Case and Review

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Cutaneous Collagenous Vasculopathy: A Rare Form of Microangiopathy Successfully Treated with a Combination of Multiplex Laser and Optimized Pulsed Light with a Review of the Literature

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Key Words
Cutaneous collagenous vasculopathy · Multiplex laser · Optimized pulsed light

Abstract
Cutaneous collagenous vasculopathy (CCV) is a rare idiopathic microangiopathy of the cutaneous vasculature characterized histologically by the presence of dilated small blood vessels with flat endothelial cells and thickened walls containing hyaline material in the upper dermis. We report an elderly patient presenting with an extensive form of CCV involving the trunk, upper and lower limbs. She was treated with Multiplex PDL 595-nm/Nd:YAG 1,064-nm laser and optimized pulsed light. This approach, which has never been reported for CCV so far, resulted in a striking and almost complete clearance of the widespread lesions. We here review our knowledge about CCV and therapeutic options available with a survey of the literature.

Introduction

Cutaneous collagenous vasculopathy (CCV) is a rare microangiopathy of unknown origin, which involves the superficial cutaneous vasculature [1]. CCV typically develops in middle-aged patients with cutaneous telangiectasia on the trunk, lower and upper limbs. Cutaneous lesions are usually asymptomatic but sometimes disfiguring. The perivascular fibrosis is thought to be due to the production of abnormal collagen by veil cells in the outer vessel walls as a result of unknown factors [1]. Although there is no cure for this usually chronic and progressive condition, vascular laser should be considered to significantly improve both skin lesions and the quality of life of affected patients. These were successfully treated for the first time with an optimized pulsed light (OPL) combined with a multiplex sequential PDL 595-nm/Nd:YAG 1,064-nm laser, and we review previous cases of CCV and available therapeutic options.

Case Report

A 77-year-old woman was evaluated for generalized asymptomatic telangiectasias (fig. 1a). The lesions had first developed by the age of 20 years on the lower legs and subsequently spread onto the thighs, arms and chest. The family history was unremarkable. The medical history revealed surgery for ovarian cystic adenocarcinoma, ischemic heart disease with arrhythmias and chronic renal insufficiency with generalized itch. The patient was on phenprocoumon, acetylsalicylic acid, oxazepam and levocetirizine.

Physical examination showed widespread telangiectasias distributed symmetrically on the legs, arms and chest. Some lesions were raised, slightly hypertrophic

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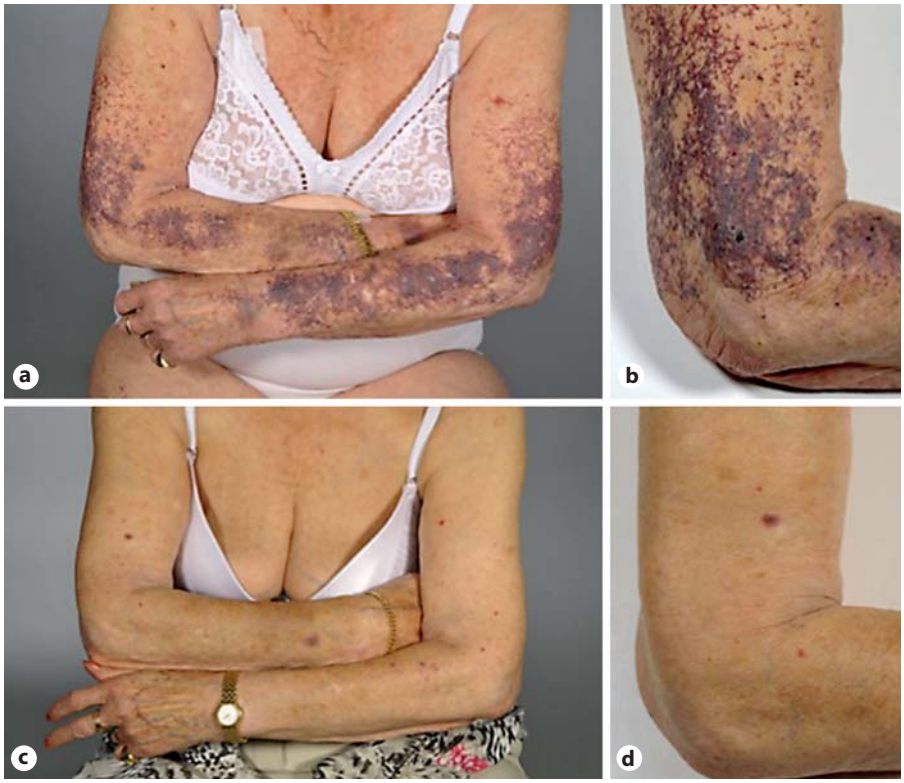

