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SHORT REPORT

Reflectance confocal microscopy for Kaposi's sarcoma treatment monitoring after intralesional vincristine chemotherapy

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Abstract

Kaposi's sarcoma (KS) is a multifocal systemic disease, originating from endothelial cells mainly affecting elderly men. Intralesional chemotherapy with vinblastine or vincristine is an effective and well-tolerated treatment in patients presenting single nodules on the skin. Despite reflectance confocal microscopy represents a useful diagnostic method for many dermatological diseases, to date, there are few data regarding the use of RCM in mucocutaneous KS. Objective of this study was to evaluate the use of RCM for therapeutic follow-up in KS patients treated with intralesional vincristine. An observational retrospective study involving patients with a histological diagnosis of classic KS was conducted. All patients were treated with intralesional vincristine; reflectance confocal microscopy images were taken for each patient at baseline (T0) and 1 month after vincristine injection. Four male patients with a median age of 76.8 years were included in the study and four nodules (one for each patient) were evaluated with RCM examination before and after vincristine injections. At 1 month from intralesional vincristine treatment, therapeutic response was confirmed at RCM examination; a reduction of inflammatory cell at the stratum spinosum level in all evaluated lesions was observed; at papillary dermis levels, black luminal structures were decreased in diameter and superficial linear canalicular structures were not represented. Aggregates of inflammatory cells and of hemosiderin deposition, at the dermal level, were reduced in number. Reflectance confocal microscopy showed to be a promising method to evaluate vincristine therapeutic response in patients with KS; further studies evaluating RCM use in KS patients in order to monitor treatment efficacy are still required.

KEYWORDS
chemotherapy, Kaposi, reflectance confocal microscopy, treatment, vincristine

1 | INTRODUCTION

Kaposi's sarcoma (KS) is a multifocal systemic disease, usually involving the skin, originating from endothelial cells mainly affecting elderly men. Patients affected by classic KS present multiple pink to red-purple-colored lesions, varying from a patch, a nodule or a plaque, often localized on the distal lower extremities.[1,2] Although, in the last decade, the use of reflectance confocal microscopy (RCM) as diagnostic tool has been studied in many dermatological diseases, including inflammatory dermatosis, benign and malignant neoplasms, as well as in cosmetic dermatology,[3–5] to date, there are few data regarding the use of RCM in mucocutaneous KS.[6] In literature there is only one study describing reflectance confocal microscopy features of KS lesions and their correlation with histopathological examination.[7]

Although many therapeutic strategies from systemic to local treatment are available for KS, the correct treatment should be tailored according to patients' characteristics. Intralesional chemotherapy with vinblastine or vincristine is an effective and well-tolerated treatment in patients presenting single scattered nodules on the skin. Few data regarding the use of intralesional doxorubicin or bleomycin have been described.[8] Vincristine is a natural alkaloid derived from the plant Vinca rosea; it has an antiblastic effect, and acts by binding to microtubules and spindle proteins, thus inhibiting the mitotic cycle.[9] To date, ultrasonography is the only non-invasive diagnostic tool that have been used to monitor the efficacy of intralesional vincristine treatment in KS patients.[10] Objective of this study was to evaluate the use of RCM for therapeutic follow-up in KS patients treated with intralesional vincristine.

2 | MATERIALS AND METHODS

2.1 | Study population

An observational retrospective study was performed at the Dermatology Unit of the University of Federico II in Naples from January 2021 to September 2021. Patients with a histological diagnosis of classic KS, presenting with cutaneous nodules were included in the study. All patients were treated with intralesional chemotherapy that was performed using insulin syringes containing vincristine. The amount of vincristine injected in each nodule was decided according to the size of the lesion and the injection was always performed by the same investigator.

Clinical (Canon Power Shot G16, 12.3 megapixel digital single-lens reflex camera) and RCM images (Vivascope 1500; Lucid Inc, Rochester, NY) acquisition was performed for each patient at baseline (T0) and 1 month after vincristine injection. For each patient, a single nodule was examined before vincristine injection and after 1 month. All procedures performed in studies involving human participants were in accordance with the Helsinki Declaration and its later amendments or comparable ethical standards. All patients provided informed written consent. Therapeutic response was divided in to complete response in case of complete resolution of the KS nodule, partial response (PR) in case of a reduction >50% of nodule volume, and no response (NR) in case KS nodule remained stable.

