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Lentigo

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A lentigo is a small pigmented macule with a sharply circumscribed border. There are multiple clinical and etiologic forms. Lentigines are often initially identified shortly after birth, although they may appear later in childhood. Certain varieties are associated with systemic abnormalities. Histologic findings include epidermal hyperplasia with increased pigmentation of the basal layer.

Lentigo is derived from the Latin word *lens* meaning *lentil*.[1] Pigmentation varies from homogeneous to variegated and from brown to black. Lentigines may evolve slowly over a number of years, or they may be eruptive, appearing in a short period. They can be either solitary or multiple, occurring anywhere on the body depending on the type of lentigo.[2] Certain varieties have associated systemic manifestations. The clinical distinction of a lentigo, as opposed to other melanocytic lesions such as melanocytic nevi or melanoma, is of major significance because of its role as a marker for UV damage or systemic syndromes.[3]

Epidemiology

Lentigines are commonly found in people around the world. Lentigo simplex is the most common form of lentigo, but its frequency has yet to be determined.[4] A study conducted by Alper and Holmes[5] revealed multiple lentigines in 18.5% of 492 black newborns and in 0.04% of 2682 white newborns. However, histologic confirmation of these lesions was lacking.

Clinical Manifestations

The clinical presentation of lentigines varies depending on their type. Various forms of lentigines appear in children and are described as follows.

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Lentigo Simplex—Lentigo simplex, also referred to as simple or juvenile lentigo, is the most common form of lentigo. The lentigines are similar in appearance to solar lentigines or "liver spots," but they lack the predilection for sun exposed areas of the body. Additionally, simple lentigines usually appear initially in childhood, as opposed to solar lentigines, which appear in adulthood.[6,7] Simple lentigines are round to oval, asymptomatic macules measuring 3 to 15 mm in diameter.[8] The margins are either jagged or smooth, and the color ranges from brown to black with even distribution of pigmentation. Lesions occur anywhere on the body and are generally few.[2]

Lentigines Profusa—Lentigines profusa, or generalized lentigines, is characterized by numerous lentigines without signs of associated abnormalities or triggering factors. The clinical appearance is similar to ephelides, but the distribution is widespread.[2] The areas most commonly involved include the trunk, extremities, palms, genitalia, and mucosal surfaces such as the conjunctiva, but the buccal mucosa and soles may be spared. The macules are dark brown to black and vary in size from 1 mm to 2 cm in diameter.[9] Cutaneous manifestations of lentigines profusa are similar to those of LEOPARD, LAMB, and NAME syndromes[10,11]; however, a notable exception is the lack of physical anomalies and defects associated with these syndromes.

Agminated Lentigines—Agminated lentigines, also known as segmental, unilateral, or partial unilateral lentigines, are characterized by numerous lentigines geographically confined to a particular body segment.[12] The distribution frequently occurs in a dermatomal pattern. Less commonly, they can be distributed in midline clusters or a checkerboard pattern, either unilaterally or bilaterally. The lesions may be noted at birth, although onset usually occurs in early childhood.[4] Clinically, they appear as dark circumscribed macules on normal background skin. This distinguishes agminated lentigines from segmental nevi in which the background skin is hyperpigmented.[2] Agminated lentigines are associated with numerous diseases.[4]

A 13-year-old girl with xeroderma pigmentosum.

Xeroderma Pigmentosum—Xeroderma pigmentosum (Figure) is a condition whose abnormalities stem from an inability of cells to repair DNA damage induced by UV light and certain chemicals. Xeroderma pigmentosum is inherited in an autosomal recessive fashion. Clinically, patients develop progressive pigmentary changes and skin atrophy. Subsequent neoplastic changes occur in the skin, often in childhood.[13] Malignancies most commonly associated with xeroderma pigmentosum are squamous and basal cell carcinomas. However, other neoplasms such as melanoma also may occur.[14] All of these neoplasms occur on sun exposed areas, particularly the head, neck, and face. The diagnosis of xeroderma pigmentosum is often delayed until the skin exhibits some evidence of solar damage. It is essential for children to avoid sun exposure whenever possible to prevent the acceleration of skin changes that lead to the formation of skin cancers.[13]

Peutz-Jeghers Syndrome—Peutz-Jeghers syndrome is an autosomal dominant condition with a high degree of penetrance. The syndrome is characterized by gastrointestinal polyps and pigmented macules. The polyps are benign hamartomas of the entire bowel, with jejunal involvement most characteristic.[15,16] The polyps result in recurrent abdominal pain and perirectal bleeding. Initially, patients are seen in early childhood with bleeding or signs of intussusception. The lentigines are brown to black to blue macules varying from 1 to 12 mm in diameter[15,16] and may be present at birth or appear during early childhood. They characteristically involve the lips, mouth, and buccal mucous membranes, with scattered lesions around the nose and face. Lesions also may appear on both the palmar and volar surfaces of the fingers and toes. There is a characteristic absence on the flexor and extensor surfaces of the rest of the body.[16] Some macules may fade with age, but buccal mucosal macules persist throughout the patient's life.[15,16] There appears to be no correlation between the extent of melanosis and the extent of polyposis. After childhood, most women with Peutz-Jeghers syndrome develop unusual sex cord tumors, which tend to be small, bilateral, multifocal, and asymptomatic. These women also have an increased risk of developing unilateral or bilateral breast cancer.[15] In addition, Sertoli cell tumors also have been noted to occur in men with the condition.

