

Bilateral nevus of Ota: A case series and literature review



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ABSTRACT

Nevus of Ota is a dermal melanocytic hamartoma clinically characterized by confluence of blue-to-gray macules, distributed along the ophthalmic and the maxillary divisions of the trigeminal nerve. It is usually unilateral and only 5–15% of cases have been reported to have bilateral involvement. This entity has been reported predominantly in darkly pigmented individuals, particularly in Asians and blacks. Case reports and case series describing this unique entity are very rare in literature. Herein, we report three cases of bilateral nevus of Ota at a tertiary care center in Eastern India. A detailed history, clinical examination, Wood's lamp examination, and histopathological correlation were done in all the cases. In all the cases, lesions started with bluish pigmentation on the sclera and out of three cases, two had palatal involvement as well.

Key words: Bilateral nevus of Ota; Nevus of Ota; Hori's nevus; Dermal melanocytosis

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INTRODUCTION

Nevus of Ota was originally described as Nevus fusco-caeruleus ophthalmo-maxillaris by Ota in 1939¹ and was renamed as Oculodermal melanocytosis by Fitzpatrick in 1956² and Oculomuodermal melanocytosis as described by Syed et al.,³ It is an extensive, bluish, and patchy, dermal melanocytosis that affects the sclera and the skin adjacent to the eye, distributed along the first and second branches of the trigeminal nerve.⁴ Nevus of Ota is usually unilateral and only 5–15% of cases have been reported to have bilateral involvement.⁵ This entity has been reported predominantly in darkly pigmented individuals, particularly in Asians and blacks.⁴ Various classification systems have been proposed to describe the nevus of Ota. According to Tanino classification, all the three cases classify as type IV and as per the Peking Union Medical College Hospital (PUMCH) classification, also, all three cases fall under type IV.

Histopathological examination shows deeply pigmented dendritic melanocytes and melanophages dissecting bundles of dermal collagen. Patients with nevus of Ota are known to be at higher risk of developing glaucoma and uveal melanoma.⁶ All the cases reported here had no visual impairment but were advised bi-annual full ophthalmic examination for early detection and prevention of complications. Nevus of Ota is often misdiagnosed as Hori's nevus, melasma, solar lentigines, or exogenous ochronosis. The first-line management is laser surgery, particularly with Q-switched lasers. The study was conducted for a period of 12 months from March 2022 to February 2023. The study population included all patients attending the dermatology outpatient department of the Indira Gandhi Institute of Medical Sciences, Patna. A total of three cases were reported during the study. A detailed history regarding the age of onset, site of lesion, duration, and any past treatment was obtained. Detailed dermatological, systemic, and wood's

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lamp examinations were carried out. Histopathological examination was also done for all cases which was consistent with clinical diagnosis.

CASE REPORTS

Case 1

A 7-year-old boy presented to the skin outpatient department with a progressive, bluish hyperpigmented lesion over bilateral cheeks. The lesion appeared first in the left eye at 6 months of age. It gradually progressed to involve the left cheek, the right cheek, and the hard palate over a period of 1 year. No history was suggestive of change in the color of lesions could be elicited. There was no evidence of neurological involvement or visual disturbance. The patient was not on medications for any other medical condition. Furthermore, there was no similar family history in this patient.

Clinical examination revealed blue-gray coalesced hyperpigmented patches on either side of the face involving anterior aspect of the left forehead, bilateral temporal, zygomatic, malar areas, upper eyelids, the left ala of nose, and the left pinna and left sclera (Figure 1a-c). A hyperpigmented irregular patch over the hard palate was also noted (Figure 1d).

On ophthalmic examination, no visual disturbance was noted. The cutaneous lesions were examined under Wood's lamp and accentuation in the intensity was not appreciated which was consistent with dermal melanosis.

