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PEUTZ-JEGHERS SYNDROME IN A LARGE FAMILY*

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The Peutz-Jeghers syndrome is a familial condition characterized by the triad of 1) mucocutaneous pigmentation, 2) benign polyp occurring in any part of the gastrointestinal tract but mainly in the jejünum, 3) autosomal dominant inheritance. 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].

Although the melanin pigmentation of the skin and mucous membrane may develop at any age, it is generally noted in infancy and early childhood[3,4]. The pigmented areas may be located on the lips, the perioral area and the buccal mucosa and less commonly, on the palms of the hands, the soles of the feet, and the toenails[5]. Histologically, an accumulation of melanin pigment and an increased number of melanocytes are to be seen in the basal layer of the epidermis[1].

Polyps are by far the most important part of this syndrome. The intestinal polyps associated with this disease are rarely found in infants but appear during puberty and adolescence[1,6,7]. The polyps which are hamartomas, are distributed throughout the gastrointestinal tract. They have a definite predilection for the jejunum and ileum, but may also be seen in the stomach, duodenum, colon or rectum[3,4,6,8].

The clinical course of Peutz-Jeghers syndrome is characterized by asymptomatic periods interspersed with episodes of intermittent colicky abdominal pain, often related to intussusception. Small bowel polyps should be removed through multiple enterotomies, and as much as possible of the small bowel should be preserved so as to avoid the development of the short gut syndrome. Colonic polyps are often asymptomatic and are usually found during the investigation of anemia.

Because of the potential serious complications associated with this syndrome, its stigmas need to be recognized by a variety of medical personnel including a

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dentist, pediatrician, internist, surgeon, dermatologist and otolaryngologist. This paper reports an experience with this rare disease that involves a large family. The current literature is also reviewed.

Case Reports

Case 1

A 58-year-old man, the father of this family, was asymptomatic. The general physical examination revealed essentially normal results except for light brown pigmented lesions on the hands (Figure 1). Findings of sigmoidoscopy, barium enema examination and upper gastrointestinal radiography were normal.

