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Evaluation of Peutz-Jeghers Syndrome in a Family

Kayhan Ozkan, MD*

Five cases of Peutz-Jeghers syndrome in one family have been studied, and a review of the history and features of the syndrome are presented. This syndrome was detected in four of six siblings and in the father. Three family members underwent surgery after small-bowel obstruction was diagnosed. A gastric polyp was removed from a fourth family member. Rectal bleeding dominated the clinical picture in two patients. Colonic polyps were also found in the three patients who had small-bowel polyps. One of the four affected siblings had mucocutaneous pigmentation, but no evidence of intestinal polyps was detected. The five affected family members have been followed up for periods of 3-1/2 to 4-1/2 years.

Peutz-Jeghers syndrome, which is inherited as an autosomal dominant condition, is characterized by mucocutaneous pigmentation and hamartomatous polyps occurring in the gastrointestinal tract. This syndrome was first reported by Hutchinson in 1896 (1,2), but it was Peutz in 1921 who reported the syndrome in seven patients, noting the close relationship between mucocutaneous pigmentation and intestinal polyposis (1,2). In 1949, Jeghers demonstrated that the disease was inherited through a simple mendelian dominant gene (1-5).

Characteristic pigmentation is usually seen in the first two to three years of life. The pigmented areas may be located on the lips, perioral area, and buccal mucosa and, less commonly, on the palms of the hands, soles of the feet, and toe nails (6). Histologically, an accumulation of melanin pigment and an increased number of melanocytes are seen in the basal layer of the epidermis (1).

Intestinal polyposis associated with this disease is rarely found in infants but appears during puberty and adolescence (1,7,8). The polyps, which are hamartomas, are distributed throughout the gastrointestinal tract; the highest occurrence is in the jejunum. The clinical course of Peutz-Jeghers syndrome is characterized by asymptomatic periods interspersed with episodes of intermittent colicky abdominal pain, often related to intussusception and hemorrhage, which is usually occult. Small-bowel polyps should be removed through multiple enterotomies, and as much small bowel as possible should be preserved to avoid the development of the short-gut syndrome. Colonic polyps are often asymptomatic and are usually found only during the investigation of anemia. This paper reports an experience with this rare disease in a large family and reviews the current literature.

Case Reports

Case 1
A 40-year-old man underwent transgastric polypectomy five years ago after gastric polyp was diagnosed. Microscopically, the gastric polyp was hamartomatous. On physical examination, characteristic pigmentation was seen on the lips, perioral area, and buccal mucosa. The patient was entirely asymptomatic after surgery, and no polyt was demonstrated on radiographs of the gastrointestinal tract and small bowel that were obtained after surgery. Findings of barium-enema examination were also negative. The patient is well after a 4-1/2 year follow-up period.

Case 2
The 20-year-old son of the man reported above was admitted with abdominal pain, distention, vomiting, and constipation of two to three days’ duration. Physical examination revealed dark brown pigmentation of the lips and buccal mucosa (Figs 1,2). Generalized abdominal distention with tenderness, abdominal rigidity, and rebound tenderness was noted. Bowel sounds were hyperkinetic. Radiographs of the abdomen showed evidence of mechanical small-bowel obstruction. A diagnosis of intussusception secondary to polyps in the small bowel was made, and the patient underwent surgery. Exploration revealed a large gangrenous mass due to jejunojejunal intussusception. After resection of this mass, enterenterostomy was performed. Three polyps, 0.5 cm, 1 cm, and 2 cm in diameter, were found in resected material. Histopathologic examination revealed their hamartomatous nature. The patient is well after a 4-1/2 year follow-up period.

Case 3
The 17-year-old son in this family was admitted, complaining of weakness. His history included resection of small bowel (to treat intestinal obstruction) and episodes of melena. Physical examination revealed dark brownish-black pigmentation located on the
Fig 1
Diffuse melanin pigmentation of nose and lip areas.

Fig 2
Typical pigmented lesions of lips and buccal mucosa.

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perioral area, buccal mucosa, hands, and soles of the feet. On radiographs of the upper gastrointestinal tract and small bowel, four separate polyps were seen in the jejunum and ileum (Figs 3A,B). In addition, three polyps were demonstrated in the rectosigmoid region on barium-enema examination (Fig 3C). Repeated gastrointestinal bleeding had reduced the hemoglobin level to 5.6 gm per 100 mL of blood. After transfusions, the patient was discharged without any complaint, and he has remained well since 1981.

Case 4
The 16-year-old daughter in this family was admitted with complaints of abdominal pain, vomiting, dizziness, and weakness of six days' duration. Her history included surgery to treat intestinal obstruction. Physical examination revealed scattered brownish-black pigmentation of the lips, buccal mucosa, palms of the hands, and soles of the feet. Abdominal distention and generalized tenderness were noted. On rectal examination, a 2- x 2-cm diameter polyp was found 5 cm from the anal verge. Radiographs of the abdomen demonstrated evidence of partial small-bowel obstruction. Symptoms of intestinal obstruction disappeared after three to four days of conservative treatment. Anemia was treated with blood transfusions. On follow-up, findings of upper gastrointestinal and small-bowel radiographic series were normal, but barium-enema examination revealed two additional polyps in the ascending and transverse colon. The patient is well 3-1/2 years later.

Case 5
The 15-year-old son in this family was asymptomatic. The general physical examination revealed essentially normal results except for dark brown pigmented lesions on the lips. Findings of sigmoidoscopy, barium-enema examination, and upper gastrointestinal and small-bowel radiography were normal. The patient has been followed-up periodically since 1983, and the sigmoidoscopic and radiographic studies have remained normal.

The clinical findings, familial incidence of pigmentation, and polyposis related to the Peutz-Jeghers syndrome in this family are presented in Tables I and II.

