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Case Report

PEUTZ–JEGHERS SYNDROME WITH INTESTINAL OBSTRUCTION - A CASE REPORT

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Abstract :

Peutz–Jeghers syndrome, also known as hereditary intestinal polyposis syndrome, is an autosomal dominant genetic disease characterized by the development of benign hamartomatous polyps in the gastrointestinal tract and hyper pigmented macules on the lips and oral mucosa (melanosis).[1] Peutz–Jeghers syndrome has an incidence of approximately 1 in 25,000 to 300,000 births[2] . The polyps in the intestines are usually the leading point for intussusception which may cause obstruction.

KEYWORDS: Peutz-jeghars syndrome, polyps, macules, intussusception.

INTRODUCTION

Peutz–Jeghers syndrome is named after Johannes Laurentius Augustinus Peutz (1886 – 1957), a Dutch Internist who worked in Ohio, USA together with his co internist, Harold Joseph Jeghers (1904-1990).

The main criteria for clinical diagnosis are:

- Family history
- Mucocutaneous lesions causing patches of hyper pigmentation in the mouth and on the hands and feet.
- Hamartomatous polyps in the gastrointestinal tract.
  Having 2 of the 3 listed clinical criteria indicates a positive diagnosis.

There are two types of PJS:

- Familial PJS may be due to a mutation in a gene called STK11. The genetic defect is passed down (inherited) through families as an autosomal dominant trait. That means if one of your parents has this type of PJS, you have a 50% chance of inheriting the nonworking gene and having the disease.
- Sporadic PJS is not passed down through families and appears unrelated to an STK11 gene mutation.

Most patients will develop flat, brownish spots (melanotic macules) on the skin, especially on the lips and oral mucosa, during the first year of life, and a patient's first bowel obstruction due to intussusception usually occurs between the ages of six and 18 years. In 1998, a gene was found to be associated with the mutation. On chromosome 19, the

gene known as *STK11* (*LKB1*)[4] is a possible tumour suppressor gene. It is inherited in an autosomal dominant pattern, which means that anyone who has PJS has a 50% chance of passing the disease on to their offspring.90-100% of patients with a clinical diagnosis of PJS have a mutation in the *STK11/LKB1* gene. Molecular genetic testing for this mutation is available clinically.[3]

CASE REPORT

A 21yr old male patient presented to us with pain abdomen for two days, distended abdomen and, obstipation for one day and vomiting two episodes. On examination, he had a pulse of 100/min and blood pressure of 100/70mmHg, moderately dehydrated, abdominal distension +++, bowel sounds – absent, P/R – rectum empty. Ultrasound abdomen showed Target sign (bowel in bowel appearance) and no signs of gangrene .Pigmented spots were present over the lower lip and also over sole of feet. His father also had similar spots. X-ray showed multiple air fluid levels. Patient was taken for laparotomy and was found to have intussusception. The intussusceptum was reduced, as no signs of gangrene were present, no resection was done. Enterotomy was done and a polyp was excised and sent for histopathology. Post-op period was uneventful. Patient was discharged and he came back two months back with pain abdomen which subsided in a day. CECT abdomen was done this time and was found to have multiple intestinal polyps were seen with intussusception.

Fig 1: Patient with spots over lip and sole of feet.

