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CASE REPORT

Sporadic Peutz-Jeghers Syndrome with Recurrent Intussusception and Malignant Change in Hamartomatous Polyps

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Abstract
Peutz-Jeghers syndrome (PJS) is a rare inherited autosomal dominant disease characterised by mucocutaneous pigmentation and multiple polyps in the gastrointestinal tract. In up to 25% of cases, there is no family history of PJS (sporadic cases). Acute intestinal intussusception due to multiple polyps is the most common complication of PJS. PJS is associated with cancers of the gastrointestinal tract and in other organs. Adenocarcinoma arising in hamartomatous polyps is heavily debated. A 23-year-old gentleman presented with sporadic PJS with recurrent ileal intussusceptions and multifocal well-differentiated adenocarcinomas arising in the background of hamartomatous polyps following hamartoma-dysplasia-carcinoma sequence, which is herein discussed. The hamartoma-dysplasia-carcinoma sequence is one of the pathways of carcinogenesis within hamartomatous polyps in PJS.

Keywords Peutz-Jeghers syndrome · Recurrent intussusception · Hamartomatous polyp · Hamartoma-dysplasia-carcinoma sequence

Introduction

Peutz-Jeghers syndrome (PJS) is an autosomal dominant rare disease characterised by multiple gastrointestinal tract (GIT) hamartomatous polyps with perioral and perianal mucocutaneous pigmentation. Its incidence ranges from 1 in 8300 to 2,00,000 live births [1]. In 1954, A. Bruwer coined the eponym 'Peutz-Jeghers syndrome'. The hamartomatous polyps, located predominantly in the small intestine (jejunum), often present with intestinal obstruction due to intussusception, abdominal pain, blood in stool, and anaemia. Germline mutation of tumour suppressor serine-threonine kinase gene, LKB1/STK11, on chromosome 9p13.3 is involved in PJS [2]. It does not have 100% complete penetrance and extremely rare sporadic cases arise from spontaneous de novo mutations [3]. Genetic testing shows considerable heterogeneity with approximately 60% of familial and 50% of sporadic cases having STK11 mutations.

We herein report a rare case of PJS with recurrent intussusceptions in a young male within 7 years associated with multifocal adenocarcinoma and concomitant dysplastic changes in the hamartomatous GIT polyps.

Case History

A 23-year-old male presented with subacute intestinal obstruction for 15 days. His past history revealed that at the age of 16 years he had undergone an ileal resection, for an ileo-ileal intussusception. The histopathology was well-differentiated adenocarcinoma reaching beyond serosa with free resected margins. Thereafter, he had received 12 cycles of adjuvant FOLFOX4, after which he was on irregular follow-up. An upper gastrointestinal endoscopy and colonoscopy were done at around 20 years that revealed multiple sessile polyps in the corpus, antrum of the stomach and duodenum, and multiple colonic polyps respectively. Family history was not significant, although none of them was ever screened for PJS. There was no history of any cancer in any of his relatives.

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Multiple hyperpigmented lesions were present on inner aspect of the lower lip and fingers (Fig. 1) of the patient. A 20 × 5 cm smooth, well-defined tender mass was palpable in the lower half of the abdomen. On per-rectal examination, 2 polyps were felt 1 cm and 5 cm from the anal verge. CECT scan revealed a large jejunoileal intussusception; multiple polypoid lesions in the stomach, duodenum, jejunum, ileum, colon, and rectum; and multiple mesenteric lymph nodes (Fig. 1). At laparotomy, a large jejunoileal intussusception was found with approximately 20 cm of jejunoileal segment invaginated into distal ileum, up to ~ 10 cm from the ileocaecal junction. There was necrosis of ~ 5 cm of jejunum intussusceptum with a 3 × 2 cm polypoid lead point (Fig. 2). The total length of the small bowel was only about 150 cm probably owing to previous surgical resection. Multiple small polyps were present throughout the jejunum, ileum, and colon. The small intestine was grossly unhealthy, edematous, and friable. There was no evidence of metastasis. Intussusception was gently reduced by retrograde pressure from the apex. Resection of the involved segment of the ileum was done with side-to-side jejunoileal anastomosis. The intraoperative course was uneventful. Final histopathology showed a well-differentiated adenocarcinoma arising in a hamartomatous polyp (multifocal in 3 polyps) (Fig. 3) with the tumour invading muscularis propria with no macroscopic tumour perforation and no lymphovascular invasion. There was no regional lymph node involvement. Another polyp came as a hamartomatous polyp with high-grade dysplasia but without any invasive component (Fig. 3). Thus, the patient had a second small intestinal adenocarcinoma stage pT2N0M0.