2.2 | RCM imaging

RCM images were acquired with a near-infrared reflectance confocal laser scanning microscope (Vivascope 3000, Lucid Inc., MAVIG GmbH, Munich, Germany); images, parallel to the skin surface, were acquired for each patient, corresponding to epidermis, DEJ, and superficial dermis. Specific RCM features, previously described by Corsetti Grazziotin et al.,[7] were analyzed for each RCM examination to evaluate treatment response. In detail, parameters taken into account in this study were: the presence of round-to polygonal mild refractive structures correlating with the inflammatory cells located in the intercellular spaces at the stratum spinosum level; regarding the vascular structures, black luminal structures increased in diameter corresponding to dilated vessels at papillary dermis levels and linear small canalicular structures representing newborn vessels; the intersection of black canalicular structures corresponding to anastomosing vessels was also analyzed. At the level of dermal stroma, three features were evaluated: refractile cells arranged in aggregates representing inflammatory cells, round-to-oval poorly refractile structures moving from vessel walls in to the dermal stroma representing erythrocytes extravasation and round-to-polygonal structures aggregated outside the vascular structures representing hemosiderin deposition. An evaluation of potential RCM features variation after vincristine chemotherapy was performed.

3 | RESULTS

Four patients with cutaneous KS nodules located on lower limbs were included in the study and four nodules (one for each patient) were evaluated with RCM examination before and after vincristine injections. All patients were males with a median age of 76.8 years (range 72–87 years). Patients presented a median number of KS nodules of 4.3 (range 2–7) and a median KS duration of 13.5 years. An overall improvement was observed in all KS patients, in particular, one patient reported complete response, whereas, PR was observed in 3 out of 4 patients. RCM images were analyzed according to two previously described RCM patterns; at baseline evaluation, round-to polygonal mild refractive structures at the stratum spinosum level were identified in all KS nodules (4/4); black luminal structures increased in diameter at papillary dermis levels and linear small canalicular structures representing newborn vessels were observed with a frequency of 75% (3/4) and 50% (2/4), respectively. Moreover, the intersection of black canalicular structures corresponding to anastomosing vessels was also observed (75%). At the level of dermal stroma, aggregates of refractile cells, round-to-oval poorly refractile structures moving from vessel walls in to the dermal stroma and round-to-polygonal structures aggregated outside the vascular structures were observed in a percentage of 50%, 75%, and 75%, respectively (Figure 1).