Table I
A Familial Incidence of Pigmentation and Polyposis of Peutz-Jeghers Syndrome

<table>
<thead>
<tr>
<th>Gender</th>
<th>Polyp</th>
<th>Pigment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Female</td>
<td>□</td>
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</table>

20 years of age (Case 2) 16 years of age (Case 4) 17 years of age (Case 3) 15 years of age (Case 5)

Discussion
The three significant features of the Peutz-Jeghers syndrome are gastrointestinal polyposis, mucocutaneous pigmentation, and inheritance through a mendelian dominant gene. The pigmented lesions of the mucosa are flat, brownish-black spots 2 to 4 mm in diameter. Although they are generally seen on the lips and buccal mucosa, they can be present on the nasal and anal mucosa. The cutaneous lesions usually appear in early childhood and gradually disappear with advancement of age. In contrast, the lesions of the mucosa are present at birth and persist throughout life (1,2). In our series, four of six patients had mucosal pigmentation that was noticed at birth. We were unable to detect
Fig 3. Case 3
Radiographs (A,B) obtained after ingestion of barium showing multiple small-bowel filling defects representing polyps. Radiograph (C) after barium showing multiple filling defects in rectosigmoid region representing polyps.
The Clinical Data of Peutz-Jeghers Syndrome in a Family

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Age/Sex</th>
<th>Pigmentation</th>
<th>Gastrointestinal Symptoms</th>
<th>Localization of Polyps</th>
<th>Follow-up Period (in years)</th>
<th>Present Status</th>
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<td>1</td>
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<td>-</td>
<td>4-1/2</td>
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<td>2</td>
<td>20/M</td>
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<td>4-1/2</td>
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<tr>
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<td>17/M</td>
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<td>4</td>
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<tr>
<td>4</td>
<td>16/F</td>
<td>Yes</td>
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<td>-</td>
<td>3-1/2</td>
<td>Well</td>
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<tr>
<td>5</td>
<td>15/M</td>
<td>Yes</td>
<td>-</td>
<td>-</td>
<td>3-1/2</td>
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</table>

cutaneous pigmentation because the siblings were between 15 and 20 years of age at the time of physical examination. Thus, in our experience, the phenomenon of gradual disappearance of the cutaneous pigmentation with advancement of age cannot be documented. The pigmentation located on the palms of the father's hands and the soles of his feet gradually disappeared after he was 35 years old, and the remaining brownish spots were barely visible.

Histologically, the more clinically significant polyps in the gastrointestinal system are hamartomas. These polyps are most commonly localized in the jejunum. Less frequent sites include the ileum, duodenum, colon, and rectum. Polyps are rarely found in the stomach (1,2,8). Interestingly, in three of our patients, there were polyps in the colon as well as in the small bowel. The histopathologic examination of the polyps revealed their hamartomatous nature. In our patients, intussusception was the most common presenting feature, occurring in the second decade of life. Hematemeses or melena from polyps in the upper or lower alimentary tract may be the presenting feature. In two of our patients, rectal bleeding was the presenting symptom, but no hematemeses was present in any of the patients. Occult hemorrhage may result in anemia before other symptoms appear (Case 3).

A definite familial tendency can be found in 40% to 55% of cases (9-11). We found that Peutz-Jeghers syndrome was present in four of six children in a single family.

Essential findings for diagnosis of this syndrome are the presence of abnormal mucocutaneous pigmentation, the presence of polyps of a hamartomatous nature in the alimentary tract, and inheritance through a mendelian dominant gene. To reach a definite diagnosis, each family member should be interviewed for a detailed medical history followed by a complete physical examination. Sigmoidoscopy, colonoscopy, gastroscopy, upper gastrointestinal radiography including small-bowel studies, and barium-enema examination should be performed. In our patients, this sequence was followed for each family member. Comparison of our cases with those previously reported is presented in Table III.

The rational approach to the management of complications of Peutz-Jeghers syndrome should be asymptomatic (1,2,8). Prophylactic treatment has no role in the management of small-bowel polyps for several reasons: first, despite frequent intestinal intussusception due to those polyps, the majority reduce spontaneously; second, these polyps have a low malignancy potential; third, extensive resection may lead to malabsorption and mortality. In view of these facts, we did not perform any prophylactic surgery, but we did resect a gangrenous segment of small bowel secondary to intussusception in one of our patients. Two of our patients in which massive gastrointestinal bleeding dominated the clinical picture required multiple blood transfusions.

Surgical intervention is often necessary to treat complications resulting from polyposis of Peutz-Jeghers syndrome. The most frequent complication is intussusception of small bowel. Rectal bleeding and hypochromic anemia are also frequent. Three of our patients underwent surgery after a diagnosis of intussusception was made. A gastric polyp was removed from the father. In two patients, rectal bleeding dominated the clinical picture, and transfusions were required.

It has been suggested that cancer may sometimes develop from hamartomatous polyps associated with this syndrome (9,12). In a study of 14 patients, Reid (13,14) found a 2% to 3% risk of malignancy with Peutz-Jeghers polyposis. It should be emphasized that there could be coincident precancerous adenomas in the duodenum, stomach, or colon masked by hamartomatous polyps of Peutz-Jeghers syndrome. Dozois et al (15) reviewed 321 reported cases of Peutz-Jeghers syndrome and added five cases of their own. They concluded that a patient with Peutz-Jeghers syndrome appeared to have a 2% risk of experiencing gastrointestinal cancer, which is higher than that in the general population. We found no malignant transformation in our series.
Peutz-Jeghers Syndrome

Table III
Previously Published Series

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of Patients</th>
<th>Pigmentation</th>
<th>Gastro-intestinal Symptoms</th>
<th>Localization of Polyps</th>
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<td>Griffith et al, 1980</td>
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References