A lumpy back: extensive cutaneous eruptive collagenomas

Daniele Agosta[1] MD, Laura Atzori[1] MD, Luca Pilloni[2] MD, Maria Angela Brundu[1] MD, Franco Rongioletti[1] MD

Affiliations: [1]Dermatology Clinic, Department Medical Sciences and Public Health, University of Cagliari, Italy, [2]Pathology Unit, Department Medical Sciences and Public Health, University of Cagliari, Italy

Corresponding Author: Prof. Laura Atzori, Dermatology Clinic, Department Medical Sciences and Public Health, University of Cagliari, Via Ospedale 54, 09124, Cagliari, Italy, Tel: 39-070-6092324, Fax: 39-070-6092580, Email: atzoril@unica.it

Abstract

A widespread form of eruptive collagenomas in a 23-year-old man is presented for the impressive iconography, challenging differential diagnosis, and histopathological considerations associated with such rare connective tissue disorders. Syndromic forms should be carefully investigated for the different course and prognosis. Treatment is a major unsolved issue as aesthetic concerns are significant, especially in young adults.

Keywords: eruptive collagenomas, histopathology, connective tissue nevi

Introduction

Abrupt and progressive growth of asymptomatic skin-color nodules on the back and limbs at puberty or early adulthood is a rare event, which requires careful assessment to exclude syndromic forms [1-5]. Skin lesions usually represent benign hamartomas in the spectrum of connective tissue nevi (CTN), whose differential diagnosis relies on histopathological findings. In fact, classification is based on the predominant component of the involved extracellular matrix and includes three major forms: collagenomas, elastomas, and mucinosis. Special staining is advisable to address the pathological distinctions, which may have controversial aspects

