Two contrasting presentations of Peutz–Jeghers syndrome

Introduction

Peutz–Jeghers syndrome is a rare autosomal dominant disorder characterized by intestinal harmatomatous polyps and associated with circum-oral pigmentation affecting the skin and oral mucous membranes (Utsunomiya et al, 1975). The prevalence of this condition is not exactly known, but is approximately 1 in 120 000, affecting males and females equally (Zanoni et al, 2003). This article describes two very different presentations of this rare condition.

Figure 1. Circum-oral pigmentation from case 1.

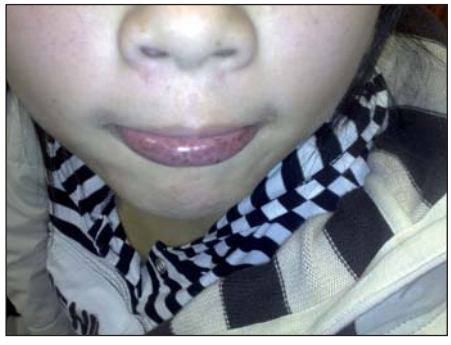


Figure 2. a. Abdominal X-ray showing an abnormally dilated loop of small bowel in the left upper quadrant.

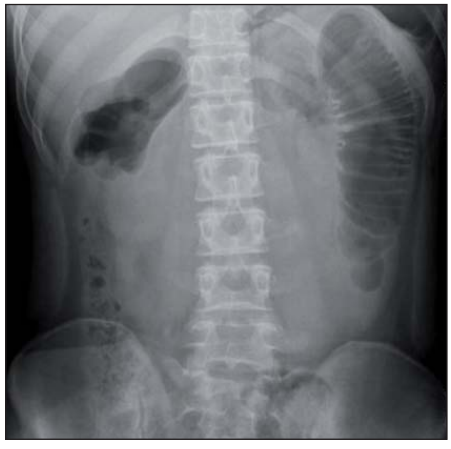
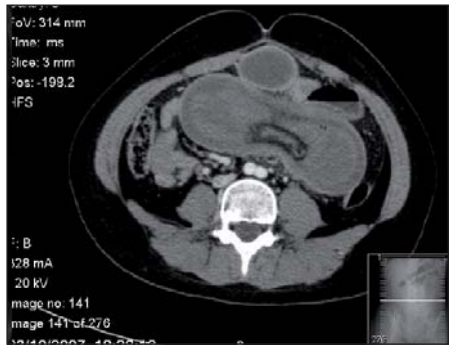


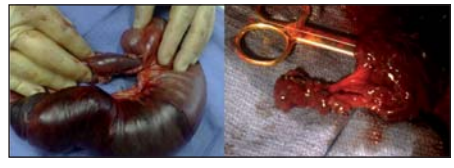
Figure 3. Computed tomography scan showing a small bowel intussusception as the cause.



Discussion

Peutz–Jeghers syndrome was first recognized in 1921 by Peutz and rediscovered by Jeghers in 1949. It is a rare autosomal dominant disorder with phenotypic variability and incomplete penetrance, estimated by registries to occur in anywhere

Figure 4. The resected small bowel segment with a small bowel polyp identified as the lead point of the intussusception.



Case Report 1

A 17-year-old girl of Chinese origin was referred as a case of suspected acute appendicitis with a 3-day history of a colicky abdominal pain which had started off in her peri-umbilical region. She had presented to another hospital 2 days before, but was discharged home after an overnight stay because her symptoms had improved. The pain had now become more severe and was associated with bilious vomiting, absolute constipation for 3 days, and increasing abdominal distension. On further questioning she had experienced a self-resolving peri-umbilical pain intermittently over the past 3 years, but had never had this investigated. Her last period was 3 months ago, and she was being investigated for irregular menstruation in China. There was no family history of any gastrointestinal problems.

On examination, she was markedly dehydrated and noted to have 'freckle-like' lesions around her mouth and on her lips (*Figure 1*). She had a pyrexia of 38.1 °C, a tachycardia of 130 beats per minute, and was normotensive. The abdomen was visibly distended, tender (mostly in her epigastrium and left upper quadrant) and absent of bowel sounds. There was no evidence of previous surgery and scars, and digital rectal examination was unremarkable with an empty rectum. Blood tests showed marginally raised white cell count (13.8×10^9/litre) and C-reactive protein (51 mg/litre), and urine tests were unremarkable with a negative β-human chorionic gonadotrophin level. A plain abdominal radiograph showed an isolated loop of small bowel in the left upper quadrant (*Figure 2*), and a computed tomography scan of her abdomen was performed showing a long intussusception of the proximal jejunum with free pelvic fluid (*Figure 3*). This segment of bowel was grossly dilated and a diagnosis of small bowel obstruction secondary to intussusception was made.

Exploratory laparotomy was performed and revealed a 45 cm-long segment of intussuscepted jejunum which was ischaemic and non-viable, thereby requiring small bowel resection and primary anastomosis. On opening of the resected specimen a small polyp was identified at the lead point of the intussusceptions (*Figure 4*). The remainder of the small bowel did not contain any palpable or visible polyps, but a Meckel's diverticulum was found and resected. Histology of the intussuscepted small bowel segment revealed three pedunculated polyps (the largest 45x25x25 cm) with branching muscle pattern and relatively bland nuclei, consistent with a diagnosis of Peutz–Jeghers syndrome. The patient made a complete uncomplicated recovery and was discharged at postoperative day five.