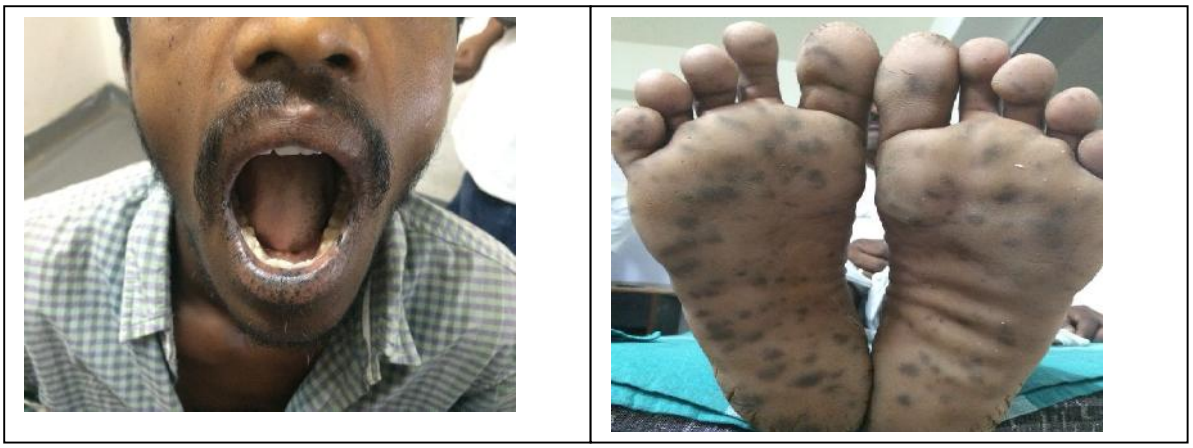
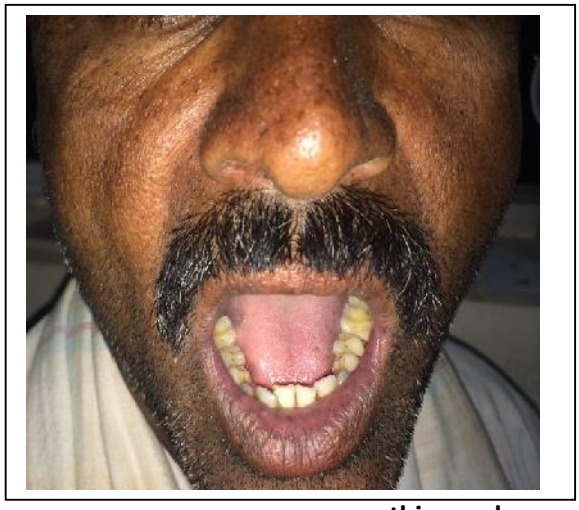


Fig 2: Patient's father with spots over lips and sole of foot.