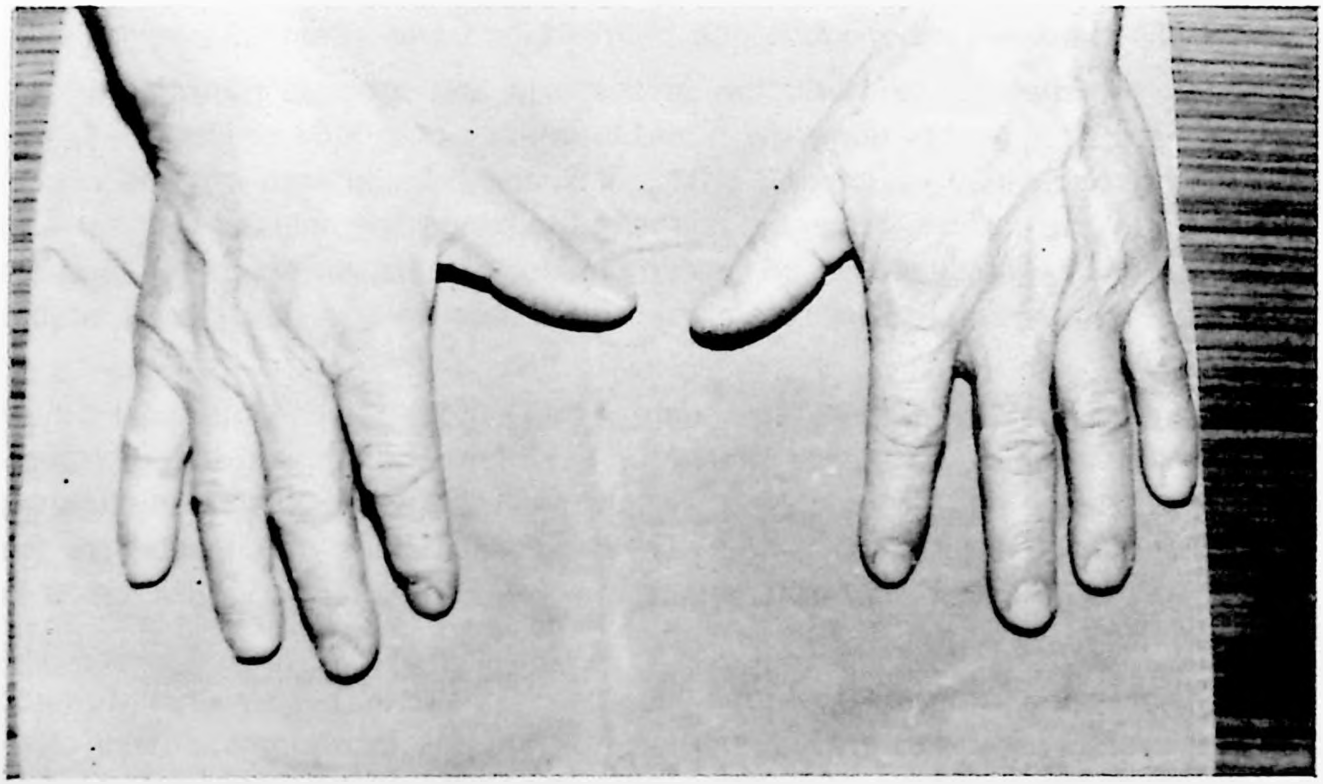

Figure 1

The 58-year-old father of the family shows light brown pigmented lesions on the hands.

Cases 2, 4, 6, 9

The 52-year-old mother and three siblings of this family were entirely asymptomatic. They had no typical pigmentation and no demonstrable polyps were found on radiographs of the gastrointestinal tract.

Case 3

A 30-year-old son in this family presented with the complaint of rectal bleeding. The general physical examination revealed essentially normal results. The findings of sigmoidoscopy and upper gastrointestinal series were normal. Barium enema revealed a polyp in the cecum (Figure 2). Periodic follow-ups at six-month intervals have been planned.