Fig. 1. a Diffuse acquired telangiectasias over the arms and chest. **b** Close-up view of the right arm. **c** Postintervention resolution of the telangiectasias over the arms and the chest. **d** Postintervention close-up view of the right arm.

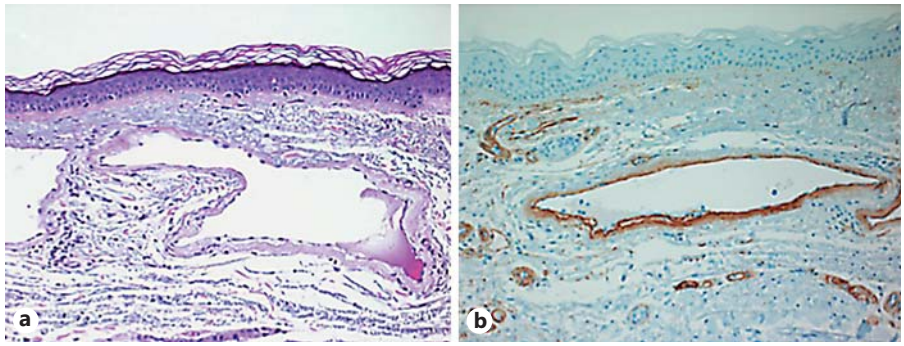

Fig. 2. a Telangiectasia of dermal capillaries with hyalinized thickening of the vessel wall. **b** The hyaline material within the thick vessel wall is positive for collagen type IV.

and more of a purple color, while some others were completely flat and bright red. There was no mucosal or nail involvement.

Light microscopy studies of a biopsy specimen obtained from the leg revealed dilated superficial cutaneous vessels with perivascular deposits of hyaline material (fig. 2a). A staining with collagen type IV was visible at immunohistochemistry (fig. 2b).

The patient desired to improve the disturbing cosmetic appearance of these extensive red-blue lesions, especially on the arms and forearms. We proposed laser treatment using a combination of a Multiplex PDL 595-nm/Nd:YAG 1,064-nm laser as well as an OPL. The following parameters were used, as spot tests first, with the laser, on the hypertrophic lesions: 595-nm pulsed dye laser, a 7-mm spot at 8.5 J/cm^2 and a 10-ms pulse duration followed sequentially by a 500-ms interval, then a pulse of 1,064-nm Nd:YAG laser at 55 J/cm^2 and a 15-ms pulse duration (Cynergy Multiplex, Cynosure, Westford, Mass., USA). This was delivered in a single pass with no overlap. Forced chilled air was used for parallel cooling. For flat lesions, we used an OPL (Limelight Cutera, Brisbane, Calif., USA) with a 520-nm filter, a 10 × 30 mm spot, fluence range of 16–18 J/cm^2, 8–9 ms of pulse width, with contact cooling and 2 perpendicular passes. The response of these tests gave a remarkable improvement. Therefore all lesions of the upper limbs and trunk were subsequently treated using the same parameters. Almost complete clearance of the telangiectasia on both arms and the chest was obtained after a total of 7 combined laser/intense pulsed light treatment sessions, performed every 4–8 weeks (fig. 1b).

Discussion

Our patient had clinical and histopathological features typically described as CCV, a distinctive primary cutaneous microangiopathy first described in 2000 [1, 2]. This entity is rare since only 25 cases have been described so far in the English literature (table 1).

