Chronic abdominal pain and diarrhea

Pigmented macules on the patient's oral mucosa provided an important clue to the diagnosis.

Mohamed Omar Warsame, MBBS; Josette R. McMichael, MD
Department of Family Medicine, Amoud University, Borama, Somaliland (Dr. Warsame); Department of Dermatology, Emory University, Atlanta, GA (Dr. McMichael)

jmcmichael@emory.edu

DEPARTMENT EDITOR
Richard P. Usatine, MD
University of Texas Health at San Antonio

The authors reported no potential conflict of interest relevant to this article.

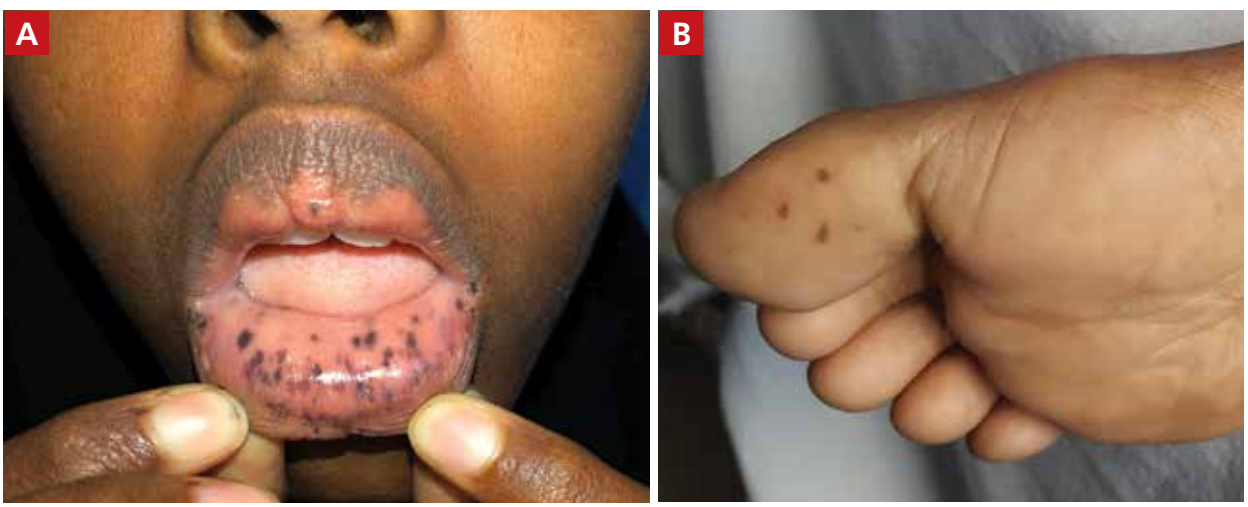
A 15-YEAR-OLD GIRL was brought to the Family Medicine Clinic in Somaliland, Africa, for evaluation of intermittent abdominal pain and watery diarrhea of 12 years' duration. Over the previous 2 months, her symptoms had worsened and included vomiting and weight loss. She denied fever, melena, or hematemesis.

Physical examination revealed a thin female with a normal abdominal exam and numerous hyperpigmented macules on the lips, buccal mucosa, fingers, and toes (**FIGURE 1**). Her family reported that the black spots on her lips had been there since birth. There was no known family history of similar symptoms or black spots.

Her hemoglobin was 10 g/dL (reference range, 12–15 g/dL). A probable diagnosis was discussed with the family, and they elected to travel to India for further evaluation due to limited diagnostic resources in their location. In India, computed tomography (CT) and ultrasonography showed duodenojejunal intussusception. Upper gastrointestinal (GI) endoscopy revealed multiple polyps from the lower stomach to the jejunum of the small bowel; colonoscopy was normal.

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE 1
Scattered hyperpigmented macules



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Numerous scattered hyperpigmented macules were present on the patient's lips and distal fingers (**A**), as well as the plantar aspect of her great toe (**B**).

