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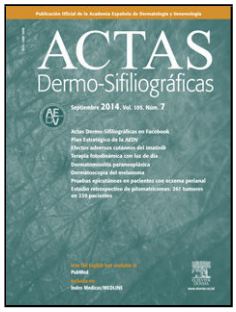

Asymptomatic slowly evolving fine wrinkled dermatosis in a man

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PII: S0001-7310(25)00113-9

DOI: https://doi.org/doi:10.1016/j.ad.2023.10.063

Reference: AD 4283

To appear in: *Actas dermosifiliograficas*

Received Date: 3 August 2023

Accepted Date: 9 October 2023

Please cite this article as: Valente C, Aparício Martins I, Duarte B, Asymptomatic slowly evolving fine wrinkled dermatosis in a man, *Actas dermosifiliograficas* (2025), doi: https://doi.org/10.1016/j.ad.2023.10.063

Sección; Casos para Diagnóstico

Title: Asymptomatic slowly evolving fine wrinkled dermatosis in a man

Título: Dermatosis finamente arrugada asintomática de lenta evolución en un hombre

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Medical history:

A man in his 60s presented to the dermatology office with a 10-year history of dermatosis that started on his trunk and gradually expanded to his proximal upper limbs. His past medical history included factor V Leiden mutation, a pulmonary embolism 7 years ago, a myocardial infarction 30 years prior, and fibromyalgia. His medication included acetylsalicylic acid, losartan, verapamil, atorvastatin, and clonazepam. There was no past pharmacological history of drug, alcohol, or tobacco use. His family history was unremarkable. Despite no pruritus or pain, he expressed dissatisfaction with his skin's appearance. Throughout the years, various treatments, such as emollients with urea, topical corticosteroids (betamethasone dipropionate cream), prednisolone, and oral fluconazole proved ineffective.

Physical examination:

Presence of symmetrical erythematous patches of fine wrinkles on his trunk and proximal arms (Fig.1).

Histopathology:

Histopathologic examination of a biopsy performed on the patient's dorsum with Hematoxylin&Eosin (H&E) staining [x40] was unremarkable (Fig.2A). Orcein staining [x40] showed a focal loss of elastic fibers in the mid-dermis (Fig.2B).

Supplementary tests:

Lab test results were unremarkable, including complete blood count; biochemistry; renal, hepatic and thyroid function; autoimmunity (tests for antinuclear and antineutrophil cytoplasmic antibodies) and viral serologies (HIV, HBV, HCV).

What is your diagnosis?

Diagnosis:

Mid-dermal elastolysis type III.

Clinical course and treatment:

We tried tretinoin cream 0.5mg/g for 2 months with minor improvement; there was no progression of the dermatosis, yet the wrinkled appearance of the patches remained unchanged.

Comment:

Mid-dermal elastolysis (MDE) is a rare acquired elastic tissue disorder that is more prevalent in middle-aged women. Although MDE is limited to the skin and has no systemic involvement, it is associated with numerous concomitant or preceding diseases, particularly autoimmune disorders.[1]

The precise pathophysiology of MDE is not completely understood. It appears to involve an enhanced elastolytic activity and a decrease in elastic fiber renewal. Multiple cells such as macrophages and fibroblasts are involved in this entity, creating an imbalance between the overexpression of matrix metalloproteinases and decreased expression of tissue inhibitors of metalloproteinases. The triggers for this enhanced elastolytic activity are not fully understood and may include genetic background, chronic inflammation, and autoimmunity.[1–3]

On physical examination, symmetrically distributed patches of well-circumscribed fine wrinkles (type I), perifollicular papular protrusions (type II), or persistent reticular erythema and wrinkling (type III) can be found on trunk and proximal limbs. Like in our case, type III is more common in older men (> 50 years).[1]

Histopathologic examination with elastica stains (like Orcein or Verhoeff–Van Gieson) is pathognomonic, revealing a band-like or focal loss of elastic fibers in the mid-dermis, with sparing of papillary and deeper reticular dermis and around the appendages.[3] Inflammatory infiltrates and macrophages/elastophagocytosis are sporadically seen. MDE belongs to the group of “invisible” dermatoses to the dermatopathologist, with no significant changes in H&E staining. Clinicopathological correlation is essential to perform additional elastica stains to establish the diagnosis of MDE.[4]