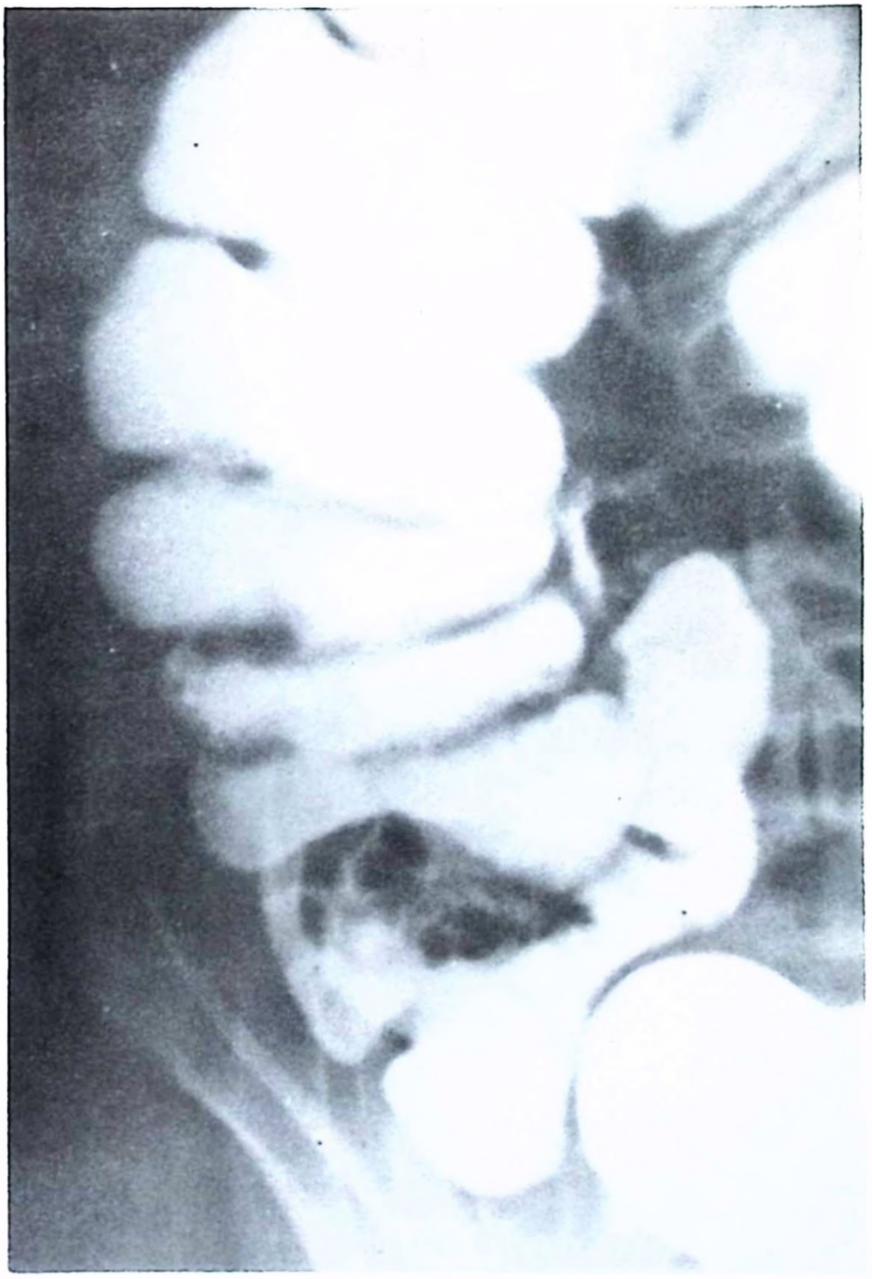

Figure 2

The barium enema of a 30-year-old son in this family exhibits a large filling defect in the cecum representing a polyp.

Case 5

A 30-year-old son in this family was admitted, complaining of abdominal pain. No typical pigmentation was found and physical examination was normal. No pathological findings were found on sigmoidoscopy and barium enema. Upper GI series and small bowel radiographs revealed a polyp, 3 cm in diameter, at the level of the Treitz ligament (Figure 3).