CCV has almost exclusively been reported in middle-aged subjects [3], even though 1 pediatric case has been reported [4]. In our patient, cutaneous telangiectasia originally developed on the lower legs and progressed subsequently to the thighs, trunk and the upper extremities in accordance with data reported in the literature [5]. Usually lesions are almost invariably asymptomatic although some itching may occur [5]. Lesions remain then relatively stable or may occasionally worsen during the summer months [2]. No mucosal involvement has been reported so far.

Light microscopy studies are essential for the diagnosis of CCV. This typically shows dilated small blood vessels in the superficial dermis and, more rarely, in the midreticular dermis. Sparse lymphocytes scattered around the vessel walls may be found. Electron microscopy studies disclose dilated postcapillary venules with flat endothelial cells and a thickened laminat-

Table 1. Survey of the literature: cases of CCV and their management

No.	Authors	Age, years	Sex	Race	Medical history	Distribution	Evolution	Treatment
1	Salama and Rosenthal [1], 2000	54	M	Caucasian	Depression	Trunk, upper and lower limbs	5 years	No
2	Davis et al. [6], 2008	59	M	Caucasian	Diabetes mellitus, hypercholesterolemia, hypertension	Forearm, chest, abdomen	7 months	No
		6	M	Caucasian	Diabetes mellitus, hypertension, psoriasis	Thigh	Unclear	No
		80	M	Caucasian	Atrial fibrillation, gastroesophageal reflux, venous insufficiency	Abdomen, thigh, back, hands	Unclear	No
3	Kanitakis et al. [8], 2010	65	M	Caucasian	Hypertension, coronary infarction, prostatic adenoma	Lower extremities, abdomen, buttocks, back	5–6 years	No
4	Monteagudo et al. [11], 2010	68	M	Caucasian	Hypertension, hypercholesterolemia, prostatic adenoma, hyperuricemia	Forearm, abdomen, lower limbs	15 years	No
5	Perez et al. [7], 2010	51	F	Caucasian	Hypothyroidism, psoriasis	Trunk, neck, upper and lower limbs, retroauricular area	16 years	No
		71	F	Caucasian	Pituitary tumor, osteoporosis	Feet, knees, upper limbs, chest, cheeks	7 years	No
6	Lloyd et al. [4], 2011	16	F	Caucasian	Mood disorders	Trunk, legs	3 years	No
7	González Fernández et al. [3], 2012	83	F	Caucasian	Atrial fibrillation, mitral valve disease, hepatitis C, hypertension	Upper and lower limbs, abdomen	>20 years	No
		74	F	Caucasian	Discoid lupus, venous insufficiency	Lower limbs		No
8	Echeverría et al. [14], 2012	42	F	Caucasian	–	Upper and lower limbs, abdomen	7 years	PDL, successful
9	Burdick et al. [2], 2012	68	M	Unknown	Macular degeneration since childhood, hypertension, hyperlipidemia, gastroesophageal reflux disease	Legs, abdomen	Several weeks	No
		59	M	Unknown	Diabetes mellitus, hypertension, hyperlipidemia, osteoarthritis, depression	Arms, legs	Several months	No
		70	M	Unknown	Hypertension, diabetes mellitus, hypercholesterolemia	Right leg	10 years	No
		41	F	Unknown	Basal cell carcinoma, inactive hepatitis	Arms	Several years	No
10	Bernard et al. [21], 2012	47	F	Unknown	Diabetes mellitus type 1, psoriasis, hypertension, hypothyroidism	Lower limbs, abdomen	1–2 years	No
11	Salama et al. [5], 2014	84	M	Caucasian	Myelodysplastic syndrome, diabetes mellitus, celiac disease, tuberculosis, tachycardia	Lower limbs and trunk	3 years	No
12	Salama [22], 2015	68	F	Unknown	Mild chronic renal failure, cryofibrinogenemia	Lower limbs	Unknown	–
		85	F	Unknown	Diabetes mellitus	Lower limbs	10 years	No
		50	F	Unknown	–	Lower limbs and upper limbs	2 years	No
		69	F	Unknown	Diabetes mellitus	Lower limbs and upper limbs, abdomen	Unknown	No
		56	F	Unknown	–	Lower limbs and upper limbs, trunk	25 years	No
		42	F	Unknown	Raynaud phenomenon	Lower limbs	>20 years	No
		73	M	Unknown	–	Lower limbs and upper limbs	2.5 years	No
13	Bardazzi et al. [23], 2014	57	F	Caucasian	Uveitis, hypertension	Legs, abdomen, buttocks, hips, trunk, arms, malar region, fingers	9 years	No
14	This study, 2015	77	F	Caucasian	Renal insufficiency, venous insufficiency, ovarian adenocarcinoma, ischemic heart disease	Upper and lower limbs, chest	>20 years	PDL/ Nd:YAG

