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Single Case

Efficacy of Siltuximab and 1,927 nm Fractional Laser for the Treatment of Cutaneous Manifestations in Castleman's Disease: The Role of Dermoscopy and Reflectance Confocal Microscopy for Lesion Evaluation

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Keywords
Castleman's disease · Fraxel · Monoclonal antibody · Multicentric disease · Reflectance confocal microscopy

Abstract
Introduction: Multicentric Castleman's disease (MCD) with cutaneous involvement has rarely been discussed in dermatologic literature, with few reports. Cutaneous lesions in MCD may induce deep scars, causing a significant impact in the daily life of the patients. The treatment of Castleman's disease (CD) is usually a challenge, especially in case of cutaneous involvement. ***Case Presentation:*** We report the case of a 35-year-old Caucasian man with a 3-year-old history of MCD with cutaneous involvement that we treated with a combined therapy characterized by siltuximab and 1,927 nm fractional laser. The patient showed a therapeutic response, characterized by a reduction of systemic symptoms and cutaneous manifestations.

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Conclusion: We believe that the combination of siltuximab and 1,927 nm fractional laser might have a synergistic beneficial role in patients with cutaneous iMCD and maximize esthetic outcomes. Anyway, additional evidence is needed to validate our findings.

Introduction

Castleman's disease (CD) is a rare inflammatory condition characterized by lymph node hyperplasia and vascular proliferation [1]. CD can be classified as unicentric (UCD) or multicentric (MCD) disease by clinical manifestations and as hyaline-vascular, plasma cell, or mixed type according to pathological findings [2, 3]. Among these variants, MCD typically presents with diffuse systemic lymphadenopathy, associated with inflammatory manifestations [3]. MCD with cutaneous involvement has rarely been discussed in dermatologic literature, albeit these lesions may induce deep scars, causing a significant impact in the daily life of the patients. The treatment of CD is a challenge, above all in case of cutaneous involvement.

Case Report

A 35-year-old Caucasian man presented with a 3-year history of multiple brownish macules and papules on the head/neck region, trunk, and upper limbs, associated with occasional mild pruritus, creating discomfort to the patient in his social life. Dermoscopy of the cutaneous lesions was characterized by a dermatofibroma-like pattern, with a peripheral hyperpigmentation and a central pale amorphous and scar-like area. Clinical examination revealed also an enlargement of cervical lymph nodes. Laboratory tests showed high erythrocyte sedimentation rate (120 mm/h), C-reactive protein (85.7 mg/L), serum IL-6 (162 pg/mL), and polyclonal hyper-gamma-globulinemia. In vivo reflectance confocal microscopy (RCM) of one erythematous lesion showed no epidermal changes with hyperreflective papillae and increased vascularization of the papillary dermis, with scattered hyperreflective cells (corresponding to inflammatory cells), along with extended fibrotic areas (Fig. 1a–f). Two cutaneous biopsies showed a dermal perivascular plasmocellular infiltrate with an increase of vascularization, as well as a lymph-node biopsy showed hyperplastic follicles and an expansion of the paracortical areas of germinal centers with accumulation of mature polyclonal plasma cells. According to the clinico-pathologic correlation, a final diagnosis of CD was made in the setting of idiopathic MCD (iMCD). Systemic treatment with siltuximab (11 mg/kg every 3 weeks, one-hour infusion) was started. The patient initially showed a Dermatology Quality Life Index (DLQI) of 25. Routine laboratory tests were obtained before each infusion. In parallel, 1,927 nm fractional laser (Fraxel re:store DUAL, Solta Medical, Hayward, CA, USA) was performed on scarring lesions, with 20 mJ/mb at 4 W, 8 MTZ/cm^2, resulting in 2.5–3.0% coverage and 500 mJ/cm^2 total energy delivered per pass. The patient was treated with 8 passes, performing one session every 3 weeks for a total of 10 months. During siltuximab infusions and fractional laser sessions, the patient did not experience side effects, besides mild pain and transitory redness; a lenitive cream was always applied for the 10 days after each fraxel laser session, avoiding sun exposure. After 15 months of treatment, the patient showed a general improvement with normalization of laboratory tests, reduction of adenopathy, and, above all, a reduction in size and pigmentation of

