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Peutz–Jeghers Syndrome: A Rare Genetic Cause of Intestinal Obstruction

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Abstract

Peutz–Jeghers syndrome (PJS) is a rare autosomal dominant disorder. The mutation is found in the serine threonine kinase (STK11)/ liver kinase B1 (LKB1) gene on chromosome 19. It impacts 1 out of 50000–200 000 individuals. Clinical menifestations include hyperpigmented lesion in oral cavity, lips, fingertips and perianal region. Abdominal pain, Anaemia, Gastrointestinal (GI) bleeding, GI polyp, Intestinal obstruction (mostly due to intussusception) and malignancy are closely interlinked with the disease. We present a 21 years old lady with characteristic hyperpigmented lesions in lips and fingertips with multiple polyps in the GI tract. The patient was presented in general emergency department with abdominal pain and vomiting. Detail workout revealed the diagnosis as PJS. We have plotted the diagnosis according to the WHO criteria due to the lacking of genetic analysis facility. Patients with PJS are at high risk of intestinal and extraintestinal malignancy. Early diagnosis and polypectomy along with surveillance for recurrence may prolong cancer free lifetime.

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Introduction

Peutz–Jeghers syndrome (PJS) is a rare autosomal dominant disorder. The genetic mutations in PJS are complex and diverse. 80% of PJS cases were found to have mutation in the serine threonine kinase (STK11) gene also known as liver kinase B1 (LKB1) gene on chromosome 19.[1] The incidence of the disease reported as 1 out of 50000–200000 individuals.[2] It was first described by Peutz in 1921 and Jeghers in 1944 and 1949.[3] Patients with PJS typically present heterogeneous phenotypes with regards to oral and GI lesions, including different onset of time, disease severity, distribution of GI symptoms and level of malignancy.[4] Patient predisposes to various malignancies such as gastrointestinal, nasal passages, bronchial tree, lung, breast, kidney, ureter, pancreatic, gallbladder, uterine, ovarian and testicular tumors.[5,6] Clinical menifestations include hyperpigmented lesion in oral cavity, lips, fingertips and perianal region. Abdominal Pain, Anaemia, Gastrointestinal (GI) bleeding, GI polyp, Intestinal obstruction (mostly due to intussusception) and malignancy are closely interlinked with the disease.[2-4,7,8] We present a case of 21 years old lady with PJS presented as recurrent subacute intestinal obstruction.

Case Presentation

This 21 years old female college student got admitted in the Department of Surgery, Community Based Medical College Hospital, Mymensingh, Bangladesh on 28.09.2022 evening

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with the complaints of abdominal pain for 7 days, occasional vomiting and constipation for same duration.

According to statement of the patient, she was reasonably well 7 days back. Then she experienced sudden onset of colicky pain in left side of the abdomen. The pain was of moderate intensity, initially localized to left side of the abdomen which later diffused to the whole abdomen with more intensity to epigastric region. Pain was not associated with chills, fever or rigor. There was no aggravating factor. Pain relieved on medication. She also gave history of occasional vomiting for about a week. It was spontaneous, projectile and bile stained. It contained mixed digested food materials. The patient gave history of infrequent passage of very small amount of hard stool in previous week. There were complaints of abdominal discomfort and fullness. She experienced similar attack of symptoms three times in last one year.

She did not give history of haematemesis or melaena. But she gave history of fresh per rectal bleeding for several days, 6 month back. The bleeding was painless, moderate in amount and eminent after defecation as dribbling. There was no perianal discomfort. There was no history of loss of appetite, anorexia, weight loss. No hunger pain or periodicity of pain. No history of jaundice. She did not give any history of other systemic illness.

She was from a middle class family. She has a sister. Her father died long past, suffering from carcinoma of the stomach. Her menstrual history was normal. She was immunized according to EPI (Expanded Program on Immunization) schedule. On general examination, the patient was found very ill looking with skinny body built. Multiple hyperpigmented spots were found on her lips and fingertips (Figure 1). On query, she stated that, these spots were from her very early childhood and did not create any problem. Her sister also has similar spots. Her father had so too, who died from carcinoma of the stomach. Her paternal aunt also has such hyperpigmented spots.

