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LETTER TO THE EDITOR

Line-field confocal optical coherence tomography, optical coherence tomography and reflectance confocal microscopy in a case of cutaneous sarcoidosis

Dear Editor,

Chronic sarcoidosis is a rare granulomatous multisystem disease and may be life threatening when lung-involvement is present. Cutaneous sarcoidosis (CS) manifests in up to 35% of the cases and may be an apparent indicator to early diagnosis.[1,2] It is crucial to distinguish between unspecific CS lesions, related to granulomatous inflammation, and specific ones, related to granuloma infiltration of the skin.[1] Usually,

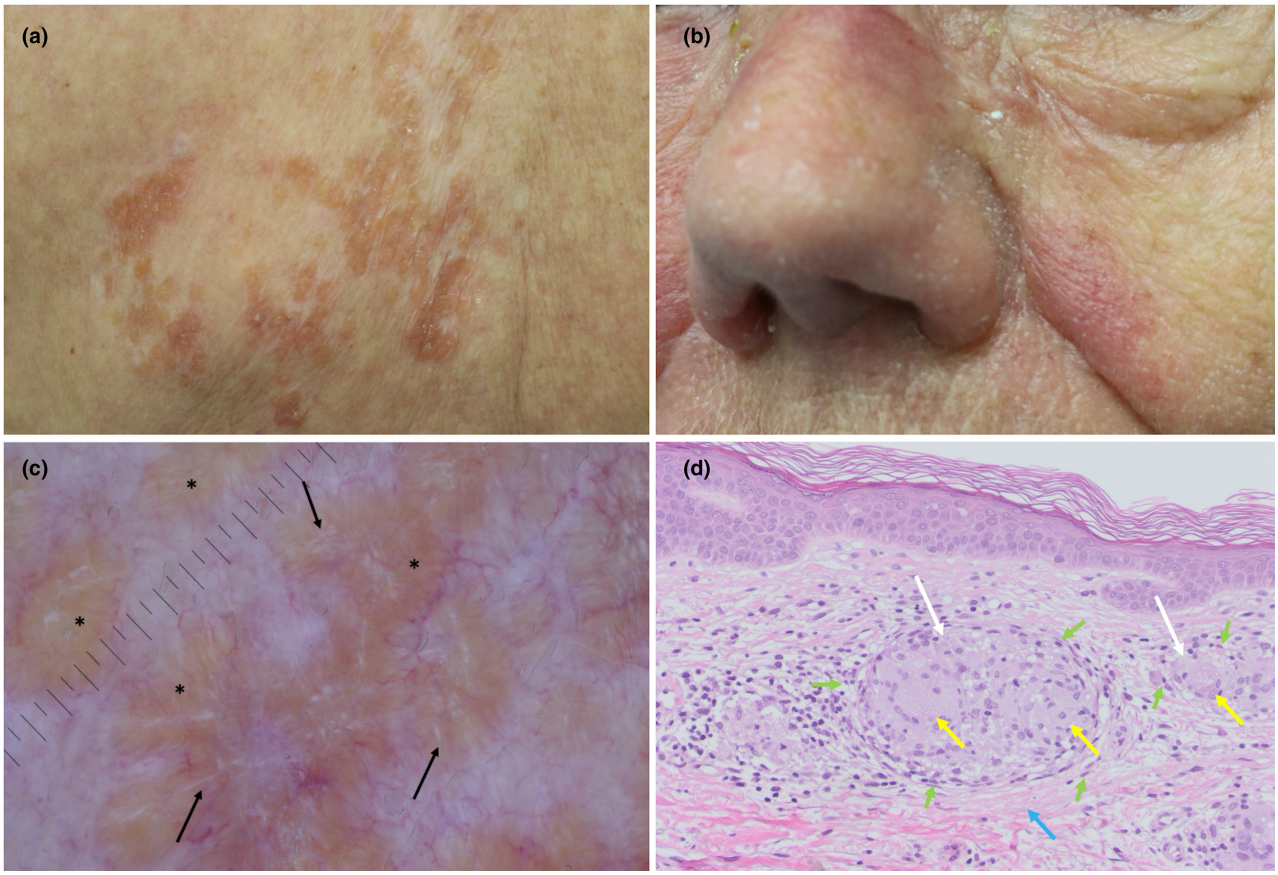

FIGURE 1 Clinical photographs (a, b), polarized contact dermoscopy (c) and histology (d) of plaque-type cutaneous sarcoidosis and Lupus pernio. (a) shows large brown-to-red plaques with atrophic regression present on the upper left back. On the right red-to-purple plaques on the nose as well as in the nasolabial folds and on the cheeks can be seen in (b) (images were taken with a Canon EOS 750D). (c) shows the dermoscopy of the back with multiple linear and branching vessels over yellowish- orange globular as well as leaf-like structures (black asterisk) with scar-like depigmented areas (black arrow). The background appears whitish atrophic with multiple fine vessels (images were captured using a DermLite® Foto II Pro dermoscope attached to a Nikon D500 digital camera, 3 Gen Inc.). (d) illustrates the histopathology of the same lesion on the back. The well-defined nodules (white arrows) correspond to sarcoidal noncaseating granulomas in the superficial dermis with epitheloid cells, multinucleated giant cells (yellow arrows) and a lymphocytic infiltrate (green arrows) surrounded by fibrous tissue (blue arrow) (haematoxylin–eosin stain; original magnification: ×10).

skin findings of CS are multiform and may imitate other skin diseases.[3–5] Hence, histology is the gold standard to detect sarcoidal noncaseating granulomas, conglomerates of epithelioid histiocytes, giant cells and macrophages. While for diagnosis of ocular sarcoidosis, optical coherence tomography (OCT) is used for visualization of inflammation, OCT is not routinely used in the diagnosis of CS.