Peutz-Jeghers Syndrome presenting with severe Anemia: A Case Report

Noor Abdulaziz Binkroom[1*], Omar Abdul-Rahman Bawazir[2], Reem Khalid Khanbash[3], Heba Mohammed Alnahdi[4], Omer Moammed Barahman[5]

[1,2]Associate Professor of Pediatrics, College of medicine and Health Sciences, Hadhramout University, Mukalla, Hadhramout, Yemen.
[3,4]Pediatric specialist, Mukalla Maternity & Children Hospital, Mukalla, Hadhramout, Yemen.
[5]Associate Professor of Surgery, College of medicine and Health Sciences, Hadhramout University, Mukalla, Hadhramout, Yemen.

Abstract

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant condition characterized by mucocutaneous pigmentation and hamartomatous polyps, primarily in the gastrointestinal tract. The syndrome is associated with complications such as gastrointestinal bleeding, intestinal intussusception, and an increased risk of malignancies both within and outside the gastrointestinal tract. We report a case of a 12-year-old boy with PJS who had no family history of the condition and was admitted for blood transfusion due to severe anemia. Clinical examination revealed muco-cutaneous pigmentation, and upper GIT (gastrointestinal tract) endoscopy identified multiple polyps, confirming the diagnosis of PJS. This case highlights the importance of doing gastrointestinal tract upper GIT endoscopy in children with unexplained severe anemia associated with muco-cutaneous pigmentation may serve as a crucial diagnostic clue for PJS.

Keywords: Peutz-Jehgers syndrome, mucocutaneous pigmentation, anemia, Yemen.

Corresponding author:
*Noor Abdulaziz Binkroom. Department of Pediatric, College Of Medicine and Health Sciences, Hadhramout University, Al-Mukalla, Yemen.
E-mail: noorbinkroom@yahoo.com
Mobile: +967-771155067

عرض نمطي لحالة فقر دم شديد نتيجة متلازمة بيتز جقر

نور عبدالعزيز بن كروم[1*]، عمر عبدالرحمن باوزير[2]، ريم خالد خنبش[3]، هبة محمد النهدي[4]، عمر محمد بارحمان[5]

الملخص:

عرض نمطي لحالة فقر دم شديد نتيجة متلازمة بيتز جقر تعتبر هذه المتلازمة من النوع النادر والسائد وراثيا. وتتميز بالاصطباغ الجلدي المخاطي السلائل الدموية في الجهاز الهضمي حيث تكون هذه السلائل مكانا للنزيف و الانسداد المعوي. كما يصاحب هذه المتلازمة خطر الاصابة بالاورام الخبيثة داخل وخارج الجهاز الهضمي. نقدم تقريرا عن حالة صبي عمره 12 عاما مصاب بمتلازمة بيتز جقرز، دون تاريخ عائلي لنفس المرض، وقد ادخل الى المستشفى لنقل الدم بسبب فقر الدم الشديد. كشف الفحص السريري عن وجود تصبغات مخاطية جلدية، كما اظهر التنظير العلوي للجهاز العلوي وجود العديد من السليلات الدموية مما اكد تشخيص الحالة. تسلط هذه الحالة الضوء على أهمية التقييم السريري الدقيق للأطفال الذين يعانون من فقر دم شديد غير مفسر، حيث يمكن أن تكون التصبغات المخاطية الجلدية دليلًا تشخيصيًا مهمًا لمتلازمة بيتز جيقر.

الكلمات المفتاحية: فقرالدم، الاصطباغ الجلدي المخاطي، الاورام الدموية في الجهاز الهضمي، اليمن.

Introduction:

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant disorder characterized by mucocutaneous pigmentation and gastrointestinal (GI) hamartomatous polyposis (1,2). The estimated incidence ranges from 1 in 8,300 to 1 in 200,000 live births and can occur in any ethnic group affecting males and females equally. Mucocutaneous pigmented lesions are present in approximately 95% of patients and may serve as the first clue to a diagnosis of PJS. These lesions appear as dark blue, brown, or black macules, primarily around the lips and oral mucosa, but they can also be found on the hands and feet. They typically emerge in infancy and tend to fade by late adolescence (3).

Gastrointestinal polyps in PJS can lead to complications such as bleeding, abdominal cramping, and bowel obstruction due to recurrent intussusception. Additionally, PJS is associated with an increased lifetime risk of malignancies both within and outside the gastrointestinal tract, including cancers of the pancreas, breast, and testis. Although testicular tumors are more commonly reported in adults, they have also been documented in pediatric patients (3, 4).

The diagnosis of PJS is based on clinical criteria, requiring the presence of at least two of the following: 1- a family history of PJS, 2- multiple pigmented macules on the mucous membranes and skin, and 3- hamartomatous intestinal polyps (5). Mutations in the **serine-threonine kinase 11 (STK11)** tumor suppressor gene have been linked to PJS, with pathogenic variants detected in 50–80% of affected families. However, the rate of spontaneous mutation in PJS remains uncertain (6).

