

PRESENTACIÓN DE CASO/CASE REPORT

Calcifying Lupus panniculitis in a patient without manifestations of systemic lupus Erythematosus

Paniculitis Lúpica calcificante en un paciente sin manifestaciones de lupus eritematoso sistémico

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Summary

Lupus panniculitis or lupus profundus is a variant of lupus Erythematosus cutaneous that primarily affects subcutaneous tissue. Clinically, it is characterized by one or several firm subcutaneous nodules and/or plaques with or without overlying epidermal changes. It is reported to occur with a frequency of 2-3% in patients with Systemic Lupus Erythematosus (SLE). Between 10 and 50 percent of patients with lupus panniculitis will have or eventually develop Systemic Lupus Erythematosus. In nearly all cases there are deep, erythematosus plaques and nodules, and some of them ulcers, which usually involve the proximal extremities, trunk, breasts, buttocks, and face. These lesions may be tender and painful and frequently heal with atrophy and scarring, turning as a chronic condition and subsequently heal with disfigurement. We describe a patient who suffers from lupus panniculitis with no association to SLE symptoms and complicated by several progressive and disabling cutaneous lesions.

Key words: lupus panniculitis, dystrophic calcification, lupus erythematosus cutaneous.

Resumen

La paniculitis lúpica o también llamada lupus profundus es una variante del lupus eritematoso cutáneo que afecta el tejido celular subcutáneo. Se caracteriza clínicamente por uno o varios nódulos subcutáneos que son firmes y/o placa con o sin cambios epidérmicos. Se ha informado su frecuencia en 2% a 3% de casos de Lupus eritematoso sistémico. Entre el 10 al 50% de los casos de paniculitis lúpica va a desarrollar lupus eritematoso sistémico. En casi todos los casos hay placas eritematosas y/o nódulos que en algunos casos se ulceran y que usualmente están localizados en las áreas proximales de las extremidades, tronco, mamas, nalgas y la cara. Estas lesiones pueden ser clínicamente dolorosas y sensibles a la presión y frecuentemente cicatrizan con desfiguración del área circundante. Describimos un paciente que padece de paniculitis lúpica sin asociación de lupus eritematoso sistémico y que se complicó con varias lesiones cutáneas progresivas y discapacitantes.

Palabras clave: paniculitis lúpica, calcificación distrófica, lupus eritematoso cutáneo.

Introduction

Lupus panniculitis or lupus profundus is a variant of lupus Erythematosus cutaneous that

primarily affects subcutaneous tissue. Clinically, it is characterized by one or several firm subcutaneous nodules and/or plaques with or without overlying epidermal changes. New

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nodules may appear while other may resolve slowly or may have long standing calcification. In nearly all cases there are deep, erythematous plaques and nodules, and some of them ulcers, which usually involve the proximal extremities, trunk, breasts, buttocks, and face. Lesions may be tender and painful and frequently heal with atrophy and scars turning as a chronic condition and subsequently heal with disfigurement. Lupus panniculitis is reported to occur with a frequency of 2-3% in patients with Systemic Lupus Erythematosus (SLE)¹⁻³. Conversely, between 10 and 50 percent of patients with lupus panniculitis will have or eventually develop systemic.

lupus Erythematosus. This entity can manifest along with symptoms and laboratory of SLE or by itself. Approximately a quarter of patients with lupus panniculitis fulfilled the American College of Rheumatology criteria of SLE. Antinuclear antibodies (ANA) are positive in 65% of patients in low titers⁴.

Lupus panniculitis has been described associated to other entities and it is not limited to patients with SLE⁵. Prognosis is generally good, despite the association to systemic manifestations.

A panniculitis associated with a patchy lymphocytic infiltrate and deposition of mucin in the overlying dermis is suggestive of lupus panniculitis⁶.

We describe a patient who suffered from lupus panniculitis with no association to SLE symptoms and complicated by several progressive and disabling cutaneous lesions.

Case report

A 50 year-old woman, housekeeping and Hispanic race, had a diagnosis of lupus panniculitis at the age of 40, when she presented with symptoms of arthralgias, headache, and malaise, weight and hair loss. She did not state relevant past medical and family history except of fibromata of uterus and migraine.

