

A Classical Presentation of Peutz–Jeghers Syndrome as Multiple Intussusceptions

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Abstract

Peutz–Jeghers syndrome (PJS) is a great mimic. Cutaneous markers should never be overlooked because they give very significant clinical information about the understanding of the underlying problem. The triad of pigmentation, polyps, and intussusception should raise the suspicion of PJS. Radiological imaging, contrast studies, and scopy directed biopsies confirm the diagnosis and help in surveillance. Hamartomatous mucosal polyps with characteristic central core of branching smooth muscle associated with a mucosa native to the site of origin are pathognomonic of PJS. Dysplasia and adenocarcinoma can develop within polyps. Almost all cases are linked to a germline mutation in LKB1/STK11 at 19p13.3. Surveillance for malignancy and genetic counseling is an integral part of management. PJS essentially needs a multidisciplinary empathetic approach. This case is presented for its classical presentation where radiological imaging played an important role in diagnosis.

Key words: Hamartomatous polyps, Intussusception, Peutz–Jeghers syndrome

INTRODUCTION

Peutz–Jeghers syndrome (PJS) is a rare autosomal-dominant syndrome commonly presenting as multiple gastrointestinal hamartomatous polyps and mucocutaneous hyperpigmentation. The pigmentations can range from dark blue to brown macules around the mouth, eyes, nostrils, buccal mucosa, palmar surfaces of hands, genitalia, and perianal region. These pigmentations to an unsuspecting mind look like freckles, but the involvement of buccal mucosa rules out the possibility. The polyps can become a lead point for recurrent intussusceptions which results in life-threatening emergency surgical procedures. The main concern is the increased risk of several malignancies owing to its pathogenesis at the molecular level.

CASE REPORT

A 22-year-old female attended surgical OPD with the complaints of intermittent colicky abdominal pain predominantly on the right side of the abdomen relieved by vomiting for the past 1 month. However, she was symptom free between the episodes. Abdominal distension, melena, menstrual irregularities, and family history were conspicuously absent.

She had undergone emergency laparotomy for ileocolic intussusception at 10 years of age and ovarian cystectomy around 13 years.

Clinically, she was anemic, and pigmentations over the mucocutaneous junction of the lips, fingers, and toes were noted [Figure 1a-c]. Her vitals and other systems were normal. A transverse scar was seen extending from the umbilicus to the right hypochondrium, and a mass was palpable in the suprapubic region which was non-tender, firm in consistency with sluggish bowel activities. Laboratory investigations were suggestive of severe anemia with hemoglobin level 5.7 g/dL, peripheral smear showed microcytic hypochromic anemia, and total count - 7100, ESR - 58, platelet count - 2.39 lakhs/cu mm, CRP - <0.6 mg/dL, coagulation profile, liver function tests, renal function test, and electrolytes were within normal

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limits. The test for occult blood in stools was found to be negative. The urine routine was normal.

Contrast-enhanced computed tomography (CECT) abdomen revealed multiple intussusceptions of small bowel involving the terminal ileum and the jejunal loops [Figures 2 and 3a and b] which was further evident after the administration of oral contrast [Figure 4a and b]. Meanwhile, she was transfused with three units of packed cells which raised her Hb to 12.5 g/dL making her clinically fit for further invasive procedures.

Upper gastrointestinal (GI) endoscopy not only revealed multiple gastric and duodenal sessile polyps [Figure 5a and b] that were biopsied but also it threw light to clinch the provisional diagnosis of PJS and the triad of pigmentation, polyps, and intussusception.

Colonoscopy was performed demonstrating multiple pedunculated polyps in the rectum, sigmoid, descending colon, and cecum [Figure 6a and b]. Multiple biopsies were

taken, and histopathological evaluation was suggestive of tubular adenomatous polyp in rectum and cecum and hyperplastic polyps in colon and stomach. Before planning for the definitive surgical procedure, she was posted for diagnostic laparoscopy which revealed multiple jejunojejunal (30 cm

from DJ flexure), ileoileal intussusceptions, and multiple adhesions between the omentum, small bowel, and peritoneal wall [Figure 7a and b]; the procedure was converted to open laparotomy, adhesions were released, and intussusception sites were resected, enteroscopy [Figure 8a and b] helped in the identification of multiple polyps along the small and the large bowel lumen, endoloop resection of larger polyps done and the lead point of intussusception was confirmed to be a polyp.. The resected bowel ends were anastomosed, and enterotomy site was closed. The patient's post-operative period was uneventful, and she is on regular follow-up.

