps with characteristic mucocutaneous pigmentation
British Society of Gastroenterology 2020[5]	1. ≥2 histologically confirmed PJ polyps 2. Any PJ polyps detected with a history of PJS in a close relative 3. Characteristic mucocutaneous pigmentation with a history of PJS in a close relative 4. Any number of PJ polyps with characteristic mucocutaneous pigmentation 5. Pathogenic variant in *STK11*

GI, gastrointestinal; PJS, Peutz–Jeghers syndrome.

there is debate about genotype-phenotype associations. Surveillance programs are appropriate in most patients with PJS as the lifetime risk of cancer is approximately 90%.[8–11]

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