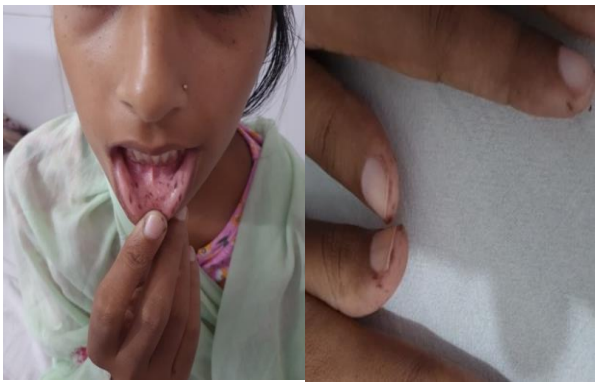

Figure 1: Multiple hyperpigmented lesion on lips and fingertips

The abdomen found scaphoid in shape with left lumber region fullness. On palpation, no definitive lump was palpable in the abdomen except the left lumbar region felt doughy. There was mild tenderness at the epigastric region. Other abdominal examination findings were normal. On per rectal examination, no herperpigmented spot was found in the perianal region. No anal fissure, haemorrhoids or rectal polyp was found.

Immediate plain X – Ray abdomen and Ultrasonography were obtained along with Complete blood count, Serum lipase, Urea, Creatinine, Electrolytes and Blood glucose level. The X – Ray showed gas distended bowel loops without any air fluid level. The distension was mild to moderate. Ultrasonography revealed “Intussusception like gut loops at left upper quadrant”. Blood count showed mild anaemia. All other investigations were within normal limit. We planned for conservative approach with clinical diagnosis as Subacute Intestinal Obstruction due

to PJS. On following day, patient's symptoms were improved on conservative modality like; nothing per oral, nasogastric suction, intravenous fluid, electrolyte and nutritional support along with wide spectrum antibiotics, antispasmodics and proton pump inhibitor. Subsequently we got CT Scan of whole abdomen which denoted colonic polyposis with descending colo-colic intussusception with subacute intestinal obstruction (Figure 2). As soon as the symptoms subsided, upper GI endoscopy and Colonoscopy were done. Upper GI endoscopy showed multiple polyps in the body of the stomach with erosive gastritis (Figure 3). Colonoscopy was able to see upto 60 cm from anal verge at which point a giant polyp was found which restricted further passage of the scope (Figure 4). Multiple polyps of different size were seen within the seen portion of the colon (Figure 5).

Biopsies were taken in both procedures. Histopathology revealed inflammatory/ hamartomatous polyp. Patient's clinical condition improved on conservative management. She was allowed oral diet and well tolerated. She was independent to her daily activity and all vitals were stable.

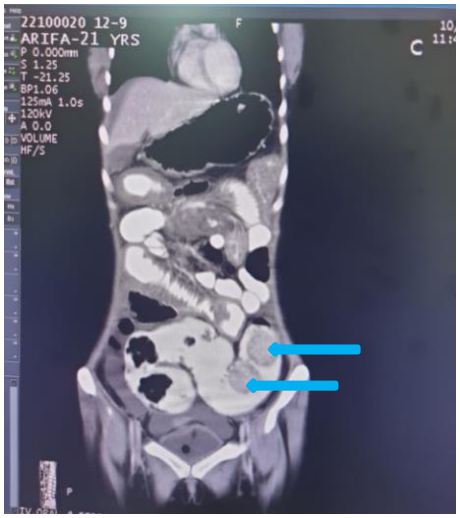

Figure 2: Giant polyps on CT scan (Blue arrow)

