

anti-cardiolipin antibodies and other anti-extractable nuclear antigens were negative. The diagnosis of infliximab-induced lupus was established and infliximab was discontinued. Prednisolone 1 mg/kg/day, was started; after four weeks all symptoms had resolved, and after two months, autoantibodies were negative and complement levels returned to normal. Three months later, he started etanercept (50 mg/week) without any adverse events.

The second case is a 60-year-old male patient, with an 8-year history of rheumatoid arthritis (RA), under adalimumab (40 mg every other week) in association with oral methotrexate (20 mg/week). Baseline laboratory investigations showed positive ANA (1/100, homogeneous pattern), in the absence of other clinical or laboratory manifestations suggestive of lupus, and negative anti-DsDNA. After 3 months of treatment, he presented arthralgia, asthenia, anorexia, malar rash and hand cutaneous vasculitis. Laboratory investigation showed normal cell blood count, positive ANA (1/320 homogeneous pattern), positive anti-DsDNA (326.2 UI/mL), complement consumption (C3 79 mg/dL, and C4 10 mg/dL). The other autoantibodies tested, namely anti-histone antibodies, were negative. Within four weeks of adalimumab suspension, rapid reduction of the clinical symptoms and biological parameters was seen and antibodies disappeared after three months.

The third case is a 44 year-old female patient, with an 11-year history of RA treated with adalimumab (40 mg every other week) in association with leflunomide (20 mg/day). At baseline, clinical manifestations suggestive of lupus were absent and ANA and anti-DsDNA were negative. After four years of treatment, she developed photosensitivity, malar rash, disseminated sub-cutaneous lupus rash, asthenia, low grade fever and arthralgia. Laboratory investigation revealed leukopenia ($3560/\text{mm}^3$), ESR 60 mm/h, CRP 55.6 mg/L, positive ANA (1/320, homogeneous pattern), positive anti-dsDNA (233 UI/mL) and positive anti-histone antibody. Complement levels were within normal range and the other antibodies tested were negative. Adalimumab was suspended and after 6 weeks all symptoms disappeared and autoantibodies turned negative. She started golimumab (50 mg/month) without recurrence.

Herein, we reported three rare cases of anti-TNF-induced lupus, two of them induced by adalimumab, which have been very rarely described in literature³.

The three cases described mirror the clinical heterogeneity that these patients can present. Since the raise of autoantibodies during the treatment can occur, and, anti-histone antibodies can be negative, the most important features to identify such patients are the clinical symptoms. It is advisable to stop the drug and, despite some controversy, the switch to other anti-TNF can be done without recurrence.⁵

References

1. Takase K, Horton SC, Ganesha A, Das S, McHugh A, Emery P, et al. What is the utility of routine ANA testing in predicting development of biological DMARD-induced lupus and vasculitis in patients with rheumatoid arthritis? Data from a single-centre cohort. *Ann Rheum Dis*. 2014;73:1695–9.
2. Atzeni F, Talotta R, Salaffi F, Cassinotti A, Varisco V, Battellino M, et al. Immunogenicity and autoimmunity during anti-TNF therapy. *Autoimmun Rev*. 2013;12:703–8.
3. De Bandt M, Sibilia J, Le Loët X, Prouzeau S, Fautrel B, Marcelli C, et al. Systemic lupus erythematosus induced by anti-tumour necrosis factor alpha therapy: a French national survey. *Arthritis Res Ther*. 2005;7:R545–51.
4. Brunasso AM, Aberer W, Massone C. Subacute lupus erythematosus during treatment with golimumab for seronegative rheumatoid arthritis. *Lupus*. 2014;23:201–3.
5. Santiago T, Santiago MG, Rovisco J, Duarte C, Malcata A, da Silva JAP. A case of infliximab-induced lupus in a patient with ankylosing spondylitis: is it safe switch to another anti-TNF- α agent? *Clin Rheumatol*. 2013;32:1819–22.