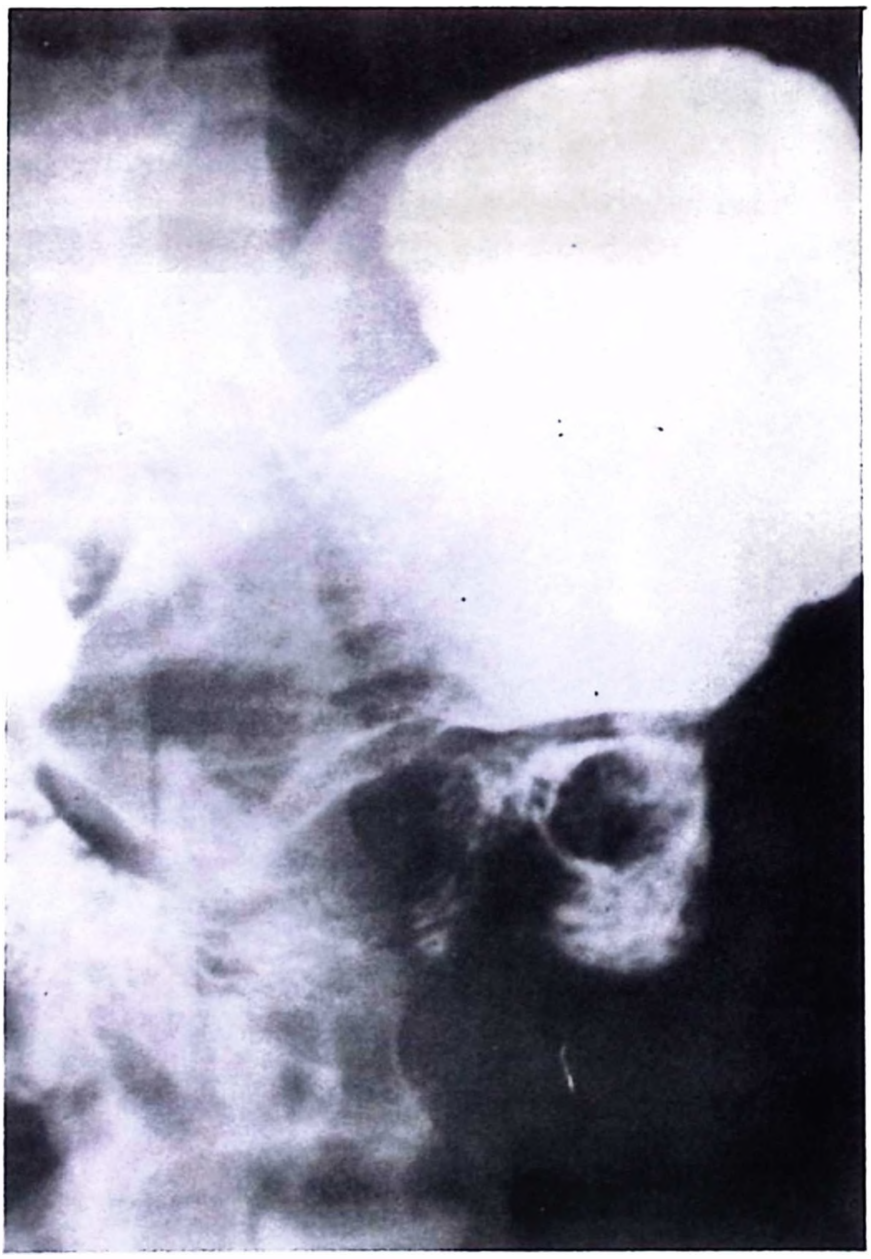

Figure 3

The upper GI series and small bowel radiographs of the 26-year-old son display a large polyp at the level of the Treitz ligament.

Case 7

The 23-year-old daughter in this family was admitted with the complaints of abdominal pain and rectal bleeding. Physical examination revealed brownish-black pigmentation located on the buccal mucosa. Sigmoidoscopy revealed two rectal polyps, 0.3 and 0.5 cm in diameter; an additional polyp, located in the cecum, was seen on barium enema (Figure 4). The patient is being kept under clinical observation.