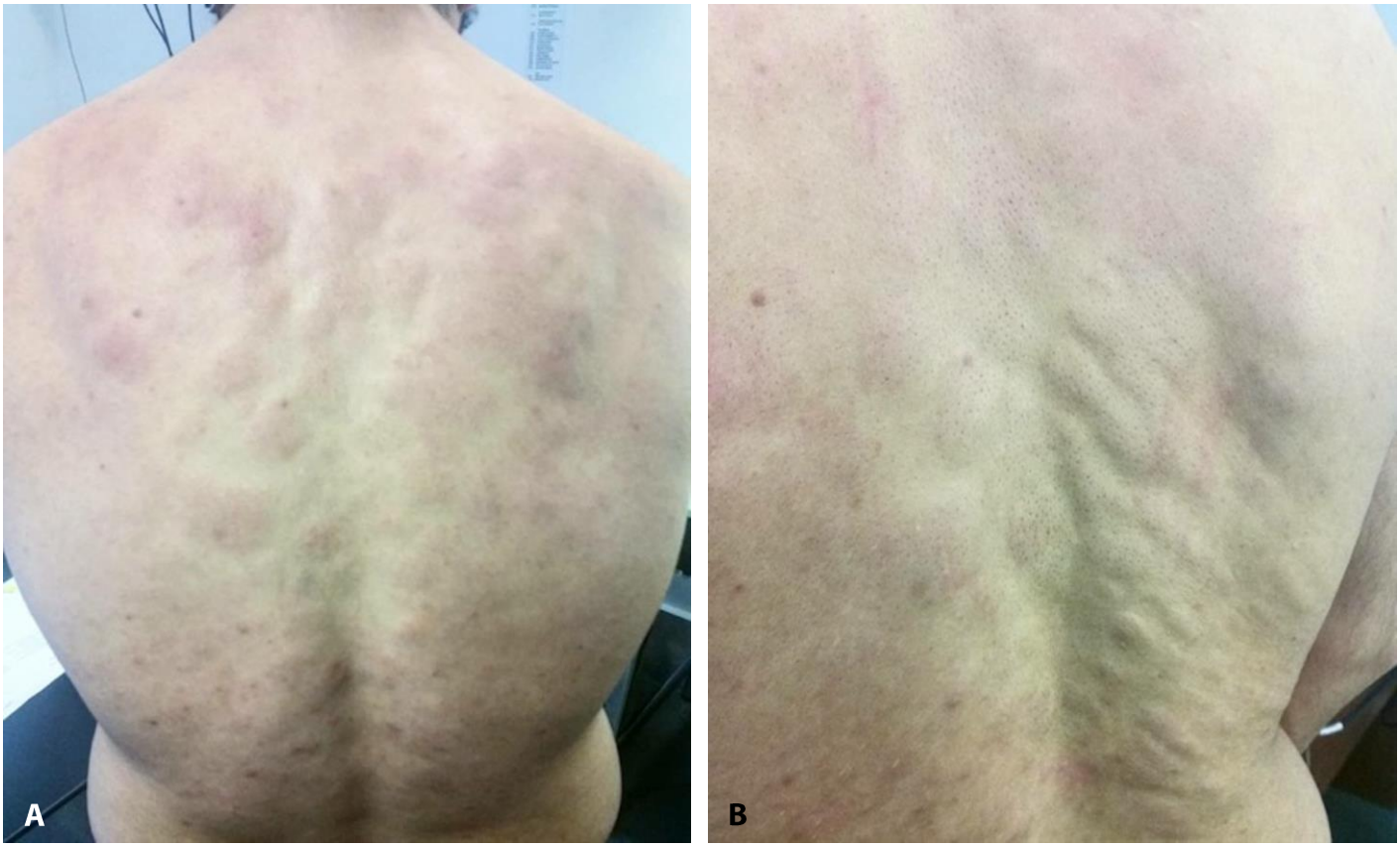

Figure 1. ***A)*** *Eruptive collagenomas. Multiple, subcutaneous, tender, light pink to skin-colored nodules, from 0.5 to 2cm, sometimes gathering into plaques on the upper and middle back of the patient.* ***B)*** *Eruptive collagenomas, a closer view of the lumpy skin appearance.*

especially concerning the concomitant elastic fiber alteration [3].

A very widespread distribution of connective tissue nevi in a 23-year-old man, involving the whole back, suggestive of eruptive collagenomas (EC), [6], is presented to highlight this uncommon presentation. The differential diagnosis and histopathological considerations regarding distinguishing collagenoma from elastorrhexis are discussed.