ed basement membrane consisting of an amorphous eosinophilic hyaline material [2, 3]. By immunohistochemistry, vascular cells of endothelial origin are CD31 and CD34 positive. The amorphous eosinophilic hyaline material is stained using antibodies directed against laminins, fibronectin and, characteristically, type IV collagen [5–7]. No amyloid deposits by Congo red staining are found.

CCV has to be differentiated from a number of other vascular disorders presenting with cutaneous telangiectasias, including benign hereditary telangiectasia, angioma serpiginosum and telangiectasia macularis eruptiva perstans [3]. Generalized essential telangiectasia (GET) [8] is another benign condition that should be differentiated from CCV. At variance with CCV, GET is more common in women and can rarely also involve the oral mucosa and conjunctiva. In contrast to CCV, in GET there are dilated vessel walls, which consist of thickened endothelial cells, but without any deposition of amorphous hyaline material [2, 9].

The question remains whether the peculiar histopathological findings of CCV are sufficient to distinguish CCV from GET as a distinct disease or whether both conditions represent different faces of a single disease. We included in the study only the certified CCV.

The mechanisms leading to the development of CCV remain unknown. Some authors have discussed a nonimmunologically related injury of the endothelial cells by unknown factors, which ultimately lead to the production of abnormal collagen and reparative fibrosis [4]. The intake of drugs, encompassing corticosteroids, lithium, tiotixene, interferon, isotretinoin, calcium channel blockers, antibiotics or antidepressants, has been thought to act as trigger [7, 10].

Conditions such as diabetes mellitus or hypertension may further contribute. Most likely CCV represents a response pattern triggered by multiple factors [2, 3, 11].

The therapy of CCV is challenging. If the patient wants a cosmetic improvement, lasers and other light sources represent the first therapeutic option. The latter are working according to the principle of selective photothermolysis [12]. When treating vascular lesions, the primary target is oxyhemoglobin [13]. Two cases of CCV have been treated by a pulsed dye laser [14]. We opted for a combination of Multiplex PDL/YAG laser on thicker, purple lesions, together with an OPL on the flatter, redder ones. The advantages of this combination of energy-based devices during the same session are: (a) the Multiplex laser, which combines PDL at 595 nm followed by YAG at 1,064 nm, is ideal for treating hypertrophic vascular lesions; this specific device has already been used successfully in treating various vascular conditions, with better vessel clearance than with a single pulsed laser [15]; (b) the OPL is an evolution of the intense pulsed light, developed in 1992 [16], as it brings true square pulse emission. This peculiarity gives a very precise control of delivered fluencies, similar to a laser, even being a noncoherent light source. Our OPL, due to its large spot size (10 × 30 mm) allowed speed, comfort and also very good cosmetic results in treating large areas when compared with a laser with a small spot size (7–10 mm). A few cases of essential telangiectasias have been published using an intense pulsed light [17–20]. To our knowledge, our case is the first describing a case of CCV successfully treated with an OPL combined with a Multiplex laser within the same session.

In conclusion, we here describe the first successful case of CCV treated with an OPL combined with a multiplex sequential PDL 595-nm/Nd:YAG 1,064-nm laser within the same session. This approach led to an impressive aesthetical improvement despite the very large affected surface. Even if a causal treatment of this difficult skin disease has not already been discovered, the combination approach used here seems very effective.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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