Differential diagnoses include anetoderma, cutis laxa, pseudoxanthoma elasticum-like papillary dermal elastolysis and annular elastolytic giant cell granuloma. Anetoderma presents with smaller, well-circumscribed areas of pouch-like herniations of flaccid skin, with loss of elastic fibers in the papillary and reticular dermis on histology. Cutis laxa presents with loose redundant skin, frequently with internal organ involvement and fragmentation of elastic fibers on histopathology. Pseudoxanthoma elasticum-like papillary dermal elastolysis resembles pseudoxanthoma elasticum clinically, with a band-like loss of elastic fibers in the papillary dermis on histopathology. Annular elastolytic giant cell granuloma comprises erythematous annular lesions with atrophic wrinkled appearance centrally, and on biopsies, a dermal granulomatous infiltrate with loss of elastic fibers centrally is seen.[3]

Treatment is challenging since, to this date, no treatment allows full recovery of the lost elastic tissue. UV radiation is thought to play a role in the pathogenesis of MDE; therefore, sun protection is recommended. Various topical and systemic treatments have been attempted, including

corticosteroids (topical and systemic), tretinoin, hydroxychloroquine, vitamin E, clofazimine, colchicine, dapsone, and mycophenolate mofetil, with modest improvement being reported.[3,5,6]

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Figure captions:

Figure 1. Clinical observation of symmetrical erythematous patches of fine wrinkles on the dorsum, proximal arms and lumbar region.

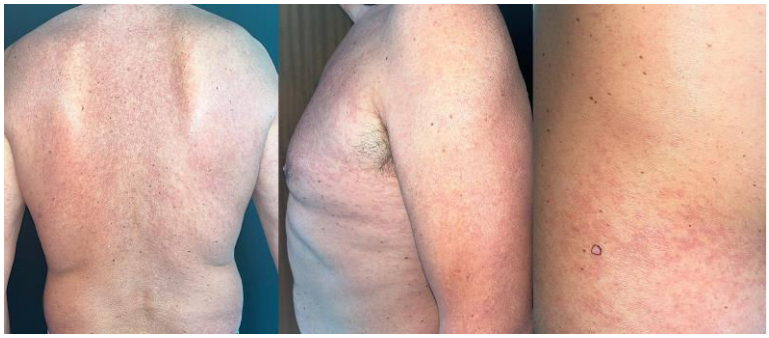
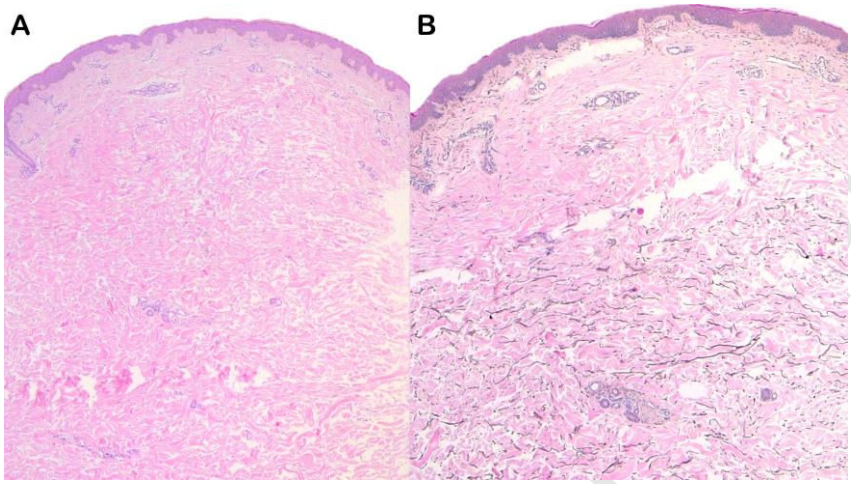


Figure 2. (A) Histology with Hematoxylin & Eosin stain [x40]. (B) Histology with Orcein staining [x40].