Dr Paul Cathcart *is ST1 Trainee in the Department of Surgery, St Mary's Hospital, London,* **Mr Omer Aziz** *is Specialist Registrar and Honorary Research Fellow, Department of Biosurgery and Surgical Technology, Imperial College London, London W2 1NY,* **Mr Anil Desai** *is Consultant Colorectal Surgeon in the Department of Surgery, Wexham Park Hospital, Slough and* **Mr Paul Ziprin** *is Consultant Colorectal Surgeon and Senior Lecturer in the Department of Biosurgery and Surgical Technology, Imperial College London*

Correspondence to: Mr O Aziz

Case Report 2

A 31-year-old Indian man presented with a 1-day history of painless bright red rectal bleeding. This was the first time he had experienced bleeding of any nature, and since its onset described passing the equivalent of a 'bowl-full' of fresh blood every hour followed by a feeling that his rectum was filling up again. The only relevant past medical history was that he had previously been investigated by his GP for iron deficiency anaemia, with no clear cause found.

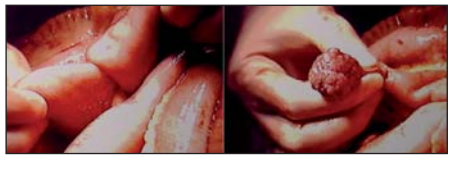
On examination the patient appeared to be very lethargic and pale with a tachycardia of 140 beats per minute and a blood pressure of 100/60 mmHg. He was resuscitated with 2 litres of colloid solution, urgent blood tests including a cross-match sent, and type O negative blood ordered. Examination of his abdomen was unremarkable but digitation of the rectum revealed a regular flow of bright red blood. A rigid sigmoidoscopy was attempted but constant pooling of blood in the scope made visualization impossible. During his first hour in the emergency department the patient had lost approximately 1 litre of fresh blood, and was not showing any signs of response to aggressive resuscitation with colloid and blood. As on-site angiographic facilities were not available and the patient was too unstable to transfer, a decision was made to intubate the patient, transfer him to the operating theatre for an on-table gastroscopy, colonoscopy, and if necessary an exploratory laparotomy.

Gastroscopy was normal and colonoscopy revealed too large an amount of blood in the colon to effectively visualize and advance the scope. A midline laparotomy was performed, revealing a blood-filled distended colon with some blood also present in 20 cm of small bowel just proximal to the ileo-caecal junction. The jejunum and ileum were also found to have multiple non-obstructing intussusceptions with large polyps acting as the lead points (*Figure 5*). Six of these polyps were excised with enterotomies, but none were actively bleeding. The distended colon was decompressed using a Savage's sucker, but found to re-distend rapidly with blood. A subtotal colectomy was performed, and the rectal stump opened to identify and ligate two bleeding polyps. An end ileostomy was formed, and thereon the patient made an unremarkable postoperative recovery. Histological examination of the resected specimen revealed that all the small and large bowel polyps were hamartomatas. In retrospect it was noted that the patient had circum-oral pigmentation that was initially missed because of his skin colour. A diagnosis of Peutz–Jeghers syndrome was made, and the patent referred for genetic screening.

between 1/600 000 to 1/300 000 people (Sarlós et al, 2007), and affect males and females equally (Zanoni et al, 2003). The genetic disorder has been mapped to chromosome 19p13.3, with most families studied having an inactivating germline mutation in the gene encoding serine/threonine kinase LKB1 (Westerman et al, 1999). This gene is ubiquitously expressed and composed of 10 exons spanning 23 kb (Mehenni et al, 1998). A second disease locus has been suggested at chromosome 19q13.4 on the basis of genetic linkage analysis in one family (Hearle et al, 2004).

The disorder is characterized by mucocutaneous pigmentation from pigment-laden dermal macrophages occurring in approximately 95% of Peutz–Jeghers syndrome patients. These may be found on the hands, feet, and even within the intestine (Zanoni et al, 2003). Gastrointestinal hamartomatous polyps are characteristic of Peutz–Jeghers syndrome, and are usually large and pedunculated. Histological appearance of these polyps includes an arborising network of connective tissue and well-developed smooth muscle that extends into the polyp. The overlying epithelium is normal, and these polyps are typically found in the jejunum and ileum.

Figure 5. a. Small bowel intussusceptions found in case 2 with (b) large polyps found as the cause.



Diagnosis of Peutz–Jeghers syndrome is usually incidental, with patients presenting a consequence of polyp formation giving rise to anaemia, melaena, intestinal obstruction and intussusception. Almost half of patients experience an intussusception, putting them at risk of multiple abdominal operations, and 14% present with a gastrointestinal bleed (Zanoni et al, 2003).

Patients have an increased incidence of both gastrointestinal and non-gastrointestinal malignancy, particularly in the lung, breast, uterus and ovary (Perzin and Bridge, 1982; Spigelman et al, 1989). The St Mark's Polyposis Registry found that in patients with Peutz–Jeghers syndrome, the relative risk of mortality from gastrointestinal malignancy is 13, with a mortality from all cancers of 48% by the age of 57 years (Spigelman et al, 1989). The risk of malignancy in Peutz–Jeghers syndrome is highest for the gastrointestinal tract (Hearle et al, 2006), with colorectal cancers (10–20% of cases) more common than those in the small intestine (5–10%) (Hearle et al, 2006). Women with Peutz–Jeghers syndrome have an approximately 6-fold increased risk of breast cancer compared to the general population (Hearle et al, 2006).

Regular follow up of these patients is necessary because of their malignancy risk; (Dunlop, 2002) suggested that surveillance of the large bowel should begin at the age of 18 years, and of the upper gastrointestinal tract from the age of 25 years. The incidence of colonic harmatomas has a varying rate of reporting, but may be as high as 53% (Utsunomiya et al, 1975). BJHM

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