Histopathological examination revealed increased pigmentation in basal cell layer. The dermis shows pigment



Figure 1: Clinical examination-revealed blue-gray coalesced hyperpigmented patches on either side of the face involving anterior aspect of the left forehead, bilateral temporal, zygomatic, malar areas, upper eyelids, left ala of nose, and left pinna (a-c). A hyperpigmented irregular patch over hard palate was also noted (d)

laden cells and perivascular chronic inflammatory cell infiltrate with melanophages (Figures 2a and b).

Mucosal biopsy from the palate was advised but was denied by the patient.

Hence by co-relating clinical and histopathological findings, we came to the diagnosis of bilateral nevus of Ota.

Case 2

A 17-year-old girl presented to the skin outpatient department with a progressive, bluish hyperpigmented patch over the left cheek and the forehead. The patient had a small hyperpigmented macule on the left sclera since birth. The patient developed a similar lesion in the left periorbital area which gradually increased in size to involve the left cheek and both side of the forehead over a period of 5–7 years. No history is suggestive of change in the color of lesions and visual disturbance could be elicited.

Clinical examination revealed grayish blue coalesced hyperpigmented patches on either side of the face involving the bilateral forehead, bilateral upper eyelids, the left temporal, zygomatic, malar areas, the left ala of nose, and left sclera (Figure 3a-c). A bluish hyperpigmented macule over hard palate was also noted (Figure 3d).

On ophthalmic and otological examination, no significant abnormality was noted. The gray-colored lesions were examined under Wood's lamp, which caused attenuation in the intensity confirming the dermal origin. Histopathological examination-revealed deeply pigmented dendritic melanocytes and melanophages dissecting bundles of dermal collagen in reticular dermis (Figures 4a and b).

Mucosal biopsy from the palate was advised but was refused by the patient. Hence by co-relating clinical and histopathological findings, we came to the diagnosis of bilateral nevus of Ota.

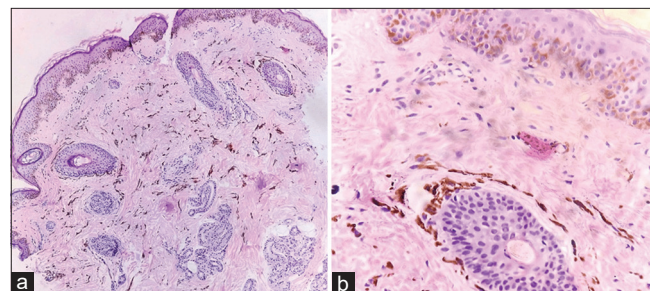


Figure 2: (a) H and E (x100) shows stratified squamous epithelial lining. The underlying dermis shows clusters of pigment laden cells. (b) (H and E, x400) the underlying dermis shows elongated dendritic melanocytes scattered within collagen bundles and melanophage extending around hair follicles

Case 3

A 29-year-old male, presented to the skin outpatient department with a bluish hyperpigmented patch over the left side of his face and in the right infraorbital area, which is stable from the last 2 years. He mentioned that his mother noticed pin-point bluish pigmentation at the left sclera at around 6 months of age. At the age of 16 years, the patient contracted tuberculosis for which he was on medication for 6 months. After this, the patient had a sudden progression of lesions to the left side of the forehead, temporal, zygomatic, and buccal areas. Lesions also progressed to involve the right infraorbital area. The patient complains of tingling sensation over lesions, on exposure to sunlight. Mucosal involvement was not present in this case.

On examination, grayish-blue coalesced hyperpigmented patches on were observed in the left midface, mainly, the left side of the forehead, temporal, zygomatic, and buccal area, and the right infraorbital area (Figure 5a-d),



Figure 3: Clinical examination-revealed grayish blue coalesced hyperpigmented patches on either side of the face involving bilateral forehead, bilateral upper eye lids, left temporal, zygomatic, malar areas, left ala of nose, and left sclera (a-c). A bluish hyperpigmented macule over hard palate was also noted (d)

