



Peutz Jeghers Syndrome: A Diagnosis Clinched on Histopathology

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ABSTRACT

Peutz-Jeghers syndrome (PJS) is an inherited, autosomal dominant disorder characterized by hamartomatous polyps in the gastrointestinal tract and pigmented mucocutaneous lesions. Data on prevalence of PJS in India is not available. PJS predisposes sufferers to various malignancies (gastrointestinal, pancreatic, lung, breast, uterine, ovarian and testicular tumors). We report here a case of 18 years old male with Peutz Jeghers Syndrome.

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Introduction

Peutz-Jeghers syndrome (PJS) is an autosomal dominant inherited condition determined by a mutation localized at 19p13.3; characterized by the occurrence of gastrointestinal hamartomatous polyps in association with mucocutaneous hyperpigmentation. The diagnosis of PJS is based on clinical findings and histopathological patterns of polyps. The disease has variable penetrance, even within families; some members will only manifest hyperpigmentation, while others may manifest pigmentations and hamartomatous polyps. The estimation of population prevalence of PJS differs between studies. The widest estimated range is from 1 in 8300 to 1 in 280 000 individuals [1,2]. Probable prevalence is around 1 in 100 000 people. Peutz Jeghers syndrome is associated with significant morbidity, variable clinical course and considerable predisposition to gastrointestinal & non-gastrointestinal malignancies. An overall recommendation for PJS patients includes not only gastrointestinal multiple polyps resolution, but also regular lifelong cancer screening. Early detection and proper surveillance are vital to minimize the risk of carcinoma. We report here a case of Peutz-Jeghers syndrome which had an interesting clinical presentation.

Case Report

18 years old male presented with complains of pain abdomen, vomiting and constipation since 3 days. The pain was periumbilical in location, insidious in onset, gradually progressive and colicky in nature. He also had multiple episodes of feculent vomiting. Physical examination revealed a tender lump palpable over the right iliac fossa and right lumbar region. No distension or guarding was present. The bowel sounds were exaggerated. Digital rectal

examination showed fecal matter that was blood stained. The other systems were within normal limits.

Laboratory investigations revealed low haemoglobin concentration: 10.1 g/dL (N: 12.5 to 16.5 g/dL). Blood indices & peripheral blood smear examination suggested microcytic hypochromic anemia. Routine blood chemistry reports were within normal range. Ultrasonography revealed features suggestive of subacute intestinal obstruction due to ileo-colic/ileo-ileal intussusception. The patient underwent emergency exploratory laparotomy with ileal resection and end to end anastomosis. The specimen was sent for histopathology examination. Post-operative course was uneventful.

We received a specimen of small intestine measuring 6 cm in length. External surface was congested. A polypoidal growth with a stalk was identified measuring 2x2x1 cm, 2.3 cm from one resected end (Fig 1a). Microscopically Sections from the polyp showed a lining of proliferating mucinous glands with a core consisting of bundles of smooth muscles that showed a characteristic arborizing pattern. Some of the glands were cystically dilated and few areas had pools of mucin (Fig 1b). No atypia or mitotic activity was seen. On basis of above findings, a diagnosis of hamartomatous polyp, ileum, was made. Keeping in mind the age of the patient, clinical presentation and pathological findings, a diagnosis of Peutz Jeghers Syndrome was suspected. The patient was thus re-examined, and found to have multiple, black coloured pigmented lesions on the lips and buccal mucosa, which the patient reported having had since childhood (Fig 2). The histological findings of hamartomatous polyp in ileum along with