In the past 8 years she developed multiple subcutaneous nodules which were seen first at elbows and then they spread to most regions of the body: Thorax, abdomen, upper, and lower extremities (figures 1, 2, 3, 4, 5 and 6).

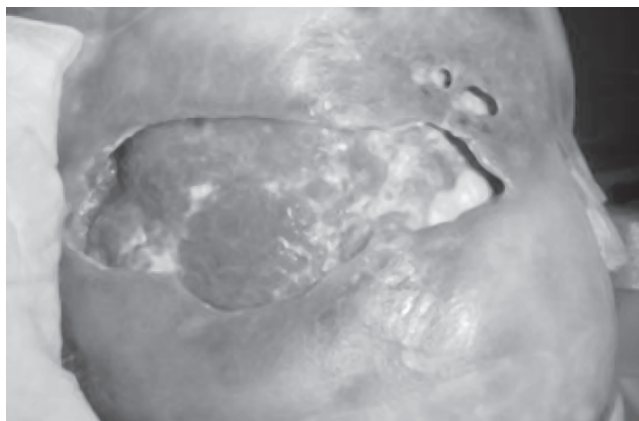


Figure 1. An extensive ulcer with debris tissue on its bottom with mild surrounding erythematous rash on the left buttock.

These lesions are characterized by being mobile, painful, hard or firm consistency, and cause fissures and ulcerations to the overlying skin with atrophy and depressions.

In the last years, the patient has undergone multiple hospitalizations due to several episodes of secondary infections and ulcerations on the nodules. It was obtained pseudomonas and staphylococcus species on cultures from one of the lesions and staphylococcus epidermidis on blood cultures requiring intravenous antibiotics. Physical examination was unremarkable except for an ulcer that reveals a debris tissue with mild surrounding erythematous rash on the left buttock (figure 1) and several firm nodules of approximately 2 to 3 centimeters localized in thorax, abdomen, upper (figures 2, 3, 4 and 5) and lower extremities (figure 6). These nodules were covered by a skin with depressions and lesions on different healing stages. Laboratory studies showed negative antinuclear antibodies (ANA), negative extractable nuclear antibodies that included anti La/SS-B, Ro/SS-A, Sm and RNP. Double stranded DNA was negative. Hemoglobin of 10.4 mg/dl, hematocrit 32%, and leucocytes 5000 x mm³ with lymphopenia, platelets 563000 x mm³, reactive C-protein 36ug/dl, erythro sedimentation globular 22mm/h, calcium 10.8 mEq/L. Proteins 5.9 g/L, albumin 2.4 g/L, globulins 3.5 g/L, alkaline phosphatase and transaminases

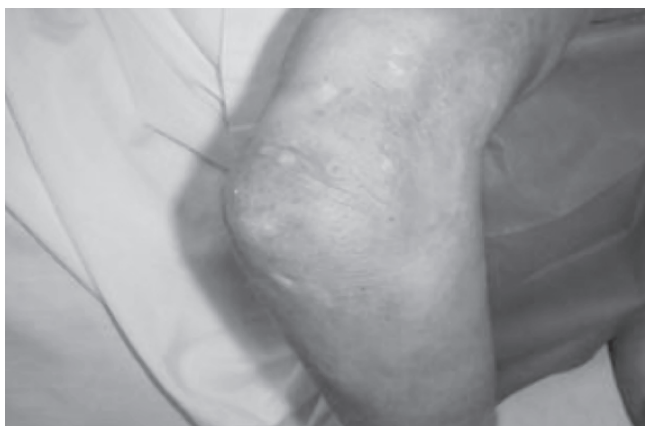


Figure 2.