Here, we report the case of a 12-year-old boy with PJS presenting with severe anemia and weight loss. His general examination was otherwise unremarkable, and there was no family history of the condition. A review of the literature on PubMed and Google suggests that this is the first reported case of pediatrics PJS in Yemen.

Case Report:

A 12-year-old male student, born to non-consanguineous parents from a rural area, presented with a history chronic of anemia requiring one blood transfusion one year before.

Upon further history-taking, he reported upper abdominal pain, particularly after consuming heavy, fatty meals, which was associated with non-projectile, non-bilious vomiting.

There was no history of melena, hematemesis, fever, changes in bowel habits, or alterations in urine color. He had no known family history of hereditary anemia or bleeding disorders. Despite maintaining a good appetite, he experienced significant weight loss. His psychomotor development was appropriate for his age, and a systemic review revealed no additional concerns.

On March 5, 2023, he was admitted to our department for blood transfusion due to severe anemia.

Physical Examination:

The patient's weight was below the 5th percentile, while his height was at the 50th percentile. He appeared severely pale but was not jaundiced. Mild tenderness was noted on palpation of the upper abdomen, though no palpable masses were detected. Notably, pigmented spots were observed on his lips, which his mother reported had been present since early childhood. Further examination revealed similar pigmentation on the buccal mucosa, palms, and soles (Fig. 1, 2, and 3).

Laboratory Investigations:

- **Complete Blood Count (CBC):**
  - Total WBC count: 4.9 × 10^9/L
  - Neutrophils: 69.9%
  - Lymphocytes: 21.8%
  - Hemoglobin (Hb): 6 g/dL
  - Mean Corpuscular Volume (MCV): 65.1 fL
  - Platelet count: 553 × 10^9/L
  - Peripheral blood smear: Microcytic hypochromic anemia
- **Additional Tests:**
  - Stool occult blood: Positive
  - Liver and renal function tests: Normal
  - Iron profile (including ferritin and serum iron): Not performed
  - Genetic study was not done

In view of the mucocutaneous pigmentation and anemia, PJS was highly suspected, the child was arranged to have endoscopy. Upper gastrointestinal endoscopy revealed multiple hamartomatous polyps in the stomach and duodenum, confirming the diagnosis of PJS (Fig. 4). A histopathological study was not performed.

