Laugier-Hunziker Syndrome

Joan Paul, MD, MPH, DTMH; Valerie M. Harvey, MD, MPH; Jennifer A. Sbicca, MD; Brian O'Neal, DO, MPH

PRACTICE **POINTS**

- Laugier-Hunziker syndrome (LHS) comprises benign mucosal pigmentation in the absence of gastrointestinal pathology.
- Differentiating LHS from Peutz-Jeghers syndrome can prevent unnecessary aggressive cancer screening protocols.
- The average age of onset of LHS is 52 years and typically occurs in white adults.
- Pigmentation in LHS is most commonly distributed on the lower lips and oral mucosa.

To the Editor:

A 55-year-old man presented with hyperpigmented brown macules on the lips, hands, and fingertips of 6 years' duration. The spots were persistent, asymptomatic, and had not changed in size. The patient denied a history of alopecia or dystrophic nails. He also denied a family history of similar skin findings. He had no personal history of cancer and a colonoscopy performed 5 years prior revealed no notable abnormalities. His medications included amlodipine and hydrocodone-acetaminophen. His mother died of "abdominal bleeding" at 74 years of age and his father died of a brain tumor at 64 years of age. Physical examination demonstrated numerous well-defined, dark brown macules of variable size distributed on the lower and upper mucosal lips (Figure 1A), buccal mucosa, hard palate, and gingiva, as well as the dorsal aspect of the fingers (Figure 1B) and volar aspect of the fingertips (Figure 1C).

A shave biopsy of a dark brown macule from the lower lip (Figure 2) was performed. Histopathologic examination

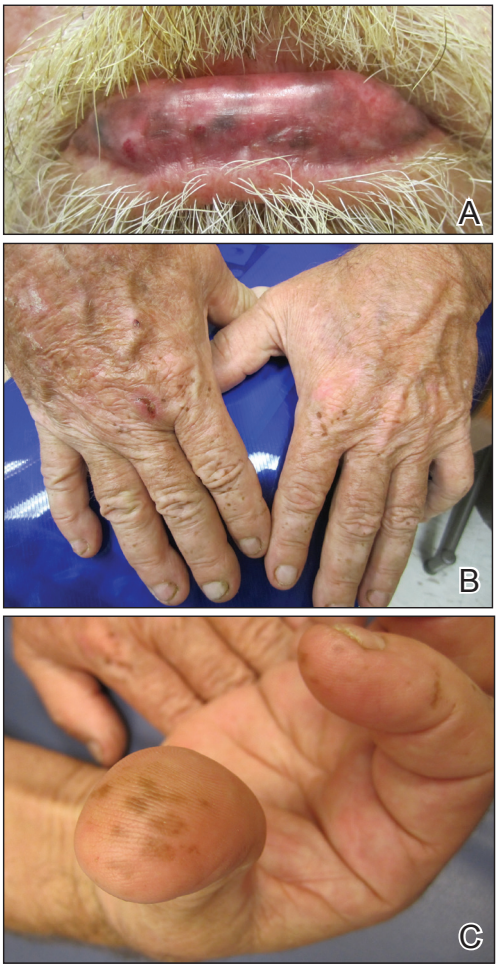

FIGURE 1. Numerous well-defined, dark brown macules of variable size distributed on the lower lip (A), dorsal aspect of both hands (B), and volar aspect of the fingertips (C).

Dr. Paul is from Kaiser Permanente, Union City, California. Dr. Harvey is from the Department of Dermatology, Eastern Virginia Medical School, Norfolk, and Hampton University Skin of Color Research Institute, Virginia. Dr. Sbicca is from the Department of Dermatology, University of Southern California, Los Angeles. Dr. O'Neal is from the Department of Dermatology, United States Naval Hospital, Yokosuka, Japan.

The authors report no conflict of interest.

The opinions expressed in this article are solely those of the authors and should not be interpreted as representative of or endorsed by the US Army, the US Navy, the Department of Defense, or any other federal government agency.

