

CASE REPORT

Necrobiotic Xanthogranuloma: Efficacy of Surgery in 2 Patients

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Abstract. Necrobiotic xanthogranuloma is a rare disease characterized by indurated nodules and yellowish-red plaques in the dermis or subdermal tissues particularly in the periorbital region; the lesions are often ulcerated. This disease is frequently associated with hematological disorders such as monoclonal gammopathy and lymphoproliferative disorders. Its pathogenesis is unknown and the small number of cases makes long-term studies difficult. We present 2 cases of periorbital lesions in which the biopsies established a diagnosis of necrobiotic xanthogranuloma. Both patients were treated with corticosteroids and cyclophosphamide, with no improvement. The lesions were excised and the periorbital regions were reconstructed with skin grafts. After 1 year of follow-up there are no signs of recurrence.

Key words: necrobiotic xanthogranuloma, ocular complications, surgery.

NECROBIOTIC XANTHOGRANULOMA: EFFICACY OF SURGERY IN 2 PATIENTS

Resumen. El xantogranuloma necrobiótico es una enfermedad poco frecuente que se caracteriza por la presencia de nódulos indurados y placas rojo-amarillentas en los tejidos dérmicos o subdérmicos, a menudo ulceradas, que asientan preferentemente en la región periorbitaria. Suele asociarse con alteraciones hematológicas como gammopatía monoclonal y trastornos linfoproliferativos. Su patogenia es desconocida y el escaso número de casos existentes hace difícil la publicación de estudios a largo plazo. Presentamos dos casos de lesiones periorbitarias cuyas biopsias establecieron el diagnóstico de xantogranuloma necrobiótico. Los pacientes se sometieron a tratamiento con corticoides y ciclofosfamida sin mejoría. Las lesiones fueron tratadas quirúrgicamente mediante escisión y reconstrucción con injertos de piel. Tras un año de seguimiento no hay evidencias de recurrencia de la enfermedad.

Palabras clave: xantogranuloma necrobiótico, complicaciones oculares, tratamiento quirúrgico.

Introduction

Necrobiotic xanthogranuloma is an extremely rare, well-defined clinical and pathologic condition that was described by Kossard and Winkelmann¹ in 1980, although it had been previously reported in the literature as atypical necrobiosis lipoidica, atypical multicentric reticulohistiocytosis, and disseminated xanthoma. It is a histiocytic lesion of unknown etiology^{2,3} that usually affects the orbital and periorbital area and other areas of the face, as well as the trunk and limbs.^{1,2,4-6} The cutaneous

manifestations of the disease include multiple indurated nodules and yellowish or violaceous plaques, which are often ulcerated.

Treatment continues to be debated; however, the lesion usually responds to oral corticosteroid therapy, alone or in combination with low-dose chemotherapy.^{7,8} These patients have a 15-year survival of approximately 95%. Morbidity and mortality are due mainly to complications of the paraproteinemias with which it is frequently associated and only rarely to malignant transformation.

Case Descriptions

Patient 1

A 50-year-old woman was seen for the first time in a dermatology department 4 years ago for the progressive onset of yellowish-orange plaques with clearly defined borders and a xanthomatous appearance that had started to

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Figure 1. Yellowish-orange plaques of xanthomatous appearance, located in the periorbital region.



Figure 3. Eyelid eversion with exposure of the superior tarsus after retraction of the full-thickness skin grafts on the eyelids, 1 month after the first operation.



Figure 2. Large plaques on the neck, upper chest, and flank. Telangiectases are seen on a yellowish, shiny surface.

develop 3 years earlier. Superficial telangiectases were also observed. The plaques were of fibroelastic consistency and were located in the periorbital regions (Figure 1), axillas, on both flanks, and in the suprasternal region (Figure 2), along with severe pruritus during acute episodes of the disease.

Three biopsies were taken from the xanthomatous plaques in the periorbital area and on the neck. Histology showed a slightly thinned epidermis, with extensive areas of hyaline necrosis and large multiple granulomas, some with a central necrobiotic area surrounded by a markedly cellular palisade. The laboratory workup revealed mild anemia with a hemoglobin of 9.2 g/dL. The biochemistry results were unremarkable. Other parameters included immunoglobulin (Ig) A 244 mg/dL,

IgM 296 mg/dL, IgG κ light chains 3110 mg/dL, and β 2-microglobulin within normal limits. No pathologic findings were observed in the bone marrow aspirate, abdominal ultrasound, or cranial computed tomography scan. The chest x-ray, electrocardiogram, and echocardiogram were reported as normal, and bone scintigraphy showed no lytic lesions or pathologic deposits. IgG monoclonal gammopathy of uncertain significance was diagnosed, and remained stable under follow-up by the hematology department. Following the diagnosis, the patient was treated with corticosteroids and cyclophosphamide boluses that were gradually discontinued, achieving a partial response and slow progression of the skin plaques.

