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Case Report

Laugier-Hunziker syndrome with xanthelasma palpebrarum in an adolescent girl: a rare association

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ABSTRACT

Laugier-Hunziker syndrome (LHS) is a rare and benign acquired disorder of mucocutaneous pigmentation characterized by hyperpigmented macules over the lips, buccal mucosa and acral sites with associated nail pigmentation. It usually occurs in middle-aged adults with a female preponderance. The pigmentary lesions respond poorly to therapy and has high chance of recurrence. The syndrome has neither malignant predisposition nor any underlying systemic abnormality. LHS is a diagnosis of exclusion. Clinical correlation is needed to rule out other causes of mucocutaneous hyperpigmentation. It is an important differential diagnosis to Peutz Jeghers syndrome. Herein we report a case of a 16-year-old female presenting with a 10-year history of asymptomatic pigmentation of oral and acral regions with nail pigmentation and was diagnosed with LHS after ruling out other possible differential diagnoses. The patient also had lesions corresponding to xanthalesma palpebrarum in the medial aspect of both the upper eyelids. Both LHS and xanthalesma palpebrarum are very unusual conditions to present in this age.

Keywords: Muco-cutaneous pigmentation, Xanthelasma palpebrarum, Acral pigmentation, Laugier–Hunziker syndrome, Mucosal hyperpigmentation, Oral pigmentation, Nail pigmentation, Melanonychia

INTRODUCTION

Laugier et al in 1970 described a rare benign idiopathic acquired disorder in five patients characterized by multifocal oral, cutaneous and mucosal pigmentation on clinical examination.[1] It is also described as Laugier-Gerbig-Hunziker syndrome (LHS), Laugier-Hunziker-Baran syndrome or idiopathic lenticular mucocutaneous pigmentation. It usually occurs in a sporadic manner, yet a few cases with familial autosomal dominant and recessive inheritance are reported.[2,3] The syndrome usually occurs in middle-aged adults with a female preponderance and is more common among those of Asian descent particularly the Chinese.[4] The usual clinical picture is multiple, asymptomatic discrete or confluent macules of varying colours and shapes measuring less than 5 mm involving the oral cavity including lips, tongue, buccal mucosa, gingiva and hard palate. It is frequently associated with melanotic streaks in nails. Rarely other sites such as face, conjunctiva, oropharyngeal regions, external genitalia, anal and vaginal mucosa may be involved. The afflicted individuals often experience aesthetic and psychosocial effects due to progressive pigmentation, perceiving it as concerning or unusual. Important differential diagnosis includes Peutz-Jeghers syndrome, Addison disease and drug-induced pigmentation and mucosal melanomas. Thus, the condition is often diagnosed by exclusion of other mucocutaneous pigmentary disorders after a thorough evaluation. Due to the original observation, only around 172 cases have been described, including cases that have been reported in related family member and very few other cases with nonclassical features or atypical oral and cutaneous presentations.[5,6] Treatment involves reassurance, and for aesthetic purposes, laser-based

therapies like Q-switched alexandrite, Q-switched Nd-YAG or diode lasers are used for melanosis, though they are associated with recurrence of lesions.[7] In our case, a 16 -year-old female presented with asymptomatic macular hyperpigmentation involving lips, oral mucosa, palmoplantar areas, and longitudinal melanonychia and homogenous pigmentation of nails without any systemic abnormalities or malignancy. A vigilant case history and investigations is usually needed to exclude other causes of mucocutaneous pigmentation, with melanonychia being key feature for diagnosing LHS.

CASE REPORT

A 16-year-old girl presented with asymptomatic multiple brown-black oval to irregular lesions on lips, buccal mucosae and tongue from 6 years of age. She further developed similar light brown lesions on the palmoplantar region and nails at the age of 10-12 years, which insidiously increased in number for the next 4-5 years during adolescence and since then it remained static. She also had elevated yellowish skin lesions over bilateral upper eyelids for 1 year. She denied any history suggestive of gastrointestinal or cardiac diseases. There was no history of any drug intake or excessive sun exposure. The rest of the skin did not show any blue-coloured lesions or soft tissue swellings or hair abnormalities. There was no family history of similar skin lesions or gastrointestinal polyps or cardiac abnormalities.

Examination revealed multiple brownish-black lenticular macules of varying sizes ranging from 1 mm to 5 mm over lips, buccal mucosae, ventral surface of tongue and hard palate (Figure 1a and b).