Diagnosis: Peutz-Jeghers syndrome

Our patient was given a diagnosis of Peutz-Jeghers syndrome (PJS) based on the characteristic pigmented mucocutaneous macules and numerous polyps in the stomach and small bowel. PJS is an autosomal dominant syndrome characterized by mucocutaneous pigmentation, polyposis of the GI tract, and increased cancer risk. The prevalence is approximately 1 in 100,000.[1] Genetic testing for the *STK11* gene mutation, which is found in 70% of familial cases and 30% to 67% of sporadic cases, is not required for diagnosis.[1]

What you'll see. The bluish brown to black spots of PJS often are apparent at birth or in early infancy. They are most common on the lips, buccal mucosa, perioral region, palms, and soles.

The polyps may cause bleeding, anemia, and abdominal pain due to intussusception, obstruction, or infarction.[2] Intussusception is the most frequent cause of morbidity in childhood for PJS patients.[3,4] Recurrent attacks of abdominal pain likely result from recurring transient episodes of incomplete intussusception. The polyps usually are benign, but patients are at increased risk of GI and non-GI malignancies such as breast, pancreas, lung, and reproductive tract cancers.[1] Most cancers associated with PJS occur during adulthood.[2]

When Peutz-Jeghers syndrome is suspected, the entire GI tract should be investigated.

Other possible causes of hyperpigmentation

PJS can be differentiated from other causes of hyperpigmentation by clinical presentation and/or genetic testing.

Laugier-Hunziker syndrome manifests with macular hyperpigmentation of the lips and buccal mucosa and pigmented bands on the nails in young or middle-aged adults. It is not associated with intestinal polyps.

Cronkhite-Canada syndrome consists of acral and oral pigmented macules and GI polyps as well as generalized darkening of the skin, extensive alopecia, loss of taste, and nail dystrophy.

Familial lentiginosis syndromes such as Noonan syndrome and NAME syndrome (nevi, atrial myxoma, myxoid neurofibroma, ephelides) have other systemic signs such as cardiac abnormalities, and the pigmentation is not as clearly perioral.

Albright syndrome manifests with oral pigmented macules but also is associated with precocious puberty and polyostotic fibrous dysplasia.

Addison disease may cause multiple hyperpigmented macules but has other systemic involvement; adrenocorticotropic hormone levels are elevated.

Juvenile polyposis syndrome manifests with GI polyps but is not associated with mucosal pigmentation.

Use these 4 criteria to make the diagnosis

The diagnosis of PJS is made using the following criteria: (1) two or more histologically confirmed PJS polyps, (2) any number of PJS polyps and a family history of PJS, (3) characteristic mucocutaneous pigmentation and a family history of PJS, or (4) any number of PJS polyps and characteristic mucocutaneous pigmentation.[2]

When PJS is suspected, the entire GI tract should be investigated. The hamartomatous polyps may be found from the stomach to the anal canal, but the small bowel most commonly is involved. The polyps may occur in early childhood, with one study of 14 children reporting a median age of 4.5 years.[5] Polyp biopsy will show smooth muscle arborization. When possible, those who meet clinical criteria for PJS should undergo genetic testing for a *STK11* gene mutation. PJS may occur due to de novo mutations in patients with no family history.[6]

Long-term management involves surveillance for polyps and cancer

Screening guidelines for polyps vary. Some suggest starting screening at age 8 to 10 years with esophagogastroduodenoscopy or capsule endoscopy and if negative, colonoscopy at age 18. Others suggest starting screening at 4 to 5 years of age.[5] The recommendation is to remove polyps if technically feasible.[3] Surveillance for Sertoli cell tumors (sex cord stromal tumors) should be done before puberty, and evaluation of other organs at risk of malignancy should begin by the end of adolescence.

CONTINUED

The pigmented macules do not require treatment. Macules on the lips may disappear with time, while those on the buccal mucosa persist. The lip lesions can be lightened with chemical peels or laser.

Our patient underwent laparotomy, which revealed a grossly dilated and gangrenous small bowel segment. Intussusception was not present and was thought to have spontaneously reduced. Resection and anastomosis of the affected small bowel was performed. The patient's postoperative course was uneventful, and her diarrhea and abdominal pain resolved. We recommended follow-up in her home city with primary care and a GI specialist and explained the need for surveillance of her condition. JFP

CORRESPONDENCE
Josette R. McMichael, MD, Department of Dermatology, Emory University, 1525 Clifton Road NE, 1st Floor, Atlanta, GA 30322; jmcmichael@emory.edu

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