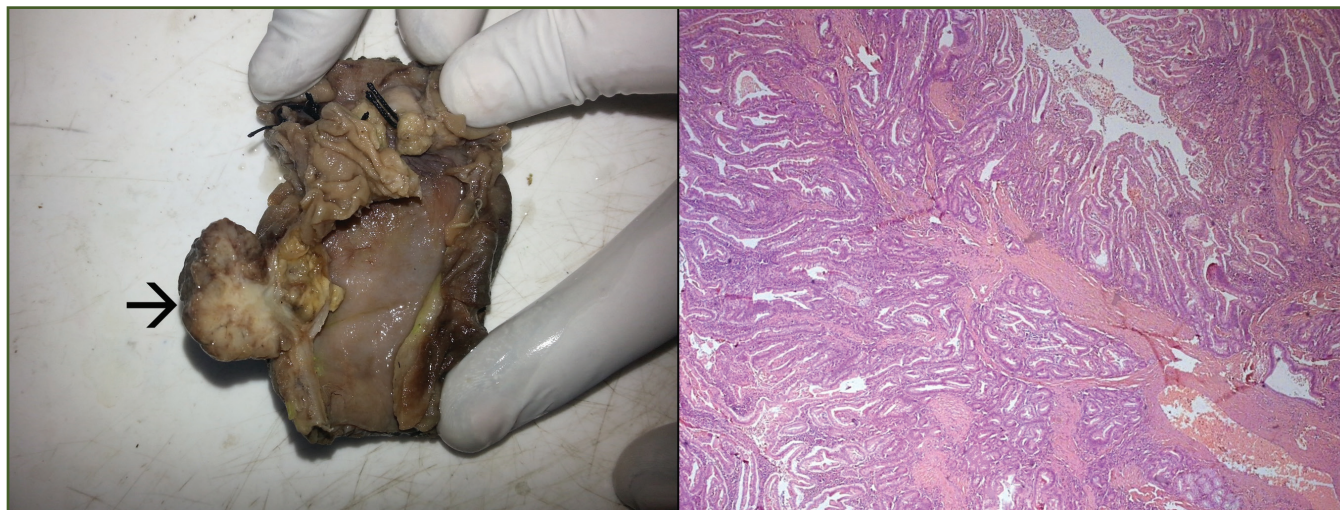


Fig. 1a: A polypoidal growth (→) projecting into the lumen of intestine. Fig1b: Arborising pattern of mucinous glands and smooth muscle H&E stain 40X



Fig. 2: Mucocutaneous pigmentation over the lips

hyperpigmentation of lips and oral mucosa were suggestive of Peutz Jeghers Syndrome (WHO criteria).

Discussion

PJS was first reported in a pair of identical twins with melanotic macules described by Connor in 1895 and illustrated by Hutchinson in 1896[3,4]. The primary description of PJS was published by Peutz in 1921 in one Dutch family (the Harrisburg family) as a gastrointestinal familial polyposis with pigmentations [5]. Jeghers specified the description in 10 cases from different families in his work in 1949 and defined the relations between pigmented lesions, gastrointestinal polyposis and increased risk of carcinoma; approximately half of his patients suffered from gastrointestinal malignancy[6]. PJS, as with the other hamartomatous syndromes, has an autosomal dominant pattern of inheritance with both familial and sporadic transmission. Nowadays, the only identifiable mutations causing PJS affect the STK11 (serine/threonine-protein kinase 11 alias LKB1) gene, located on chromosome 19p13.3 [7]. This gene was identified in 1998. It encodes for a multifunctional serine-threonine kinase, important in second messenger signal transduction. The serine-threonine kinase modulates cellular proliferation, controls cell polarity, and seems to have an important role in responding to low cellular energy levels [8]. This gene has been reported in 80% of patients with PJS. Up to 25% of recorded cases of PJS do not have family history. Those sporadic cases probably arise due to new mutation of STK11 gene or low penetration [9]. In the present case,

there was no positive family history of Peutz-Jeghers syndrome. The Peutz-Jeghers syndrome consists of two major components: hamartomatous polyposis of the gastrointestinal tract and mucocutaneous pigmentation [10]. Mucocutaneous pigmentation is a characteristic finding of PJS and is present in most, but not all, patients who have the disease. The hyperpigmented lesions contain melanotic deposits and commonly manifest in infancy and childhood. Pigmented lesions could fade during puberty and adulthood [9]. The pigmented lesions are often seen on the lips, around the mouth, eyes, nostrils, on the buccal mucosa; and sparsely on the fingers, soles of the feet, palms, anal area and intestinal mucosa [10]. The mucocutaneous lesions of PJS are considered to be hamartomatous in origin and without potential of becoming malignant. Gastrointestinal hamartomatous polyps are another classic finding of Peutz-Jeghers syndrome. Although these polyps are most commonly found in the small intestine, they can occur anywhere from stomach to rectum. The median time to first presentation with polyps is about 11-13 years of age and approximately 50% will have experienced symptoms by the age of 20 years [10]. Patients with PJS often present with a history of intermittent abdominal pain due to small bowel intussusception caused by the polyps. Some intussusceptions spontaneously reduce; others lead to development of small bowel obstruction. Peutz-Jeghers polyps can also ulcerate, leading to acute blood loss or chronic anemia. Although Peutz-Jeghers polyps are most commonly found in the gastrointestinal system, they can also occur in extraintestinal sites such as kidney, ureter, gallbladder, bronchial tree, nasal passages etc.