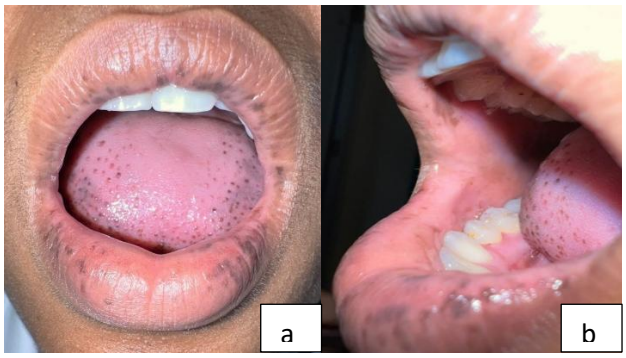

Figure 1: (a) Multiple discrete hyperpigmented macules present over the lips and tongue, and (b) multiple discrete hyperpigmented macules present over the lips and buccal mucosa.

Multiple tiny light brown, irregular and angulated macules less than 5 mm were prominently present on the palmoplantar skin (Figures 2 and 3).

Nail pigmentation was present in the form of longitudinal hyperpigmented streaks and diffuse pigmentation on the fingernails (Figure 4).

Her toenails had complete homogenous hyper-pigmentation (Figure 5).

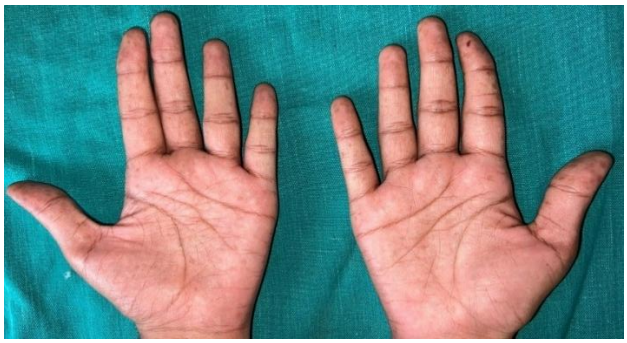

Figure 2: Multiple discrete hyperpigmented macules present over the palmar skin.

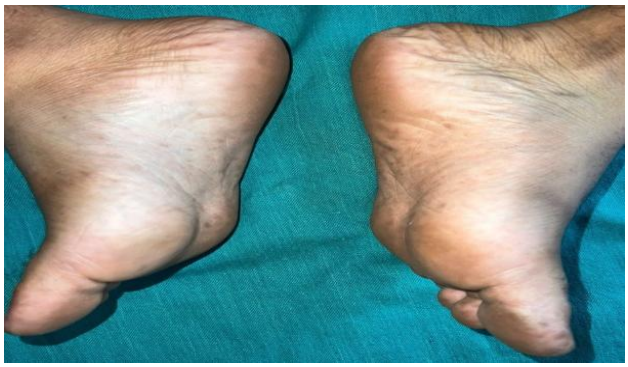

Figure 3: Multiple discrete hyperpigmented macules present over the plantar skin.

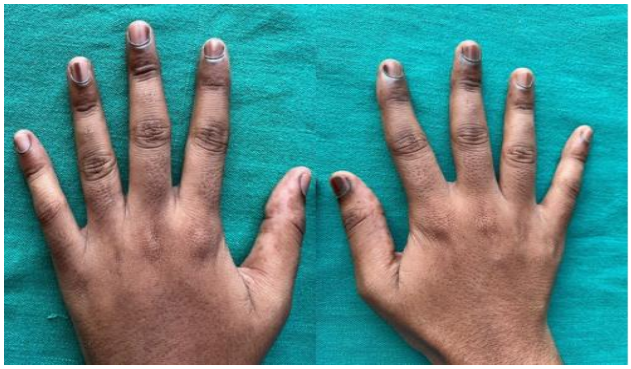

Figure 4: Longitudinal melanonychia (black arrow) and diffuse nail pigmentation (white arrow) in the fingernails.

She also had two yellowish soft plaques of size 2×1 cm present on the medial aspects of both upper eyelids suggestive of grade I xanthelasma palpebrarum (Figure 6).