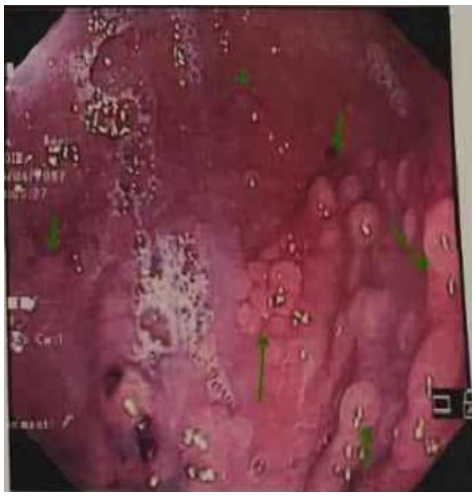

Figure 3: Multiple polyps in the body of stomach seen on endoscopy

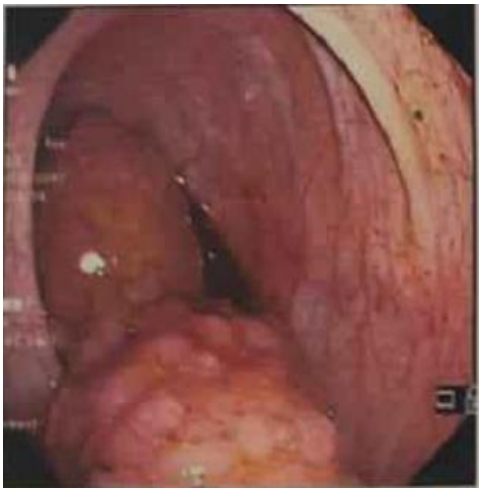

Figure 4: Giant polyp in the descending colon seen on colonoscopy

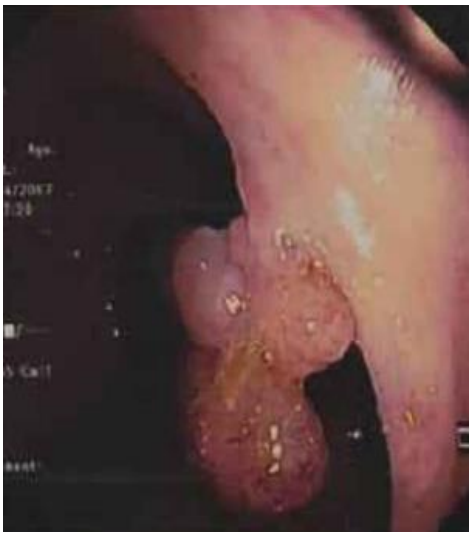

Figure 5: Multiple polyps in the sigmoid colon seen on colonoscopy

Upon the basis of clinical and investigation findings and as per World Health Organization (WHO) diagnostic criteria, she was diagnosed as a case of Subacute intestinal obstruction due to PJS. Genetic study could confirm the diagnosis but lack of facility bound us to stop. We planned for colonoscopic polypectomy and survey of the whole colon. Patient and her relatives, including mother and sister (who has similar spot) were counseled regarding the disease and treatment options. They were informed about the options, resources and facilities for further treatment. Contact and data sharing was done with the Department of Colorectal Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU) and they agreed to attend the patient. Patient was transferred to BSMMU where she underwent laparotomy followed by jujunal resection and colonic polypectomy. Histopathology revealed Peutz–Jeghers Polyposis.

Discussion

PJS has got diversity in both genotyping and phenotyping.[4,7] The mutation is mostly in the STK11/LKB1 gene on chromosome 19.[7] The earliest menifestation of clinical features is oral hyperpigmentation which has been reported as early as 2nd year of life.[4] The most frequent presenting symptom found intussusception with the median age of 19 years. The median age of diagnosis of first cancer was 32 years.[9] Oral lesions appear prior to GI symptoms, and the severity of these may reflect the severity of GI phenotypes. This early onset (pre-puberty) of PJS may be an indicator of the development of serious GI complications.[4] Hamartomatous polyps are found in approximately 80% of the cases predominantly in the jejunum, followed by the ileum, the stomach and large intestine.[6] It can also be found in extraintestinal sites including the nasal passages, bronchial tree, lung, breast, kidney, ureter, pancreatic, gallbladder, uterine, ovarian and testicular tumors.[5,6] Although the hamartomatous polyps are known with low malignant potential, individuals with this disease are at elevated risk of acquiring malignancies.[3] Overall lifetime GI cancer risks of 55–85% and the reported lifetime risk for any cancer varied according to the literature between 37% and 93% at the age of 60–70 years.[3,8]