Individuals with PJS are at risk for the development of gastrointestinal & non-gastrointestinal malignancies. Among the non-gastrointestinal type; pancreas, lung, breast, uterus, cervix, ovary, testis & thyroid being the major sites of malignancies[11]. In a study of Hearle N et al, 96 cancers were found among 419 PJS patients [12]. This study reported the risks of developing gastrointestinal cancer (31%), breast cancer (31%), gynecologic cancer (18%), pancreatic cancer (7%), and lung cancer (13%) by 60 years of age. Individuals with PJS are also at risk for developing rare sex cord tumors. Women are at risk for sex cord tumors with annular tubules and men are at risk for developing Sertoli cell tumors. The Peutz-Jeghers polyp varies in size from <1 cm to >3.5 cm in diameter, and may be pedunculated or sessile. Because it appears to be composed of non-neoplastic tissue normally found at the site, the Peutz-Jeghers polyp is generally considered a hamartomatous polyp but with an abnormal growth pattern. The most characteristic feature of a Peutz-Jeghers polyp is a central core of smooth muscle that extends into the polyp

in an arborizing fashion (Christmas tree like appearance) and that is covered by either normal or hyperplastic mucosa native to the involved site. Adenomatous & carcinomatous changes have been described in Peutz-Jeghers polyps [13]. Epithelial misplacement, also referred to as pseudoinvasion, is another feature seen in some Peutz-Jeghers polyps. It is characterized by cystically dilated benign glands and supporting lamina propria within the submucosa, muscularis propria, or subserosal layers of the gut adjacent to a polyp and extravasated mucin pools.

This feature can mimic the appearance of invasive adenocarcinoma. However, noting the lack of epithelial dysplasia, the presence of supporting lamina propria and the absence of a desmoplastic stromal reaction can help avoid this interpretive error. The diagnosis of PJS is established by the presence of histopathologically confirmed hamartomatous polyps and at least two of the following clinical criteria: a family history of PJS, the presence of mucocutaneous pigmentation and the presence of small-bowel polyps.

Typical imaging features of Peutz-Jeghers syndrome consist of multiple polypoid lesions involving the stomach, small bowel and colon. Although the polyps are often detected with barium studies, they can also be identified with US or CT. Some authors have suggested using US or magnetic resonance (MR) imaging for follow-up imaging to reduce the lifetime radiation burden. Another important imaging finding in Peutz-Jeghers syndrome is intussusception (10).

Over the years, the standard therapy for Peutz-Jeghers syndrome has been laparotomy and bowel resection to remove symptomatic gastrointestinal polyps that cause persistent or recurrent intussusceptions. However, some patients require multiple surgical resections, which can lead to short gut syndrome. Because of this, it has been recommended that endoscopy be performed to remove all polyps. During each laparotomy, the small bowel should be examined by means of intraoperative enteroscopy (IOE). Nowadays, double balloon enteroscopy (DBE) in combination with capsule enteroscopy are the gold standard for the diagnosis and treatment of the small bowel hamartomatous polyps (12).

Conclusion

Peutz-Jeghers syndrome is a rare, autosomal dominant disorder characterized by mucocutaneous pigmentation & gastrointestinal hamartomatous polyps. Because of the increased risk of both gastrointestinal and non-gastrointestinal malignancies in PJS, careful screening of

the patients is recommended. It is necessary to investigate all first-degree relatives of the patient. This case report was presented because of the rarity of this condition and the interesting clinical presentation.

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Competing Interests

NONE DECLARED

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