[6] Only two case reports on CS using reflectance confocal microscopy (RCM) exist.[7,8] Line-field confocal OCT (LC-OCT) is a further development of OCT, allowing visualization of epidermal and dermal (non-)pigmented structures at cellular resolution, using en-coupe/en-face and 3D imaging modalities.[9]

On the upper left back of a 78-year-old woman, a large brownish plaque was noticed (Figure 1a). Red-to-purple plaques and nodules on the nose, nasolabial folds and on both cheeks were retrospectively identified as lupus pernio (Figure 1b). The lesion on the back was examined using dermoscopy, OCT (VivoSight Dx®, Michelson Diagnostics Ltd), LC-OCT (deepLive™®, DAMAE Medical) and RCM (VivaScope® 1500, MAVIG GmbH).

Polarized contact dermoscopy revealed multiple linear and branching vessels, yellowish-orange globular and leaf-like structures with depigmented scar-like areas. The background had a whitish atrophic appearance with multiple fine branching vessels (Figure 1c). In 3D-LC-OCT subepidermal hyporeflective ovoid formations, embedded into hyperreflective connective tissue, were observed (Figure 2a). OCT provided an overview by depicting multiple dark nodules due to a deeper penetration depth, revealing dermal hypervascularization (Figure 2c). Using RCM, hyporeflective ovoid nodular structures, increased surrounding vascularization and inflammatory infiltrates were visualized in the papillary dermis (Figure 2d). In en-face-LC-OCT and RCM bright beaded-like structures and enlarged hyperreflective cells within each individual nodule surrounded by a bright stroma and accompanied by smaller hyperreflective cells were seen (Figure 2b,d). From the specific site where dark nodules were found, punch biopsy was taken and sarcoidal non-necrotizing granulomas were confirmed histologically (Figure 1d). In correspondence to histology, RCM and (LC-)OCT were able to identify hyporeflective round-to-ovoid subepidermal structures as granulomas. The surrounding bright stroma corresponded well with concentric fibrosis. Using LC-OCT, the cellular resolution allowed the possible identification of smaller hyperreflective cells as lymphocytes