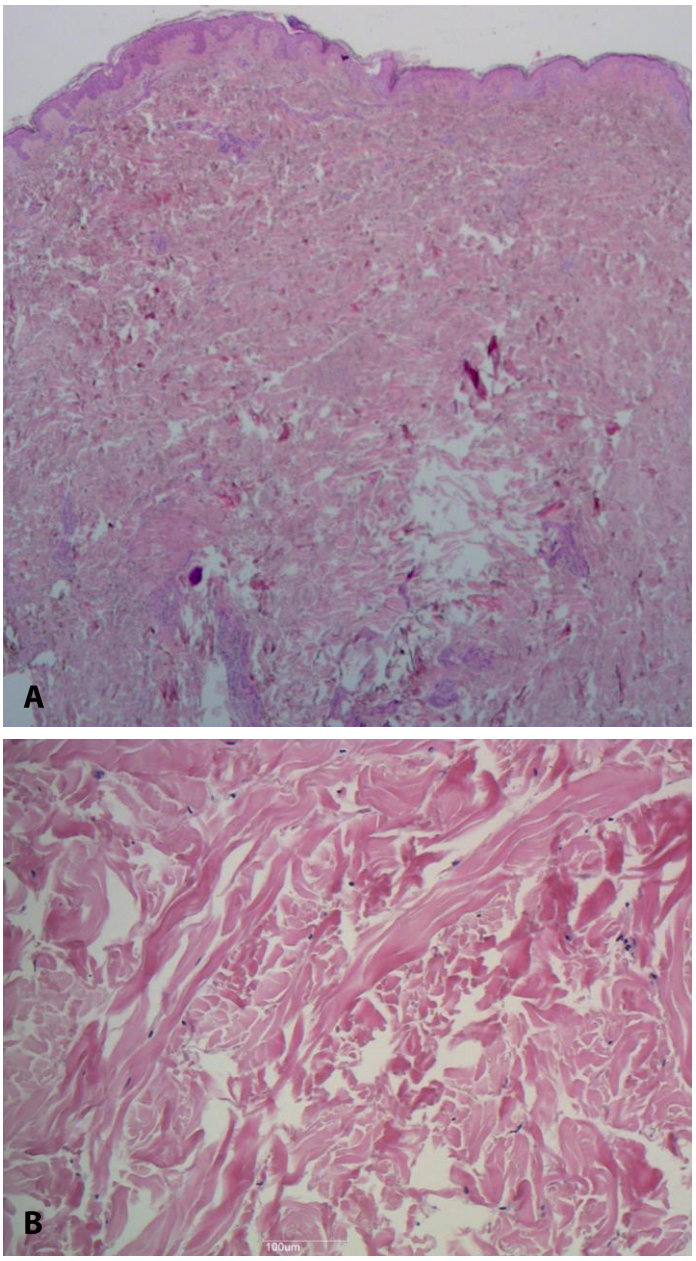

Figure 2. ***A)*** *H&E staining of skin biopsy showing a thickened dermis, made of dense collagen bundles, 2.5×.* ***B)*** *Magnified view of the collagen bundles, coarse and thickened, 20×.*

Case Synopsis

A 23-year-old man presented with a 3-year history of multiple, symmetrical, asymptomatic nodules. He was treated with topical corticosteroids without improvement. On examination, the subcutaneous, tender nodules were extensively distributed on the upper and middle back; they were variable in color from light pink to skin colored and in size from 0.5 to 2cm [**Figure 1**]. No trauma or inflammation preceded the manifestations and no other similar cases were reported in the family. Joint hypermobility was otherwise noted, with easy right shoulder dislocation. The same joint hypermobility was present in his second-born brother and a maternal uncle. However, no other skin signs, history of pathological fractures, or gastric or cardiologic disorders were disclosed. A genetics consultation was performed and excluded a known concurrent syndromic disease.

A skin biopsy from a nodular lesion of the right lumbar region showed a thickened dermis made of coarse and dense dermal collagen bundles, with apparently decreased elastic tissue, as well as fibroblasts [**Figures 2-4**]. Weigert special stain and factor XIIIa immunohistochemistry were performed, confirming prevalent collagen involvement composed of haphazardly arranged fibers, compatible with collagenomas. The study of the elastic fibers excluded elastic tissue disorders and showed only a proportional reduction or dilution with respect to the thickened collagen bundles; a normal number of fibroblasts was exhibited [**Figures 3, 4**].

Case Discussion

Collagenomas are uncommon disorders but represent a major form of connective tissue nevi, whose pathogenesis is elusive. However, they are generally considered benign hamartomas [5, 6]. Collagenoma classification distinguishes among localized and generalized forms, acquired or inherited, isolated or associated with internal malformations (Table 1). The hereditary, syndromic forms are autosomal dominantly transmitted, with associated signs and symptoms such as the

dermatofibrosis lenticularis in the Buschke-Ollendorff syndrome, the shagreen patch in tuberous sclerosis, and the familial cutaneous collagenomas with cardiac disorders.

Acquired collagenoma includes several localized forms [7-9], which usually occur in a single body region, such as the genitalia. Morphological variants are described, including the plantar cerebriform collagenoma, zosteriform collagenoma, knuckle pads, and papulo-linear collagenomas. Plantar cerebriform collagenomas can be associated with Proteus syndrome [10].