The patient was referred to the plastic surgery department for the periorbital plaques, which made eyelid closure very difficult despite the medical treatment, leading to the appearance of bilateral corneal ulcers. En bloc resection of the xanthogranulomas on the upper and lower eyelids was performed; the defect was covered using a partial-thickness skin autograft. During the first month of follow-up, the fully attached grafts developed considerable retraction that led to bilateral corneal reexposure and eyelid eversion with exposure of the superior tarsus (Figure 3). Three months later, the patient underwent a second operation, in which the retracted grafts were excised, the levator muscle of the upper eyelid was released at its lower insertion, and the resulting defect was covered with a partial-thickness skin graft to the lower eyelids and full-thickness graft (taken from the inguinal region) to the upper eyelids. The procedure was completed with lateral canthoplasty to reduce the palpebral fissure and a temporary tarsorrhaphy to protect the cornea and prevent graft retraction during the first few days after the operation. The tarsorrhaphy

was released on the fourth day and showed fully attached grafts. After 1 year of follow-up, there was no evidence of recurrence of the disease in the periorbital area, upper eyelid mobility was good, and no signs of palpebral retraction were observed.

Patient 2

A 55-year-old woman with no relevant history consulted for bilateral periorbital lesions consisting of the confluence of various asymptomatic, rough, yellowish-brown papulonodular lesions from 18 months earlier (Figure 4). Because of plaque progression and the appearance of bilateral conjunctivitis due to difficult eyelid closure, she was seen in the dermatology department, where necrobiotic xanthogranuloma was diagnosed by biopsy of the lesion. The laboratory workup and the bone marrow biopsy were normal. An abdominal ultrasound was also normal. The patient was treated with corticosteroids and cyclophosphamide boluses; however, there was no response and the cutaneous plaques progressed. She was referred to the plastic surgery department for surgical treatment. The periorbital plaques were excised, and the defects were covered with partial thickness skin grafts. After 1 year of follow-up, there were no signs of palpebral retraction, skin lesions at any other site, or hematologic disease.

Discussion

Necrobiotic xanthogranuloma occurs with equal frequency in men and women between 50 and 60 years, although cases have been reported in adolescents.⁹ Many theories have been proposed in an attempt to elucidate the pathogenesis of this disease.² It is often associated with abnormal laboratory tests, including increased erythrocyte sedimentation rate, leukopenia, neutropenia, anemia, thrombocytopenia, hypergammaglobulinemia, cryoglobulinemia, positive antinuclear antibodies, and positive rheumatoid factor.^{7,10} Glucose levels are usually normal, and blood lipids may be normal, elevated, or decreased.^{6,9} The most common laboratory finding (>70% of cases) is paraproteinemia, usually an IgG κ or λ light-chain monoclonal gammopathy.^{2,3,5}

The cutaneous manifestations of the disease usually appear in the periorbital region, neck, trunk, and limbs. The most serious complications are related to the periorbital area and include ulceration of the palpebral fold, conjunctivitis, keratitis, uveitis, and even blindness.¹¹ In the 2 patients we describe, periorbital involvement prevented eyelid closure, which caused exposure of the eyeball and thus led to ulcers in the first patient and conjunctivitis in the second. It is not rare to observe



Figure 4. A, Periorbital xanthomatous plaques in patient 2. B, 3 months after surgery.

involvement of mucosae and of organs other than the skin, such as the lung, oral mucosa, larynx, kidneys, heart, liver,¹⁰ or central nervous system.¹² The condition can also present as a solitary tumor not associated with a neoplasm or paraproteinemia,^{11,13} as in our second patient.

There is a strong association between necrobiotic xanthogranuloma and the development of certain malignant neoplasms. Because the condition is rare, there are very few series of patients. The longest series in the literature were published by Finan and Winkelmann⁹ with 22 cases and, more recently, Mehregan and Winkelmann⁶ with 32 cases. Various therapeutic options are currently available, but none is curative, and some patients achieve no response or only partial response.^{6,9} The literature contains reports of the use of alkylating agents (usually at low doses), such as methotrexate, melphalan, chlorambucil,^{2,3,6,8} hydroxychloroquine, nitrogen mustard, azathioprine, and cyclophosphamide.⁷ The use of intralesional or topical

corticosteroids or oral glucocorticoids at high doses can have variable effects.⁸ Some reports also mention radiotherapy for localized ocular involvement¹⁴ and subcutaneous α -2a interferon in lesions resistant to other therapeutic options.^{4,15} Nonetheless, treatment appears to be palliative and most patients show a slowly progressive clinical course.⁷ According to published data, surgical excision of the lesions has been associated with recurrences (42%) and increased disease activity and, therefore, should be avoided.^{2,5,16} In the 2 patients we describe, we opted for surgical resection following failure of the corticosteroid therapy and cyclophosphamide boluses, despite the likelihood of postoperative recurrence. Nevertheless, after 1 year of follow-up, both patients were still lesion-free in the periocular area.

In our study, both patients' lesions were consistent with the typical presentation described in the specialized literature. In contrast, surgery was effective following failure of the medical treatment. Although the surgical option is usually unadvisable, our patients remain recurrence-free and no increase in disease activity had been observed. Extensive surgical excision of the periorbital plaques and the use of partial thickness skin grafts to cover the defects made complete eyelid closure possible, thus preventing the serious complications of continuous eye exposure. The absence of mucosal lesions and local control of the disease by surgery led to a favorable clinical course in both patients, with no recurrences or progression of the hematologic disease to date.

Conflicts of Interest

The authors declare no conflicts of interest.

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