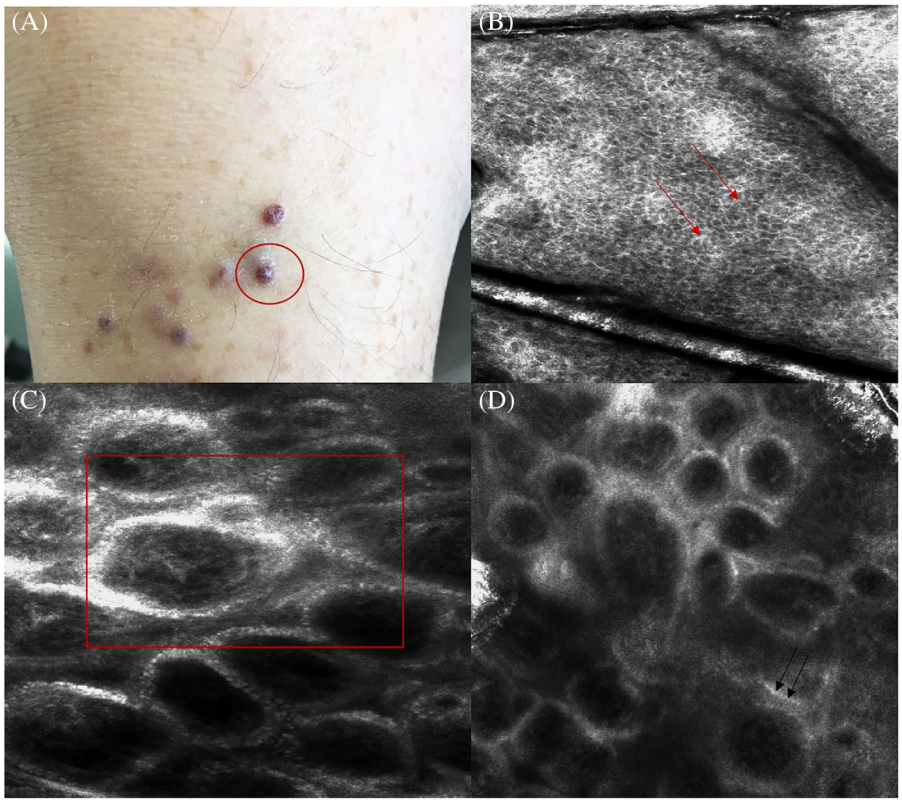

FIGURE 1 (A) Clinical appearance of KS nodule of the lower limb at baseline (red circle); RCM examination images taken with Vivascope 3000: (B) round-to polygonal mild refractive structures (red arrows) in the intercellular spaces at the stratum spinosum level corresponding to inflammatory cells; (C) black luminal structures increased in diameter at the papillary dermis corresponding to dilated vessels (red square); (D) linear small canalicular structures corresponding to newborn vessels

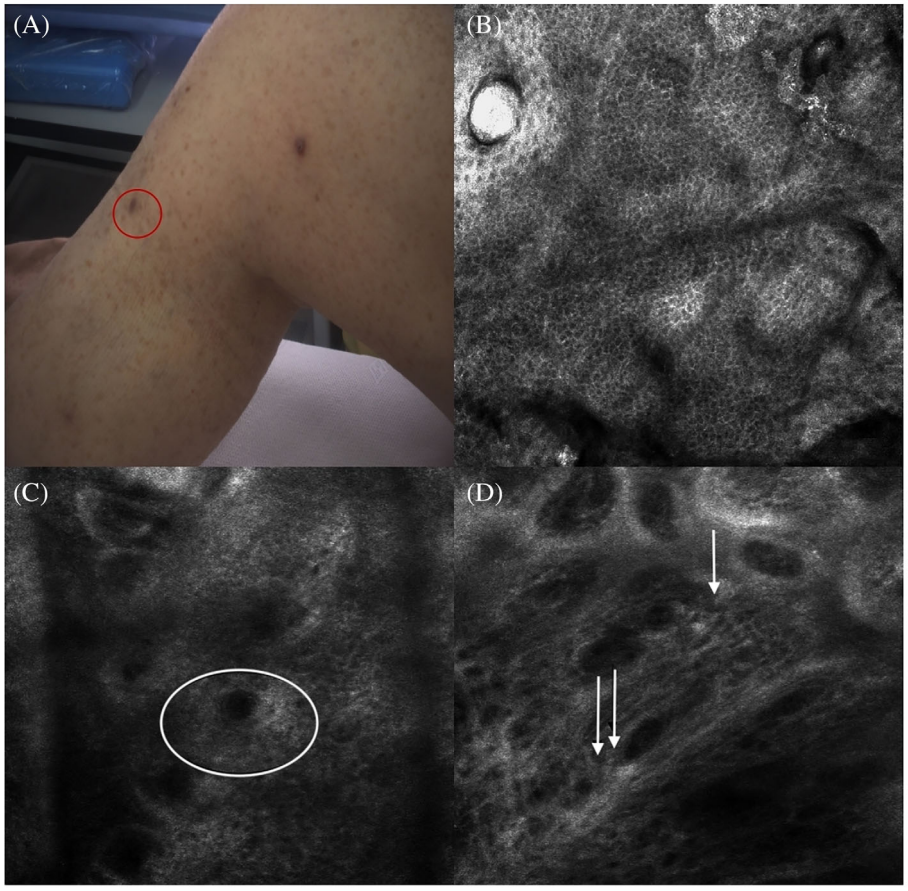

FIGURE 2 (A) Clinical appearance of KS nodule of the lower limb after 1 month from intralesional vincristine (red circle); RCM examination images taken with Vivascope 3000: (B) reduction of inflammatory cells at the stratum spinosum level; (C) black luminal structures decreased in diameter at the papillary dermis (white circle); (D) vascular structures replaced by collagen fibers in the dermis (white arrows)

At 1 month from intralesional vincristine treatment, all evaluated RCM features were significantly decreased. Therapeutic response was confirmed by the reduction of inflammatory cell at the stratum spinosum level in all evaluated lesions; at papillary dermis levels, black luminal structures were decreased in diameter and superficial linear canalicular structures were not represented yet. Aggregates of inflammatory cells and of hemosiderin deposition, at the dermal level, were reduced in number. RCM examination confirmed the therapeutic response. The amount of RCM specific features reduction was observed to be proportional to the degree of therapeutic response (Figure 2).