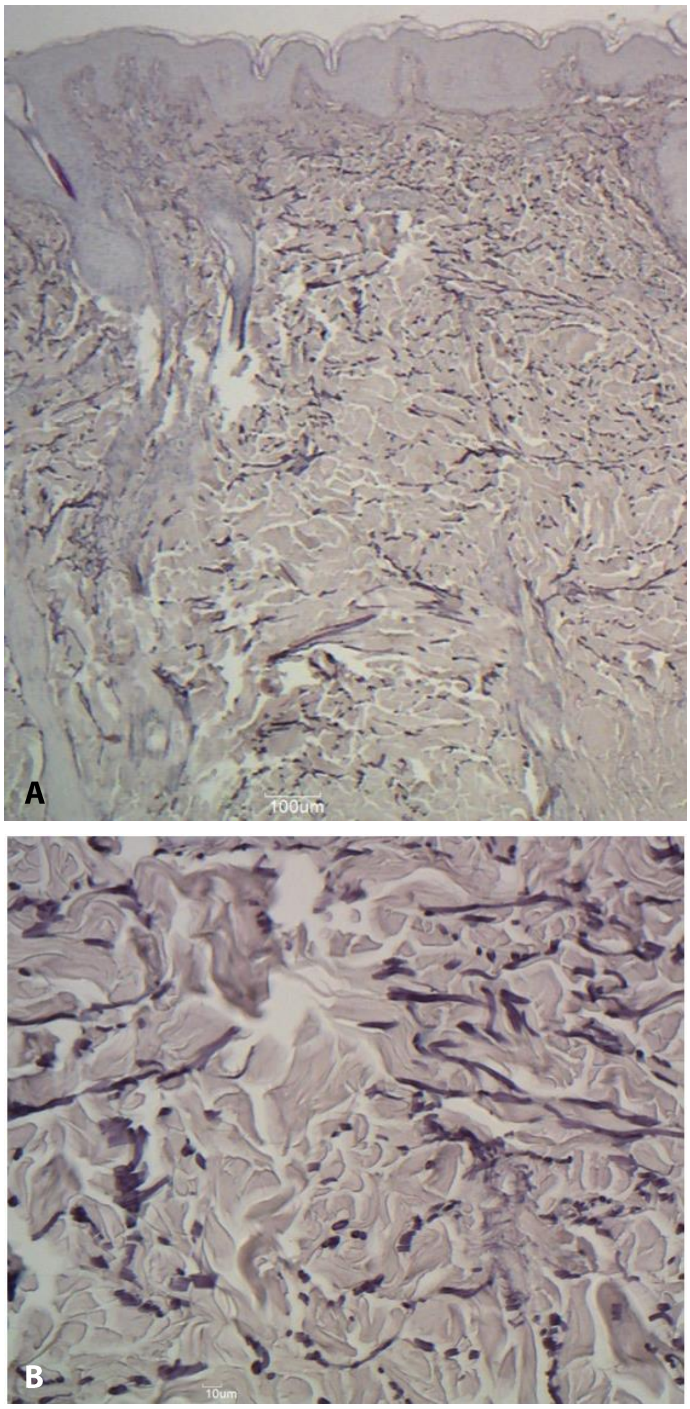

Figure 3. *The study of the elastic fibers showed not specific alterations, with a proportional decrease in respect to the thickened collagen bundles. Weigert stain, 4×, 10×.*

The very widespread presentation in our patient, together with the clinical-pathologic findings supported the final diagnosis of eruptive collagenoma (EC), firstly described by Cramer in 1966 [6]. Eruptive collagenomas are characterized by the sudden appearance of symmetrical asymptomatic multiple firm, skin-colored papules or nodules on trunk and upper limbs. There is no gender or racial predilection; the course is slowly progressive and permanent. Also supportive of the EC diagnosis, our patient had no family history of similar lesions and the onset was in early adulthood, which is typical. Eruptive collagenomas have been reported in Multiple endocrine neoplasia type 1 [11], but our investigations excluded any systemic finding. The observed joint hypermotility that was present in the family suggested a possible association with Ehlers-Danlos syndrome [12], but this was excluded by genetic consultation. The impressive generalization of the subcutaneous nodules gave the appearance of a lumpy bumpy surface, grossly different from the pebbling skin described in Hunter syndrome [13].

The histopathology was pathognomonic of collagenomas [14], showing a thickened reticular dermis made of haphazardly packed collagen bundles, with decreased elastic fibers and fibroblasts. Focal absence of elastic fibers in collagenomas is a controversial topic; some authors consider that the elastic fiber alterations should be considered part of the same spectrum of disease, which includes nevus anelasticus and papular elastorrhexis [15]. Our findings support that collagenoma is different from papular elastorrhexis, as the collagen was mature, just augmented and thickened, with a normal number of fibroblasts (**Figure 4**). The elastic fibers were not fragmented or coarse, just more widely spaced. These likely appear decreased related to a dilution phenomenon in respect to the excessive collagen accumulation.

Etiopathogenesis of EC remains unknown, but a decrease in collagenase activity may play a role, with consequent type 1 collagen accumulation [16].