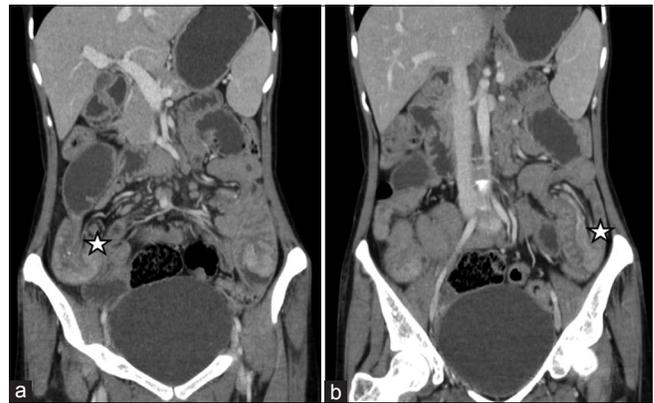


Figure 3a & 3b :CECT reformatted coronal view of the abdomen in venous phase shows multiple intussusceptions(asterix) involving the involving the distal ileum and the jejunal loops

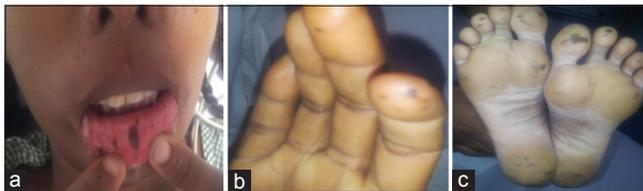


Figure 1: 1a,1b and 1c:Melanin pigmentation involving the mucocutaneous junction of lips , fingers (1b)and toes(1c)



Figure 4: 4a & 4b : Delayed images obtained after administration of oral contrast reveal formation of another intussusceptions in the proximal jejunum(arrow head), not seen on prior images and the distal jejunal loops(left arrow)



Figure 2: CECT axial view of the abdomen in venous phase shows multiple intussusceptions(asterix) involving the distal ileum and the jejunal loops

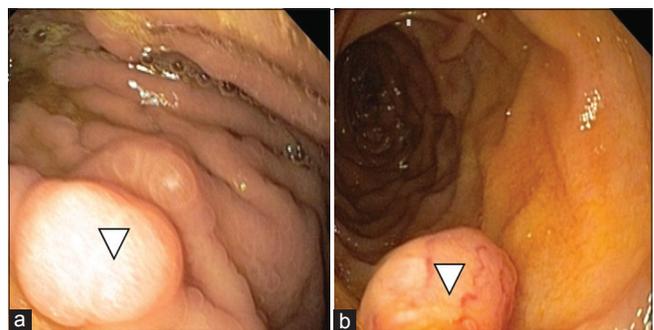


Figure 5a & 5b : Upper Gastro intestinal endoscopy showed multiple gastric and duodenal sessile polyps(arrow head)

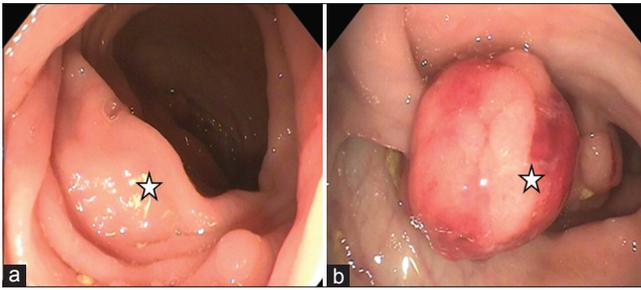


Figure 6a & 6b : Colonoscopy showed pedunculated polyps(asterix) in the rectum , Sigmoid colon , Descending colon

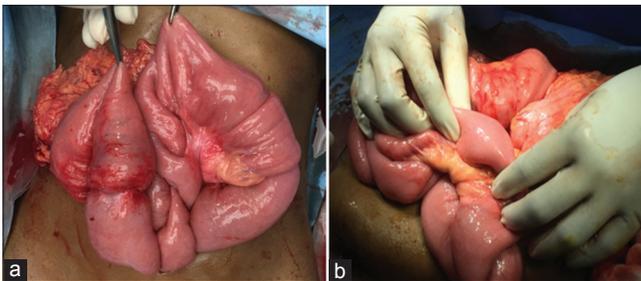


Figure 7a & 7b: Laparotomy done to remove adhesions and intussusceptions were resected at ileoileal site

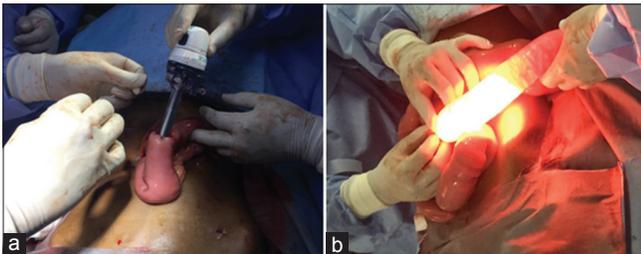


Figure 8a & 8b : Diagnostic enteroscopy revealed multiple polyps along the large and small bowel. Larger ones were removed using endoloop

The patient’s history, imaging findings in CECT abdomen, endoscopy, laparotomy, and histopathological findings were conclusive of PJS.