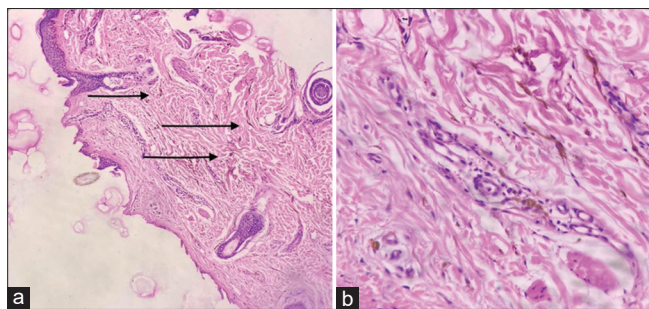


Figure 4: (a) H and E (×100): deeply pigmented dendritic melanocytes and melanophages dissecting bundles of dermal collagen in reticular dermis. (b) H and E (×200): elongated dendritic melanocytes scattered with collagen bundles

On ophthalmologic and otological examination, no abnormality was noted. The lesions were examined under Wood's lamp, which caused attenuation in the intensity consistent with melanosis of dermal origin.

Histopathological examination-revealed elongated dendritic melanocytes scattered with collagen bundles (Figures 6a and b).

Hence by co-relating clinical and histopathological findings, we came to the diagnosis of bilateral nevus of Ota.

DISCUSSION

Nevus of Ota was originally described as nevus fusco-caeruleus ophthalmo-maxillaris by a Japanese dermatologist Ota in 1939.¹ Its alternate designations include oculodermal melanocytosis² and oculomucodermalmelanocytosis.³

It is a dermal melanocytic hamartoma clinically characterized by confluence of blue-to-gray macules, distributed along

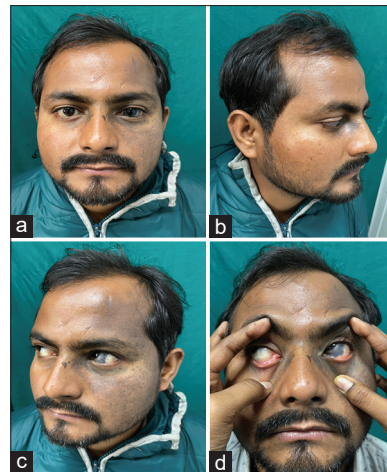


Figure 5: Clinical examination-revealed grayish blue coalesced hyperpigmented patches on the left side of forehead, temporal, zygomatic, and buccal area and right infraorbital area (a-c). Involvement of the left sclera was also noted (d)

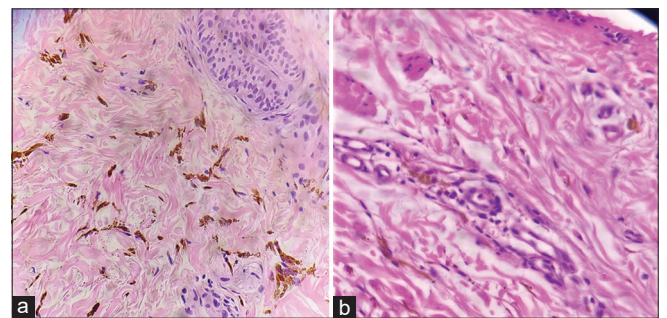


Figure 6: (a) H and E (×400) elongated dendritic melanocytes scattered with collagen bundles. (b) H and E (×400) pigment laden cells in the dermis

the ophthalmic and the maxillary divisions of the trigeminal nerve.⁴ It mainly involves periorbital region, as well as the temple, forehead, scalp, nose, ears, palate and malar area. Other frequent sites of involvement are the tympanum (55%), nasal mucosa (30%), pharynx (25%), and palate (20%).⁵ The involvement of the ipsilateral sclera which is a characteristic feature is seen in about two-third of patients.⁶ It is usually unilateral and only 5–15% of cases have been reported to have bilateral involvement.⁵ Nevus of Ota occurs predominantly in people of Asian and African descent and is quite rare in Caucasian population.⁷ It has a female preponderance as approximately 80% of all reported cases are females. The lesion has two peaks of onset: the first (~50–60% of all cases) is during infancy (<1 year) with the majority present at birth, and the second (40–50%) is around puberty. Onset between the ages of 1 and 11 years, and after 20 years is unusual.⁸