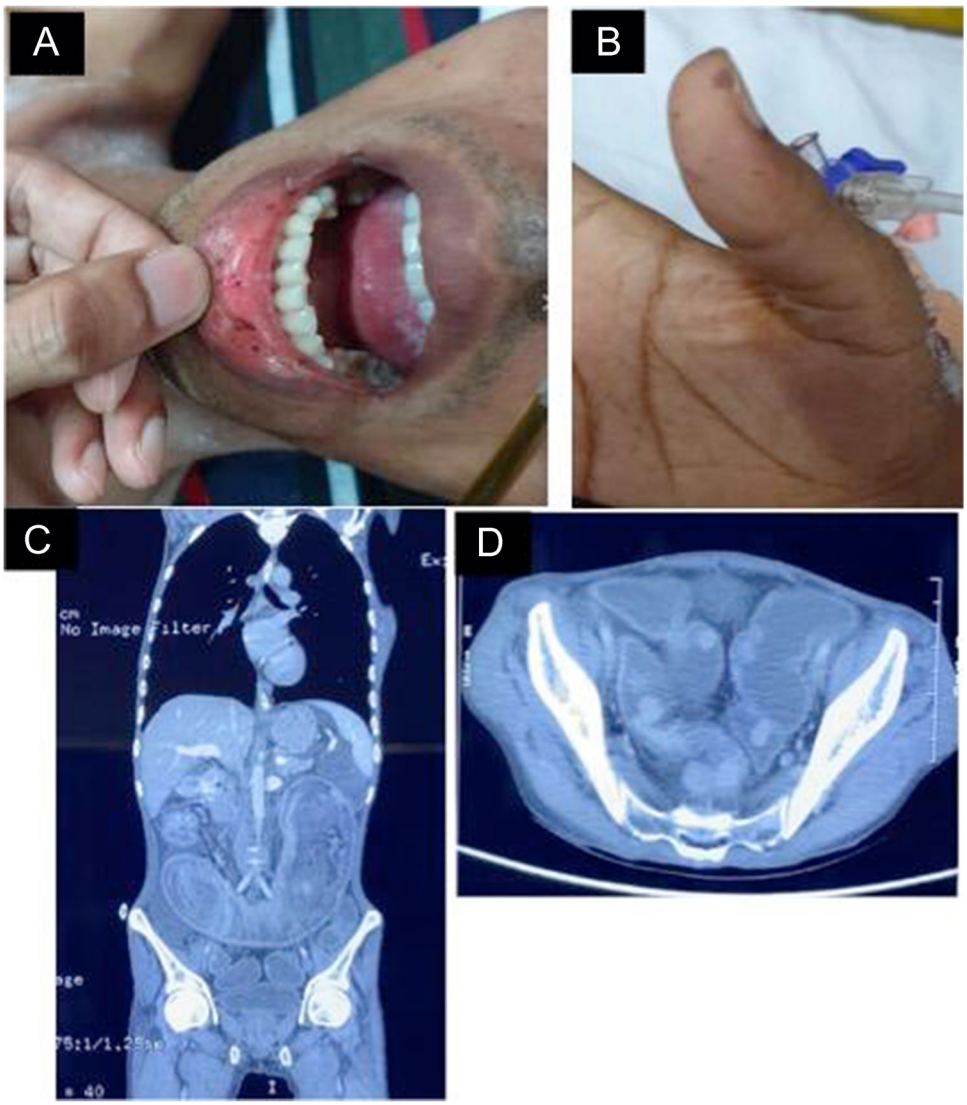

Fig. 1 **A, B** Hyperpigmented melanin spots on inner aspect of lower lip; thumb. **C, D** CECT scan showing intussusception and multiple polyps in sigmoid colon and rectum