4 | DISCUSSION

In literature there are different studies showing the efficacy and safety of vincristine treatment for KS.[11] However, previous studies have been limited by the absence of an objective measure evaluating treatment improvement. To date, there is only one study reporting the use of sonographic examination[10] as a non-invasive diagnostic method to monitor disease activity and to assess clinical response to therapy. In the recent scenario, the use of RCM has been studied in many dermatological diseases, including inflammatory disorders, skin neoplasms, and cosmetic dermatology[3,4]; few data describing its use in KS lesions have been reported[7,8]; in particular there is only one study describing specific RCM features observed in KS lesions. This is the first study showing the promising role of RCM examination in monitoring KS lesions during intralesional vincristine treatment. In fact, a progressive reduction in all RCM parameters evaluated, corroborated by clinical evaluations, was observed during the follow-up evaluation; a reduction in diameter and in number of vascular structures was reported maybe due to the cytotoxic action of vincristine that acts by destroying endothelial cells. Limitations of this study was the low number of patients involved, the retrospective design of the study and the lack of specific RCM features to evaluate; further studies evaluating RCM use in KS patients in order to monitor treatment efficacy are still required.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICS STATEMENT

This article is based on previously conducted studies and all human participants gave their written informed consent.

AUTHORSHIP

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

DISCLOSURES

Alessia Villani, Gabriella Fabbrocini, Tiziana Peduto, and Massimiliano Scalvenzi have nothing to disclose.

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REFERENCES

1. Buonaguro FM, Tomesello ML, Buonaguro L, et al. Kaposi's sarcoma: aetiopathogenesis, histology and clinical features. *J Eur Acad Dermatol Venereol*. 2003;17:138-154.
2. Schwartz RA, Micali G, Nasca MR, Scuderi L. Kaposi sarcoma: a continuing conundrum. *J Am Acad Dermatol*. 2008;59:179-206.
3. Ardigo M, Cota C, Berardesca E, Gonzalez S. Concordance between in vivo reflectance confocal microscopy and histology in the evaluation of plaque psoriasis. *J Eur Acad Dermatol Venereol*. 2009;23:660-667.
4. Pellacani G, Guitera P, Longo C, Avramidis M, Seidenari S, Menzies S. The impact of in vivo reflectance confocal microscopy for the diagnostic accuracy of melanoma and equivocal melanocytic lesions. *J Invest Dermatol*. 2007;127:2759-2765.
5. Wortsman X, Wortsman J, Orlandi C, Cardenas G, Sazunic I, Jemec GBE. Ultrasound detection and identification of cosmetic fillers in the skin. *J Eur Acad Dermatol Venereol*. 2012;26:292-301.
6. Villani A, Scalvenzi M, Peduto T, Cinelli E, Fabbrocini G, Di Stefani A. Dermoscopy and reflectance confocal microscopy of Kaposi's sarcoma: an overview. *J Eur Acad Dermatol Venereol*. 2021;36:e272-e274. doi:10.1111/jdv.17831
7. Grazziotin TC, Cota C, Buffon RB, Araújo Pinto L, Latini A, Ardigò M. Preliminary evaluation of in vivo reflectance confocal microscopy features of Kaposi's sarcoma. *Dermatology*. 2010;220(4):346-354. doi:10.1159/000297561
8. Epstein JB, Lozada-Nur F, McLeod WA, Spinelli J. Oral Kaposi's sarcoma in acquired immunodeficiency syndrome. Review of management and report of the efficacy of intralesional vinblastine. *Cancer*. 1989;64:2424-2430.
9. Odom RB, Goette DK. Treatment of cutaneous Kaposi's sarcoma with intralesional vincristine. *Arch Dermatol*. 1978;114:1693-1694.
10. Nazzaro G, Genovese G, Tourlaki A, Passoni E, Berti E, Brambilla L. Ultrasonographic intraoperative monitoring and follow-up of Kaposi's sarcoma nodules under treatment with intralesional vincristine. *Skin Res Technol*. 2019;25:200-203.
11. Brambilla L, Bellinvia M, Tourlaki A, Scoppio B, Gaiani F, Boneschi V. Intralesional vincristine as first-line therapy for nodular lesions in classic Kaposi sarcoma: a prospective study in 151 patients. *Br J Dermatol*. 2010;162:854-859.

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