Correspondence: Joan Paul, MD, MPH, DTMH, 3555 Whipple Rd, Building A, Union City, CA 94587 (joannypaul@gmail.com).

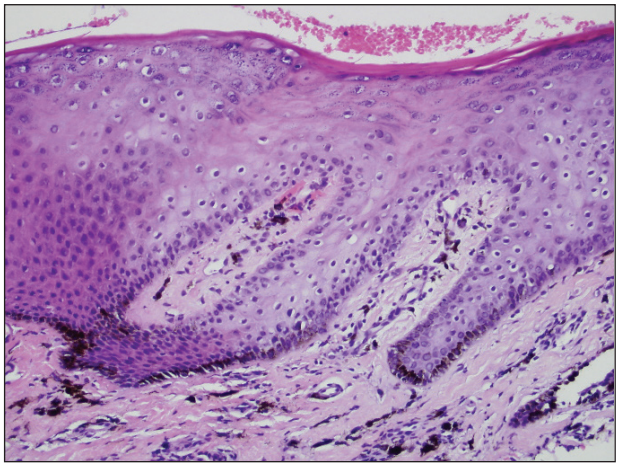

FIGURE 2. A shave biopsy of a dark brown macule from the lower lip displayed pigment-laden macrophages in the papillary dermis (H&E, original magnification ×40).

revealed pigmentation of the basal layer of the epidermis with pigment-laden cells in the dermis immediately deep to the surface epithelium. Immunoperoxidase stains showed a normal number and distribution of melanocytes.

A diagnosis of Laugier-Hunziker syndrome (LHS) was made given the age of onset; distribution of pigmentation; and lack of pathologic colonoscopic findings, personal history of cancer, or gastrointestinal tract symptoms.

Benign hyperpigmentation of the lips and fingers has been reported.[1] The average age of onset of LHS is 52 years, and it typically is diagnosed in white adults.[1,2] In LHS, pigmentation is most commonly distributed on the lips, especially the lower lips and oral mucosa.[2] Pigmentation of the nails in the form of longitudinal melanonychia is present in approximately half of cases.[2,3] There also may be pigmentation of the neck; thorax; abdomen; and acral surfaces, especially the fingertips.[1-3] Rarely, pigmented macules can occur on the genitalia or sclera.[1,2] Unlike Peutz-Jeghers syndrome, the diagnosis of LHS does not result from a germline mutation and carries no risk of gastrointestinal polyposis or internal malignancy.[3,4] The histopathology of a pigmented macule of LHS shows a normal number and morphology of melanocytes. Epidermal basement membrane pigmentation is common, with pigment-laden macrophages evident in the papillary dermis.[3]

The differential diagnosis of multiple lentigines is broad and includes Peutz-Jeghers syndrome; LEOPARD (lentigines, electrocardiographic conduction abnormalities, ocular hypertelorism, pulmonary stenosis, abnormalities of genitalia, retardation of growth, deafness) syndrome; Carney complexes, including LAMB (lentigines, atrial myxoma, mucocutaneous myxoma, blue nevi) and NAME (nevi, atrial myxoma, myxoid neurofibroma, ephelide) syndromes[5]; primary adrenocortical insufficiency (Addison disease); and idiopathic melanoplakia.[2] Peutz-Jeghers syndrome, an autosomal-dominant syndrome with mucocutaneous lentigines, has a similar clinical appearance to LHS; therefore, it is necessary to exclude this diagnosis due to its association with intestinal hamartomatous polyps and internal malignancies (Table).[3,6,7]

Peutz-Jeghers syndrome is characterized by mucocutaneous hyperpigmentation and intestinal hamartomatous polyposis and is associated with internal malignancies of the colon, breast, pancreas, stomach, small intestines, ovaries, lung, and Sertoli cells in men.[6,7] Associated gastrointestinal tract malignancies in descending order of frequency are colon (39%), pancreatic (36%), gastric (29%), and small intestine (13%).[1] It is caused by a germ line mutation of the serine/threonine kinase 11 gene, *STK11.* Although the appearance and distribution of the

