Late-onset focal dermal elastosis: Report of a case and review of the literature

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Abstract

Late-onset focal dermal elastosis is a rare cutaneous condition classified as an increased dermal elastic tissue disorder. It is distinguished clinically by multiple papules with a preference for the neck and other flexures, as well as histologically by focally increased elastic fibers in the reticular dermis. Several elastic tissue disorders in the skin have a similar clinical presentation. The distinction between late-onset focal dermal elastosis and other pseudoxanthoma elasticum mimickers is critical because they are not associated with systemic lesions. We present a case of late-onset focal dermal elastosis and conduct a literature review on this unusual condition.

Introduction

Several elastic tissue disorders share a similar clinical presentation in the skin, *i.e.* multiple small papules symmetrically distributed in the flexural areas. Pseudoxanthoma elasticum (PXE) represents the prototype of such clinical picture, but a number of other elastic tissue disorders may present with a similar appearance of "PXE-like" features. Late-onset focal dermal elastosis (LOFDE) is a rare, acquired cutaneous disorder first described in 1995,[1] characterized clinically by multiple papules in a PXE-like appearance, without systemic alterations, and histologically by focally increased elastic fibers in the reticular dermis. We report here on a case of LOFDE and review the scientific literature on this unusual condition.

Case report

A 70-year-old Italian woman presented with a 4-year history of a bilateral, slowly extending, papular eruption of the axillae. Cutaneous examination showed 2-4 mm firm, yellow white, partly coalescing, non-follicular papules symmetrically distributed along the posterior axillary folds (Figure 1). No other cutaneous folds were affected. The lesions were asymptomatic, but the patient referred that at first, they were itchy and erythematous. Her medical history revealed a primary cutaneous follicular non-Hodgkin lymphoma of the right groin 15 years previously, treated with surgery, chemotherapy, and radiotherapy. A grade 1 urinary bladder carcinoma was removed one year before. No ocular, cardiovascular, gastrointestinal or pulmonary symptoms were present.

A punch-biopsy of a representative papule showed dermal fibrosis at H&E staining. Verhoeff elastic tissue stain showed increase of thick, interlacing elastic fibers in the mid and deep reticular dermis. Fragmentation, calcification or phagocytosis of elastic fibers were no seen. Mild atrophy of the epidermis and edema in the papillary dermis were also evident (Figure 2).

Discussion

LOFDE is a rare cutaneous condition classified within the disorders of increased dermal elastic tissue.[2] Increase of dermal elastic tissue is a feature seen in a number of inherited and acquired disorders, including LOFDE, linear focal elastosis, elastofibroma, nevus elasticus, and Buschke-Ollendorff syndrome. Elastic tissue disorders presenting with a PXE-like appearance, *i.e.* symmetrical, non-follicular papules distributed along the major folds, often require histology and elastic tissue stains to be diagnosed. Distinction of LOFDE and other PXE mimickers from PXE is critical, as they are not associated to systemic lesions.

PXE is a genetic disease induced by autosomal recessive mutations in the ABCC6 gene, that make elastic tissue prone to mineralization.[3] The onset is in childhood or early adolescence, with yellowish papules appearing and coalescing on the major folds. Later on, skin laxity develops. Histology is characteristic, showing fragmentation of the elastic fibers and calcium deposits in the dermis. Internal organs may be affected. Mineralization of the Bruch membrane of the retina leads to angioid streaks and retinal hemorrhages. Involvement of the internal elastic lamina and tunica media of small- and medium-sized arteries may cause vascular disorders such as gastrointestinal bleeding, as well as cardiac and cerebral ischemia.

