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Peutz-Jegher's syndrome – a case report

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Abstract

Peutz-Jegher's syndrome is a hereditary disorder characterized by melanocytic macules on the lips and buccal mucosa and multiple gastrointestinal hamartomatous polyps. It is caused by a mutation localized on chromosome 19p13.3. Skin and mucosal pigmentation may be present at birth and usually occur in early childhood, but occasionally may develop later. It is associated with an increased risk of malignancy for gastrointestinal carcinoma and also for breast, ovarian, testiscular, pancreatic and gallbladder cancer. We report a 12-year-old girl who presented with disseminated petty yellowish macules on the bridge of her nose, numerous brown to bluish black macules on her lips and buccal mucosa. Mucocutaneous pigmentation has been present from the age of five, with a negative family history. In our patient, esophageal endoscopy was normal, while the endoscopy of stomach and duodenum revealed multiple diminutive polyps. After clinical evaluation, there were no indications for therapy. Further follow up was suggested. Continuous surveillance is very important for patients with Peutz-Jegher's syndrome in order to reduce risks of cancer and prevent other morbidity and mortality.

Key words

Peutz-Jegher's Syndrome; Intestinal Polyposis; Child; Hyperpigmentation; Endoscopy, Gastrointestinal; Follow-Up Studies

Peutz-Jegher's syndrome (PJS), also known as periorofacial lentiginosis, is a hereditary disorder characterized by melanocytic macules on the lips, buccal mucosa and multiple gastrointestinal hamartomatous polyps. PJS was first described by Peutz in 1921, and later, by Jeghers, in 1949.

PJS is inherited as an autosomal-dominant trait, and the gene has been mapped to chromosome 19 p 13.3, the serine/threonine protein kinase-11 gene (STK11) involved in the growth control regulation (1).

Buccal lesions tend to be permanent, while the cutaneous may fade. The acral, periorbital lesions and conjunctival pigmented macules can also be seen. The hallmark of PJS, are hamartomatous polyps that may occur in every part of the gastrointestinal tract.

The lifetime risk for gastrointestinal carcinoma is high and exceeds 50%, and there is an increased incidence of breast, ovarian, testicular, pancreatic, and gallbladder cancer (2).

Case report

A 12-year-old girl was admitted to our Clinic with disseminated petty yellowish macules on the bridge of her nose (Figure 1) and numerous brown to bluish-black macules (up to 5 mm in diameter) on her lips and on buccal mucosa (Figure 2). She was the first child from the first, well controlled, full term pregnancy. The rest of the physical findings were normal. Mucocutaneous pigmentation has been

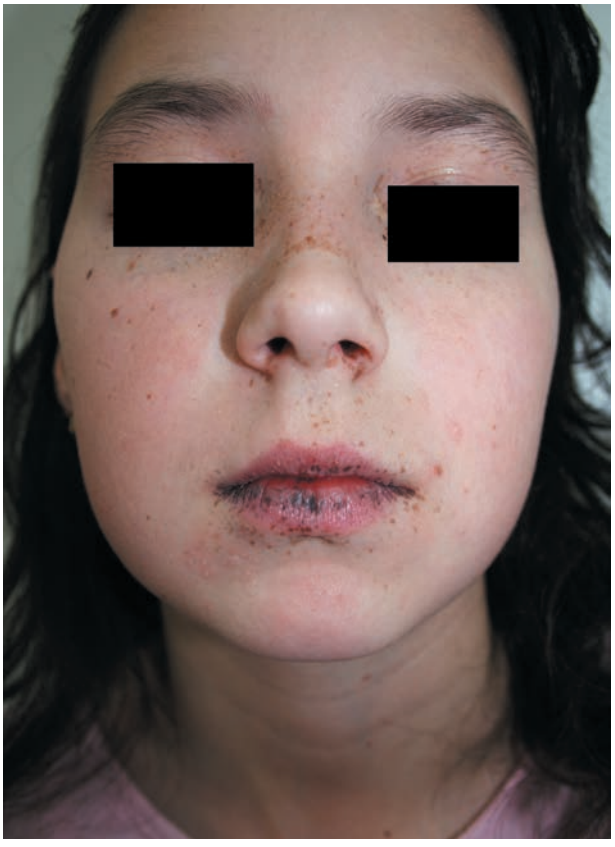

Figure 1. a) Disseminated petty yellowish macules on the bridge of the nose; b) Hyperpigmented macules on the lips

present from the age of five, with a negative family history. Routine laboratory blood and urine tests were normal. The stool examination for occult blood was negative. Esophageal endoscopy was normal, while the endoscopy of stomach and duodenum revealed multiple diminutive polyps. Presence of polyps and pigmented macules on the lips, confirmed the diagnosis Peutz-Jeghers syndrome.

