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Nevus of Ota in Children

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Nevus of Ota, synonymously termed oculodermal melanosis, *is an uncommon dermal melanosis most commonly seen at birth in children of Japanese descent, though it can affect individuals of any age or ethnicity. The disease tends to persist and extend locally, becoming increasingly prominent with age, puberty, and postmenopausal state. Treatment should begin early after diagnosis using multiple sessions of laser photothermolysis to avoid darkening and extension of the lesion. Important associated disorders include ipsilateral glaucoma; intracranial melanocytosis; and rarely cutaneous, ocular, or intracranial melanoma. Recommendations are discussed for managing nevus of Ota in children.*

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Nevus of Ota is a rare disorder characterized by melanocytic pigmentation of the sclera and ipsilateral skin along the distribution of the ophthalmic and maxillary branches of the fifth cranial nerve. Hulke[1] is credited with first describing oculodermal melanosis (nevus of Ota) in 1861. In 1916, Pusey[2] observed a Chinese student affected by the disorder. In 1939, Japanese dermatology professor Masao Ota[3] characterized and descriptively named the disorder *naevus fusco-caeruleus ophthalmomaxillaris*. Yoshida[4] conducted a large statistical study of Japanese patients with nevus of Ota and further elaborated clinical aspects of the disease. In 1956, Fitzpatrick et al[5] renamed the syndrome *oculodermal melanocytosis*.

Nevus of Ota affects females approximately 5 times more often than males.[6] It is known to affect individuals with darker-pigmented skin, is seen most commonly in individuals of Japanese descent, and is less likely to present in individuals of Chinese or Korean descent, though individuals descending from the Indian subcontinent, Africa, and Europe also may be affected.[7] In early surveys of Japanese patients at dermatology clinics, the incidence of nevus of Ota was determined to be 0.4% (110/27,500).[4] Cowan and Balistocky[8] calculated the incidence of oculodermal melanocytosis in black patients to be 0.016%. A study of 2914 Chinese children in Calgary, Alberta, Canada, reported an incidence of oculodermal melanocytosis of 0.034% (1/2914).[9]

Clinical Manifestation

The typical nevus of Ota is a unilateral facial discoloration that is macular, speckled, and bluish gray or brown, with edges that blend with bordering skin (Figure).[10] The dermatomal distribution of pigment characterizes this diagnosis in most cases. Typical locations (in order of decreasing frequency) include the skin of the upper and lower eyelids, temples, zygomatic region, and forehead.[5,11] The area affected usually lacks hair and is ordinarily unilateral, though 5% of patients demonstrate bilateral pigmentation.[10]

The disease tends to persist and extend locally, becoming increasingly prominent with age, puberty, and postmenopausal state. Approximately 60% of cases present at birth or shortly thereafter, with the

A 12-year-old girl of sub-Saharan descent with nevus of Ota.

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remainder presenting at puberty.[6,10] Patients have reported heightened pigmentation with fatigue, menstruation, insomnia, environmental temperature extremes, and cloudy weather.[5,6,10,11]

Oculodermal melanocytosis is not known to follow a recognizable inheritance pattern, though there are cases of families with multiple members affected by the condition.[6] Other disorders that may be associated with the nevus of Ota include the related nevus of Ito, telangiectatic nevi in phakomatosis pigmentovascularis, nevus flammeus, and neurofibromatosis.[11-13] Nevus of Ota has been associated with Sturge-Weber and Klippel-Trenaunay-Weber syndromes; a neurodevelopmental error may be common to all 3 disorders.[14,15]

Associated melanosis of the ipsilateral eye occurs in approximately 2 of 3 cases of nevus of Ota. The most commonly affected structure is the sclera, though pigmentation of the ipsilateral iris, conjunctiva, retina, cornea, choroid, extraocular muscles, and retrobulbar fat also have been described.[11,16] Optic nerve involvement occurs in 1% to 4% of patients.[16] Ipsilateral sensorineural hearing loss also has been described. Pigmentation of other mucosal surfaces of the head and neck may occur, involving the nasal and oral mucosa, tympanic membrane, and external auditory canal. Palatal pigmentation is rare and occurs most frequently in patients with bilateral nevi of Ota.[6,16] Patients with bilateral nevi of Ota often have extensive mongolian spots.[6,7]