Dear Editor and Reviewers,

Thank you for considering our work for publication. We appreciate the helpful comments on the manuscript and have revised it to include the given suggestions. Please find below our responses:

- *Revisor nº1: English should be improved. There are some grammatical errors. Some examples: "What is it your diagnosis?" should say "What is your diagnosis? "Histopathology examination of …" should say "Histopathologic examination of" "Orcein staining [x40] showed no change…." ??? "Diferencial" should say differential diagnosis "the likelihood of effectively treating the already wrinkled skin areas becomes significantly diminished" this phrase is confusing*

We made the proper changes as advised. In page 1: 'What is your diagnosis?'. In page 1 and 2: 'Histopathologic examination'. In page 1: 'Orcein staining [x40] showed loss of elastic fibers in the mid-dermis'. In page 2: 'Differential diagnosis'. In page 2: 'Treatment is challenging since, so far, no treatment allows for full recovery of the lost elastic tissue.'

- *Did the authors perform any laboratory investigations?, especially regarding autoimmunity?*

A blood analysis was performed and revealed no abnormalities. We added this information on page 1: 'Additional tests: Laboratory testing was unremarkable, including complete blood count; biochemistry; renal, hepatic and thyroid function; autoimmunity (tests for antinuclear and antineutrophil cytoplasmic antibodies) and viral serologies (HIV, HBV, HCV).'

- *Please improve the histopathological description. Perhaps in the second part of the article, explain the histopathological features that allow a correct diagnosis.*

We made the proper changes in the histopathological description in page 1, line: "Histopathology: Histopathologic examination of a biopsy done on his dorsum with Hematoxylin&Eosin (H&E) staining [x40] was unremarkable (Fig.2A). Orcein staining [x40] showed a focal loss of elastic fibers in the mid-dermis (Fig.2B).'

We made the proper changes in the second part, page 2, line: 'Histopathologic examination with elastica stains (like Orcein or Verhoeff–Van Gieson) is pathognomonic, revealing a band-like or focal loss of elastic fibers in the mid-dermis, with sparing of papillary and deeper reticular dermis and around the appendages.[3] Inflammatory infiltrates and macrophages/elastophagocytosis are sporadically seen.'

- *When the authors say "they belong to the group of invisible dermatosis", I think they should be more specific, of course the authors mean invisible dermatosis to the pathologist point of view, but please clarify better. They also say clinicopathological correlation is essential, but*

in fact what it is essential, is the performance of additional techniques such as orcein or Verhoeff-van Giesonor or lichens red stains.

We made the proper changes in page 2, line: 'MDE belongs to the group of "invisible" dermatoses to the dermatopathologist, with no significant changes in H&E staining. Clinicopathological correlation is essential to perform additional elastica stains that allow the diagnosis of MDE.'

- *Please discuss a little bit more the differential diagnosis.*

We made the proper changes in page 2, line: 'Differential diagnoses include anetoderma, cutis laxa, pseudoxanthoma elasticum-like papillary dermal elastolysis and annular elastolytic giant cell granuloma. Anetoderma presents with smaller, well-circumscribed areas of pouch-like herniations of flaccid skin, with loss of elastic fibers in the papillary and reticular dermis on histology. Cutis laxa presents with loose redundant skin, frequently with internal organ involvement and with fragmentation of elastic fibers on histopathology. Pseudoxanthoma elasticum-like papillary dermal elastolysis resembles pseudoxanthoma elasticum clinically, with a band-like loss of elastic fibers in the papillary dermis on histopathology. Annular elastolytic giant cell granuloma comprises erythematous annular lesions with atrophic wrinkled appearance centrally, and on biopsies, a dermal granulomatous infiltrate with loss of elastic fibers centrally is seen.'

- *Please check reference formating (references should be in superscript in the text, not in square brackets [])*

We made the proper changes as advised.

- *Revisor nº2: Incluir el tipo de dermatosis que padece el paciente en la respuesta "Diagnóstico" (tipo I, II ó III) que posteriormente se exponen en el bloque de comentario*

We made the proper changes in page 1, line: "Mid-dermal elastolysis type III.".

- *Comentarios del editor. Clinical and histopathological pictures, must be improved as the lesions are difficult to see in the clinical picture and the white contrast and contrast is low in the histopathological pictures, both in the one with HE and in the one with orcein staining.*

We made the proper changes as advised.

Best regards,