After the clinical evaluations, there were no indications for therapy. Further follow up was suggested.

Discussion

Peutz-Jegher's syndrome is a rare autosomal dominant hereditary disease characterized by mucocutaneous pigmentation and gastrointestinal polyposis (2, 3). Hemminki et al. identified the linkage of PJS to chromosome 19 and demonstrated mutations in the serine/threonine kinase gene (4). STK11 gene, mapped at 19p13.3, encodes the serine-threonine protein kinase that regulates cell-cycle metabolism, cell polarity, and also has tumor suppressor functions (3). There are no certain data about the prevalence or incidence of PJS. Prevalence of PJS is estimated from 1 in 8.300 to 1 in 280.000 individuals (1).

Mucocutaneous melanin pigmentations are present in 95% of patients with PJS, and they may have a tendency to disappear in time. Predilection sites for pigmentations are the lips, the peri- and intraoral regions and less commonly the rectum, feet, vulva, and conjunctiva. There is a variation in size, number and color of pigmentations (1).

Perioral pigmention is an external hallmark of PJS. In other hamartomatous polyposis syndromes including Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome and Juvenile polyposis syndrome, the pigmentation of the perioral region is not present. Another differential diagnosis of PJS is Laugier-Hunziker syndrome, characterized by benign melanotic pigmentation of the lips and oral cavity but without systemic manifestations and gastrointestinal polyposis (5).

For children with SPJ, colonoscopy screening is recommended every 2 years, starting from the onset of symptoms, or in early adolescence if there are no symptoms. From the age of 10 years, endoscopy of the upper gastrointestinal tract is recommended (2). In our patient, the upper gastrointestinal endoscopy of esophagus was normal, but the endoscopy of stomach and duodenum revealed multiple diminutive polyps.

The diagnosis of PJS is based on criteria including at least two polyps, one polyp and mucocutaneous pigmented lesions, or one polyp and positive family history of PJS (6).

Around one third of patients with PJS are diagnosed before the age of 10 years, and almost two thirds of cases develop first clinical manifestations before the third decade of life (5). In our patient, mucocutaneous pigmentations have been present from the age of 5 years, with negative family history. Negative family history in some patients indicates a possibility of *de novo* germline mutations. Approximately 30% of PJS cases occur without any previous family history, as a result of spontaneous genetic mutations (7).

Individuals with PJS are at an increased risk for colorectal and small intestinal cancer, ductal, breast cancer, lung, thyroid, pancreatic, uterine, Sertoli cell testicular, and ovarian sex cord tumors. In a large study, that included 419 PJS patients, the reported

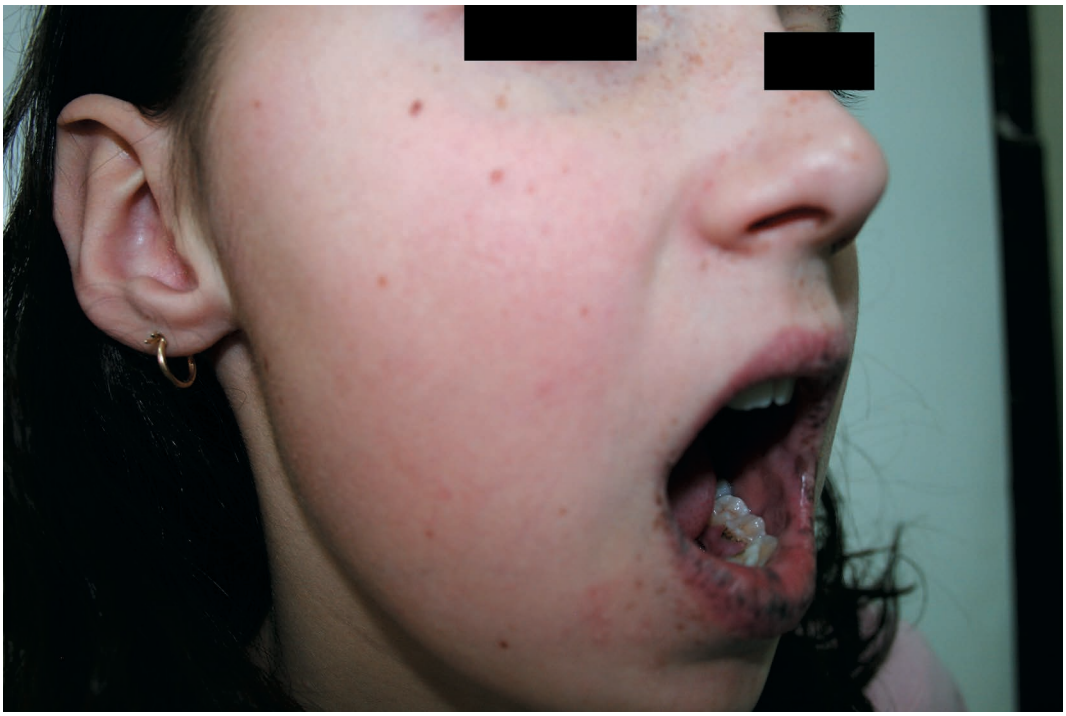

Figure 2. Brown to bluish-black macules on the lips and on the left buccal mucosa