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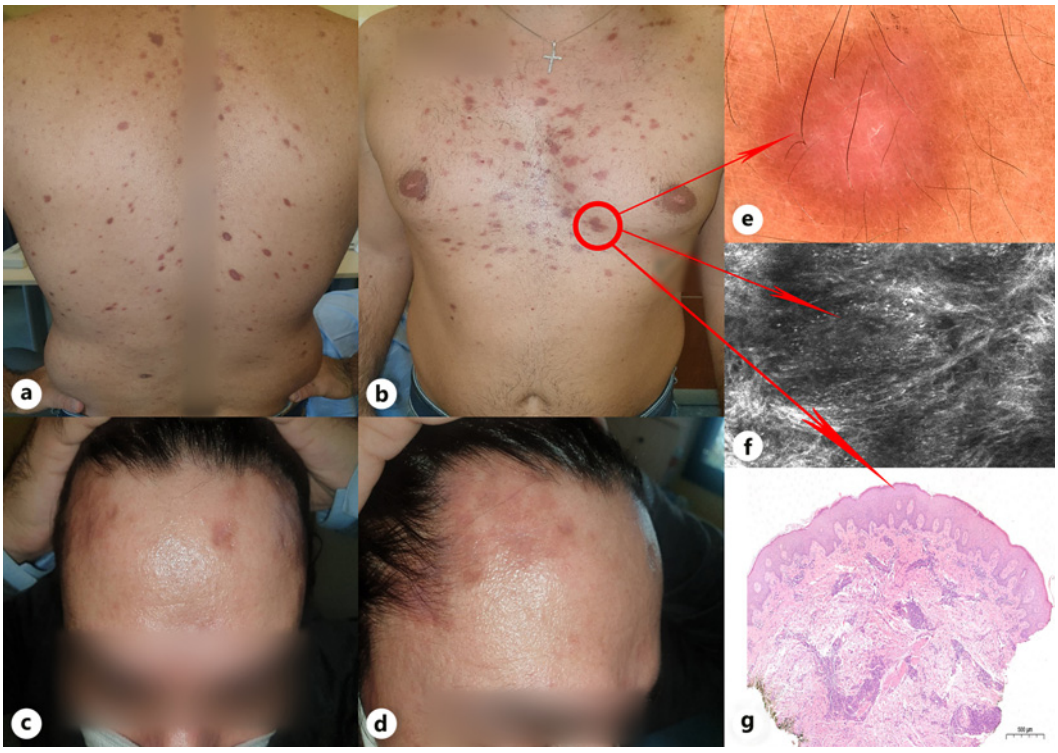

Fig. 1. Multiple brownish papules on the back (**a**); multiple brownish papules on the chest (**b**); multiple brownish papules on the head/neck region (**c**); multiple brownish papules on the head/neck region, lateral view (**d**); dermoscopy of one lesion showed peripheral hyperpigmentation, with central pale amorphous brownish area, consistent with dermatofibroma-like pattern (**e**); RCM of one lesion showed increased vascularization of the papillary dermis along with extended fibrotic areas and scattered hyper-reflective cells, corresponding to dermal plasma cells. The general RCM features show a dermatofibroma-like pattern with inflammatory cells (**f**); cutaneous biopsy of one lesion showed dermal perivascular plasmocellular infiltrate, with mild remodeling of collagen bundles (Hematoxylin and eosin. ×100) (**g**).

cutaneous lesions, leading to DLQI = 5. Dermoscopy was characterized by persisting, but reduced, dermatofibroma-like pattern with decreased pigmentation and erythema and reduction of the central scarring area, while RCM showed the thickening of dermal fibers with remodeling of superficial dermis and absence of dermal inflammatory infiltrate (Fig. 2a–f). Currently, after 23 months of follow-up, the patient shows no cutaneous or systemic signs of recurrence.

Discussion

To date, only seven reports on cutaneous iMCD have been published in the literature so far [1–5]. Consensus guidelines recommend an anti-IL-6 monoclonal antibody, siltuximab, with or without corticosteroid as the first-line therapy. However, there is no specific recommendation for the treatment of cutaneous manifestations in iMCD. Considering the scarring features of the skin lesions, we arbitrarily decided to associate 1,927 nm fractional laser therapy with siltuximab. Specifically, by targeting water as its chromophore, the 1,927 nm fractional laser induces a dense array of microscopic, columnar thermal zones of tissue injury, extending down to a depth of 300 μm, leading to gentle photothermal damage and