Clinically, PJS patients often present with a history of intermittent abdominal pain, which is due to bowel intussusception caused by the polyps. This may be reduced spontaneously or develop acute bowel obstruction. Individuals affected with PJS may also present with acute blood loss and chronic anemia due to the ulceration of polyps.[3] Our patient presented with abdominal pain with history of per rectal bleeding which correlates with rectal/colonic polyp disease. She had history of recurrence of the symptoms. She had a lot of investigations. Most of the investigations were within normal limit except few of them showed mild anaemia. Her treatment focused on acuteness and extent of the symptoms and emphasis were given to relieve the pain. Keeping in mind the age and sufferings of the young lady, methodical approach to general examination proceeded. At first instance, the lips drew the attention and further query was made. As these spots did not create any problem to her daily activity and there are other family members with similar spots, the patient did not think any significance of mentioning this. But finally these spots became the diagnostic tool for her sufferings.

According to WHO diagnostic criteria, a diagnosis of the syndrome should be considered in an

individual who satisfies any one of the following: 1) three or more Peutz-Jeghers polyps confirmed by histology; or 2) any number of Peutz-Jeghers polyps with a family history of the syndrome; or 3) typical visible mucocutaneous pigmentation with a family history of the syndrome; or 4) any number of Peutz-Jeghers polyps and typical visible mucocutaneous pigmentation.[10] Gene testing is not necessary to diagnose PJS.[5] Recently, different diagnostic techniques have been added to the traditional small bowel follow-through and enteroclysis, to assess for small bowel polyps. These include wireless capsule endoscopy, MRI enterography and balloon assisted enteroscopy which could be therapeutic as well.[5]

Our patient was admitted through the general emergency department in the evening with the complaints of abdominal pain and vomiting. Initial assessment was done with the routine haemogram, X – Ray Abdomen and Ultrasonography and was diagnosed as a case of subacute intestinal obstruction. On next morning, during the formal review of the case, the diagnosis was revised and suspicion of PJS was made. Further investigation included CT Scan of whole abdomen, Upper GI Endoscopy and Colonoscopy. Biopsies were taken during both Endoscopic and Colonoscopic procedure and finally the criteria for diagnosing the disease were met.

Despite the scarce evidence, there are available guidelines for the management of PJS in adults, and, most recently, recommendations for its diagnosis and management in the pediatric population were published by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN).[11] Based on the reviewed literature and expert opinion, recommendations and statements were formulated by European Hereditary Tumour Group (EHTG) Guideline on (1) clinical genetic, (2) gastrointestinal, (3) surgical, (4) pancreatic,(5) breast, and (6) gynecological management.[8] At present, PJS treatment mainly includes endoscopic polyp resection and surgical operation and as the PJPs are usually small, sessile, multiple, and difficult to remove, patients always need multiple endoscopic treatments.[12] Surveillance protocols for individuals with Peutz-Jeghers syndrome have two key objectives; one is to identify sizeable intestinal polyps that could lead to intussusception and obstruction or bleeding and anemia. The other is to identify malignancy at an early stage.[10]

Conclusion

The scarcity of prevalence of PJS seems once in a lifetime disease for a physician. Clinical suspicion for rare causes of chronic disease should be kept in mind. Formal history and examination is the key point to elicit pathognomic features of diseases. Due to high incidence of malignant transformation, PJS patients should be well counseled regarding benefit of surveillance and risk of loss to follow up state. Early diagnosis and polypectomy along with surveillance for recurrence may prolong cancer free lifetime.

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