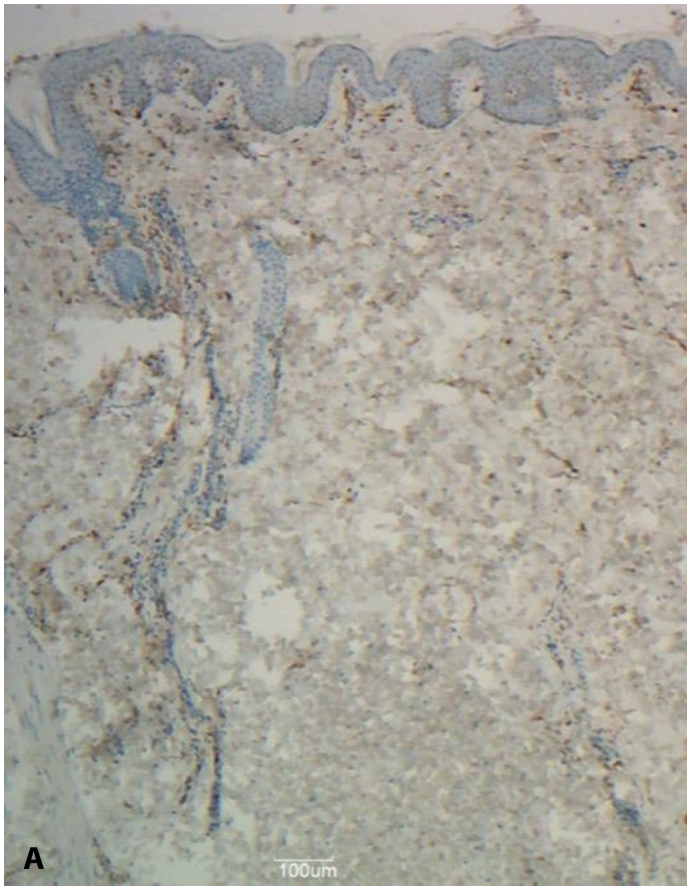

Figure 4. *The number of fibroblasts was normal, without apparent alterations at factor XIIIa immunohistochemistry, 4×, 20×.*

Hormonal influences were suggested for the predominant onset during puberty and pregnancy [6].

Dedicated clinical trials or treatment recommendations are few; EC are often left untreated because of the risk of scarring sequelae. Surgical excision is performed for diagnostic purposes or when particular lesions are more visible or become symptomatic [6]. The use of intralesional triamcinolone acetonide, alone or in combination with hyaluronidase, was effective in isolated corymbose collagenoma, more extensive familial cutaneous collagenoma, and acquired linear nodular collagenoma [17, 18]. The corticosteroid effect may regulate fibroblast synthesis, reducing the release of transforming growth factor β1 (TGFβ1) in favor of basic fibroblast growth factor (bFGF), which in turn inhibits fibroblast mitosis and collagen synthesis.

Our patient was not interested in intralesional treatment because of the extensive areas to be treated and injection pain. He was otherwise disappointed with the scarring results of the simple biopsy. Thus, the decision for surveillance with annual follow up was mutually agreed.

Conclusion

Eruptive collagenomas are benign acquired disorders of the connective tissue, with sudden onset and sometimes wide spread involvement, that can produce relevant aesthetic complaints and require assessment to exclude syndromic forms. The diagnosis relies on histopathological findings characterized by dermal thickening consisting of haphazardly arranged collagen fibers. Special staining is advisable to investigate the relative decrease of elastic tissue and differentiate it from elastorrhexis or nevus anelasticus.

Potential conflicts of interest

The authors declare no conflicts of interests.