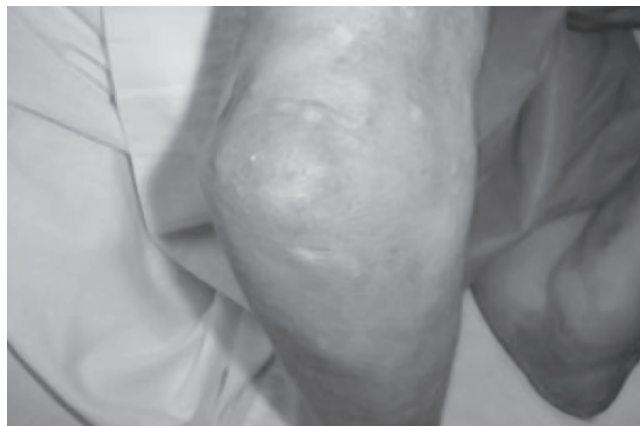


Figure 4.



Figure 3.



Figure 5.

Figures 2, 3, 4, 5. Multiple erythematous nodules and indurated plaques along with depressed areas are appreciated in upper extremities. Note the diversity of the healing process in different stages.



Figure 6. Indurated and depressed violaceous healing plaques with nodules over thighs.

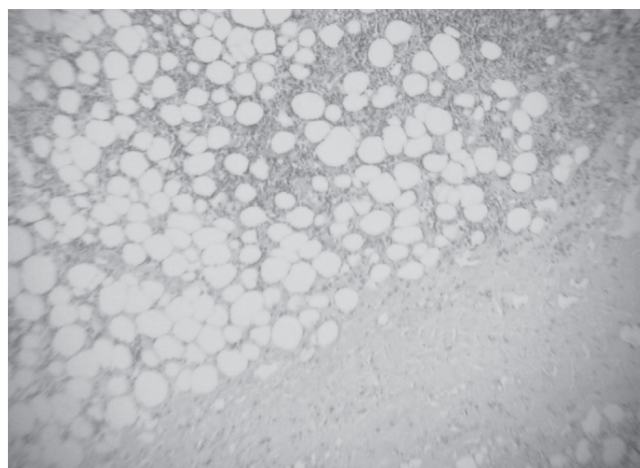


Figure 7. Hyalinization of septa between fat subcutaneous lobules in addition to inflammatory infiltrates. Hematoxylin and eosin stain.

were unremarkable. Levels of serum phosphorus were normal. Creatinine was normal and urinalysis showed: protein negative, bacteria +, 3 erythrocytes, 8-10 leucocytes. A urine culture was negative. Chest x-rays showed multiples soft tissue calcifications around axillary's vessels. Radiographs of lower limbs and pelvis demonstrated calcifications in muscles and blood vessels. No bone lesions were found in these projections or in the skull x-rays. Thyroid gland and cortisol tests in blood were normal. Skin biopsy of ulcer on left buttock area revealed fat tissue with multiple chronic inflammatory fragments predominately lymphoid populations. Muscular tissue was appreciated with chronic inflammation and coexistence of multiple foci of dystrophic calcification and hyalinization of septa between fat subcutaneous lobules in addition to inflammatory infiltrates (Figure 7). The Histopathologic diagnosis was lupus panniculitis and dystrophic calcifications.

Discussion

At the beginning of the 20th century (1912), almost simultaneously, two authors, Otto Kren⁷ and Oppenheim⁸ named a new entity called lupus profundus⁹. Lupus panniculitis or profundus diagnosis is made by primarily both clinical and histological findings. Usually, clinical picture is well established and one or several firm, asymptomatic, large subcutaneous nodules in patients with or without SLE is the most frequent clinical presentation¹⁰. It can lead to cutaneous and subcutaneous atrophy with occasional ulceration¹¹ as seen in our patient. According to Winkelmann, lupus profundus histopathology lesions consist in an inflammatory process with perivascular and perianexial lymphoid infiltrate predominance on lymphoid conglomerates that suggests germinal centers in addition to collagen hyalinization, fibrinoid necrosis, mucinosis, perivasculitis and microcalcifications that are seen depending on the grade of calcification. It may be microcalcifications in fat or may be large cumulates of calcifications which compromise lobules or septa, and when are large enough it enable us to register them on plain radiographs^{12,13}. It is uncommon to observe calci-

fications in lupus panniculitis lesions and when they are documenting is seen in old lesions as reported by Winkelmann in 1970 and Peter in 1989¹⁴. In these cases, patients suffered from pain as happened in our patient who complained of pain on buttocks and thighs when sitting.