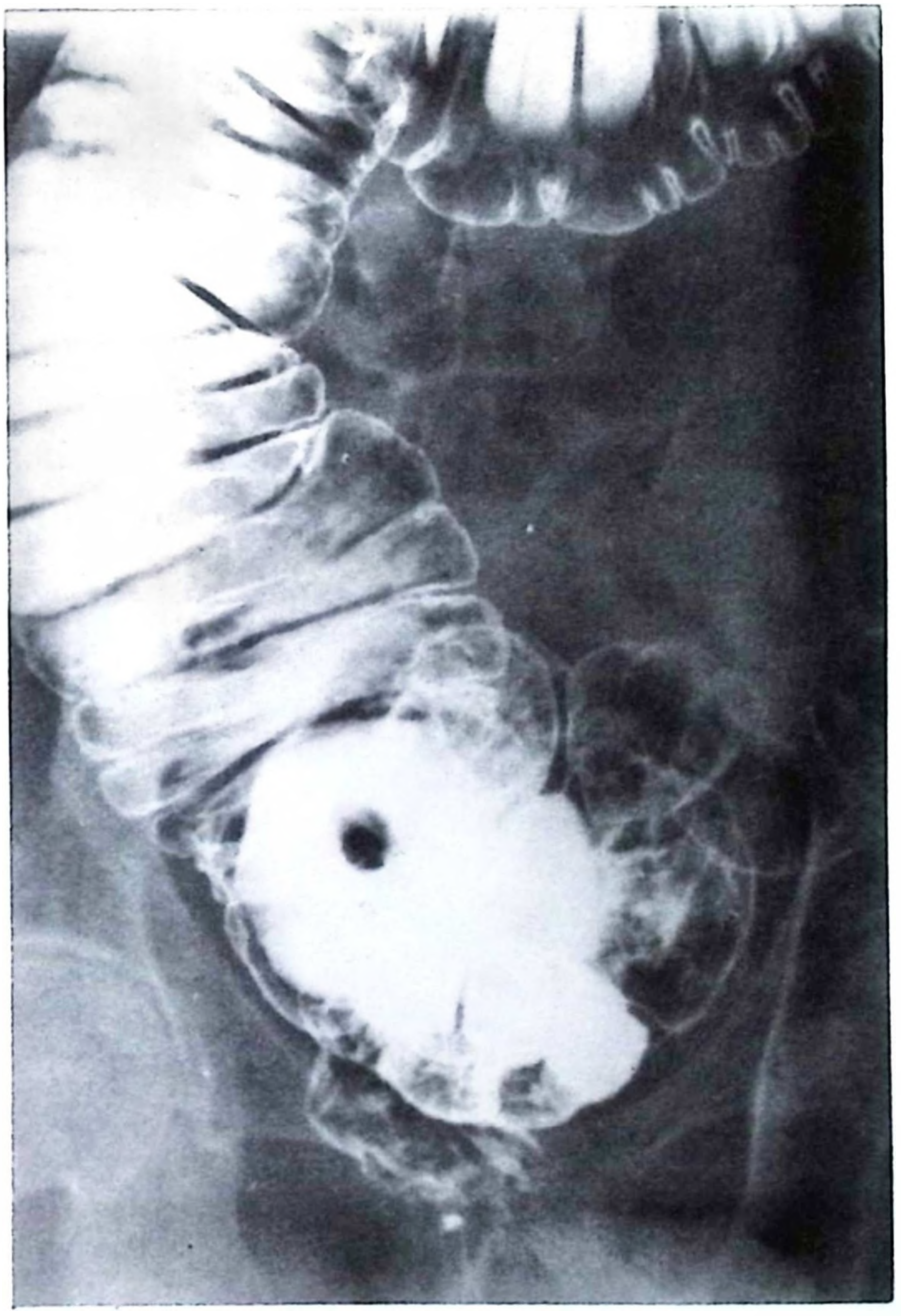

Figure 4

The barium enema of the 23-year-old daughter exhibits a polyp in the cecum.

Case 8

The 21-year-old daughter in this family was asymptomatic. The general physical examination revealed normal findings. Sigmoidoscopy and barium enema were normal. Upper GI series and small bowel radiographs revealed a polyp, with a diameter of 0.5 cm, located in the ileum.

Case 10

The 17-year-old daughter in this family was asymptomatic. No pigmentation was found. Sigmoidoscopy and upper GI and small bowel series were unremarkable. Barium enema revealed two polyps located in the cecum and the descending colon with diameters of 0.5-1 cm.

Case 11

The 15-year-old son in this family was asymptomatic. The general physical examination revealed normal findings. Sigmoidoscopy and upper GI and small bowel series were negative. On barium enema, a 3 cm polypoid lesion was seen in the region of the splenic flexura.

Case 12

The 10-year-old daughter in this family was admitted with diarrhea and pigmentation of the lips (Figure 5). Sigmoidoscopy revealed polyps in the rectum