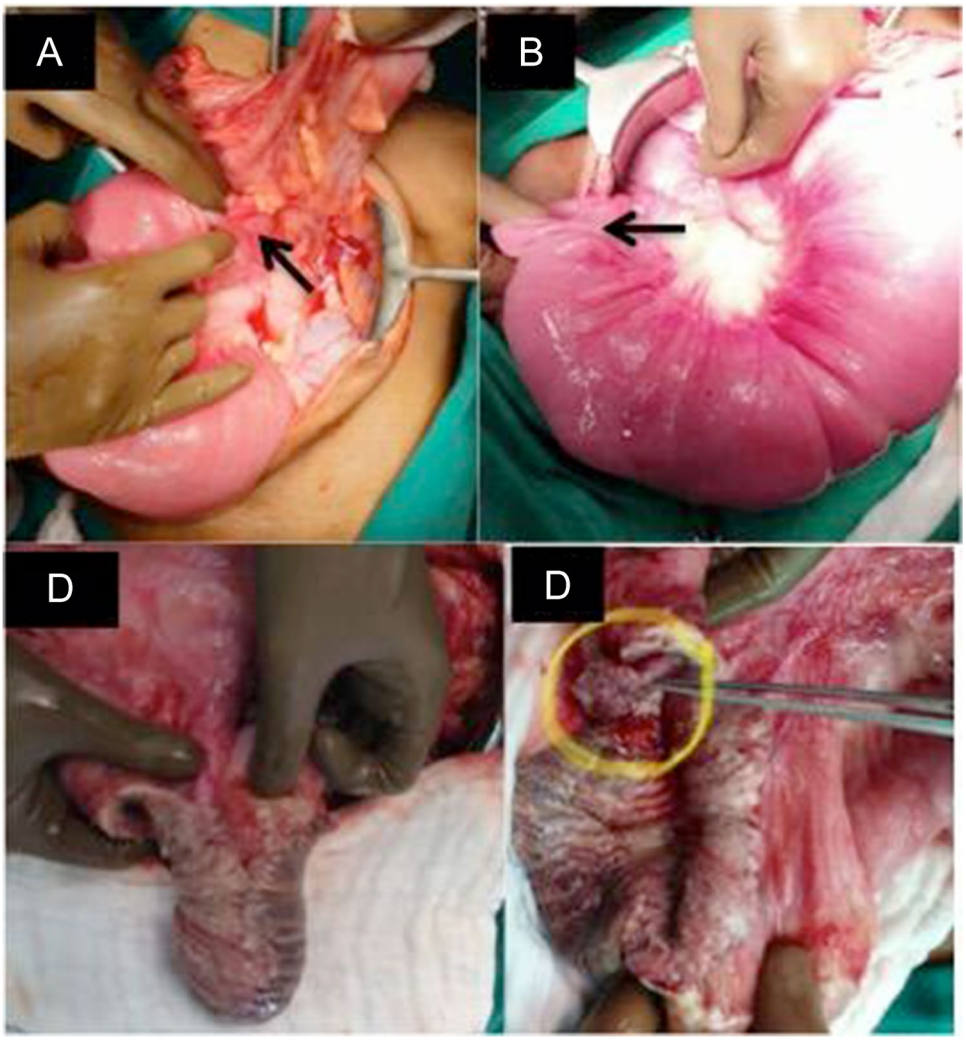

Fig. 2 Clinical operative photograph showing the following: **A, B** The start of the jejunoileal intussusception close to the duodeno-jejunal flexure and the end point close to the ileocaecal junction; **C, D** the necrosed intussusceptum with lead point polyp

Discussion

The WHO describes the following criteria for diagnosing PJS: three or more histologically confirmed Peutz-Jeghers polyps, or any number of Peutz-Jeghers polyps with a family history of PJS, or characteristic mucocutaneous pigmentation with a family history of PJS, or any number of Peutz-Jeghers polyps, and characteristic mucocutaneous pigmentation [4].

