

Case Report

A Case of Peutz-Jeghers Syndrome with Multiple Intussusceptions

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ABSTRACT

Peutz-jeghers syndrome (PJS) is an autosomal dominant cancer syndrome with variable penetrance and characterised by hamartomatous polyp in gastrointestinal tract with mucocutaneous pigmentation. Approximately one third of PJS patients present in the first decade of life, the rest of them present by second or third decade with equal predilection for both males and females. The most common site of Peutz-jeghers polyp is jejunum. Most of the cases are associated with germline mutations in LKB1/STK11 located on chromosome 19p13.3. The most frequent presentation is intermittent abdominal pain due to intestinal obstruction or intussusception. However intussusception in adults are rare compared to children. Here we present a case of 22 years female who presented with Peutz-jeghers syndrome with multiple intussusceptions.

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Introduction

In 1921, Johannes Peutz, a dutch physician noted a relationship between intestinal polyps and mucocutaneous pigmented macules. Harold Jeghers, an American physician was the first person to publish the description of the term “Peutz-jeghers syndrome” (PJS). PJS is a rare inherited autosomal dominant cancer syndrome with variable penetrance. Approximately one third of PJS patients present in the first decade of life, the rest of them present by second or third decade with equal predilection for both males and females. It is characterised by hamartomatous polyps throughout the gastrointestinal tract and mucocutaneous pigmentation. Less than 5% of cases with PJS lack abnormal mucocutaneous pigmentation and less than 5% with pigmentation lack polyps. Its incidence is 1 in 300,000 births^[1].

Case Report

22years female presented with complaints of intermittent abdominal pain and abdominal distension for 1week and two to three episodes of vomiting with past history of surgery for ileocolic intussusceptions 10 years back. On examination, pigmentation over mucutaneous junction of lips ,fingers and toes were noted. The patient had severe anemia with haemoglobin of 5.4 gm%. CECT –abdomen showed intussusceptions at various levels involving ileoileal and jejunojejunal segments with partial, subacute intestinal obstruction and few calcified mesenteric lymph nodes. UGI scopy showed multiple gastric and duodenal sessile polyps and biopsy taken from these showed H.Pylori associated chronic gastritis and hyperplastic polyp. Colonoscopy showed pedunculated polyps in rectum, sigmoid colon, descending colon and mucosal thickening noted in caecum. Biopsies were taken and it showed tubular adenoma in rectum and caecum, hyperplastic polyps in descending and sigmoid colon. Patient was taken up for diagnostic laparoscopy which showed multiple intussusceptions at ileoileal, 30 cm from duodenojejunal flexure, jejunojejunal levels. Also multiple adhesions from omentum to small bowel noted. Laparotomy was done. After removing the adhesions, intususception was reduced followed by small bowel resection and anastomosis. Resected segment sent for histopathological examination.

Gross: The resected small bowel segments were sent as two separate specimens. One segment measuring 13.5cm and the other measuring 11.5 cm in length. Thickness of the bowel wall is around 0.5 to 0.8 cm. Both segments showed sessile polyp on mucosal surface measuring 4×3×3 cm and 3×3×2.5 cm respectively (fig: 1).

Microscopy of polyps showed glandular epithelium resting on a tree -like branching smooth muscle framework that arises from muscular mucosa which gives ‘Christmas tree’

or arborescent- like appearance at low power (fig: 2). The smooth muscle fibres of muscularis mucosa are thick and broad centrally and thin peripherally. The smooth muscle fibres separating the glands gives a lobulated appearance in some foci (fig: 3). In high power, epithelium lining the glands are benign looking without any atypia and the diagnosis of Peutz-jeghers polyp was made (fig: 4).



Fig. 1: Gross: Segments of small intestine showing polyp.