Rita Fonseca,* Eva Mariz, Miguel Bernardes, Lúcia Costa

Rheumatology Departmente, São João Hospital, Oporto, Portugal

* Corresponding author.

E-mail address: anaritapfonseca@gmail.com (R. Fonseca).

2173-5743/

© 2016 Elsevier España, S.L.U. and Sociedad Española de Reumatología y Colegio Mexicano de Reumatología. All rights reserved.

A Case Report of Pseudoxanthoma Elasticum and Systemic Lupus Erythematosus: An Uncommon Association?[☆]



Presentación de un caso de Pseudoxantoma elasticum y lupus eritematoso sistémico: ¿una asociación infrecuente?

To the Editor,

Pseudoxanthoma elasticum (PXE) is a rare hereditary disorder that affects connective tissue and consists of a progressive calcification of the elastic fibers of the skin, the Bruch membrane in the retina and cardiovascular system. Its prevalence in the general population is estimated to be 1:25,000–100,000 population, with a slight predominance of women.¹ It frequently presents as yellowish papular lesions, which can converge and form plaques with an irregular morphology and a “paved” aspect due to the fact that the skin becomes laxer and more redundant.

The association of this disorder with other systemic connective tissue diseases is rare. To date, there have been 6 cases associated with rheumatoid arthritis,^{2–5} 2 with systemic lupus erythematosus

(SLE)⁶ and another associated with ankylosing spondylitis.⁷ We describe a case of PXE in a patient with SLE.

The patient was a 46-year-old woman, an active smoker, who had been diagnosed with SLE at the age of 28 years. She began with a nephrotic syndrome secondary to World Health Organization class IV diffuse proliferative lupus nephritis, which was treated with mycophenolate mofetil. This achieved resolution of the nephrotic syndrome, and she had been asymptomatic since then. During a check-up, she mentioned the development of asymptomatic skin lesions on her neck and in axillae. Physical examination revealed papular lesions measuring around 3 cm \times 7 cm, distributed on both sides of her neck. They were yellowish and lax, like “goosebumps” (Fig. 1), and she had others that were similar but smaller in the axillae. A specimen was taken for a skin biopsy which showed the existence of a high number of fragmented elastic fibers in the dermis (Fig. 1), a finding compatible with PXE. The study was completed with an examination of the fundus which showed nothing abnormal and renal ultrasound which revealed no signs of disease.

Pseudoxanthoma elasticum is a hereditary connective tissue disease related to a mutation in the *ABCC6* gene located on chromosome 16p13.1, that encodes the multidrug resistance protein 6 (MRP6), which is one of the family of adenosine triphosphate-dependent membrane transport proteins, which are mostly expressed in the liver and kidneys. Two types of inheritance have been described: autosomal recessive in 90% of the cases and autosomal dominant, much rarer. Mutation in the *ABCC6* gene

[☆] Please cite this article as: Muñoz Gómez MM, Novella Navarro M, Ramírez Gómez M, Navas-Parejo A. Presentación de un caso de Pseudoxantoma elasticum y lupus eritematoso sistémico: ¿una asociación infrecuente? *Reumatol Clin*. 2017;13:183–184.

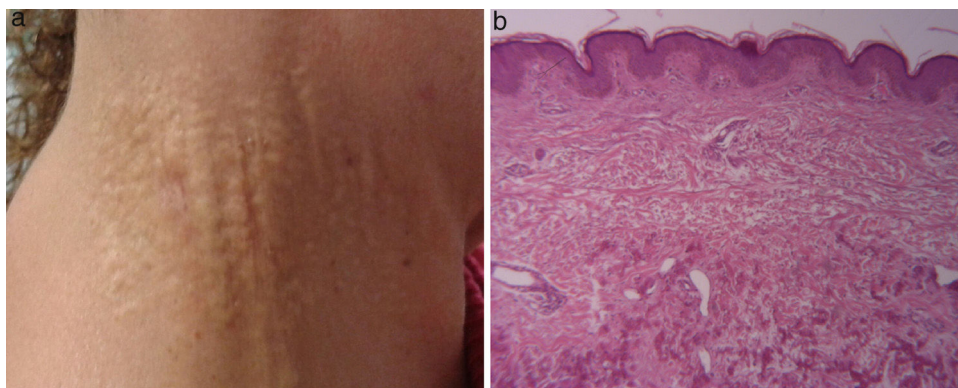


Fig. 1. (a) Yellowish papular lesions looking like “goosebumps” in right neck region, surrounded by normal skin. (b) Hematoxylin-eosin staining: sample of calcified elastic fibers in reticular dermis.