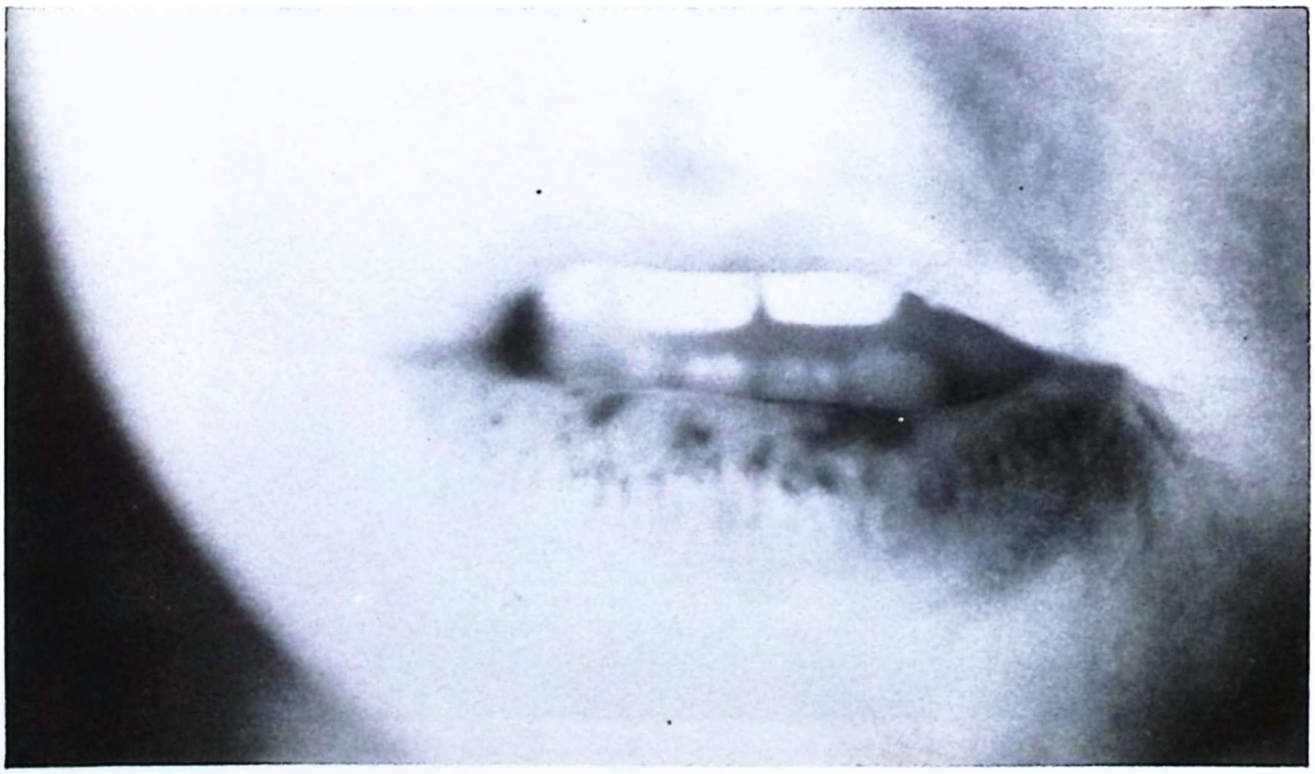

Figure 5

Typical pigmented-lesions of lips seen in case 12.

and three of them were removed. Histopathologic examination showed their hamartomatous nature. Two years later, this child was admitted again complaining of vomiting and constipation. Radiographs of the abdomen showed evidence of mechanical small bowel obstruction. A diagnosis of ileo-cecal intussusception secondary to the polyps was made and the patient underwent surgery. Exploration revealed a large mass due to ileo-cecal intussusception. In addition, a second large polyp, proximal to the mass, and causing complete obstruction, was detected. Several other polyps were noticed throughout the GI system. The two polyps causing intussusception as a leading point and causing almost complete obstruction were removed with partial small bowel resections. Histopathologic examination revealed that these polyps were hamartomas.

The clinical findings, familial incidence of pigmentation, and polyposis related to the Peutz-Jeghers syndrome in this family are presented in Figure 1 and Table I.