Other cutaneous conditions, without systemic involvement, share a similar clinical presentation with PXE, and must be considered in the differential diagnosis. PXE-like papillary dermal elastolysis (PXE-PDE) affects predominantly females in late adulthood. It is characterized by band-like loss of elastic tissue in the papillary dermis, with normal collagen fibers. White fibrous papulosis of the neck presents with multiple, symmetrical, non-confluent, whitish papules on the neck, caused by increase in the papillary dermal collagen and loss of elastic fibers in the papillary and reticular dermis. Because of the common characteristics, *i.e.* late onset, similar clinical presentation, histologic features typical of intrinsic aging (decreased elastic fibers in the papillary dermis with or without increased collagen fibers), these conditions

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have been classified under the term "age-related fibroelastolytic syndromes".[4] Nevus elasticus (or elastoma) is a connective tissue nevus, histologically featuring increased dermal elastic tissue. It is either congenital or appears during the first years of life as single or multiple, disseminated or clustered yellow papules or nodules in the face, trunk and extremities. The disseminated nodular form (dermatofibrosis lenticularis disseminata) may be heritable and in association with osteopoikilosis (focal addensation of bone tissue) constitutes the autosomal dominant Buschke-Ollendorff syndrome. Age of onset and the different distribution of the cutaneous lesions help to differentiate this syndrome from LOFDE.[2]

Linear focal elastosis also displays a histologic picture of increased elastic tissue staining in the reticular dermis. Elastic fibers appear fragmented and aggregated. The clinical presentation displays asymptomatic, yellow or red, indurated and palpable linear cords, distributed symmetrically in the lumbar-sacral region and proximal extremities. It preferentially affects males and is not considered an age-dependent, nor actinic process.[2] Finally, a case of "papillary dermal elastosis" in a 33-year-old woman has been reported, characterized by scattered 1–2 mm white-to-yellow papules on the upper back and neck region. Histologically, foci of clumped, granular elastic tissue, alternating with foci of decreased elastic fibers were seen within the papillary dermis. Based on the focal clumping of elastic fibers and young age, it has been proposed that this case may be distinct from PXE-PDE.[5] LOFDE clinically presents with a longstanding history of progressively increasing, 2-4 mm flat-topped papules, symmetrically distributed in the flexural areas (neck, axillae, groin, popliteal and antecubital folds), which may coalesce in plaques. Lesions may be asymptomatic or pruritic. It is characterized histologically by focal increase, in the reticular dermis, of normal appearing elastic fibers, which present, with elastic tissue staining, as aggregates among collagen fibers without calcium deposition. The papillary dermis is unaffected.[1] LOFDE is not associated to systemic diseases; so far, no specific treatment has been described. LOFDE affects preferentially patients after the sixth decade, but a few reports relate to younger patients (18 years in the case of Tajima *et al,* 1996; around 30 years in the two familiar cases of Camacho *et al.,* 2012; 39 years in the case 2 of Wang *et al.,* 2012).[6-8] The term "focal dermal elastosis" has been proposed as an update of the nomenclature to include also these earlier presentations.[9] However, the cases in younger patients differ also in other clinical features from classic presentation, *e.g.* association with acrogeria,[6] familiarity,[7] or acral distribution.[5,7] From a review of the cases reported in the literature (Table 1) it appears that under the term of LOFDE have been grouped heterogeneous clinical presentations, solely on the basis of the histologic trait of increased dermal elastic tissue. The pathogenesis of LOFDE is still unclear. Clinical (late onset in non-exposed areas) and histologic features (absence of solar elastosis) suggest that the condition may result from an intrinsic aging process rather than from sun damage. It has been suggested that an increased elastin synthesis, rather than a reduction of elastin degradation, is involved in LOFDE, as mRNA levels of elastin as well as the expression of other molecules related to elastin metabolism, such as fibrillin-1, fibulin-5, latent transforming growth factor-ß-binding protein-2 (LTBP-2) and LTBP-4 are increased.[10,11] Location on flexural regions might suggest a role for repetitive mechanical stress. The condition may have a higher prevalence and be underreported, because it is clinically subtle and often asymptomatic, and histopathological recognition requires elastic fiber staining in addition to routine histology. In the first report of LOFDE, Authors stated that they had seen several similar cases in the elderly but could not confirm the diagnosis by histological examination.[1]