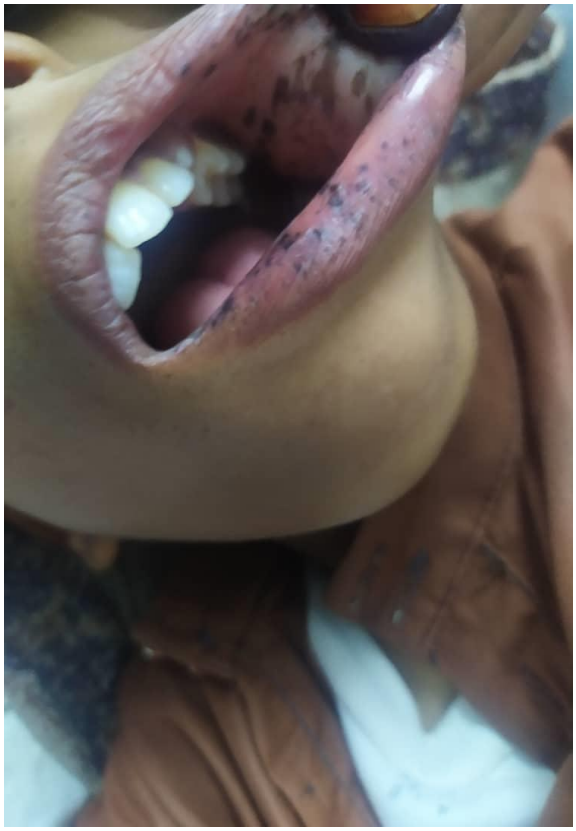

Figure 1: The child face shows pigments on lips and buccal mucosa

Figure 2: The child hand shows pigmented macules on finger tips

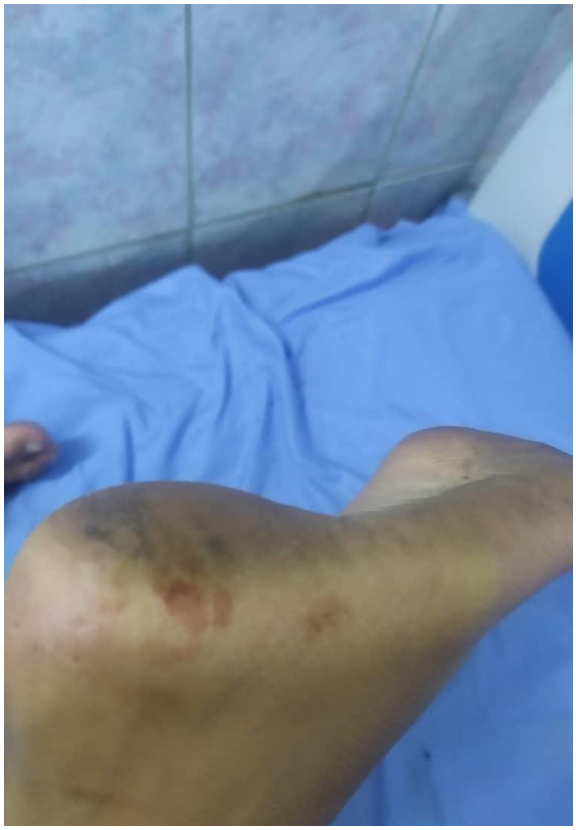

Figure 3: The child feet shows pigmented macules

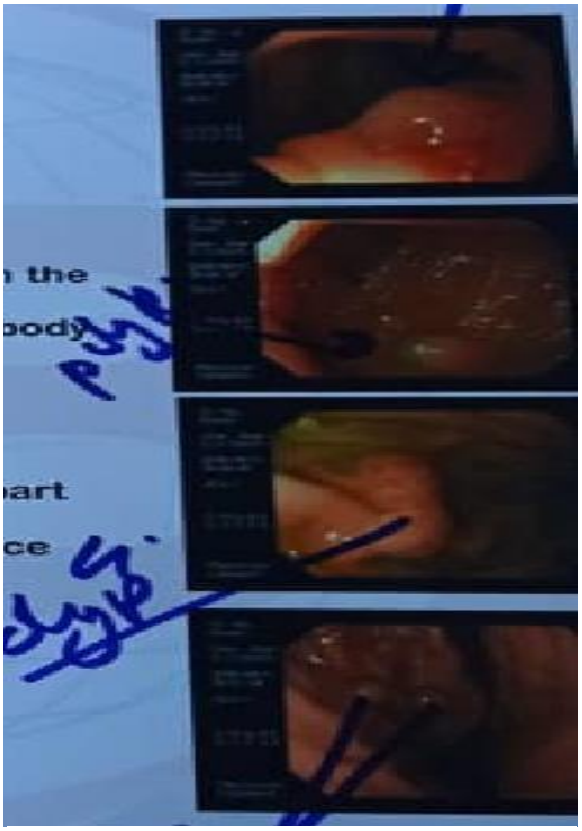

Figure 4: Upper endoscopy shows polyps in stomach and duodenum

Discussion:

Peutz-Jeghers syndrome (PJS) is characterized by a triad of mucocutaneous pigmentation, gastrointestinal hamartomatous polyps, and an increased risk of various malignancies (7). In pediatric patients, the hallmark manifestations of PJS are complications related to gastrointestinal polyps, such as abdominal pain, intussusception, and anemia (8,9), findings consistent with our case.

In their study on Chinese patients with PJS, Wu *et al.* (7) reported that mucocutaneous pigmentation may be the only initial clinical finding. Similarly, in our case, PJS was suspected based on the presence of lip pigmentation. Mucocutaneous pigmentation in PJS is most commonly located on the lips (94% of patients), followed by the buccal mucosa (64%), hands (74%), and feet (62%). These lesions typically appear at birth or in early infancy, though they may occasionally emerge later in life (8). Our patient exhibited pigmentation in all these areas, with particularly extensive involvement of the buccal mucosa (Figures 1, 2, and 3). The family reported that these pigmented lesions had been present since early childhood but had not raised any concerns. No other family members exhibited similar pigmentation.

In pediatric PJS, gastrointestinal symptoms are the most common reason for seeking medical attention (10). Abdominal pain is one of the cardinal symptoms of PJS (8). In our case, the child experienced chronic upper abdominal pain but did not develop intussusception or require surgical intervention.

Ortegón-Gallareta *et al.* (10) described unexplained weight loss and some degree of malnutrition in patients with PJS, findings that were also present in our case.

Patients with PJS are at an increased risk of developing malignancies later in life (7). However, pediatric-onset tumors are not negligible. Beggs *et al.* reported that 9% of children with PJS developed testicular tumors at a mean age of 8.6 years (6).

Additionally, feminizing gonadal tumors have been described in prepubertal children with PJS (11, 12). This highlights the importance of careful examination for PJS-associated pigmentation in pediatric patients presenting with malignancies. In our case, the child had normal testes and no family history of malignancy.

Genetic testing and counselling are available for individuals with suspected PJS and for relatives of confirmed PJS patients to detect STK11 gene mutations, enabling early diagnosis and preventive interventions to reduce gastrointestinal complications and malignancies (7,13). Unfortunately, such facilities are unavailable in our institution.

Treatment

Polypectomy is recommended for symptomatic polyps, as in our case, and prophylactic polypectomy is advised for polyps larger than 10 mm during endoscopy (4,14). Our patient was referred to a specialized center for further management due to the presence of a highly vascular polyp. Additionally, screening for melanotic spots was recommended for his younger sister and other family members.

Conclusion:

This case highlights the importance of recognizing mucocutaneous pigmentation in children with unexplained severe anemia and/or weight loss, as it may serve as a crucial diagnostic clue for Peutz-Jeghers syndrome.

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