Calcification on deep soft tissues is rare and reports of cases are known in a renal transplantation and caciphylaxis which differ from our case. Other changes described as common findings are foci of lymphocytes with or without germinal centers, hyalinization of septa, fat lobules, and lymphocytes within the vessel walls or on the perivascular tissue¹⁵. Lesions will show variable degrees of calcification (mainly in old established lesions) or sometimes with intense calcium deposits on previously damage fat lobules with hyaline necrosis frequently limited by a collagenic pseudocapsule⁷.

Lesions have a chronic clinical course with remissions, recurrences and resolutions. They are commonly accompanied by large areas of depression and lipoatrophy¹⁶ as was seen in our patient.

Pathogenesis of calcium deposits is not clear but it is well documented that parathyroid hormone and vitamin D are not key factors. It was suggested that tissue alkaline phosphatase may activate extracellular pyrophosphatase (that normally inhibits calcium deposits) generating phosphates along with denaturized proteins of necrotic cells produced by inflammation of panniculitis^{17,18}. This latter induces the production of phosphate calcium and calcareous deposits on lesions and is documented in dystrophic calcinosis¹⁹. These calcareous deposits damage the cytosolic sites producing cellular deposits and death. On elastic, collagenous and subcutaneous tissues, calcareous deposits may contribute to further calcareous deposition and worsening the cellular necrosis, an acid environment and interfering on the action of the calcification inhibitors and pyrophosphatases^{11,14,20}.

This case not fulfils the American College of Rheumatology criteria for SLE. Therefore, Lupus panniculitis was diagnosed without any other disease manifestation. These lesions were

progressive and caused a great burden in the patient's activities of daily living due to its sequels.

The treatment was challenging in this patient who had a poor outcome. She was on antimalarial agents and colchicine.

Management of patients with lupus panniculitis includes antimalarials that were used the first time by Thurson and Curtis^{9, 21}, azathioprine²², cyclophosphamide¹⁴ and dapsone. Thalidomide was recommended in lupus panniculitis by Burrows, especially when it is associated to partial C4 deficiency²³. It has been reported the management of older lesion calcifications with colchicine as was used in our patient²⁴.

Some cases may respond to a combination of antimalarials such as hydroxychloroquine 200 mg and quinacrine 100 mg daily when a single drug is ineffective²⁵. Other treatments include probenecid²⁶, low doses of warfarin^{27,28} and diltiazem m^{18,29,30}. Systemic glucocorticoids should be reserved for widespread and resistant lesions. Intralesional glucocorticoids are usually ineffective and may exacerbate the atrophic healing process³¹. Calcifying Lupus panniculitis in a patient without manifestations of systemic lupus Erythematosus]. Adjuvant treatments include topical care and prevention from injury. Surgical debridement or resection of individual lesions may be attempted when all other modalities have failed and there is appreciable debilitation. Surgical treatment includes the presence of recurrent infection, painful masses, ulcerations, and local functional impairment³².

In conclusion, we here report a case of lupus panniculitis with extensive dystrophic calcifications and any manifestation of SLE or other connective tissue disease. This is a case of lupus profundus associated to late dystrophic calcinosis due to calcium salt deposits derived from inflammatory process generated by a panniculitis process. These calcifying lesions which are found in perivascular and deep subcutaneous tissues, ulcerate, extrude and migrate through the surface of the skin revealing an aspect of whitish and chalk-like tissue. We highlight this case for the severity of lupus panniculitis and was originated after several years of a secondary and severe dystrophic calcinosis.

It has been described lupus panniculitis associated to discoid lupus, subacute cutaneous lupus, and systemic lupus erythematosus. It has been described cases of acute calcifying panniculitis or secondary panniculitis to renal failure and/or calciphylaxis and also described in severe dystrophic calcinosis as we described in the present case^{33,34}. Although there are different reports of lupus calcinosis, up to we know there are not reports on lupus calcinosis associated to panniculitis as is this case⁵.

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