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Conjunctival blue nevus in a child – Case report and review of literature

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ABSTRACT

Purpose: To report a rare case of a conjunctival blue nevus in a child.
Observations: A 10-year-old girl underwent an excisional biopsy for an atypical growing melanocytic conjunctival lesion. The diagnosis of a conjunctival blue nevus was confirmed on histopathology. We describe the histopathology and the anterior segment optical coherence tomography features of a blue nevus in a 10-year-old child along with a review of literature.
Conclusion and importance: Conjunctival blue nevus is rare and has rarely been reported in a child. Multimodal imaging may help document lesion progression. This condition should remain in the differential for a growing, pigmented conjunctival lesion.

1. Introduction

Conjunctival nevus is a common benign melanocytic ocular surface tumor with a low risk of malignant transformation and is classified histopathologically as compound, sub-epithelial, junctional, and blue nevi.[1] Although other types of nevi are more common, conjunctival blue nevi are rare, representing only 0.6–3 % of ocular surface melanocytic lesions.[1,2] In the dermatology literature, blue nevi originate embryologically from neural crest cells but are arrested in their migration during the course of development and remain fixed in the deeper layers of the skin.[3] These lesions get their name because of the characteristic blue color that they exhibit from the scattering of light through the layers of the surface epithelium.[4]

We report a rare case of a 10-year-old female who presented with a growing melanocytic conjunctival lesion with an atypical pigmentation pattern in the right eye which, after biopsy and histopathological analysis, was confirmed to be a conjunctival blue nevus. We report the clinical course, histopathology, and the unique anterior segment optical coherence tomography (AS-OCT) features of the lesion along with a review of the existing literature.

2. Case report

A 10-year-old prepubertal female presented to the Stanford Ocular Oncology service with the chief complaint of a dark spot in the right eye that was first noted by her parents three years ago. She was otherwise healthy with a non-contributory past medical history of recurrent otitis media and systemic allergy to amoxicillin.

On ocular examination, visual acuity was 20/20 and intraocular pressure was 17 mm Hg in both eyes. The left eye slit lamp and bilateral fundus examinations were unremarkable. On slit lamp examination, the right eye had an irregularly shaped, minimally elevated conjunctival lesion encroaching the limbus but not involving the cornea with both episcleral and deep conjunctival pigmentation. No intralesional cysts were noted and the lesion measured 1.2mm × 1.4mm (Fig. 1A). AS-OCT (Heidelberg Spectralis, Heidelberg Germany) through the lesion (Fig. 1B) demonstrated a deep conjunctival stromal lesion with hyperreflectivity and shadowing without cysts but with intact epithelium and no scleral invasion. The differential diagnosis included primary acquired melanosis, atypical conjunctival nevus, or less likely a malignant conjunctival melanoma. At this time, observation was elected.

At six months of follow-up, visual acuity was still 20/20 in both eyes. Slit lamp examination of the right eye demonstrated an increase in

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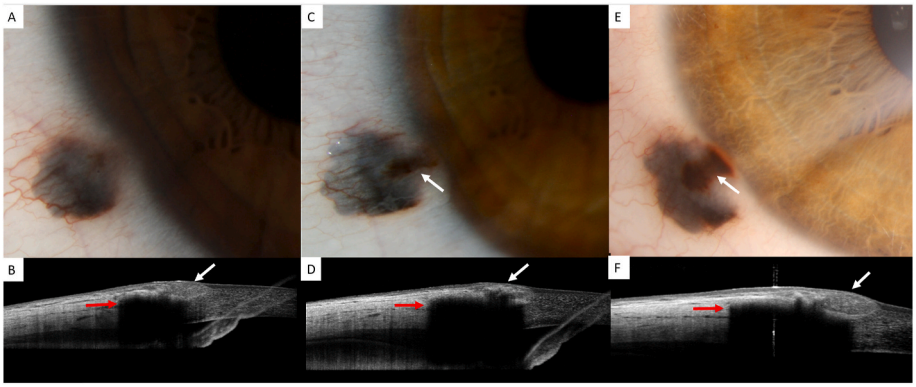