risk for gastrointestinal cancers was 57% by the age of 70 (8). Early screening and detection of cancer were recommended to prevent morbidity and mortality (9).

Our recommendation, according to the guidelines for the management of gastrointestinal polyposis, was control endoscopy of the gastrointestinal tract every second year up to the age of 18, and later annually.

Conclusion

It is very important to bear in mind that Peutz-Jegher's syndrome presents with pigmented lip macules, because of the risk for developing gastrointestinal and other cancers in any patient who presents with pigmented lip macules.

Continuous surveillance through regular endoscopy, laboratory, radiologic investigation, referrals for genetic counseling and surgery are crucial recommendations for managing this inherited condition in order to reduce risks for cancer, and prevent other morbidity and mortality.

Abbreviations

PJS - Peutz-Jegher's syndrome
STK11 - Serine/threonine protein kinase-11 gene

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Peutz-Jegher's sindrom - prikaz slučaja

Sažetak

Uvod: Peutz-Jegher sindrom je nasledno oboljenje sa karakterističnim hiperpigmentovanim makulama na usnama i bukalnoj mukozi kao i mnogobrojnim gastrointestinalnim polipima. Mutacija na hromozomu 19 p 13.3 smatra se odgovornom za ovaj sindrom. Prevalencija ovog sindroma se kreće od 1 na 8.300 do 1 na 280.000 pripadnika opšte populacije.

Promene na koži i sluznicama mogu postojati od rođenja, ali češće se javljaju tokom ranog detinjstva, a u nekim slučajevima mogu se razviti i u kasnijem životnom dobu. Postoji povećan rizik od maligniteta gastrointestinalnog trakta kao i karcinoma dojke, jajnika, testisa, pankreasa i žučne kese.

Prikaz slučaja: Prikazujemo devojčicu uzrasta 12 godina sa diseminovanim žućkastim makulama na korenu nosa i brojnim mrkim i tamnoplavim makulama na usnama i na bukalnoj sluzokoži levo. Promene na koži i sluznicama su bile prisutne od pete godine života. Porodična anamneza je bila negativna. Kod naše pacijentkinje endoskopija jednjaka je bila uredna, dok su u želucu i duodenumu otkriveno više diminutivnih polipa. Nakon kliničke evaluacije nije bilo indikacija za terapiju. Savetovano je dalje praćenje.

Diskusija: Dijagnoza se postavlja na osnovu postojanja kriterijuma koji podrazumevaju postojanje: najmanje dva polipa, jednog polipa i prisustva mukokutanih pigmentacija, ili jednog polipa i pozitivne porodične anamneze o postojanju obolelih srodnika. Perioralna pigmentacija je od patognomoničnog značaja za postavljanje dijagnoze. U Cowden sindromu, Bannayan-Riley-Ruvalcaba sindromu i u sindromu juvenilne polipoze prisutni su hamartomski polipi ali ne i pigmentacija perioralne regije. Nasuprot tome, u Laugier-Hunziker syndromu karakteristične su benigne melaninske pigmentacije na usnama i orafaringealnoj sluznici ali nisu pristni sistemski znaci niti gastrointestinalna polipoza.

Zaključak:Kontinuirano praćenje je veoma važno kod pacijenata sa Peutz-Jegher sindromom radi smanjenja rizika od karcinoma i drugih morbiditeta i mortaliteta. Kod dece sa Peutz-Jegher sindromom, kolonoskopiju treba izvoditi svake dve godine počevši od pojave simptoma, u asimptomatskim slučajevima početi u ranoj adolescenciji. Endoskopski pregled gornjeg dela gastrointestinalnog trakta treba započeti od desete godine života.

Kod svakog pacijenta sa hiperpigmentovanim makulama na usnama uvek u diferencijalnoj dijagnozi treba isključiti postojanje Peutz-Jegher sindroma.

Ključne reči

Peutz-Jegher sindrom; Intestinalna polipoza; Dete; Hiperpigmentacija; Gastrointestinalna endoskopija; Follow-up studije