Corneal limbal xanthogranuloma in Erdheim-Chester disease

Adult orbital xanthogranulomatous disease is a rare non-Langerhans cell histiocytic condition with 4 clinical subtypes: adult-onset xanthogranuloma, adult-onset asthma with periocular xanthogranuloma, necrobiotic xanthogranuloma (NBX), and Erdheim-Chester disease (ECD). We report, to our knowledge, the first case of ECD with limbal infiltration.

A 52-year-old woman presented with xanthomatous cutaneous lesions around her eyes and flexural folds of submammary skin. Subsequent full body imaging revealed sclerotic lesions in her sternum, left rib, and bilateral femurs and tibias. There were no intracranial or orbital lesions. Bone biopsy of the sternal lesions confirmed ECD. The patient was treated with oral steroids and then cladribine by hematology. Two-monthly interval imaging with positron emission tomography showed stable systemic disease.

The patient was referred to the eye clinic with a progressively enlarging left ocular lesion that had been present since her initial diagnosis. Ocular examination revealed a 5 mm well-defined yellow deposit along the superonasal limbus (Fig. 1). There were multiple yellow deposits along her nasal lower eyelid bilaterally. She did not have any optic neuropathy, and her orbital examination was normal.

Biopsy of the lesion showed a subepithelial stromal deposit of foamy macrophages with bland nuclear features (Fig. 2). The cells showed pale eosinophilic cytoplasm with indistinct cytoplasmic borders and ovoid nuclei on highest magnification. Strong and diffuse immunoreactivity for CD68 and CD163 confirmed a histiocytic nature. The lesion also was positive for factor XIIIa but negative for Langerin, CD1A, S100, and BRAF V600E. These identical immunohistochemical features were demonstrated in a previous sternal bone biopsy for this patient.

Fig. 1—Clinical photograph showing xanthomatous lesion on limbus in left eye and multiple lower lid xanthelasmas.
Systemic ECD manifestations typically involve the metaphysis of lower extremity bones, skin, heart, lungs, kidneys, large blood vessels, and retroperitoneal space. Ocular involvement of ECD has been reported in the orbit, lacrimal gland, recti muscles, lids, and conjunctiva. In general, xanthogranulomatous epibulbar lesions are rare and may appear as yellow, elevated lesions with irregular borders showing fixation to sclera and extension to the plica semilunaris. Our case is the first documentation of an ECD xanthogranulomatous lesion with limbal involvement.

Histologically, ECD typically shows foamy histiocytes with small nuclei and surrounding fibrosis, multinucleated giant cells, and Touton giant cells. Immunohistochemistry shows histiocytes that are positive for CD68, CD163, factor XIIIa, and fascin and negative for CD1a and CD207 (Langerin). S100 is usually negative but can be weakly or focally positive in 20%–30%. The BRAF V600E mutation is present in over half of ECD cases. Our case of corneal limbus ECD demonstrated a majority of typical pathologic and immunohistochemical features in keeping with the diagnosis.

A pooled study of case series has previously been performed to assess clinical and immunohistochemical features of adult orbital xanthogranulomatous disease subtypes. Periocular skin lesions are present in 95% of of adult—onset asthma with periocular xanthogranuloma cases, 85% of NBX cases, 50% of adult—onset xanthogranuloma cases, and 42% of ECD cases. These conditions are generally positive for CD68, CD163, and factor XIIIa. Necrobiosis with palisading epithelioid histiocytes is most commonly seen in NBX.

Differential diagnoses for xanthogranulomatous epibulbar lesions include juvenile xanthogranuloma, xanthoma disseminatum, Langerhans cell histiocytosis, limbal amyloidosis, fibrous histiocytoma, and Rosai-Dorfman disease. These diagnoses may be distinguished from ECD by their clinical features and histologic characteristics.

In conclusion, we report the first known case of ECD involving the corneal limbus. For patients with known ECD who present with corneal lesions, it may be a manifestation of their disease and may be appropriately managed with excisional biopsy. In patients with no known disease, ophthalmologists should consider ECD as a differential diagnosis for corneal lesions.

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Rare case of extramacular choroidal macrovessel

Choroidal macrovessel (CM) is a rare, mostly unilateral vascular anomaly of the choroidal circulation. These abnormally large vessels may cause disturbances in the overlying retinal pigment epithelium (RPE) and the development of subretinal fluid. Some CMs can even masquerade as a choroidal tumour or parasitic infestation. Reports showing early filling of CMs during indocyanine green angiography (ICGA) suggest that most CMs are arterial in nature. The short posterior ciliary circulation is comprised of a medial and lateral posterior choroidal artery (PCA); the latter may represent the origin of most CMs and may explain why almost all previously reported CMs arise in the macula. An extramacular origin for CM is rare, and to our knowledge, there are only 2 cases described in the literature. Of these 2 cases, only 1 was illustrated with retinal imaging, which appears to show an origin of the anomalous vessel within the macula.

In this correspondence, we describe and illustrate an extramacular CM that clearly originates in an extramacular location superior to the optic disc, as shown with ultra-wide-field (UWF) ICGA. This work was completed at the retinal disorders and ophthalmic genetics division at the Stein Eye Institute, University of California—Los Angeles.

A 58-year-old patient was referred for an evaluation of floaters and photopsia in the left eye for 5 days. Past medical history included hypertension and hypothyroidism secondary to thyroidectomy to treat thyroid cancer 8 years prior. Ocular history was remarkable for anisometropic myopia with a spherical equivalent of −2.25 D in the right eye and −6.50 D in the left eye.

On examination, visual acuity was 20/25 OD and 20/20 OS with normal anterior segments OU. Ophthalmoscopy demonstrated RPE mottling superior to the optic disc OS (Fig. 1A). UWF fundus autofluorescence showed a corresponding area of hyperautofluorescence (Fig. 1B). Optical coherence tomography B-scans through this region showed a large (380 μm in height) choroidal vessel with overlying subretinal fluid, focal elevation of the RPE–Bruch membrane complex, and elongated photoreceptor outer segments (Fig. 2). UWF ICGA revealed early arterial filling of a large dilated and tortuous extramacular CM originating superior to the optic disc and extending into the superior periphery without late leakage or staining (Fig. 3A). There was marked asymmetry of choroidal venous drainage, with reduced venous drainage directed toward the inferonasal vortex ampulla (Fig. 3B).

Otero-Marquez et al. reported a possible association of CM with myopia. They reviewed the fundus images of 13 cases of CM and identified features of high myopia, including fundus tessellation and peripapillary atrophy in 11 of these patients. The patient reported herein exhibited high myopia with a refraction of −6.50 D OS. Of interest, retinal arterial tortuosity was identified only in this subject’s left eye. The coexistence of CM with retinal arterial tortuosity in other non-Langerhans cell histiocytoses. Blood 2012;120:2700–3.


Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this correspondence.