It has been suggested that the process underlying the development of PJS GIT polyps may be mechanical rather than being true hamartomas. Mutation in the LKB1/STK11 gene results in disruption of cell polarity pathways resulting in mucosal prolapse and this 'pseudoinvasion' may be mistaken for invasive carcinoma [5].

PJS is associated with increased rates of both GIT malignancies (lifetime risk of 57–63%) [6] like colon, small bowel, stomach, and pancreas and non-gastrointestinal malignancies like ovary, uterus, cervix, and breast. Small intestine and colorectal carcinomas are most common with up to 15% of patients developing two primary carcinomas [1]. The development of cancer in PJS remains controversial with possibilities of it arising de novo from normal GIT mucosa and/or cancer degeneration of PJS polyp. Some believe the theory that hamartomatous PJS polyps have no malignant potential but there are findings, albeit rare, that refute this theory. A hamartoma-adenoma-carcinoma pathway has been proposed and is based on the reports finding adenomatous foci within PJS polyps and cancer arising within PJS polyps.[5, 7]. The hamartoma-dysplasia-carcinoma pathway has also been reported although it is extremely rare [8]. Latchford et al. found only six cases of atypia or dysplasia in over 1000 PJS polyps and none of the polyps exhibited adenomatous foci or malignant changes [5]. Perzin et al. first demonstrated adenocarcinoma developing in a hamartomatous polyp [4]. Our case had a demonstrable hamartoma-dysplasia-carcinoma sequence in multiple PJS polyps.

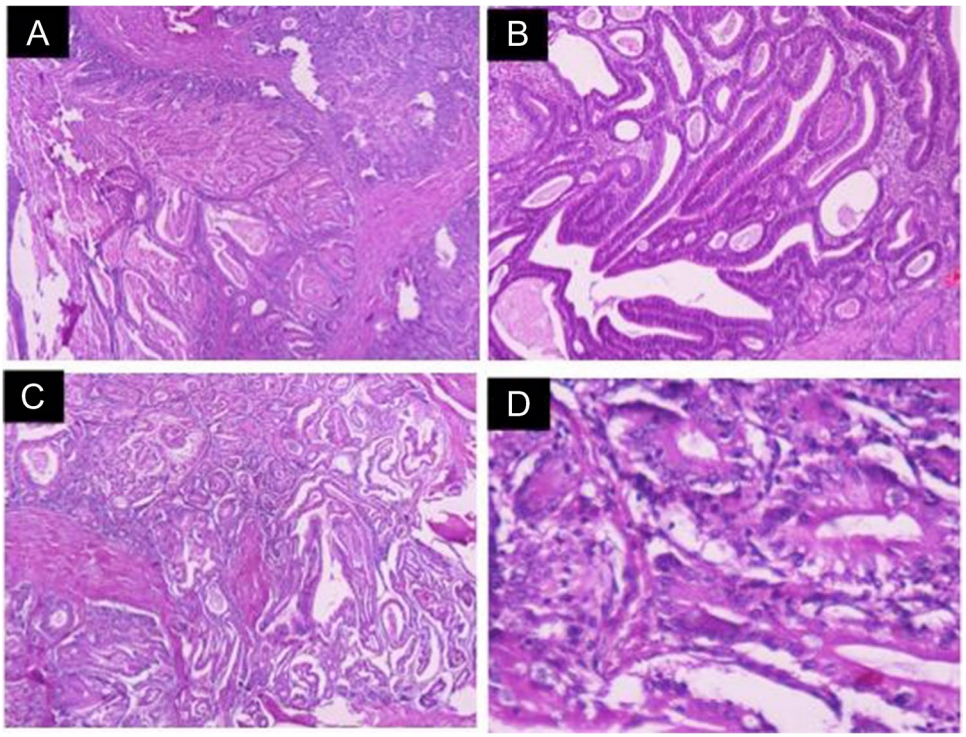

Fig. 3 Histological photomicrograph H&E stain showing the following: **A, B** the hamartomatous polyp (40×) and dysplasia (100×) in the polyp; **C, D** carcinoma changes in the polyp at 40× and 100× magnification

Declarations

The authors declare no competing interests.

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