Nevi of Ota have the potential to undergo melanomatous change. Malignant degeneration occurred in 4.6% of reported cases of oculodermal melanocytosis and was more frequent in light-skinned patients.[17-19] In one study, white individuals accounted for approximately 76% (36/47) of cases of malignant melanoma.[18] The average age at diagnosis of melanoma is approximately 60 years,[11] though there is no known association between the age of the nevus and development of melanoma. Malignant change occurs most frequently within the choroid but may develop in the skin, orbit, meninges, and brain.[11,17,19,20] The majority of these primary melanomas develop ipsilateral to the nevus.[18] The combination of nevus of Ota and meningeal melanocytoma also has been described.[21]

Cutaneous malignancy frequently manifests as new or enlarging subcutaneous nodules, as opposed to the ABCD (asymmetry, border irregularity, color, diameter) spectrum of changes typically seen in melanoma, representing a malignant blue nevus that did not arise at the dermoepidermal junction.[17] Additionally, melanoma may develop in clinically resolving nevi.[12] Intracranial melanoma rarely occurs in patients with nevus of Ota, and these cases involve the leptomeninges more often than the dural and parenchymal tissues.[13] Consequently, periodic dermatologic evaluation is warranted in these patients, along with biopsy of rapidly changing nevi.

Another well-known complication associated with oculodermal melanocytosis is glaucoma in the ipsilateral eye, which has been described in approximately 10% of patients.[12,22] Glaucoma may be detected at birth or any age, is usually open angle,[22,23] and typically is asymptomatic with gradual loss of visual acuity. The pathophysiologic process leading to glaucoma in these patients is most likely deposition of melanocytes within the trabecular meshwork at the iridocorneal angle.

Histopathology

Biopsy specimens of nevi show an epidermis with increased melanocytes but no activity at the dermoepidermal junction. Fusiform, bipolar, elongated, heavily pigmented, dendritic melanocytes with extracellular sheaths are scattered at various levels within the upper dermis and mid-dermis.[10,24] These melanocytes do not alter the overlying architecture of the skin, a characteristic that helps distinguish nevus of Ota from other dermal melanocytoses.[25] Malignant change has the histologic appearance of a malignant blue nevus.

Pathogenesis

Although the pathogenesis is not precisely known, it is generally believed that nevus of Ota represents a failed migration of melanocytes from the neural crest to the dermoepidermal junction and subsequent arrest within the dermis.[26]

Contrary to the spontaneous regression of mongolian spots, most nevi of Ota do not improve with age. The lesions may darken or extend during puberty and in postmenopausal women. It is hypothesized that these aberrant dermal melanocytes may be influenced hormonally by a mechanism within the hypothalamic-pituitary-ovarian axis.[5,10]

Nevi of Ota were originally classified based on clinical descriptions of pigmentation: type I (small lesions), type II (moderately sized lesions), type III (extensive lesions), and type IV (bilateral lesions).[6] In 1991, nevi of Ota were histologically reclassified according to the location of melanocytes within the dermis, including superficial, deep, diffuse, superficial dominant, and deep dominant types.[27] This newer classification is more relevant for predicting patient response to treatment because superficial melanocytes are most amenable to therapy.

Differential Diagnosis

Nevus of Ota belongs to the family of circumscribed dermal melanocytoses (Table), along with the

mongolian spot and cellular blue nevus, and may be misdiagnosed as an ectopic mongolian spot. Mongolian spots are homogeneously pigmented and characteristically contain melanocytes in the lower half of the dermis, whereas the nevus of Ota is a speckled, superficial, dermal melanocytosis.[10,28,29] The face is an unusual location for a mongolian spot, which most commonly occurs in the sacrococcygeal region. Additionally, mongolian spots lack malignant potential and are not associated with glaucoma.

The nevus of Ito, or nevus fusco-ceruleus acromiodeltoideus, is histologically identical to the nevus of Ota. The difference between the two is that the dermal melanocytes follow the distribution of the posterior supraclavicular and lateral brachiocutaneous nerves.[26] An acquired melanocytosis resembling the nevus of Ota is Hori nevus. Hori nevus describes acquired development of bilateral macular nevi that typically occur in women in their 30s and 40s but, unlike nevi of Ota, lack mucosal involvement.[30]

Common blue nevi may resemble nevi of Ota. Blue nevi are papulonodules or plaques that may contain hair and occur anywhere on the skin while sparing the mucus membranes.[31] They contain higher concentrations of melanocytes in the mid-dermis and lower dermis than nevi of Ota and typically persist with age.[28] Similar to nevi of Ota, cellular blue nevi have malignant potential.