Though the pathogenesis of nevus of Ota is not well-understood, there are currently several mechanisms that have been described to account for the origin of the melanocytes. First, melanocytes move from the neural crest to the skin during early embryonic life. Failure of complete migration into the epidermis before birth with ensuing dermal nesting and melanin production produces characteristic blue patches.⁹ Second, stress and trauma that causes increased secretion of proopiomelanocortin, a precursor of melanocyte-stimulating hormone can also be a potential mechanism. Other than this, role of GNAQ mutations that causes G-coupled protein to be constitutively turned on, history of previous radiotherapy/radiation exposure, and hormonal factors have also been implicated.¹⁰

To date, three classification systems have been proposed to describe nevus of Ota. Among them, Tanino's classification has been widely accepted. It was coined by Tanino in 1939. He classified nevus of Ota into 7 types according to the skin involvement area: Type I (mild): Type A is periocular. Type B involves the zygomatic region. Type C involves the forehead. Type D involves the only nose. Type II (moderate): Similar to type I but worse in severity. Type III (intensive): Periocular, nose, and scalp involvement. Type IV: Bilateral involvement.¹¹

However, several studies have demonstrated that Tanino's classification leaves a considerable portion of patients unexplained.¹² For this, a new system was developed by a Chinese group in 2013, called PUMCH classification. This classification is based on the innervation area of the trigeminal nerve branches, composed of 5 types and 14 subtypes. The 5 types were as follows: Type I, pigmentation involving one branch of the trigeminal nerve; Type II, pigmentation involving two branches of the trigeminal nerve; Type III, pigmentation involving all three branches

of the trigeminal nerve; Type IV, bilateral type; Type V, no accompanied by other cutaneous complications.¹³

According to Tanino classification, all the three cases classify as type IV and as per PUMCH classification, also, all the three cases fall under type IV.

On histopathological examination, nevus of Ota classically shows deeply pigmented dendritic melanocytes and melanophages dissecting bundles of dermal collagen.¹⁰ In our case series, in all the three cases, biopsy reports were compatible with diagnosis of nevus of Ota. The third classification system was proposed by Hirayama and Suzuki according to the distribution of the dermal melanocytes. Ota's nevus was divided into 5 types: superficial (type S), superficial dominant (type SD), diffuse (type Di), deep dominant (type DD), and deep (type De). These histological types correlate with the color and location of the nevus: the most brownish lesions represented type S or type SD which are frequent on cheeks, whereas the most bluish lesions showed types Di, DD, or De which are frequent on the eyelid, temple, and forehead.¹⁴

The main social impact of nevus of Ota is the cosmetic concern. However, in cases where the sclera is commonly affected, ocular complications such as increased intraocular pressure and glaucoma can occur. Other complications include uveitis, cataracts, retinitis pigmentosa, and uveal melanoma.⁷ Monosomy of chromosome 3 and gain of the long arm of chromosome 8q is a significant risk factor for uveal melanoma and predicts poor outcome.¹⁰ All the cases reported here had no visual impairment but were advised bi-annual full ophthalmic examination for early detection and prevention of development of these complications.¹⁵

The closest differential diagnosis of our cases is Hori's nevus. Hori's nevus also known as acquired bilateral nevus of Ota-like macules is an acquired dermal melanocytic disorder characterized by bilateral blue-gray to gray-brown macules of the zygomatic area and less often the forehead, upper outer eyelids, and nose.¹⁶ Hori's nevus differs clinically from bilateral nevus of Ota, as it often is an acquired condition, has less intense, brown-to-gray pigmentation, usually has symmetric involvement of skin of face, and spares eye, and the oro-nasal mucosa.¹⁷ Whereas, bilateral nevus of Ota generally presents at birth, has an intense blue-to-gray pigmentation involving the face asymmetrically and mucosal involvement is very frequent. On histopathology, nevus of Ota shows the presence of melanocytes in both the epidermis and dermis, whereas, in Hori's Nevus, deep dermal sparing is seen.¹⁶