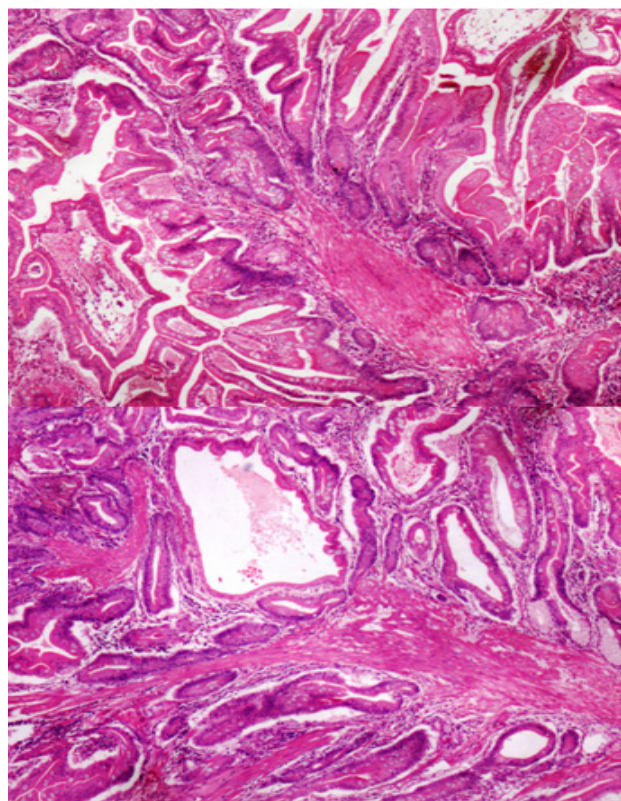


Fig. 2: (a,b): 40x H&E- “Christmas tree appearance”- Glands resting on branching tree like smooth muscle fibres of muscularis mucosa. The smooth muscle is broad and thick centrally and thin peripherally.

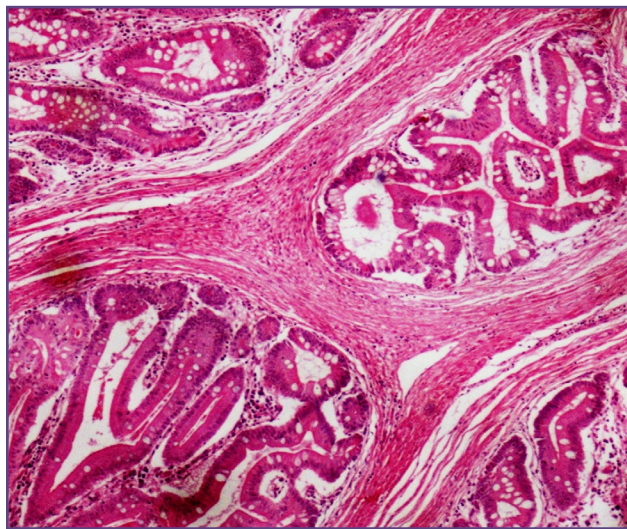


Fig. 3: 40x H&E-Smooth muscle fibres separating group of glands giving a lobular appearance.

Discussion

Peutz-Jeghers syndrome, an autosomal dominant syndrome is characterised by hamartomatous polyp involving the GIT and mucocutaneous pigmentation. In GIT, most common site of hamartomatous polyp is small intestine followed by colon and stomach. In small intestine, polyps involve jejunum followed by ileum and duodenum^[2]. Apart from GIT, hamartomatous polyps can also occur at extraintestinal sites such as nose, bronchi, gallbladder, bile duct, urinary bladder, ureter. The polyps can have adenomatous component in 16 % of cases. Our patient also had adenomatous component in rectum and caecum. Mucocutaneous pigmentation is characterised by flat, pigmented freckle-like lesions most commonly seen around vermilion border of lips in 95% of cases followed by buccal mucosa in 80% of cases. Other sites include hands, feet, genitalia, around nose and eyes. These lesions are benign and have no malignant potential.

The genetic basis for PJS is germline mutations in LKB1/STK11 located on chromosome 19p13.3. However, up to 25% of PJS have no family history but represent spontaneous mutation. LKB1/STK11 encodes serine-threonine kinase that phosphorylates and activates the members of the AMPK (AMP-activated protein kinase)-related subfamily of protein kinases. LKB1/STK11 is a tumor suppressor gene, which plays important role in G1 cell cycle arrest, cell polarity, p53-dependent apoptosis, and cellular energy levels. 80% of patients with PJS had mutations involving this gene. Common mutations are frameshift and nonsense mutations in exons 1–6^[3].