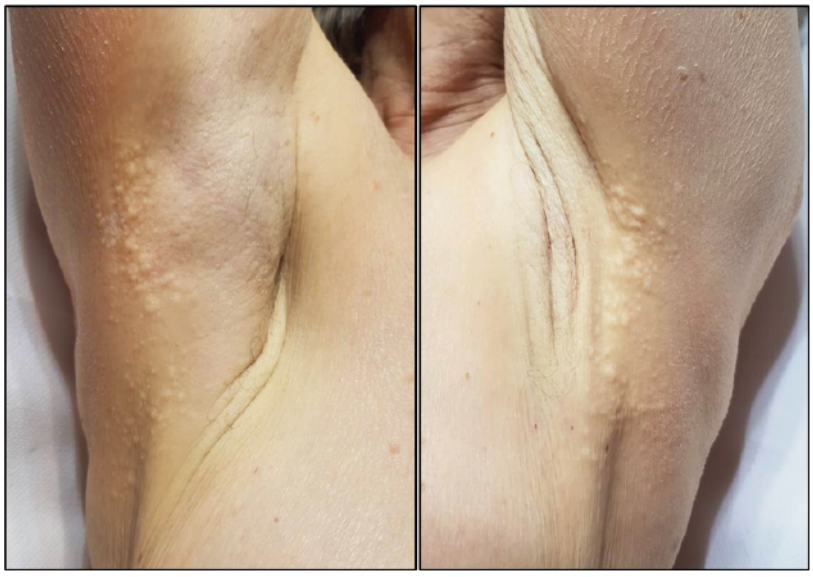

Figure 1. Clinical presentation of late-onset focal dermal elastosis: yellow-white non-follicular papules symmetrically distributed along the posterior axillary folds.

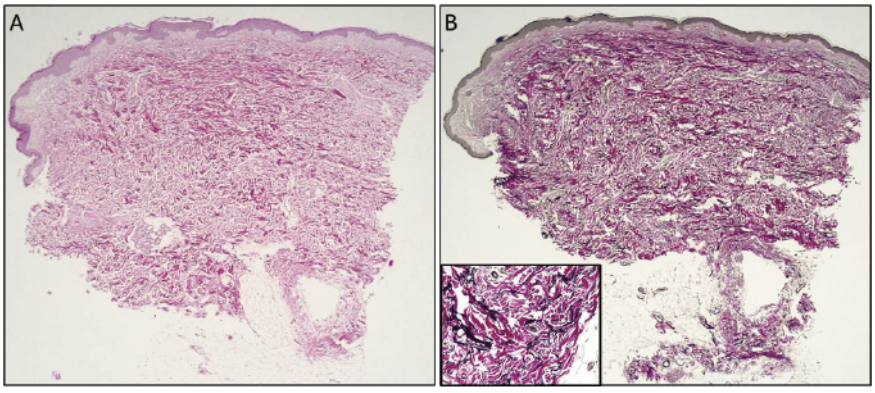

Figure 2. Histologic findings. A) dermal fibrosis without calcification (H&E, 2,5x); B) increase of thick, interlacing elastic fibers in the mid and deep reticular dermis (Verhoeff elastic tissue stain, 2,5x). Inset: elastic fibers without fragmentation.

Table 1. Cases of late-onset focal dermal elastosis.