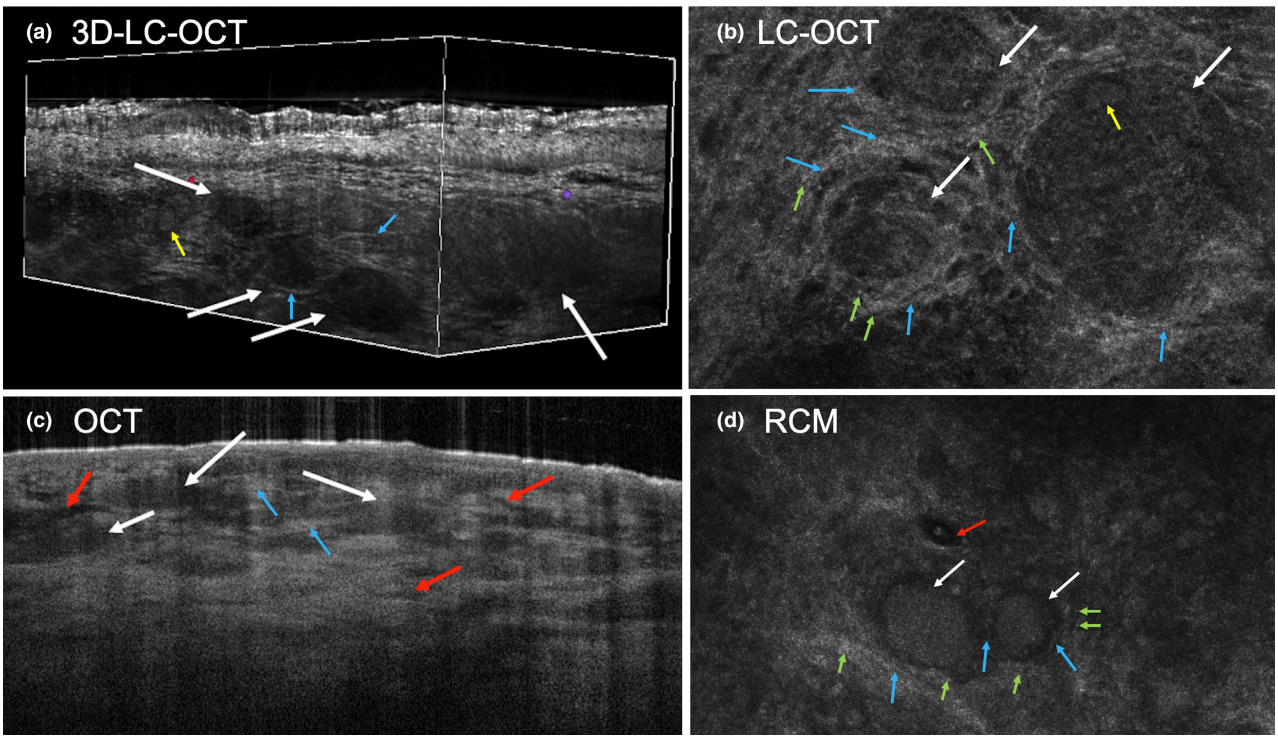

FIGURE 2 Reflectance confocal microscopy (RCM), optical coherence tomography (OCT), horizontal and 3D-view of line-field confocal optical coherence tomography (LC-OCT) of Plaque-type cutaneous sarcoidosis. (a, b) Show dark elliptic nodules (white arrows) surrounded by bright connective tissue (blue arrows) corresponding to granulomas in a cellular resolution in the 3D and horizontal view of LC-OCT (deepLive™® DAMAE Medical, Paris, France, image size: $1.2 \times 0.5\,mm^2$, lateral and axial resolution: $1.1\,\mu m \times 1.3\,\mu m$). Due to the cellular resolution enlarged hyperreflective cells (yellow arrows) within the granuloma may correspond to giant cells, whereas smaller hyperreflective cells (green arrows) in the surrounding of the granuloma may be lymphocytes. The same features can be seen in histology (Figure 1d). Structural OCT in (c) illustrates multiple ovoid hyporeflective nodules (white arrows) in an hyperreflective surrounding stroma (blue arrows) with enlarged blood vessels (red arrows) (VivoSight Dx®, Michelson Diagnostics Ltd, Maidstone, Kent, United Kingdom, image size: $6 \times 1\,mm^2$, lateral and axial resolution: $7.5\,\mu m \times 10\,\mu m$). RCM (VivaScope® 1500, MAVIG GmbH, Munich, Germany, image size: $500\,\mu m \times 500\,\mu m$, lateral and axial resolution: $1\,\mu m \times 3–5\,\mu m$) at a depth of approximately $100\,\mu m$ zoomed in (d) and in comparison, with horizontal view of LC-OCT (b) shows also corresponding hyporeflective round-to-ovoid nodules with bright beaded-like structures (white arrows) surrounded by a small rim of fibrous tissue (blue arrows) with single hyperreflective inflammatory cells (green arrows) and an increased vascularization (red arrows).

and enlarged hyperreflective cells within the granuloma as possible giant cells (Figure 2a,b), whereas OCT cannot visualize cellular structures due to its lower resolution. Necrotizing granulomas would look different showing a dark centre.

Since CS is a masquerader in dermatology, we were encouraged to see that subepidermal granuloma, the groundbreaking feature in histology, can be visualized using RCM and (LC-) OCT. By dermoscopy only, the identification of CS might be challenging since diverse variants are described.[3–5] When diagnosis of CS is considered, RCM and (LC-)OCT may provide a feasible and noninvasive approach for lesion imaging and may help to narrow the diagnosis of CS. Especially in cases where the skin region of interest is vulnerable to punch biopsy, noninvasive imaging may allow identification of subepidermal granuloma and to obtain a more significant histological result, when the region of interest is imaged and identified prior to biopsy. This might be significant, since in 80% cases, CS develops before or at the time of diagnosis of the systemic form.[10] Detection of subepidermal elliptic dark structures using (LC-) OCT and RCM, corresponding to granulomas in histology, may help to guide the diagnosis of CS eventually.

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CONFLICT OF INTEREST STATEMENT
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DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT
The patient in this manuscript has given written informed consent to the publication of her case details.

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