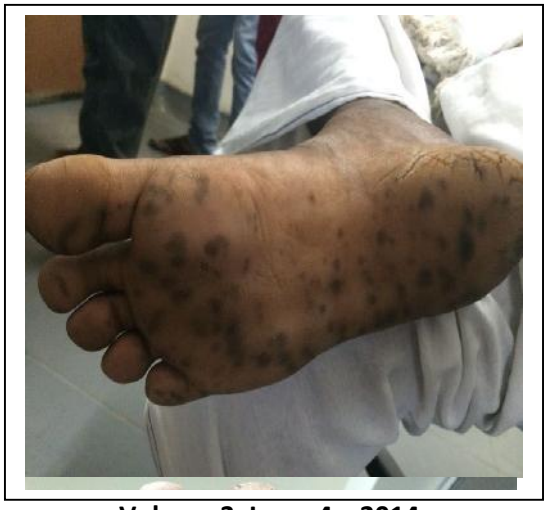


Fig 3: intra-operative findings

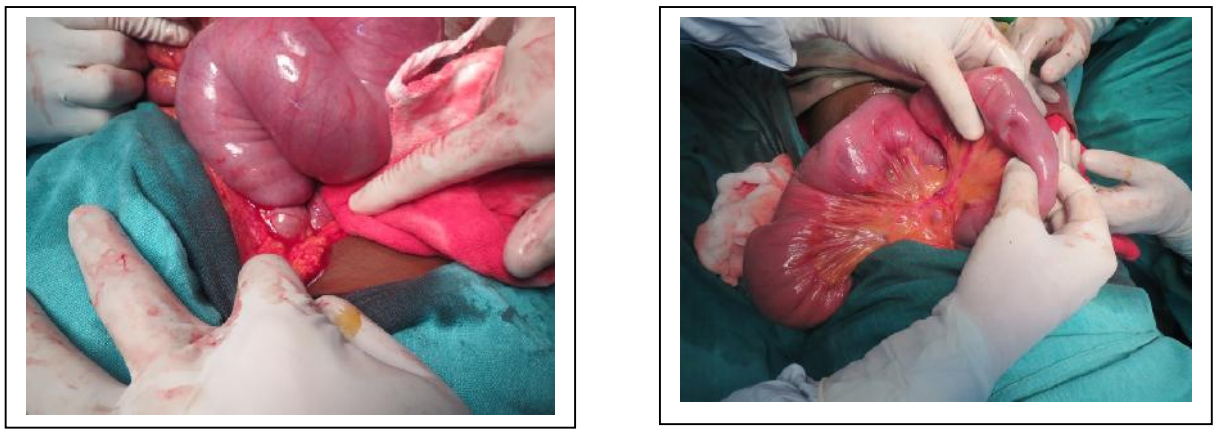


Fig 4: Polyp excised and Histopathology picture

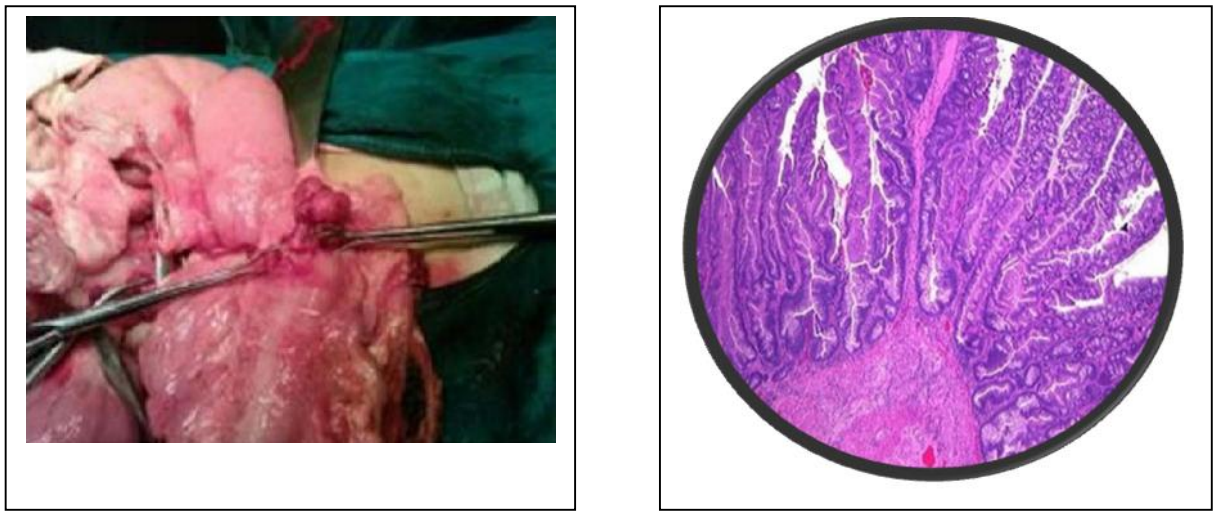
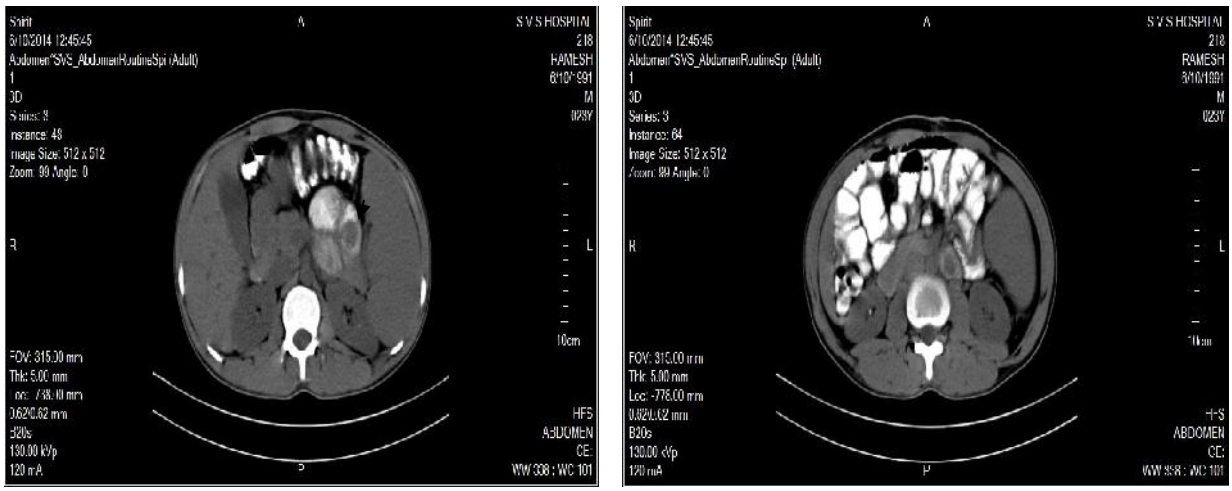