Differences Between Laugier-Hunziker and Peutz-Jeghers Syndromes

	Laugier-Hunziker Syndrome	Peutz-Jeghers Syndrome
Mode of transmission	Sporadic	Autosomal dominant *(STK11* gene)
Location of lentigines	Lips and fingers	Mouth, nostrils, hands and feet
Age of onset of lentigines	Adult onset (average age, 52 years)	Birth to infancy
Risk of malignancy	None	Colon, pancreatic, gastric, small intestinal, breast, ovarian, lung, and Sertoli cell (in men) cancers

Abbreviation: *STK11*, serine/threonine kinase 11.

mucocutaneous lentigines is similar to individuals with LHS, by contrast the lentiginosis in individuals with Peutz-Jeghers syndrome is present from birth or develops during infancy.[6] Aggressive cancer screening guidelines aid in early detection and begin at 8 years of age with a baseline colonoscopy and esophagogastroduodenoscopy; future screening is dictated by the presence or absence of polyps. If no polyps are detected at 8 years of age, a colonoscopy and esophagogastroduodenoscopy are repeated at 18 years of age and then every 3 years until 50 years of age.[8]

In an adult patient, the diagnosis of LHS can be made clinically and a correct diagnosis prevents frequent and unpleasant gastrointestinal tract cancer screening examinations. Lampe et al[2] described a man with LHS who was incorrectly diagnosed with Peutz-Jeghers syndrome and experienced a colonic perforation as a complication of a screening colonoscopy. Their case report underscores the importance of making the correct diagnosis of LHS to avoid undertaking unnecessary aggressive cancer screening regimens.[2]

Although LHS is a benign condition that does not require treatment, Q-switched alexandrite or erbium:YAG laser therapy has been shown to improve the pigmentary findings associated with LHS.[9,10] It has been suggested that LHS should be renamed Laugier-Hunziker pigmentation[2] or mucocutaneous lentiginosis of Laugier and Hunziker[1] to differentiate LHS as simply a disorder of pigmentation rather than a potentially morbid genetic defect, as in Peutz-Jeghers syndrome.

REFERENCES

1. Moore RT, Chae KA, Rhodes AR. Laugier and Hunziker pigmentation: a lentiginous proliferation of melanocytes. *J Am Acad Dermatol.* 2004; 50(5 suppl):S70-S74.
2. Lampe AK, Hampton PJ, Woodford-Richens K, et al. Laugier-Hunziker Syndrome: an important differential diagnosis for Peutz-Jeghers Syndrome. *J Med Genet.* 2003;40:E77.
3. Baran R. Longitudinal melanotic streaks as a clue for Laugier-Hunziker syndrome. *Arch Dermatol.* 1979;115:1148-1149.
4. Grimes P, Nordlund JJ, Pandya AG, et al. Increasing our understanding of pigmentary disorders. *J Am Acad Dermatol.* 2006;54 (5 suppl 2):S255-S261.
5. Bertherat J. Carney complex (CNC). *Orphanet J Rare Dis.* 2006;1:21.
6. Giardiello FM, Brensinger JD, Tersemette AC, et al. Very high risk of cancer in Peutz-Jeghers Syndrome. *Gastroenterology.* 2000;119:1447-1453.
7. Brosens LA, van Hattem WA, Jansen M, et al. Gastrointestinal polyposis syndromes. *Curr Mol Med.* 2007;7:29-46.
8. Beggs AD, Latchford AR, Vasen HF, et al. Peutz-Jeghers syndrome: a systematic review and recommendations for management. *Gut.* 2010;59:975-986.
9. Zuo YG, Ma DL, Jin HZ, et al. Treatment of Laugier-Hunziker syndrome with the Q-switched alexandrite laser in 22 Chinese patients. *Arch Dermatol Res.* 2010;302:125-130.
10. Ergun S, Saruhanoğlu A, Migliari DA, et al. Refractory pigmentation associated with Laugier-Hunziker syndrome following Er:YAG laser treatment [published online December 3, 2013]. *Case Rep Dent.* 2013;2013:561040.