LEOPARD Syndrome—LEOPARD syndrome, or multiple lentigines syndrome, is a condition associated with lentigines, electrocardiographic conduction defects, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, retardation of growth, and deafness.[16,17] This complex dysmorphogenetic disorder is autosomal dominant with variable penetrance.[10,11] Diagnosis may be difficult because most patients exhibit only 3 to 5 of the characteristic criteria. Lentigines are the most typical and one of the most frequent features.[11] Lentigines are present at birth, and their numbers continue to increase until puberty. Numerous macules occur on the neck and trunk but also erupt on the genitalia, scalp, palms, and soles.[10,11,18] There is typically some sparing of the face. In some cases, lentigines may be limited to one side of the body.[17,18] If lentigines are absent, a diagnosis of LEOPARD syndrome can be made if a patient has an immediate relative with the disorder and has features in at least 3 other categories.[11,16]

Lentigines/Myxoma Syndromes

The following syndromes are associated with lentigines and myxomas, which can be cardiac, mucocutaneous, or both.

LAMB Syndrome—LAMB syndrome is associated with lentigines, atrial myxomas, mucocutaneous myxomas, and blue nevi.[16] The lentigines are brown and can be as large as 1 cm in diameter. They are commonly found on the face, lips, sclera, and vulva. The mucocutaneous myxomas appear on various sites of the body as papules or dermal nodules and most commonly occur on the tongue, oral mucosa, genitalia, breasts, and shoulders. Cardiac myxomas occur most often in adulthood but can, on rare occasions, occur in childhood. They are usually atrial myxomas, which can cause valvate obstructions and embolic episodes.[19]

NAME Syndrome—NAME syndrome, a possible variant of LAMB syndrome, is a combination of nevi, atrial myxomas, myxoid neurofibromas, and ephelides.[20,21] Lentigines arise as flat, pigmented, pale to dark brown macules that often begin at birth and are accentuated in the summer months. The

most common areas affected include the neck, trunk, and thighs; however, the palms and soles also may be affected.[20]

Carney Syndrome—Carney syndrome is characterized by cardiac, cutaneous, and mammary myxomatous masses, as well as lentigines, blue nevi, testicular tumors, and endocrine disorders.[22,23] Organ involvement is often multicentric and bilateral in young patients.[23] Cutaneous myxomas are most prevalent on the eyelids but also can be found on the nipples, face, scalp, ears, oral mucosa, neck, trunk, limbs, and perineum. Single or multiple cardiac myxomas often lead to fibrosis or calcification. There are 2 types of pigmented macules, namely blue nevi and lentigines. Lentigines are usually 0.2 to 2 mm in diameter with irregularly shaped jagged margins. Their color ranges from brown to black, and distribution is widespread throughout the body, often coalescing to form large brown patches. Lentigines are most commonly located on the face, ears, eyelids, and vermilion borders of the lips. Less commonly, they occur on the conjunctiva, extremities, vulva, and glans penis. Buccal macules are rare in contrast to Peutz-Jeghers syndrome.[15,22] Endocrine involvement varies but includes calcifying, pigmented, neuroectodermal tumors; pituitary adenomas with acromegaly and gigantism; and adrenocortical disease leading to Cushing syndrome. Testicular tumors include Sertoli cell, Leydig cell, and adrenal rest tumors. Mammary involvement features gynecomastia and myxomatous enlargement of the stroma.[22]

Histology

Lentigo simplex exhibits a slight to moderate elongation of the rete ridges with melanocyte proliferation in the basal layer, increased melanin in both melanocytes and basal keratinocytes, and the presence of melanophages in the upper dermis.[1,6] Both lentigines profusa and agminated lentigines are similar in appearance.[4,9,12]

Xeroderma pigmentosum lentigines show hyperkeratosis with epidermal atrophy. A few rete ridges also may be elongated. The basal cell layer contains increased pigment with a variable number of melanocytes, and the upper dermis may contain chronic inflammatory cells.[13] Peutz-Jeghers syndrome lentigines have marked hyperpigmentation of the basal layer but do not always display increased melanocytes.[15,16] LEOPARD syndrome lentigines exhibit increased pigment content of the epidermis and increased melanocytes containing melanosomes that are distributed either singly or in the form of micronests.[10,11]

LAMB syndrome lentigines show elongated rete ridges associated with marked hyperpigmentation of the basal layer.[19] NAME syndrome is characterized by lentigines with increased pigmentation of both the basal and spinous epidermal layers.[20,21] Carney syndrome lentigines exhibit hyperpigmentation of the basal layer and melanocytic hyperplasia, with or without rete ridge elongation.[22]

Differential Diagnosis

Lentigines may have to be differentiated from other pigmented lesions such as ephelides, flat seborrheic keratosis, actinic keratosis, melanocytic nevi, lentigo maligna, and melanoma. These lesions not only may appear similar clinically but also may require skillful distinction histologically.

Treatment

Isolated lentigines can be treated with simple cryosurgery, which is often successful because melanocytes are susceptible to freezing with the use of liquid nitrogen. Destruction of melanocytes is known to occur at temperatures of –4°C to –7°C, while squamous cells resist injury even at –20°C.[24]

The use of lasers has been shown to be effective in the treatment of lentigines. The frequency-doubled Q-switched Nd:YAG laser, the 532-nm diode-pumped vanadate laser, and the HGM K1 krypton laser have all been employed with success.[25,26]

Noninvasive agents such as topical creams also have been used. After several months of application, the combination of tretinoin cream and hydroquinone cream have shown to lighten lentigines.[7,27]

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