DISCUSSION

Polyposis syndromes are broadly classified as adenomatous and non-adenomatous polyposis syndromes.

Adenomatous polyposis syndrome includes familial adenomatous polyposis which can be classic/attenuated FAP. Classic FAPs are associated with congenital retinal pigment epithelial hypertrophy with a presentation at 10–15 years of age, whereas attenuated FAP has a median presentation between 40 and 50 years of age. Other categories are Gardner’s syndromes associated with osteomas, desmoids, and skin cysts. Turcot’s syndrome

is associated with central nervous system tumors and medulloblastomas. Both Gardner’s and Turcot’s syndrome have a median age of presentation between 10 and 15 years of age.

Non-adenomatous polyposis syndrome includes a spectrum of PJS, Juvenile polyposis, Cowden syndrome, Cronkhite–Canada syndrome, and tuberous sclerosis.

Juvenile polyposis has a median presentation of <5 years of age with juvenile polyps and pulmonary arteriovenous malformations and digital clubbing. Cowden’s syndrome presents in <15 years of age with hamartomatous polyps, lipomas, ganglioneuromas, inflammatory polyps, benign skin tumors, malignant thyroid, or breast lesions. Cronkhite–Canada syndrome manifests in >50 years of age with hamartomatous colon polyps, crypt dilatation, edema in non-polypoid mucosa, nail atrophy, hair loss, abnormal skin pigmentation, cachexia, and anemia.

PJS presents with arborizing polyps which are found in small intestine > colon > stomach, skin macules, increased risk of thyroid, breast, pancreatic, GIT, genitourinary malignancies.

The World Health Organization (2010) diagnostic criteria for PJS include any of the following:

- Three/more histologically confirmed PJ polyps
- Any number of PJ polyps with a family history of PJS
- Characteristic prominent mucocutaneous pigmentation with a family history of PJS, or
- Any number of PJ polyps and characteristic prominent mucocutaneous pigmentation.

The historical aspect of this eponymous syndrome dates back to 1896, when John McHutchinson reported the dermatological finding in identical twins, one of them died from intussusception. In 1921, the association of polyps with mucocutaneous macules was described by Jan Peutz in a Dutch family.^[1] Jeghers, on the other hand, published a report named “Generalized intestinal polyposis and melanin spots of the oral mucosa, lips, and digits,” in 1949, with Jeghers *et al.*^[2] Thus, the eponym PJS was introduced by a radiologist named Bruwer *et al.*^[3]

The pathogenesis of PJS is most commonly the germline heterozygous loss of function mutation in the gene LKB1/STK 11 present in half of the individuals with familial PJS and sporadic PJS. Family history is negative in up to 45% of individuals which may be due to *de novo* germline mutation.^[4] The LKB1/STK11 is a serine/threonine kinase that regulates polarization, growth, and metabolism which is located on chromosome 19p13.^[5] Since this

gene is also a tumor suppressor gene, the mutation also causes high risk of neoplasia in these patients.^[6,7] The GI carcinomas arise independently of the hamartomatous polyps, indicating that it is not preneoplastic precursor lesions. However, recently it has been seen that there can be adenomatous changes in these polyps with foci of adenocarcinomas.^[8] Other carcinomas are the breast, testicular, and pancreatic malignancies.^[9] Extraintestinal polyps can occur in the respiratory system, sinuses, and urogenital tract.

Our subject of interest fulfilled the first and fourth category of the WHO guidelines of diagnostic criteria with multiple mucocutaneous pigmentation, polyposis histology proven, and multiple intussusceptions, and since there was no family history, she was categorically assigned as sporadic PJS. Further, she had tubular adenomatous polyps in the cecum and rectum warranting close surveillance.

Imaging Studies

A wide range of imaging studies is helpful in PJS which includes:

- Upper GI endoscopy
- Capsule endoscopy
- Magnetic resonance imaging enteroclysis
- CT scanning with oral contrast medium
- CT enterography
- Colonoscopy
- Intraoperative enteroscopy
- Double-balloon enteroscopy
- Endoscopic ultrasonography.

Surveillance is an important aspect in these patients which is done by two yearly upper GI endoscopy, two yearly small bowel radiography, colonoscopy every 3 years, ultrasound, CEA, PAP smear,^[10] and periodical review with thorough clinical examination to pick up early signs.

CONCLUSION

PJS is a rare genetic disorder that requires a multidisciplinary approach with specialized care. An empathetic approach should be the fundamental quality of the medical assistance given for such patients as they require multiple surgical procedures and are prone to an array of malignancies and sequelae. Patients with PJS should be given psychological advice and genetic counseling to lead a near normal life.

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