Fig. 1. A - Clinical image from the first visit – Focal, well-demarcated, 1.2 × 1.4 mm in size, minimally elevated, pigmented, brown-black conjunctival lesion, with no cysts and mobile overlying conjunctiva, just encroaching the limbus, not involving the cornea. Fig. 1B - anterior segment optical coherence tomography (AS-OCT) Horizontal section through the lesion – suggests a homogenous mass within the conjunctival stroma (white arrow), with no intrinsic cysts and dense posterior shadowing due to pigmentation (red arrow). Fig. 1C - Clinical image from the second visit – Similar lesion as compared to the previous visit but increased elongation and a new focus of irregular pigmentation within an area of lighter pigmentation close to the limbus (white arrow). Fig. 1D - AS-OCT Horizontal section through the lesion – demonstrated new hyperreflectivity and shadowing corresponding to the new focus of dark pigmentation (white arrow). Fig. 1E - The conjunctival lesion enlarged with increased pigmentation toward the limbus (white arrow) and pigmentation within the center of the lesion and extending into the peripheral cornea. Fig. 1F - AS-OCT at this visit was suggestive of a deeper stromal lesion with focal areas of bright hyperreflectivity and shadowing. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

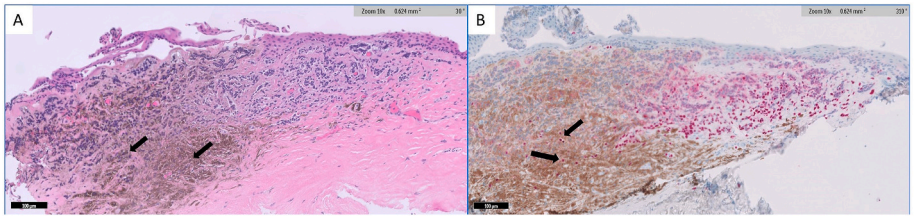

Fig. 2. A - Hematoxylin and eosin staining of a section of the conjunctival biopsy tissue showing heavily pigmented dendritic melanocytic cells in the conjunctival substantia propria, arranged as sheets, surrounded by collagen and melanophages (black arrows). (Original magnification: 10×). Fig. 2B - SOX-10 is a nuclear red stain. Nuclear staining of the pigmented spindle-shaped melanocytes is observed, indicating SOX-10 expression (black arrows). This staining pattern confirms the presence of SOX-10 positive cells, supporting the diagnosis of melanocytic origin. (Original magnification: 10×). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

conjunctival pigmentation within the lesion with radial elongation to 1.1 × 1.5 mm with a new focus of irregular, episcleral dark pigmentation within an area of lighter pigmentation close to limbus extending over the lesion radially with mobile overlying conjunctiva (Fig. 1C). The corresponding AS-OCT (Fig. 1D) demonstrated a new focus of hyperreflectivity and back shadowing corresponding to the new area of dark pigmentation. Again, observation was elected.

At one year follow-up, the visual acuity was maintained but the lesion had increased dark hyperpigmentation. The superficial pigmentation had increased along the radial margins and now the pigmentation had a bi-level appearance with the previously noted dark episcleral pigmentation and a more superficial tongue of brown hyperpigmented tissue within the center and extending into the peripheral cornea. Corneal involvement included focal pigmentation of the corneal subepithelial layer by approximately 0.5mm (Fig. 1E). The AS-OCT now demonstrated a deeper conjunctival stromal lesion with focal areas of bright hyperreflectivity and shadowing (Fig. 1F). Further, there were no cysts, as typically seen with a benign conjunctival nevus and corneal involvement was now confirmed along the peripheral limbus demonstrating sub epithelial involvement.

Due to lesion progression, corneal involvement, and lack of cysts within the lesion on AS-OCT, excisional corneal, conjunctival, and lamellar scleral biopsy was elected by the parents. First, an absolute alcohol corneal epitheliectomy was performed followed by a wide (2–3mm) margin excisional conjunctival biopsy. Intraoperatively, the conjunctival portion appeared full thickness and approached the scleral margin; therefore to ensure complete resection, a partial lamellar scleral resection was performed. The corneal pigmentation extended beneath the epithelial surface and was scraped flush to the anterior stroma. Freeze-thaw cryotherapy was applied along the cut conjunctival edges and the ocular surface was reconstructed with amniotic membrane.

On histopathological analysis, hematoxylin and eosin staining of the conjunctiva demonstrated pigmented dendritic melanocytes admixed with dense collagen bundles in the conjunctival stroma (Fig. 2A). SOX-10 staining highlighted the pigmented spindle-shaped melanocytes (Fig. 2B). The final diagnosis was conjunctival blue nevus without scleral involvement.