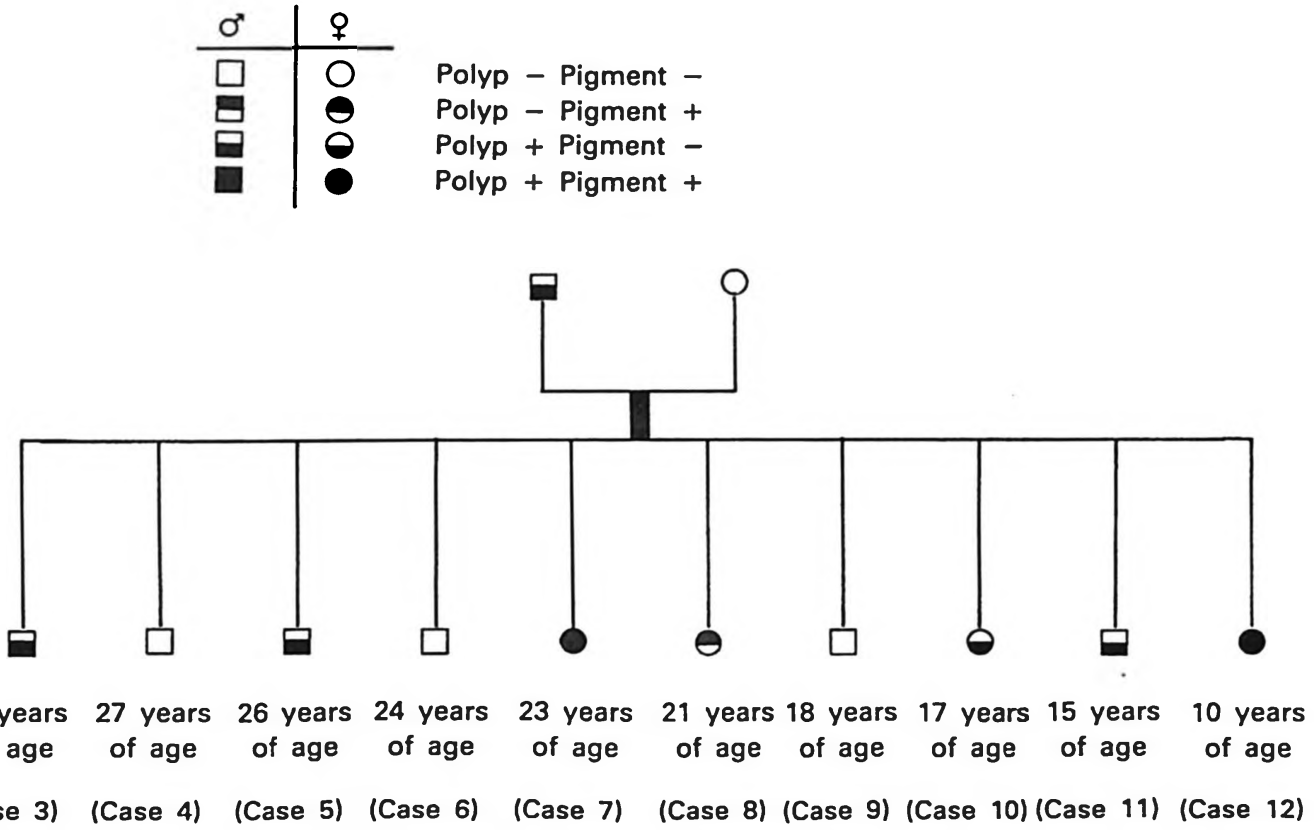

Figure 1

Familial incidence of pigmentation and polyposis with the Peutz-Jeghers syndrome.

TABLE I

The Clinical Data of Peutz-Jeghers Syndrome in a Family

Case no.	Age/Sex	Pigmentation	GI symptoms	Localization of polyps			Present status
				Stomach	Small bowel	Colon	
1	58/M	+	–	–	–	–	well
2	52/F	–	–	–	–	–	well
3	30/M	–	Rectal bleeding	–	–	+	well
4	27/M	–	–	–	–	–	well
5	26/M	–	Abdominal pain	–	+	–	well
6	24/M	–	–	–	–	–	well
7	23/F	+	Abdominal pain Rectal bleeding	–	–	+	well
8	21/F	–	–	–	+	–	well
9	18/M	–	–	–	–	–	well
10	17/F	–	–	–	–	+	well
11	15/M	–	–	–	–	+	well
12	10/F	+	+	–	+	+	well