Ocular mucosa, genital mucosa, hair and the rest of the skin were apparently normal. Routine haematological and biochemical parameters were within normal reference range. Lipid profile was done to rule out disorders of lipid metabolism and was found to be normal. Endoscopic evaluation of the gastrointestinal tract (GIT) was done in

view of intestinal involvement which was found to be normal. Cardiac echocardiogram was done and was normal. The lack of a family history coupled with the absence of any polyps on the endoscopic examinations of GIT as well as the clinical features led to the diagnosis of LHS. The patient and her family members were reassured about the benign nature of the disease. The patient was advised sun protection. Since LHS is benign and doesn't have systemic implications except the cosmetic concern, treatment was not necessary. The patient was lost to follow up.

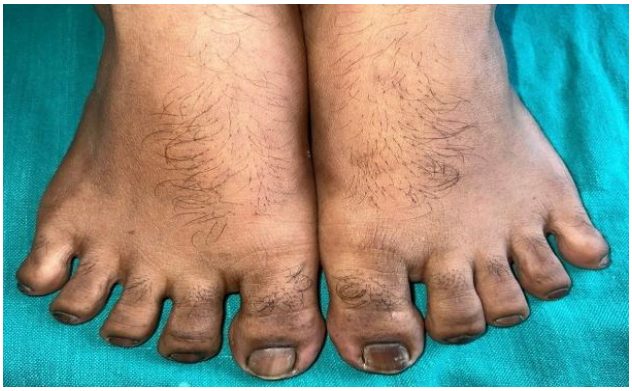

Figure 5: Homogenous pigmentation of toe nails.

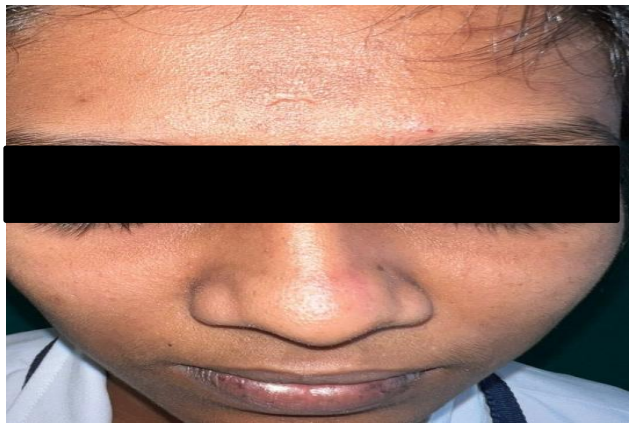

Figure 6: The xanthelasma palpebrarum lesions are not visible.

DISCUSSION

LHS also known as idiopathic lenticular mucocutaneous hyperpigmentation is a rare, benign pigmentary disorder presenting with pigmentation over mucosa, nail and acral sites. Laugier and Hunziker were the first to describe this syndrome in 1970 as an acquired condition of unknown etiology presenting as adult-onset oral pigmentation and genital lesions. Later, Baran described the typical nail lesions which included longitudinal melanonychia occurring in 50% of the patients.[8] LHS predominantly affects females with a 2:1 ratio and an average age of onset at 52 years. It's typically sporadic, but there have been reports of familial cases with both autosomal dominant and recessive inheritance patterns.

The disease develops due to alteration in melanocytes, which cause more melanosomes to be produced and transported to the basal layers, resulting in melanin buildup in basal epidermal keratinocytes. One study reports a rise in non-nested intraepidermal melanocytes.[9] Ultrastructural studies reveal an increase in melanosomes, varying in size and structure.

The lesions mainly appear on the lips, buccal mucosa, and hard palate. Fingernails are the most commonly affected area other than the oral mucosa, impacting about two-thirds of cases. Baran categorized nail pigmentation into three types: a single 1 to 2 mm wide longitudinal streak, double 2 to 3 mm wide longitudinal streaks laterally, and uniform pigmentation covering either the radial or ulnar half. Veraldi et al described a fourth type: complete nail pigmentation.[10] All four types can simultaneously affect multiple fingernails and/or toenails. There's no nail dystrophy associated to occur with this syndrome. The pseudo-Hutchinson sign might be present.

The mucocutaneous lentiginosis associated with Laugier–Hunziker can be challenging to differentiate from other conditions. Many of these below mentioned conditions have serious underlying abnormalities that necessitate multidisciplinary management.