Fig 5: CECT images showing GI Polyp and intussusception



DISCUSSION

This patient had hyper pigmented macules over this lips and sole of feet. On

Laparotomy, polyps were found on enterotomy. There is positive family history as his father also has hyperpigmented patches over lips and feet as shown previously .There is also history of repeated, unexplained abdominal pains, history of unexplained bleeding P/R. Considering all this , it is a case of Peutz-Jeghars syndrome , as it satisfies all three criteria .

Definitive diagnosis can be made by molecular gene testing for mutations in *STK11/LKB1* gene [4].

Surgical management

Patients with Peutz-Jeghers syndrome (PJS) usually undergo numerous surgeries during their lives. These surgeries include laparotomy and laparoscopy for both gastrointestinal involvement and extra intestinal complications. Surgical treatment of extra intestinal cancers detected through surveillance procedures is frequently required. Laparotomy and resection may be necessary, as indicated, for small intestinal intussusception, obstruction, or persistent intestinal bleeding. Laparoscopic-assisted enteroscopy may offer a less invasive option for polyp removal.

Pharmacologic Management

Chemo preventive strategies for familial adenomatous polyposis syndrome management have led to investigation into cyclooxygenase (COX) inhibitors for Peutz-Jeghers syndrome (PJS). Rossi et al demonstrated that COX-2 was highly up-regulated in a murine model of Peutz-Jeghers syndrome LKB1 mutant mice.[7]Polyps recovered from patients with Peutz-Jeghers syndrome also showed a significant correlation between LKB1 staining and COX-2, suggesting COX-2 is integral to the tumorigenesis pathway in Peutz-Jeghers syndrome.[8] A decrease in polyp burden was reported in COX-2 knockout LKB-1 mutant mice, analogous to LKB-1 mutant mice treated with celecoxib. In that report, Udd et al reported an uncontrolled, open-labelled pilot study in humans and noted reduced gastric polyposis in patients treated with celecoxib.[9] Celecoxib use in Peutz-Jeghers syndrome, although promising, remains to be tested and currently cannot be routinely recommended in any age group.

Given that modulation of PI3-kinase is critical to the function of STK11, and in turn, one of the major downstream mediators of PI3-kinase signalling is mammalian target of rapamycin (mTOR), inhibition of mTOR offers potential therapeutic possibilities in chemoprevention in Peutz-Jeghers syndrome. Rapamycin has been shown to be effective in reducing polyp burden in a murine model of Peutz-Jeghers syndrome.[10] In addition, RAD001 (everolimus) has been proposed as a potential chemo preventive agent and reportedly effective in achieving a partial remission in a patient with Peutz-Jeghers syndrome with advanced pancreatic cancer.[11]Currently, the use of mTOR inhibitors is not recommended as standard of care in adult and paediatric patients with Peutz-Jeghers syndrome.