References

1. Tjarks BJ, Gardner JM, Riddle ND. Hamartomas of skin and soft tissue. *Semin Diagn Pathol*. 2019; 36:48-61. [PMID: 30573326].
2. Arora H, Falto-Aizpurua L, Cortes-Fernandez A, Choudhary S, Romanelli P. Connective tissue nevi: a review of the literature. *Am J Dermatopathol*. 2017; 39: 325-341. [PMID: 28426484].
3. Saussine A, Marrou K, Delanoe P, et al. Connective tissue nevi: an entity revisited. *J Am Acad Dermatol*. 2012; 67: 233-239. [PMID: 22014540].
4. Perez AD, Yu S, North JP. Multiple cutaneous collagenomas in the setting of multiple endocrine neoplasia type 1. *J Cutan Pathol*. 2015; 42: 791-795. [PMID: 26769154].
5. Uitto J, Santa Cruz DJ, Eisen AZ. Connective tissue nevi of the skin. Clinical, genetic, and histopathologic classification of hamartomas of the collagen, elastin, and proteoglycan type. *J Am Acad Dermatol*. 1980; 3: 441-461. [PMID: 7217375].
6. Sharma R, Verma P, Singal A, Sharma S. Eruptive collagenoma. *Indian J Dermatol Venereol Leprol* 2013; 79:256-8. [PMID: 23442476].
7. Bisherwal K, Singal A, Pandhi D, Girotra V. Solitary Collagenoma of the Labium Majus: A Rare Occurrence. *Indian J Dermatol* 2017;62:312-314. [PMID: 28584376].
8. Khanna D, Goel K, Khurana K. Isolated plantar cerebriform collagenoma. *Indian J Dermatol Venereol Leprol*. 2012; 78: 666. [PMID: 22960845].
9. Kumar S, Singh SK, Bansal A, Bansal M. Isolated Collagenoma on the Scalp: A Rare Presentation. *Int J Trichology*. 2013;5: 88-90. [PMID: 24403773].
10. Biesecker LG, Happle R, Mulliken JB, et al. Proteus syndrome: diagnostic criteria, differential diagnosis, and patient evaluation. *Am J Med Genet*. 1999; 84: 389–395. [PMID: 10360391].
11. Xia Y, Darling TN. Rapidly growing collagenomas in multiple endocrine neoplasia type I. *J Am Acad Dermatol*. 2007; 56:877-80. [PMID: 17188781].
12. Sidwell RU, Francis N, Grahame R, Pope FM, Bunker CB. Connective tissue naevus (collagenoma) in a patient with benign joint hypermobility syndrome (Ehlers-Danlos syndrome type III) *Clin Exp Dermatol*. 2003; 28:323-5. [PMID: 12780726].
13. Srinivas SM, Maganthi M, Sanjeev GN. Pebbling of skin: Cutaneous marker of Hunter syndrome. *Indian Dermatol Online J*. 2017;8: 62–63. [PMID: 28217482].
14. Almeida Hl Jr, Breunig Jde A, Wolter M, et al. Light and electron microscopy of eruptive collagenoma *J Cutan Pathol*. 2009; 36:35-8. [PMID: 19775392].
15. Ryder HF, Antaya RJ. Nevus anelasticus, papular elastorrhexis, and eruptive collagenoma: clinically similar entities with focal absence of elastic fibers in childhood. *Pediatr Dermatol*. 2005; 22:153-7. [PMID: 15804307].
16. Uitto J, Bauer EA, Santa Cruz DJ et al. Decreased collagenase production by regional fibroblasts cultured from skin of a patient with connective tissue nevi of the collagen type. *J Invest Dermatol* 1982; 78: 136–40. [PMID: 6276472].
17. Yadav S et al. Isolated corymbose collagenoma responding to intralesional triamcinolone acetonide and hyaluronidase injections. *Dermatol Ther*. 2013; 26:419-23. [PMID: 24099074].
18. Saki N, Dorostkar A, Heiran A, Aslani FS. Satisfactory treatment of a large connective tissue nevus with intralesional steroid injection. *Dermatol Pract Concept* 2018; 8:12-14. [PMID: 29445568].

Table 1: Classification of cutaneous collagenomas.

Type of transmission	Specific syndromes or pattern of distribution	Skin manifestations	
INHERITED COLLAGENOMAS	Buschke-Ollendorff syndrome	Connective tissue nevi (dermatofibrosis lenticularis disseminatae) and sclerotic bony lesions (osteopoikilosis)	
	Tuberous Sclerosis	Shagreen patch	
	Familial cutaneous collagenoma (FCC)	Collagenomas and cardiac disorders	
ACQUIRED COLLAGENOMAS	LOCALIZED	Plantar cerebriform collagenoma	Plantar surface with a cerebriform pattern, sometimes associated with Proteus syndrome
		Zosteriform collagenoma	zosteriform distribution
		Knuckle pads collagenoma	dorsal aspects of the metacarpophalangeal and interphalangeal joints
		Papulolinear type collagenoma	dorsum of the hands and fingers
	GENERALIZED	Eruptive collagenomas	Non-familial history Abrupt onset