Peutz-Jeghers Syndrome: In Siblings with Palmer-Plantar Pigmentation

1Suresh KV, 2Prashanth Shenai, 3Laxmikanth Chatra

1Postgraduate Student, Department of Oral Medicine and Radiology, Yenepoya Dental College and Hospital, Mangalore Karnataka, India

2Professor, Department of Oral Medicine and Radiology, Yenepoya Dental College and Hospital, Mangalore, Karnataka, India

3Professor and Head, Department of Oral Medicine and Radiology, Yenepoya Dental College and Hospital, Mangalore Karnataka, India

Correspondence: Suresh KV, Postgraduate Student, Department of Oral Medicine and Radiology, Yenepoya Dental College and Hospital, Mangalore, Karnataka, India, e-mail: dr_suri88@yahoo.co.in

ABSTRACT

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant disorder characterized by typical pigmented perioral macules, pigmented spots in the oral mucosa and digits along with hamartomatous polyps in the gastrointestinal tract. The pigmented macules usually appear during infancy or early childhood and have a tendency to increase in size during adolescence. The characteristic clinical course includes recurrent episodes of polyt-induced bowel obstruction, abdominal pain and gastrointestinal bleeding. In addition to polyposis, the risk of gastrointestinal and extragastrointestinal malignancies is significantly higher in patients with PJS.

We report two unique cases of Peutz-Jeghers syndrome in sibling with intestinal polyposis and mucocutaneous pigmentation with a definite family history. An overview on differential diagnosis and therapeutic aspects of the disease has been discussed.

Keywords: Hamartomatous polyps, Perioral macules, Mucocutaneous pigmentation, Peutz-Jeghers syndrome.

INTRODUCTION

Peutz-Jeghers syndrome (PJS) is an autosomal dominant disease characterized by polyps and mucocutaneous pigmentation that typically manifests in childhood and early adulthood with a common presentation of bowel obstruction and severe abdominal pain. Diagnostic criteria include hamartomatous intestinal polyps, mucocutaneous pigmentation and a family history of the syndrome. Manifestations of the disease may first be encountered by the dental professional during routine examination by the presence of pigmented spots in the oral cavity. Because oral manifestations may precede gastrointestinal onset, dentist may function as part of an interdisciplinary team and aid in early detection, management and surveillance of this syndrome.

CASE HISTORY

Case 1

A 38-year-old male patient reported to the department with a chief complaint of decay in right upper back tooth region since 3 months which was associated with food lodgement. Past medical history revealed surgery in abdominal region 18 years back for severe abdominal pain, vomiting and bleeding. Family history revealed his sister also underwent abdominal surgery for the same reason 16 years back and his father has been diagnosed with carcinoma of intestine 25 years back. General physical examination and review of other systems revealed no abnormalities.

On extraoral examination, presence of multiple, well demarcated brownish-black pigmented macules on lips, perioral region, palms and soles were noticed (Figs 1 and 2). Pigmented macules started at the age of 12 years, initially present only on the lips and gradually involving the perioral regions. By the age of 20 years, macules started fading off.

On intraoral examination, there was multiple, discrete, well demarcated brownish-black pigmented areas measuring about 2 to 4 mm seen on labial mucosa and buccal mucosa. On palpation pigmented areas were flat, smooth, nontender and had the same consistency as that of adjacent mucosa (Fig. 3).
Case 2
A 34-year-old female patient who is younger sibling of case 1 was also called for examination. She revealed a similar history of having undergone an abdominal surgery 16 years ago. On examination, (introral, extraoral) similar brownish black pigmented macules are seen on lips, labial mucosa, buccal mucosa (Figs 4 and 5, Table 1).

Based on the history (abdominal surgery) and clinical examination (pigmented macules on lips and extremities), a provisional diagnosis of Peutz-Jeghers syndrome was considered (Table 2).

Differential diagnoses of other mucocutaneous pigmented lesions considered were Laugier-Hunziker syndrome, Cronkhite-Canada syndrome, Carney syndrome and Leopard syndrome.

Previous investigation reports (case 1 and 2) included barium meal, abdominal ultrasonography and histopathology.

Barium meal showed distension of small intestine. USG revealed fluid filled areas with distension of bowel loops. Histopathology report showed polypoidal hyperplasia of mucosal glands with some areas showing increased mucous secretion with no evidence of malignancy. All these features were suggestive of jejunal polyp (Figs 6 to 8).

Correlating the history, clinical examination (mucocutaneous pigmentation) and previous investigation reports (distension of bowel loops, jejunal polyp), a final diagnosis of Peutz-Jeghers syndrome was made.