Peutz-Jeghers syndrome (PJS) is a hereditary autosomal dominant condition with high penetrance. PJS is characterized by the development of hamartomatous polyps in the gastrointestinal tract and distinctive melanotic macules, which typically appear in infancy or early childhood. A hallmark of this syndrome is the presence of multiple melanotic macules resembling freckles around the peri-orifical areas, while in LHS, pigmentation is limited to the intraoral region. While pigmentary nail changes can occur in PJS, they are quite rare.[11] Patients may experience symptoms of gastrointestinal bleeding or intestinal obstruction. Studies have indicated an increased risk of both gastrointestinal and extraintestinal malignancies, including cancers of the breast, uterus, cervix, ovaries, testicles and pancreas. By age 57, there is an estimated 48% probability of cancer mortality for affected individuals. As a result, comprehensive surveillance protocols have been developed for PJS patients, which includes biennial full gastrointestinal endoscopic evaluations, early breast cancer screening and annual gynaecological examinations.

Physiological pigmentation of mucosa and nails can also pose a confusion as black pigmented striations on the nails are common among individuals with skin types V and VI, affecting around 15-20% of Asians and up to 70% of African-Americans over 20 years old. These striations are more frequently observed on digits used for grasping or those that are more prone to trauma.

Vitamin B12 deficiency can cause a reversible mucocutaneous and nail pigmentation. This darkening of the skin can be effectively reversed by taking vitamin B12

supplements.[12] The condition is particularly noticeable in the creases of the palms, dorsum of the hands and feet, flexures, oral mucosa and on recent scars. Additionally, there are haematological and neurological effects associated with this deficiency.

Drug-induced pigmentation generally develops after prolonged use, either over months or years, and often fades once the medication is stopped. The most frequent culprits are tetracyclines, antimalarials, phenothiazines and chemotherapy drugs. Patients with AIDS may exhibit hyperpigmentation due to medications such as zidovudine or emtricitabine. Smoker's melanosis is a pathological pigmentation frequently seen in anterior gingiva but associated pigmentation of the nails is not encountered.[13]

Addison's disease is characterized by the adrenal glands producing inadequate amounts of cortisol and aldosterone. This results in skin and mucous membrane darkening, along with elevated adrenocorticotropic hormone levels in the bloodstream. Bandler syndrome is a rare genetic skin disorder that marks the onset in infancy seen as hyperpigmented spots on the hands, nails and oral mucosa.[14] It also involves intestinal vascular malformations that may lead to severe gastrointestinal bleeding.

McCune-Albright syndrome features pigmentation on the lips and genitals, typically on one side and without affecting the nails. This condition is also characterized by early-onset puberty in females and polyostotic fibrous dysplasia. LAMB syndrome/Carney syndrome is a rare autosomal dominant hereditary disorder of pigmentation of the skin mucosa, atrial and mucocutaneous myxomas and multiple blue nevi. LEOPARD syndrome is a complex of multifocal organ abnormalities due to germline missense mutation of PTPN11 gene manifested by numerous lentigines, electrocardiographic abnormalities, hypertelorism, pulmonary stenosis, abnormalities of genitalia, retardation of growth and deafness.[15]

In our case report, typical discrete lenticular hyperpigmentation was noted over classical sites like the lips, oral mucosa, acral sites and nails. In the absence of systemic abnormalities or malignancy, this led to the diagnosis of LHS. The affected nails did not show dystrophy. The case was sporadic and there was no history of any family member being affected. The age of onset of the disease was earlier compared to previous studies. An associated finding of xanthelasma palpebrarum with no lipid abnormality was a novel finding.

The importance of this disorder lies in distinguishing it from other pigmentary disorders of the oral mucosa that have systemic associations, particularly PJS, which necessitates additional investigations and aggressive management. Hence, LHS should be considered when diagnosing middle-aged patients who exhibit mucocutaneous and nail hyperpigmentation without systemic signs or symptoms. Recognizing LHS allows for the exclusion of more severe pigmentary diseases and prevents unnecessary diagnostic procedures.

CONCLUSION

LHS is a rare cause of muco-cutaneous pigmentation. Understanding this benign condition is crucial because it closely resembles some syndromes with systemic implications, helping to avoid unnecessary investigations, treatments and follow-ups. This case is notable for its rarity, unusual age of onset and the presence of xanthelasma palpebrarum, which is uncommon in this age group. Also, palmo-plantar involvement and nail involvement with homogenous hyperpigmentation is uncommonly reported in LHS.

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