Patient Monitoring

Ideally, patients with Peutz-Jeghers syndrome (PJS) should be followed by a multidisciplinary team that is familiar with the syndrome. The aim of the initial consultation and continued follow up is to educate the patient and family on the illness, outline a schema for continued disease surveillance, offer genetic counselling, and, if appropriate, offer genetic

testing to the extended family. Support, including identification of psychologically at-risk individuals, needs to be factored in this holistic management approach.[12] Counselling and testing of asymptomatic but at-risk individuals is geared toward limiting the likelihood of Peutz-Jeghers syndrome patients presenting with complications, including malignancy, inherent to their disease, as well as advice regarding potential preventive strategies, including cancer-surveillance measures.

Periodic surveillance and removal of larger polyps aims to reduce the likelihood of complications in Peutz-Jeghers syndrome. Hence, surveillance for gastric and small-bowel polyposis should begin at age 8-10 years and continue at 2-year intervals.[13] When small bowel polyps are present, there is broad consensus amongst quaternary referral centres that they be removed before symptoms and obstruction become evident. A regular surveillance-based, clean-sweep enteroscopy (double-balloon or intraoperative assisted and push-enteroscopy) is suggested to decrease the risk of obstruction, surgical resection and, long term, the risk of short bowel syndrome.[14, 15, 16]

Follow-up care should be supervised by a gastroenterologist familiar with Peutz-Jeghers syndrome. Patients with Peutz-Jeghers syndrome should undergo an annual CBC count, as well as an annual physical examination that includes evaluation of the breasts, abdomen, pelvis, and testes. Lifelong cancer surveillance is advocated.[3]

A recent review by Beggs and co-workers summarized the current recommendations for cancer surveillance in patients with Peutz-Jeghers syndrome and pooled the published recommendations to date.[17, 18, 19] Recommendations were based on literature review, cohort studies, and systematic review. Recommendations focused on upper intestinal, colorectal, pancreatic, breast, and genitourinary (reproductive) organ surveillance.

- Upper gastrointestinal tract - Annual haemoglobin concentration, esophago-gastroduodenoscopy (EGD) every 2-3 years, small bowel series/enteroscopy (possible alternatives: wireless capsule endoscopy, magnetic resonance enterography) every 2 years, although there is no consensus on from what age (e.g., 10 y, 18 y, 25 y) to start
- Colorectal - Colonoscopy or flexible sigmoidoscopy and barium enema every 2-3 years from the time of first symptoms or in late teens/25 years onwards
- Pancreatic - Annual abdominal ultrasound or annual/every-other-year endoscopic ultrasound from age 25-30 years onwards
- Breast - Regular breast examination (monthly to 6 monthly) from age 18 years onwards, mammography (or MRI) every other year (annually after age 50 y)
- Genitourinary in women - Annual pelvic examination, pelvic ultrasound, and cervical smears; some reviews recommend serum CA 125, endometrial biopsy annually from age 20 years onwards
- Genitourinary in men - Annual testicular examination; ultrasound if symptomatic from birth

The Cancer of the Pancreas Screening (CAPS) Consortium summit in 2012 addressed pancreatic cancer screening recommendations in at-risk populations, including persons with Peutz-Jeghers syndrome. Periodic screening of all individuals with Peutz-Jeghers syndrome was recommended from age 50 years onwards. Suitable modalities for initial screening included endoscopic ultrasonography, MRI/magnetic resonance cholangio-pancreatography (MRCP), CT scanning, abdominal ultrasound, and endoscopic retrograde cholangio-pancreatography (ERCP). The ideal frequency for surveillance, however, was not defined.

CONCLUSION

Peutz–Jeghers syndrome is rare and studies typically include only a small number of patients. Even in those few studies that do contain a large number of patients, the quality of the evidence is limited due to pooling patients from many centers, selection bias (only patients with health problems coming from treatment are included), and historical bias (the patients reported are from a time before advances in the diagnosis of treatment of Peutz–Jeghers syndrome were made). Probably due to this limited evidence base, cancer risk estimates for Peutz–Jeghers syndrome vary from study to study.[5]

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