Since both the patients had already undergone surgical resection of proximal jejunum and they were not esthetically concerned about perioral macules, no treatment was rendered. However, all the necessary investigations (barium meal, abdominal USG, intestinal endoscopy) were repeated once again which revealed no abnormalities. They were asked to undergo periodic screening of all the systems once in 2 years.

DISCUSSION
Peutz-Jeghers syndrome was first reported in a pair of identical twins by Connor in 1895 and illustrated by Hutchinson in 1896. It is named after Dr Johannes Peutz and Dr Harold Jeghers who described a relation between mucocutaneous pigmentation and intestinal polyposis.\textsuperscript{1,2} PJS is caused by mutations in the gene coding for serine threonine kinase, located on the P arm of chromosome 19.\textsuperscript{3}

The prevalence of PJS differs between studies. The widest estimated range is from 1 in 8300 to 1 in 280000 individuals. The disease has variable penetrance, even within families; some members will only manifest hyperpigmentation, while others may manifest pigmentation and hamartomatous polyps.\textsuperscript{2} The median age of diagnosis was 23.5 years, family history was positive in one-half of cases, and mucocutaneous pigmentation was observed in almost all patients (93%).\textsuperscript{4}

The pigmented macules may be present at birth or appear during infancy, early childhood and have a tendency to increase in size during adolescence.\textsuperscript{4} Macules appears round, oval or irregular patches of brown or almost black pigmentation, measuring 1 to 5 mm in diameter and are irregularly distributed over the lips, buccal mucosa, gingiva and hard palate. The pigmented lesions may also occur on the face especially around the nose and the mouth but are smaller and often < 5 mm in size.\textsuperscript{5}

Large macules are rarely seen over the palms of the hands, the tips of the fingers and toes. Malignant transformation of these lesions is extremely rare. Hyperpigmentations can even disappear during adolescence. Early investigators noted that the cutaneous pigmentation pattern can fade with age. However, buccal mucosal lesions tend to persist.\textsuperscript{6} This is important for clinicians who are attempting to establish the diagnosis in

<table>
<thead>
<tr>
<th>Table 1: Differential diagnosis of pigmented lesions similar to Peutz-Jeghers syndrome\textsuperscript{4}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leopard syndrome</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Laugier-Hunziker syndrome</td>
</tr>
<tr>
<td>Carney syndrome</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Cowden’s syndrome</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
individuals suspected of Peutz-Jeghers syndrome, only few cases of PJS having only pigmentation without polyposis have been reported.

Present case (case 1 and 2) had large hyperpigmented macules over both his palms and soles which is very unusual.

Intestinal manifestations include numerous polyps in the jejunum, ileum and less frequently in the colon, rectum, stomach and duodenum.7 The median age of occurrence of polyps is about 11 to 13 years of age, and approximately 50% will experience symptoms by the age of 20 years.8

During the first three decades of life, anaemia, rectal bleeding, abdominal pain, obstruction and/or intussusception are common complications.8,9 Patients with PJS have a 10 to 18 fold greater lifetime cancer risk than the general population. The greatest risk is for gastrointestinal malignancy of the colon and duodenum. The risk of other cancers, especially of the reproductive organs, breasts, pancreas and lungs is nine times greater among these patients than the general population.10

The present cases had jejunal polyps without evidence of malignancy. They were surgically excised and showed no recurrence after 18 years of follow-up.

The differential diagnosis of pigmented lesions similar to PJS includes Leopard syndrome which is characterized by lentigines, electrocardiographic abnormalities, ocular hypertelorism, pulmonary stenosis along with abnormalities of genitalia, retarded growth and deafness. However, the absence of intestinal polyposis helps to differentiate this from PJS.4 Laugier-Hunziker syndrome characterized by pigmentation of oral mucosa, palmoplantar area, fingers, toes and genital region can be considered. But in this condition, there will not be any family history of hamartomatous polyposis. Carney syndrome presenting as pale brown to brown lentigines, myxomas of the skin, heart and breast; endocrine tumors; and schwannomas are also excluded as there will not be any history of intestinal polyposis in this condition. Another condition with the similar mucocutaneous lesions and oral papillomatosis is the Cowden syndrome.4,5

The differential diagnosis for polyposis similar to PJS can also be considered like familial juvenile polyposis, which is characterized by
colorectum. But, mucocutaneous pigmentation is not seen in this condition. Cronkhite-Canada syndrome which is characterized by gastrointestinal polyposis, alopecia, dermal pigmentation and atrophy of the nail beds can be included in the differential diagnosis.4,10