Other differentials include melasma, solar lentigines, lichen planus pigmentosus, exogenous ochronosis, and

Table 1: Clinico-demographic factors and associations reported with Bilateral nevus of Ota

S. No.	Author	Year	Country	Demographics	Associated features
1.	Mohta et al. ¹⁷	2021	Rajasthan, India	26-year-old male, B/L face	Oral mucosal involvement nevus of Ito Port wine stain
2.	Harvey ⁶	2019	London, UK	5-year-old boy, B/L face	Nevus spilus
3.	Adil et al. ²⁰	2018	UP, India	19-year-old female, B/L face since birth	Hard palate mucosal involvement
4.	Syed et al. ³	2018	TN, India	22 year old female, B/L sclera, malar area	Hard palate mucosal involvement
5.	Sharan et al. ²³	2005	Australia	73-year-old Anglo-Indian female	Diffuse retinal pigmentation choroidal melanoma
6.	Rathi ²¹	2002	Siliguri, India	30-year-old female, B/L midface	Hard palate mucosal involvement
7.	Kolde et al. ²²	2001	Berlin	43-year-old male, periorbital skin involvement	Hard palate mucosal involvement
8.	Halasa ²⁴	1970	Lebanon	58-year-old male, B/L face involved	Malignant melanoma of ciliary body Vitiligo Nevi flammie

Mongolian spots. These can be differentiated by the type of pigmentation, history, and site of lesions.¹⁸ Persistent Mongolian spot occurs in adult with nevus of Ota, most commonly in individuals with bilateral lesions.¹⁹ However, no such association was appreciated in our cases. In two of our cases, hard palate mucosal involvement also was present. Similar findings were reported by Adil et al.,²⁰ Syed et al.,³ Rathi,²¹ and Kolde et al.,²² Apart from this, other associations have also been reported with bilateral nevus of Ota in other studies which is summarized in Table 1.

Nevus of Ota is particularly challenging to treat. Patient should be counseled on the benign nature of the condition. The first-line management is laser surgery, with Q-switched ruby laser (694 nm) surgery being the treatment of choice.²⁵ It targets dermal melanocytes and melanophages by their selective photothermal and photomechanical destruction, thereby decreasing the pigmentation.²⁶ Other lasers such as Q-switched alexandrite (755 nm) and Q-switched Nd: YAG lasers (1064 nm) may also be employed. A randomized, split-face clinical trial of Q-switched alexandrite laser versus Q-switched Nd: YAG laser in the treatment of bilateral nevus of Ota demonstrated equal efficacy of both lasers. However, patients tolerated QS Nd: YAG laser better than QS Alex laser as pain was more severe for QS Alex than for QS Nd: YAG laser.²⁷

CONCLUSION

Bilateral nevus of Ota is a very rarely encountered condition in the Indian subcontinent with only few cases reported in the literature. Majority of the patients consult dermatologists for cosmetic concerns as it poses significant psychosocial impact in patient's life. It is often misdiagnosed as Hori's nevus, melasma, lichen planus pigmentosus, and drug induced pigmentation. This case series contributes to the growing body of literature on the disease and will help the dermatologists in early diagnosis and treatment that would considerably reduce patient's stress later in life. This

study also emphasizes on the need for clinicians to be aware of its rare and potentially life-threatening complications, i.e., glaucoma and ocular/cutaneous melanoma and highlights the importance of regular biannual review with ophthalmologists and dermatologists.

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Authors' Contributions:

PK – Critical revision of the manuscript; **V** – Concept, design, design of study, analysis, and interpretation; **PUK** – Manuscript writing and manuscript editing; **RS** – Concept and design of the study and review of literature.

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