Year	Ref.	Sex	Age	Duration	Site	Clinical aspect	Symptoms	Histology	Associations
1995	1	M	85	10 years	Thighs, lower abdomen, groins, popliteal fossae and antecubital fossae	Multiple yellow papules with a peau d'orange appearance	Asymptomatic	Focal increase in normal-appearing elastic fibres in the mid- or deep dermis	
1995	1	F	65	6 years	Neck, thighs, groins, antecubital and popliteal fossae	Papules	Asymptomatic	Focal increase in normal-appearing elastic fibres in the mid- or deep dermis	
1996	6	F	18	Not reported	Neck, inguinal area and axilla	Multiple yellow papules	Asymptomatic	Focal increase in normal-appearing elastic fibers in the dermis.	Acrogeria
1999	12	F	72	2 years	Sides of the neck, axillae, and antecubital fossae	Multiple yellowish 3-mm papules	Asymptomatic	Atrophic epidermis, increased concentration of normal elastic fibers in the middermis	Diabetes mellitus
1999	12	F	69	Not reported	Sides of the neck	Multiple yellowish, 1- to 3-mm papules	Asymptomatic	Atrophic epidermis, increased concentration of normal elastic fibers in the middermis	iabetes mellitus, Dhypothyroidism
2005	13	F	73	10 years	Neck, upper trunk and axillae	Coalescent flat pale yellow lesions forming a cobblestone pattern	Asymptomatic	Elastosis in the upper reticular dermis, foca l increase in structurally normal elastic fibres	Asthma and allergic rhinitis
2010	14	F	87	3 months	Posterior neck	Yellow plaque	Pruritus	Increased elastic tissue	
2012	7	F	53	20 years	Dorsum of the hands, wrists, abdomen, thighs	Yellowish, flat-topped, smooth, 2- to 4-mm-diameter papules	Asymptomatic	Increase of abnormal (thick and interlacing) elastic fibers in the deep and mid reticular dermis	Familial
2012	7	F	48	20 years	Dorsum of the hands	Yellowish, flat-topped, smooth, 2- to 4-mm-diameter papules	Asymptomatic	Increase of abnormal (thick and interlacing) elastic fibers in the deep and mid reticular dermis	Familial
2012	8	F	75	12 months	Posterolateral neck, anterior chest and axillae papules 2-5 mm	White-yellow non -follicular	Occasionally pruritic	Increased aggregates of elastic fibers in the reticular dermis	
2012	8	F	39	6-8 months	Posterior neck, back, antecubital and popliteal fossae, thighs, forearms and wrists	2–4 mm flesh-colored-to-yellow papules	Asymptomatic	H&E: thickened collagen bundles elastic tissue stain: increased aggregates of thickened, branched elastic fibers in the mid-dermis	
2012	15	F	72	3 years	Neck, anterior chest	2-5 mm pale yellow papules	Mild itching	Atrophic epidermis, focal accumulation of normal-appearing elastic fibres in the reticular dermis	
2014	16	F	48	years	Neck	Yellow cobblestone plaque	Asymptomatic	Elastic degeneration with perivascular dermatitis	
2016	17	F	54	5 years	Neck, antecubital and popliteal fossae, flexor surface of both forearms, and inner aspect of the thighs	>100, 2- to 4-mm, firm, yellow, dermal papules	Asymptomatic	Focal increase in the concentration of elastic fibers	Mitral valve prolapse
2018	11	F	73	10 years	Arms, trunk	Whitish yellow papules and coalesced plaques on the axilla, trunk and extremities	Asymptomatic	Increased elastic fibers in the mid- to lower dermis	
2018	18	F	74	1 week	Bilateral axillae to yellowish papules coalescing into plaques in a cobblestone pattern	Flesh-colored	Mild itch	Increased dermal elastic fibers wit h occasional fragmentation	Hypothyroidism
2018	19	F	70	5 years	Bilateral axillae	White papules coalescing into plaques with a cobblestoned appearance	Asymptomatic	Foci of thickened and clumped elastic fibers in the deep reticular dermis	
2020	9	F	59	20 years	Anterior shoulders, antecubital fossae, and medial thighs	Flat yellowish subcutaneous nodules forming a cobblestone pattern	Asymptomatic	Increased density of normal-appearing dermal elastic fibers with no evidence of fragmentation	
2021	Present case	F	70	4 years	Posterior axillary folds	Yellow-white papules	Mild itch at the onset	Increase of thick, interlacing elastic fibers in the mid and deep reticular dermis	

Conclusions

The typical clinical features of LOFDE can be summarized as follows: late onset, prevalence in female, predilection for the neck and other flexures, asymptomatic or mildly pruritic (especially at the onset), no association with systemic diseases. Focal increase of elastic fibers in the reticular dermis is the histologic hallmark of the condition. Since it is still uncertain if the cases at variance with these characteristics belong to the same, unique entity, we think that the original nomenclature should be reserved to indicate the classic presentation.

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