Postoperatively, no recurrence was noted on the conjunctival surface, though a minute focus of anterior stromal corneal pigmentation persists. No systemic surveillance was indicated, and no signs of ocular recurrence were noted.

3. Discussion

We herein report an atypical case of a rare conjunctival blue nevus in a child with documented enlargement, corneal involvement, and unique AS-OCT findings not typically noted in more common conjunctival nevi. “Blue nevus” was first described by Max Tieche in 1906.[5] Blue nevi usually occur on the skin but have been reported in various sites including the ocular surface.[1,6,7]

The name blue nevus may not be helpful to ophthalmologists when attempting to make a clinical diagnosis of this condition. When these nevi occur in the skin, they tend to appear blue in color due to the scattering effect of light as it passes through a colloid dispersion - known

Table 1
Review of clinical findings in patients with conjunctival blue nevus.

Author (Year)/ Journal name	Report type	Age (in years)	Sex	Location of nevus	No. of lesions	Excision	Pathology	Size (mm)	Recurrence	Progression to melanoma
Blicker[10](1992) Ophthalmology	Case report	71	F	OD – lower lid and inferior fornix	1	Excision of the right lower lid forniceal lesion and multiple conjunctival and lid margin biopsy	Melanocytic proliferation within substantia propria without involvement of epithelium spindle-shaped cells	N/A	N/A	No
Demirci[14](2000) Arch Ophthalmol	Case report	41	M	OS – Inferior fornix and inferior bulbar conjunctiva	1	"No-touch" technique excisional biopsy and double freeze-thaw cryotherapy	Melanocytic proliferation in the substantia propria with no junctional or epithelial component. Heavily pigmented dendritic cells with bland nuclei In one area, nuclear atypia indicative of malignant transformation into melanoma was present	N/A	13 months follow-up no recurrence	Yes
Shields[1] (2004) Arch Ophthalmol.	Case series	51 (Mean)	–	2 – Bulbar 1 – Fornix 1 – Tarsal	4	N/A	N/A	N/A	N/A	1
Berman[15] (2008) Survey of Ophthalmology.	Case report	55	F	OS – Limbal, bulbar, tarsal, plical and fornicial conjunctiva. All tumors were within conjunctival stroma but one showed evidence of intraepithelial pigmentation	6	"No-touch" technique excisional biopsy and double freeze-thaw cryotherapy. Partial lamellar conjunctivosclero-keratectomy	Pigmented spindle-shaped cells without junctional or epithelial component. Intraepithelial pigmentation with no atypical melanocytic hyperplasia	Bulbar 0.75 x 0.75 Limbus 7 x 6 Plica 3 x 2 Tarsus 3.5 x 3 Fornix 5 x 4 Fornix 2 x 2	12 months follow-up with no recurrence	Yes
Jakobiec[12] (2010) Cornea.	Case report	13	F	OD – Epibulbar conjunctiva (during surgery, tumor noted to be attached to sclera)	1	Initial: Subtotal excisional biopsy (Did not get all the lesion) Second: Excision of the conjunctivo-corneal lesion with the reconstruction of the conjunctiva with amniotic graft and, sclerectomy cryotherapy.	1st Path: Spindled pigmented cells growing within conjunctival connective tissue 2nd Path: Spindle cells	1st surgery: 1 x 1 2nd surgery: 5 x 1 x 1	After initial surgery: Over 2.5 years, the lesions recurred & become more elevated. After second surgery: 1.5 years follow-up no recurrence	No
He[16] (2017) Ann Clin Lab Sci.	Case report	29	M	OD – Perilimbal conjunctiva	1	"No-touch" technique excisional biopsy and double freeze-thaw cryotherapy	Heavily pigmented dendritic cells. Macrophages with melanophages were present surrounding tumor cells	16 x 8 x 6	8 years follow-up; no recurrence	Yes
Quhill[7] (2017) Ocular Oncology and Pathology.	Case report	16	M	OD – Bulbar conjunctiva	1	Incisional biopsy	Melanised cells in the subepithelial zone. spindled and wavy with circular melanosomes	3 x 2 x 1	N/A	No
Sayed-Ahmed[6] (2018) HHS Public Access.	Case series	55 ± 15 (Mean)	12 M 9 F	13 – Bulbar, 3 – Tarsal, 3 – Fornix, 2 –	23	"No-touch" technique excisional biopsy	2 patients – cellular blue nevi 19 patients – Simple blue nevi	Largest: 10 x 8 Smallest: 0.5 x 0.5	N/A	No follow-up 20.2 months ±28, (range