Another condition with multiple adenomatous polyposis in the large bowel, benign extraintestinal lesions (lipomas, fibromas, sebaceous and epidermoid cyst, osteomas, desmoids) is the Gardner’s syndrome. Basal cell nevus syndrome can be considered as another differential diagnosis as it is characterized by multiple gastric hamartomatous polyps, multiple basal cell carcinomas, frontal bossing, hypertelorism, bifid ribs, bone cysts (especially mandible).4,10,11

The diagnostic criteria for PJS proposed by Giardello12 and colleagues require histopathological confirmation of hamartomatous gastrointestinal polyps and two of the following features: Small bowel polyposis, family history and pigmented skin and/or mucosal brown macules. In the present cases, the polyps were hamartomatous and were present in the jejunum. Both the patients had typical mucocutaneous pigmentation which favored familial inheritance.

Treatment of pigmented macules causing cosmetic disfigurement is successfully treated by Q-switched lasers and intense pulsed light (IPL). However, repigmentation generally noticed within one year.

Current recommendations advocate prophylactic endoscopic removal of all polyps. Recent guidelines support complete colorectal surveillance with either colonoscopy or flexible sigmoidoscopy.13

Table 2: Differential diagnosis for polyposis similar to Peutz-Jeghers syndrome4

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial juvenile polyposis</td>
<td>Multiple juvenile polyps primarily in the colorectum.</td>
</tr>
<tr>
<td>Cowden’s syndrome</td>
<td>Gastrointestinal hamartomas.</td>
</tr>
<tr>
<td>Cronkhite-Canada syndrome</td>
<td>Gastrointestinal polyposis.</td>
</tr>
<tr>
<td>Familial adenomatous polyposis (Gardner’s syndrome)</td>
<td>Multiple adenomatous polyposis in the large bowel.</td>
</tr>
<tr>
<td>Basal cell nevus syndrome (Gorlin syndrome)</td>
<td>Multiple gastric hamartomatous polyps.</td>
</tr>
</tbody>
</table>

Table 3. Summarizes the recommendations, which the oral health care provider should consider while managing PJS patients4

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thorough review of medical history</td>
<td>− Attention to complains of abdominal pain and bleeding</td>
</tr>
<tr>
<td>Thorough extraoral and intraoral examination</td>
<td>− Evaluate the presence and extension of mucocutaneous pigmentation</td>
</tr>
<tr>
<td>− Evaluate soft tissue for presence of oral ulcers and glossitis as an indicator for anemia or severe malabsorption</td>
<td>− Presence of anemia; defer elective surgical treatment if hemoglobin is &lt; 10 gm/dL.</td>
</tr>
<tr>
<td>If unknown history of PJS</td>
<td>Consult physician to determine overall medical status of the patient</td>
</tr>
<tr>
<td>− Detailed history of the disease including date of diagnosis, course of disease, treatment to date and medications.</td>
<td>− Obtain complete blood count to evaluate hemoglobin, hematocrit, platelet count and electrolytes</td>
</tr>
<tr>
<td>− If unknown history of PJS suspected, referral to primary physician or gastroenterologist is advised.</td>
<td>− If unknown history of PJS suspected, referral to primary physician or gastroenterologist is advised.</td>
</tr>
<tr>
<td>Monitor patients for postoperative bleeding as well as appropriate wound healing</td>
<td>− Periodic evaluation to assess changes in oral mucosa, dentition and/or existing pigmentation is advised.</td>
</tr>
<tr>
<td>Reinforce importance of proper oral hygiene and balanced diet.</td>
<td>− Reinforce importance of proper oral hygiene and balanced diet.</td>
</tr>
</tbody>
</table>

Dental Management of Peutz-Jeghers Syndrome Patients

Modifications in the dental treatment for PJS patients compared with otherwise healthy patients are required only when they present with complications as discussed previously (Table 3).

Although perioral pigmentation is commonly seen in PJS, palmoplantar pigmentation is rare and presently reported cases with hyperpigmented macules over the soles have never been reported.

It is suggested that any patient presenting with multiple mucocutaneous pigmentsations, anemia and bleeding should be investigated for polyps of gastrointestinal.13

CONCLUSION

PJS is an autosomal dominant disease characterized by intestinal polyposis and mucocutaneous pigmentation. Since oral manifestations may precede gastrointestinal onset, oral health care providers may play a significant role in detection and surveillance of PJS. Therefore, dentist should become familiar with this condition in order to provide optimal oral health care to individuals affected by this disease.

ACKNOWLEDGMENTS

My heartfelt gratitude to Dr Veena KM, MDS, Professor and all the staff members of Oral Medicine and Radiology, Yenepoya Dental College.
REFERENCES