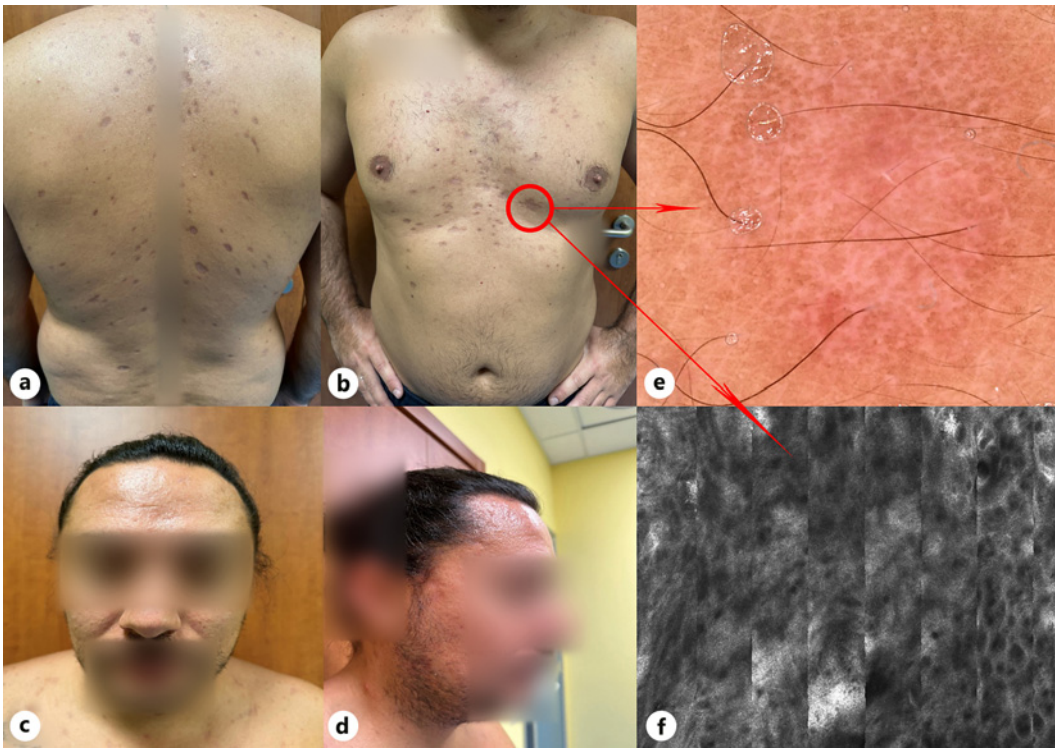

Fig. 2. Improvement of cutaneous lesions after 15 months of follow-up, with combined siltuximab and 1,927 nm fractional laser treatment (**a**–**d**); dermoscopy showing reduction of erythema, with central scarring area and peripheral hyperpigmentation, in the setting of dermatofibroma-like pattern (**e**); RCM showing only fibrotic bundles with remodeling of superficial dermis in absence of hyper-reflective inflammatory cells (**f**).

relative boost of collagen production, along with reduction of pigmentation, as observed in our patient. Finally, dermatoscopy and RCM, although not specific to diagnose iMCD, both proved useful to evaluate the therapeutic response in a noninvasive way.

CD is a very rare disease, and cutaneous involvement is even rarer. Consequently, large-scale interventional trials comparing different treatment regimens are difficult to design and perform in this specific setting. Therefore, notwithstanding the limitations of reporting data from a single patient, we believe that a combination of siltuximab and 1,927 nm fractional laser might have a synergistic beneficial role for patients with cutaneous iMCD and maximize esthetic outcomes. Of course, additional evidence is needed to validate our findings. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000536483).

Statement of Ethics

Written informed consent was obtained from participant for publication of the details of their medical case and any accompanying images. Study approval statement was not required for this study in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization: Giovanni Paolino, Marco Ardigò, Emanuel Della-Torre, and Santo Raffaele Mercuri; writing – original draft preparation: Giovanni Paolino, Marco Ardigò, Emanuel Della-Torre, Luca Moroni, and Matteo Riccardo Di Nicola; writing – review and editing: Giovanni Paolino, Marco Ardigò, Emanuel Della-Torre, Luca Moroni, Nathalie Rizzo, Matteo Riccardo Di Nicola, Vittoria Giulia Bianchi, Lorenzo Dagna, Giuseppe Alvise Ramirez, and Santo Raffaele Mercuri. All authors approved the final version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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