The clinical presentation depends upon the site of location of polyps. Patients with small intestinal polyp present

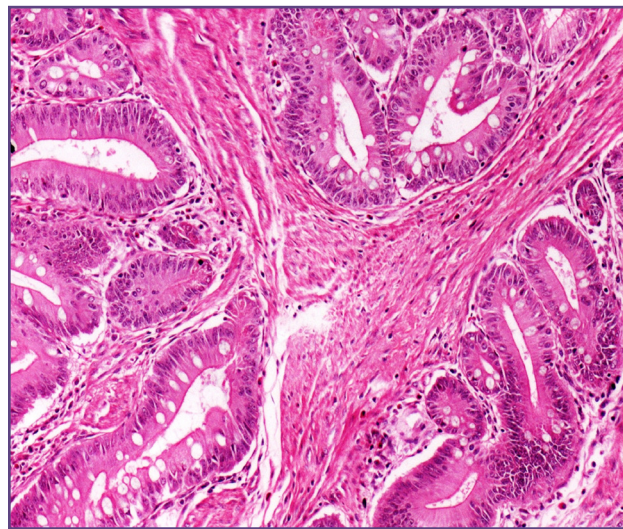


Fig. 4: 100x H&E- Glands shows no atypia.

with symptoms of obstruction and abdominal pain whereas those with large intestinal polyps present with bloody stools. However the most frequent presentation is intermittent abdominal pain due to intussusception. Intussusception is rare in adults compared to children. Also the site of intussusception vary in both. In children, it involves colon whereas small intestine is the common site in adults. Other rare presenting features include anemia, hematochezia, hematemesis, prolapse of polyp^[4]. In a series of 222 patients with Peutz-Jeghers syndrome (PJS), Utsunomiya et al noted the following distribution of presenting gastrointestinal symptoms: Obstruction – 42.8% of patients, Abdominal pain caused by infarction – 23% of patients, Rectal bleeding caused by ulceration – 13.5% of patients, Extrusion of polyp – 7% of patients.

At the time of presentation, 3 to 6% of patients with PJS are found to have neoplastic change. They have a 15-fold increased risk of developing intestinal cancer compared with that of the general population^[5]. The hamartomatous polyps in PJS can have adenomatous foci that can evolve into cancer as the age progresses. The evolution of hamartoma-adenoma-carcinoma has been demonstrated for stomach, small bowel, and colorectal polyps in PJS. The other associated malignancies which occur outside the gastrointestinal tract include lung, breast, uterus, gonads, prostate, thyroid, multiple myeloma, skin, and pancreas. Sex cord tumors with annular tubules and adenoma malignum of uterine cervix in women and testicular Sertoli cell tumors in male are other uncommon tumors seen with this syndrome^[6].

The clinical diagnosis of PJS is made if any one of the following criteria is present:

1. Two or more histologically confirmed Peutz -jeghers polyp
2. Any number of Peutz-jeghers polyp with a family history
3. A family history of PJS with characteristic mucocutaneous pigmentation.
4. Characteristic mucocutaneous pigmentation with any number of Peutz-jeghers polyp^[7].

The polyps may lack characteristic diagnostic features when ischemic necrosis occurs secondary to intussusceptions. Also in the colon and rectum, prolapse may cause histopathological changes that can mimic peutz-jeghers polyp which can be a diagnostic problem in case of solitary polyps. Epithelial structures in smooth muscle fibres can misled to diagnosis of invasion in cancer. Occasionally, there is herniation of cystically dilated epithelial structures in to the bowel wall extending up to serosa and forms tumor masses analogous to colitis cystica and jejunitis cystica profunda. This is known as pseudoinvasion which is reported in 10 % of PJS polyps. Epithelial misplacement can be differentiated from neoplasia under microscopy by the presence of benign looking glands, presence of lamina propria, absence of desmoplastic response around the glands.

Surveillance in patients with PJS is done to detect early cancers and to prevent morbidity due to its complications. Hence, periodic surveillance for gastric and small-bowel polyposis should begin at the age of 8-10 years and continue for every 2-year intervals. Screening should include all possible investigations to detect both intestinal and extraintestinal malignancies in all the patients with PJS such as colonoscopy, upper endoscopy, if possible wireless capsule endoscopy, CT, MRI or ultrasound of the pancreas, chest X-ray, mammography and pelvic examination with ultrasound in women, testicular examination in men, carbohydrate antigen 19-9 (CA-19-9), and cancer antigen (CA 125)^[8]. Surgical excision of lesions include the following : Endoscopic polypectomy for diagnosis and control of symptoms. Laparotomy and resection are reserved for repeated intussusception or persistent intestinal bleeding.

Conclusion

We are presenting this case of Peutz-Jeghers Syndrome for its rarity and to highlight the diagnostic challenges in histopathology. The appropriate diagnosis of Peutz-Jeghers polyp will help in proper screening of intestinal and extraintestinal malignancies associated with it, facilitating the early diagnosis and further management.

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Competing Interests

None Declared

Reference

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