provokes an absence of MRP6, which leads to an accumulation of substances with a high affinity for elastic tissues, resulting in the distortion of calcium deposits and fragmentation of elastic fibers.

Cutaneous manifestations include asymptomatic yellowish papules distributed symmetrically from the start of the neck that can extend to the flexure area. Although not pathognomonic, a characteristic ocular finding is the presence of angioid streaks that represent calcium deposits on the Bruch membrane. They can cause rupture of blood vessels, leading to neovascularization and retinal hemorrhage, resulting in a loss of visual acuity. In the cardiovascular system, calcification of the walls of small and medium-sized arteries can produce premature atheromatosis. The diagnosis of PXE is based on clinical suspicion and should be confirmed by a histological study, which reveals fragmentation and distortion of elastic fibers in the reticular dermis and the accumulation of calcium carbonate and phosphates in the extracellular matrix.

The pathophysiological mechanism that demonstrates the possible association between PXE and other inflammatory connective tissue diseases has not yet been established; however, the first case of association was described decades ago and, since then, there have been reports of 9 more cases. Nevertheless, when they are analyzed, no special feature has been identified that would enable us to reach conclusions. Still, given that PXE can be accompanied by potentially serious ocular and vascular manifestations, it is important that clinicians be aware of this possible association.

References

- Bergen AA, Plomp AS, Schuurman EJ, Terry S, Breuning M, Dauwerse H, et al. Mutations in *ABCC6* cause pseudoxanthoma elasticum. *Nat Genet.* 2000;25:228–31.
- Richette P, Palazzo E, Kahn MF. Coexisting pseudo-xanthoma elasticum and rheumatoid arthritis. Three cases and review of the literature. *Joint Bone Spine.* 2001;68:513–6.
- Satoh M, Akizuki M, Hama N, Akama H, Matsushita Y, Kawai S, et al. Rheumatoid arthritis in a patient with pseudoxanthoma elasticum. *Intern Med.* 1993;32:508–9.
- Praderio L, Marianj F, Baldini V. Pseudoxanthoma elasticum and rheumatoid arthritis. *Arch Intern Med.* 1987;147:206–7.
- Klingel R, Poralla T, Dippold W, Meyer zum Büschenfelde KH. Pseudoxanthoma elasticum (Grönblad-Strandberg syndrome) and rheumatoid arthritis. *Dtsch Med Wochenschr.* 1990;115:1911–6.
- Le Scannff J, Sève P, Dalle S, Kodjikian L, Thomas L, Broussolle C. Coexisting pseudoxanthoma elasticum and lupus erythematosus: report of two cases. *Int J Dermatol.* 2007;46:622–4.
- Nagant de Deuxchaisnes C, Bourlond A. Grönblad-Strandberg syndrome and ankylosing spondylarthritis. *Arch Belg Dermatol Syphiligr.* 1967;23:77–85.

María del M. Muñoz Gómez,^a Marta Novella Navarro,^a
María Ramírez Gómez,^{b,*} Antonio Navas-Parejo^b

^a *Servicio de Reumatología, Hospital Universitario San Cecilio, Granada, Spain*

^b *Departamento de Nefrología, Hospital Universitario San Cecilio, Granada, Spain*

* Corresponding author.

E-mail address: mari936@hotmail.com (M. Ramírez Gómez).

2173-5743/

© 2016 Elsevier España, S.L.U. and Sociedad Española de Reumatología y Colegio Mexicano de Reumatología. All rights reserved.