Other pigmentation disorders that must be considered in the differential diagnosis include lentigo maligna, ochronosis, phytophotodermatitis, and Riehl melanosis.[32] Melasma also may resemble nevus of Ota, but this acquired dyschromia is characterized by epidermal melanosis in sun-exposed areas and thus would appear brownish rather than bluish gray.

Treatment

Treatment for oculodermal melanocytosis has evolved greatly over the past 4 decades. Makeup may be applied to cover and blend the lesion with the surrounding skin but offers only temporary improvement in cosmesis and requires diligent daily application.[33,34] Achievement of long-term depigmentation is the current goal of therapy.

The 2 most effective treatment options are lasers and cryosurgery, with the most promising being Q-switched laser treatment with ruby, alexandrite, or Nd:YAG lasers.[35-41] These lasers selectively induce photothermolysis of pigment-containing cells of the epidermis and dermis. Watanabe and Takahashi[37] treated 114 Japanese patients with nevus of Ota using pulse therapy with the Q-switched ruby laser and noted successful depigmentation without scarring or damage to surrounding skin. Histologic examination of skin treated with the ruby laser demonstrated destruction of melanocytes in the epidermis and papillary dermis, with less of an effect on melanocytes in the reticular dermis. Transient hyperpigmentation may be noted after the first laser treatment and the rate of successful depigmentation increases with multiple laser treatments.[35]

A major complication of laser treatment is residual hypopigmentation or hyperpigmentation of the treated area, which is more common in patients treated with the ruby laser.[38] Epidermal melanocytes are not permanently damaged by Q-switched alexandrite laser therapy; thus, there is a lower incidence of posttreatment dyspigmentation.[39] Although concern has been raised regarding possible induction of malignant predisposition in laser-treated melanocytes of giant congenital nevi, malignancy

Circumscribed Dermal Melanocytoses in the Differential Diagnosis of Nevus of Ota

Disease	Reference(s)
Cellular blue nevus	Velez et al[28]
Common blue nevus	Kopf and Weidman[10]
Incontinentia pigmenti	Hori and Takayama[25]
Nevus of Ito	Dutton et al[11] Hori and Takayama[25] Hirayama and Suzuki[27]
Mongolian spot	Hirayama and Suzuki[27]
Neurocutaneous melanosis	Balmaceda et al[13]

after ruby laser treatment has not been reported with the nevus of Ota.[40]

Dermabrasion followed by cryotherapy with carbon dioxide snow is an older method that may effectively remove a nevus of Ota containing melanocytes in the more superficial aspects of the dermis.[33] The efficacy of cryotherapy increases with multiple treatment sessions over an extended period of time and is associated with pain, dermal scarring, and atrophy; the technique generally is ineffective for treating blepharal nevi and nevi of Ota with deep dermal melanocytes.[35,37] Other treatments that have been used include dermabrasion alone, surgical excision, and skin grafting of larger nevi.[33]

Kono and colleagues[41] compared Q-switched ruby laser treatment in children and adults and ascertained that children (mean age, 3 years) required fewer treatment sessions and had greater response rates with lower complication rates than adults. Approximately 0.6% to 1.2% of patients experience recurrence.[41] In adults, repigmentation may occur within 2 to 3 years of successful treatment with Q-switched alexandrite or Nd:YAG lasers.[38]

Management

Nevus of Ota may be clinically diagnosed. Confirmatory biopsy is indicated in patients of any age when the diagnosis is uncertain or in rapidly expanding or nodular lesions suggestive of malignancy.[17] Periodic examination should be conducted twice a year for early diagnosis of glaucoma or the more rare complication of malignancy. Patients with uncomplicated nevi of Ota should be instructed to return for evaluation if the lesion changes or becomes symptomatic. Because malignancy in nevus of Ota tends to occur more frequently in light-skinned individuals,[17,19] there should be a lower threshold for biopsy. Regardless of whether or not the sclera is pigmented, patients should be referred for ophthalmologic examination at the time of diagnosis and regularly thereafter because asymptomatic glaucoma is a concern. Any report of visual change, ptosis, or neurologic deficit requires further ophthalmologic and neurologic investigation and possibly magnetic resonance imaging.

When diagnosing nevus of Ota in neonatal and pediatric populations, one must recognize the rare co-occurrence of neurodevelopmental disorders and conduct appropriate examinations. Treating the nevus of Ota soon after diagnosis during childhood is preferred to avoid increasing pigmentation and enlargement with advancing age.[33] There is no harm associated with early treatment[33] and children may avoid the psychological anguish if treated before entering school.

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