Discussion

The three significant characteristics of the Peutz-Jeghers syndrome are gastrointestinal polyposis, mucocutaneous pigmentation, and inheritance through a mendelian dominant gene. The lesions are usually dark brown to black, measure 2 to 5 mm in size and are flat. The lips and the buccal mucosa are the most frequent sites. They can be present on the extremities and on nasal and anal mucosa. In our series, three of the twelve patients had mucocutaneous pigmentation. The cutaneous lesions usually appear in early childhood and gradually disappear with age. In contrast, the lesions of the mucosa are present at birth and persist throughout life[1,2]. This fact makes it doubly important to examine both the lips and the oral cavities closely. Özkan[3], however, was unable to document this phenomenon of the gradual disappearance of the cutaneous pigmentations with the advancement of age. In our series, we could not demonstrate this phenomenon clearly either.

Histologically, the polyps are hamartomas. These polyps are most commonly localized in the jejunum. Less frequent sites include the ileum, colon and rectum. Interestingly, in our series, colonic polyps were present in five cases. In contrast, small bowel polyps were detected in three of our cases. The diagnosis of hamartomatous polyps was made in case 12. In two of our patients, rectal bleeding was the presenting symptom. Intermittent abdominal pain was the only complaint in two of our cases. Intussusception and complete intestinal obstruction dominated the clinical picture in one case.

A definite familial tendency can be found in 40% to 55% of cases[9,10]. We found that Peutz-Jeghers syndrome was present in 7 of 10 children (70%) in this single family. This ratio seems to be high as compared to the literature, suggesting a high degree of penetrance.

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 GI radiography including small-bowel studies, and barium enema examination should all 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 II.

TABLE II

Previously Published Series

Reference	No. of Patients	Pigmentation	Gastro-intestinal symptoms	Localization of polyps			No. of operations
				Stomach	Small bowel	Colon	
Bartholomew et al[4], 1962	10	10	9	1	8	–	7
Burdick et al[10], 1963	10	8	4	6	3	5	5
Neely and Gillespie[15], 1967	4	4	4	–	4	–	4
McAllister and Richards[1], 1977	1	1	1	–	–	1	1
Joishy et al[2], 1979	1	1	1	1	–	1	1
Griffith and Bisset[7], 1980	3	3	3	–	3	1	3
Özkan[3], 1985	5	5	3	1	3	3	4
Present 1985	8	3	4	–	3	5	2

Surgical intervention is often necessary to treat complications resulting from polyposis of Peutz-Jeghers syndrome, but prophylactic treatment has no role in the management of this syndrome for several reasons: First, despite frequent intestinal intussusception due to intestinal polyps, the majority reduce spontaneously; secondly, these polyps have a low malignancy potential; thirdly, extensive resection may lead to malabsorption and mortality. In view of these facts, we did not perform any prophylactic surgery, but we performed two separate resections

secondary to intussusception in one of our cases. In two patients, rectal bleeding dominated the clinical picture but no transfusions were required.

The question of malignancy in Peutz-Jeghers syndrome is not completely resolved. It has been suggested that cancer may sometimes develop from the hamartomatous polyps associated with this syndrome[9,11]. In a study of 14 patients, Reid[12,13] found a 2% to 3% risk of malignancy with this Peutz-Jeghers polyposis. Dozois et al[14] 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 gastrointestinal cancer, which is higher than that in the general population. However, in several series, no malignant transformations have been reported at all[1,3,7]. We found no malignant transformation in our series.

Summary

Twelve cases of Peutz-Jeghers syndrome in one family have been studied, and these are presented together with a review of the history and features of the syndrome. This syndrome was detected in seven of the ten siblings and in the father. One family member underwent repeated surgery after small bowel obstruction was diagnosed. In addition, multiple polyps were removed from the rectum. Rectal bleeding dominated the clinical picture in two patients. Three of the siblings had small bowel polyps, five of the siblings had polyps in the colon. A colonic polyp was also found in one patient who had a small bowel polyp. Two of the seven affected siblings and the father of the family had mucocutaneous pigmentation.

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