Novel insights in Erdheim-Chester disease using *in vivo* reflectance confocal microscopy

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CLINICAL PRESENTATION

A 61-year-old man presented with a 3-year history of slowly progressive yellowish plaques involving both eyelids (Fig 1). He also complained of intermittent retro-orbital headache, bilateral lower extremity pain, and increasing fatigue over the preceding year. His medical history was otherwise unremarkable.

CONFOCAL MICROSCOPY APPEARANCE

Upon reflectance confocal microscopy, epidermal examination showed a normal honeycomb pattern. At the dermal-epidermal junction and upper dermis, clusters of multinucleated roundish structures were found along with discoid-shaped bright cells (Fig 2).

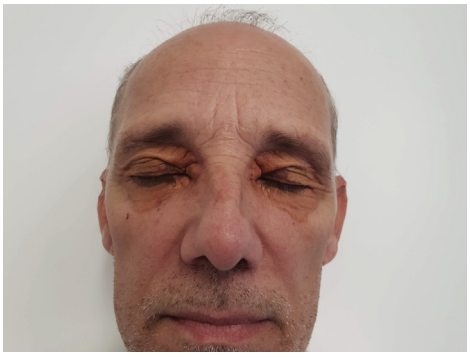

Fig 1. Erdheim-Chester disease, clinical presentation. Extensive yellowish periorbital xanthelasma-like lesions.

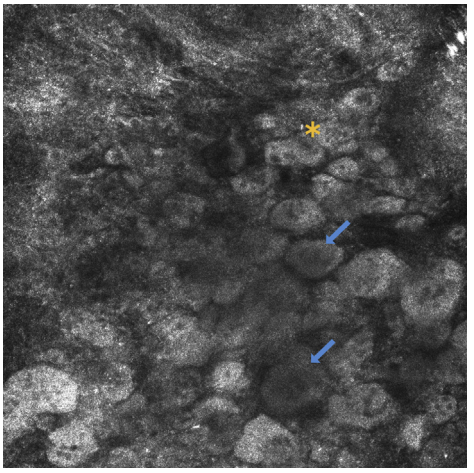

Fig 2. Erdheim-Chester disease, reflectance confocal microscopy appearance. Basic image (0.5 × 0.5 mm) at the superficial dermis level enables the observation of large, multinucleated, and hyperrefractile roundish structures (*yellow asterisk*) together with discoid-shaped cells with a peripheral bright ring (*blue arrows*).

HISTOLOGIC DIAGNOSIS

Histopathologic examination revealed papillary and reticular dermis filled with foamy histiocytes admixed with scattered Touton giant cells and lymphocytes (Fig 3, *A*). Immunohistochemically, the foamy histiocytes were $CD68^{+}$ (Fig 3, *B*) and $S\text{-}100^{-}$ and $CD1a^{-}$.

Further investigation found retro-orbital masses, osteosclerosis of the distal long bones, pleural and

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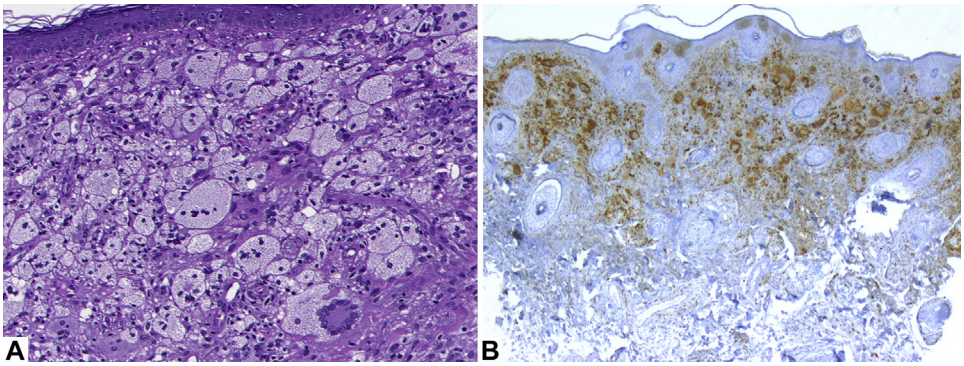

Fig 3. Erdheim-Chester disease, histopathologic examination. **A**, Dermal infiltrate of foamy histiocytes and Touton cells. Thickened collagen bundles and increased fibroblastic proliferation. **B**, CD68 immunostaining showing numerous positive histiocytes. (**A**, Hematoxylin-eosin stain; original magnification: ×200; **B**, CD68 stain; original magnification: ×40.)

pericardial effusion, and retroperitoneal fibrosis. A diagnosis of Erdheim-Chester disease was made, and the patient was started on vemurafenib after BRAF V600E mutation was identified.

KEY MESSAGE

Erdheim-Chester disease is a rare multisystemic histiocytosis that was recently recognized as a neoplastic disorder.[1] Its most common presentation is periorbital xanthelasma-like lesions, which should be differentiated from xanthelasma palpebrarum and other periorbital xanthogranulomas.[2]

The role of reflectance confocal microscopy has already been described for the diagnosis of other non-Langerhans histiocytoses.[3] In the present case, the confocal features of multinucleated roundish structures and discoid-shaped bright cells corresponded well to those of foamy histiocytes and Touton cells, respectively. These novel confocal features should be regarded in correlation to all clinical data because adult xanthogranulomatous diseases share histopathologic similarities. A skin biopsy is still required for confirmation and it permits molecular studies that are important for treatment decisions.

Therefore, even if present in only one quarter of patients, cutaneous findings and adequate confocal and histopathologic examinations will uncover important clues to further systemic investigation.

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