(continued on next page)

Table 1 (*continued*)

Author (Year)/ Journal name	Report type	Age (in years)	Sex	Location of nevus	No. of lesions	Excision	Pathology	Size (mm)	Recurrence	Progression to melanoma
				Caruncular, 1 – Episcleral and 1 at limbus.			All 23 had spindle-shaped nevus cells in substantia propria	Most lesions were between ~1.5 - 3 x 1.5–4 mm. Exceptions such as 6.5 x 5; 7x4; 6x1; 5.5 x 2.5		2 weeks -103 months)
Roelofs[17] (2020) Ocular Oncology and Pathology.	Case report	61	F	OS – Sub conjunctival lesion in the nasal perilimbal area. (Perilimbal sclera from 8 to 10 o'clock)	1	Lamellar sclerectomy	Localized melanocytic proliferation with features of blue nevus arising within the area of ocular melanocytosis	5 x 3 mm	weeks later, a small area of pigmentation was noted along the superior margin of the previous resection	No
Charles[18](2022) Ophthalmic Plastic and Reconstructive Surgery.	Case report	42	F	OS – Tarsal surface of the left lower eyelid	1	Wedge resection biopsy	Nonpigmented spindled and epithelioid cells. Melanocytes and melanophages	2 x 2 mm	N/A	N/A
Suller[19] (2022) Orbit.	Case report: 1	32	F	OS – Upper eyelid involving meibomian gland line and muco-cutaneous junction.	1	Incisional biopsy	Proliferation of spindled to ovoid melanocytes and pigmented macrophages	7 x 5.5 mm	11 months follow-up no tumor recurrence	No
Suller[19] (2022) Orbit.	Case report: 2	86	F	OS – Inferior lacrimal punctum,	1	"No-touch" technique excisional biopsy and double freeze-thaw cryotherapy.	Subepithelial/ dermal proliferation of heavily pigmented spindled melanocytes in sclerotic stroma	1.5 x 1.5 mm	4 months follow-up no tumor recurrence	No
Mruthyunjaya (2024) current case	*Case report*	*10*	*F*	*OD – Minimally elevated episcleral pigmentation with mobile conjunctival and radial pigmentation to edge of limbus. Focal pigmentation within the corneal bowman's layer by 0.*5mm	*1*	*Post excisional biopsy, partial scleral dissection, amniotic membrane, cryotherapy.*	*Benign nevus, favor blue nevus (melanocytes extend to the transected base of the biopsy)*	*2 × 2.4 mm*	*2 months follow-up no tumor recurrence*	*No*

OD Ocular dexter, OS Ocular sinister, N/A Not available.

as the Tyndall effect – which, in these cutaneous cases, would be the melanin found in the dermal layers causing light to scatter and changing the color viewed by the naked eye. In addition, the thickness and depth of the nevus also play a role in the shade of coloration. When blue nevi occur on the ocular surface, they tend to take on a grey-brown appearance and resemble other forms of pigmented conjunctival nevi, but not a characteristic blue color.[4] This is due to the difference in the thickness of the conjunctiva compared to the skin, as the thin conjunctiva does not cause adequate light disturbance to reflect other wavelengths and hence gives them the usual brownish color seen with the more common conjunctival nevi.

On slit lamp examination, blue nevi appear as well-circumscribed, brown-black, focal, elevated conjunctival lesions with an absence of intralesional cysts, the latter differentiates them from benign common junctional, compound, and subepithelial nevi.[6,8,11] On histopathology, blue nevi are characterized by the presence of heavily pigmented, loosely arranged spindle or dendritic cells within the conjunctival substantia propria. On immunohistochemistry, the melanocytic cells are positive for S-100 protein, Melan-A, and SOX-10. Blue nevi are typically located deeper into the conjunctival stroma, similar to the current case, whereas junctional nevi are arranged in discrete nests within the conjunctival epithelium or the epithelial and subepithelial junction.[8] Compound nevi develop from junctional nevi as the nevus cells descend from the epithelium into the superficial substantia propria.[8] Lesions that are noted to grow or are large at presentation can be removed.

Pigmented conjunctival lesions in children and blue nevi in particular are usually managed by observation. A study by Negretti et al. included 77 pediatric patients with a mean age of 12 years (range 4–20),

of which 65 (84 %) were observed. While 12 (16 %) underwent excisional biopsy, only one had conjunctival melanoma, suggesting a low rate of malignancy in this population.[9] In a case series of 23 cases of conjunctival blue nevi in 21 patients that were removed, all underwent excisional biopsy followed by double freeze-thaw cryotherapy. None of these recurred or presented with new evidence of conjunctival melanoma over a mean 20.2 months (±28, range 2 weeks–103 months) follow-up period.[6] However, in our case, due to the accelerated growth of the lesion, atypical location and to rule out malignancy, surgical excision was decided.

The diagnosis and follow-up of conjunctival lesions can be aided using AS-OCT. Shields et al. and Huange et al. both reported AS-OCT features of conjunctival nevi and identified intralesional cysts, which are sometimes hard to see on clinical examination, as an important prognostic factor for benign lesions.[1,8] On AS-OCT of our patient, the nevus appears as a well-demarcated lesion with intense back shadowing, due to the heavy pigmentation, but without clear cysts. We were able to demonstrate the evolution of the blue nevus on serial imaging sessions. In a novel finding, AS-OCT identified progressive corneal involvement – subepithelial at the level of Bowman's layer-corneal stromal junction. This finding, which was confirmed on histology, aided in our surgical planning to include corneal epitheliectomy and to avoid deep stromal dissection (Fig. 1).

Compared to its cutaneous counterpart, conjunctival blue nevus is a rare condition as outlined in Table 1. The earliest case of a conjunctival blue nevus was reported by Blicker in 1992.[10] In a study of conjunctival nevi in adult patients by Shields et al. only 4 out of 410 (1 %) presented with blue nevi. (Table 1).[1] The mean age of patients with blue nevi was 51 [range 40–70].[1] Sayed-Ahmed et al. reported a large case series of 21 patients with 23 blue nevi of the ocular surface with an average age of 55 years and ranged from 27 to 82 years, the most common site was the bulbar conjunctiva, followed by tarsal and palpebral conjunctiva.[6]

Further, the current case is unique in that the histopathologically confirmed blue nevus was identified in a young child. Conjunctival melanocytic nevi are common in the pediatric population. In a study of 57 pediatric conjunctival melanocytic lesions, McDonnell et al., identified only one blue nevus under the age of 20, but the exact age of the patient was not reported.[11] The youngest case ever reported of a conjunctival blue nevus was by Jacobeic and colleagues in 2010 where a 13-year-old female was diagnosed with an epibulbar conjunctival blue nevus.[12] The diagnosis was confirmed on histology, but the lesion recurred after two and a half years, and the patient had to undergo a second surgery for its complete excision.[12] This indicates the rarity of ocular blue nevus in the young population and highlights the unique nature of our patient who was diagnosed at the age of 10 years.

Malignant transformation of blue nevus is rare. The term "malignant blue nevus" or "blue nevus like melanoma" has been applied to several different clinicopathologic entities, arising from a cellular or common blue nevus.[13] The latter are noted to be aggressive and metastasize to different regions of the body especially if the diagnosis is delayed.[18] In the ophthalmic literature, malignant melanoma arising from blue nevus has been reported in only two cases (Table 1) and neither in children.[1,14] Our patient will be monitored lifelong for signs of recurrence which may increase the risk of malignant transformation.

4. Conclusion

We report a case of a 10-year-old female with a rare, histologically confirmed, blue nevus of the conjunctiva and peripheral cornea. The clinical presentation differed from a typical cystic conjunctival nevus with documented growth. AS-OCT can be used to aid in diagnosis and surgical planning. Though rare, we suggest that long-term follow-up is required for these lesions to monitor for the risk of growth, recurrence, and malignant transformation.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

CRediT authorship contribution statement

Yasser Yahya: Writing – original draft. **Purna Nangia:** Writing – review & editing, Writing – original draft. **Hunain Ahmad:** Data curation. **Rachel L. Frauches:** Writing – review & editing. **Jonathan H. Lin:** Supervision. **Prithvi Mruthyunjaya:** Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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