

## CAS CLINIQUE/CASE REPORT

# SUBCUTANEOUS NODULAR SARCOIDOSIS AND SYSTEMIC INVOLVEMENT SUCCESSFULLY TREATED WITH DOXYCYCLINE

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El Sayed F, Dhaybi R, Ammoury A. Subcutaneous nodular sarcoidosis and systemic involvement successfully treated with doxycycline. *Leb Med J* 2006 ; 54 (1) : 42-44.

**ABSTRACT :** Subcutaneous nodular sarcoidosis is a rare cutaneous manifestation of systemic sarcoidosis. We report a new case in a 45-year-old woman with a 7-year history of subcutaneous nodules and a new onset of dyspnea. She was treated with corticosteroids but her disease recurred upon withdrawal.

A 6-month course of doxycycline in a dose of 200 mg/d led to complete remission. We also emphasize the value of systemic work-up and regular screening in such cases.

## INTRODUCTION

Subcutaneous sarcoidosis or Darier-Roussy sarcoid is a rare cutaneous expression of sarcoidosis, occurring in less than 6% of patients with sarcoidosis. It is characterized by subcutaneous nodules, mainly on extremities, showing typical histopathological features of sarcoidosis localized to the subcutaneous tissue [1]. Association with early benign hilar adenopathy or with the later stages of sarcoidosis requires an initial workup for systemic involvement followed by periodic screening [2]. We report a new case of subcutaneous sarcoidosis successfully treated with doxycycline.

## CASE REPORT

A 45-year-old woman presented with erythematous to violaceous nodules and plaques on arms and trunk developing since 7 years ago. At that time, a skin biopsy showed typical features of cutaneous sarcoidosis while chest X-ray was normal. The patient was considered to have localized cutaneous sarcoidosis and was put on simple clinical observation. Recently, she started complaining from a NYHA II dyspnea without alteration of the general status. Clinical examination showed the presence of several deep-seated nodules, 1 to 4 cm, on the external sides of both arms (Fig. 1) ; a 6 cm violaceous

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El Sayed F, Dhaybi R, Ammoury A. Sarcoïdose nodulaire sous-cutanée avec atteinte systémique traitée avec succès par doxycycline. *J Méd Lib* 2006 ; 54 (1) : 42-44.

**RÉSUMÉ :** La sarcoïdose nodulaire sous-cutanée est une manifestation cutanée rare de sarcoïdose systémique. Nous rapportons un nouveau cas chez une femme de 45 ans ayant une histoire de nodules sous-cutanés depuis 7 ans avec la survenue récente d'une dyspnée. Elle avait été traitée par corticothérapie avec une rechute lors du sevrage. Un traitement par doxycycline à la dose de 200 mg/j aboutissait à une rémission complète. Nous soulignons la valeur d'un bilan systémique avec un suivi régulier de telles situations cliniques.

plaque was also noted in the upper back. Histological examination of a skin biopsy of the right arm showed several noncaseating epithelioid granulomas involving the entire thickness of the dermis accompanied by giant cells and minimal lymphocytic infiltrate. Complete blood count, erythrocyte sedimentation rate, electrolytes, liver function tests, lactate dehydrogenase and antinuclear antibodies were within normal limits. Serum calcium was normal but calciuria was decreased (73.8 mg/24 h). Angiotensin converting enzyme level was increased up to 122 IU/l (normal < 100 IU/l). Purified protein derivative for tuberculosis was negative. Chest X-ray revealed bilateral hilar lymphadenopathy while the CT scan of the chest showed both, hilar and mediastinal involvement.



FIGURE 1

Two violaceous, 4 cm in diameter, deep-seated nodules, located on the external aspect of the right arm.

Pulmonary function tests revealed a decline in the diffusing capacity for carbon monoxide with evidence of obstructive disease. The CD4/CD8 ratio was increased up to 6.6 on bronchoalveolar lavage. Ophthalmologic examination was normal. All signs and symptoms resolved within 2 months of treatment with systemic corticosteroids in a dose of 1.5 mg/kg, but recurred upon their withdrawal. After such an incomplete response to corticosteroids, a 6-month course of doxycycline in a dose of 200 mg/day led to complete remission of pulmonary and cutaneous lesions.

## DISCUSSION

Sarcoidosis is an idiopathic, systemic, noncaseating, granulomatous disease involving multiple system organs. Cutaneous manifestations occurring in 25 to 35% of patients often enable the dermatologist to be the first physician to make the diagnosis. Cutaneous sarcoidosis may be classified as specific and nonspecific lesions. Specific lesions display features of noncaseating granulomas, and include papules, plaques, lupus pernio, scar sarcoidosis and other rare morphologies such as hypopigmented patches. Erythema nodosum is the most common nonspecific cutaneous lesion of sarcoidosis [2]. Pulmonary manifestations are frequently found in lupus pernio and scar lesions, while erythema nodosum is generally associated with a benign and self-limited course. The frequency of females among patients with skin involvement is significantly higher than the one among other sarcoidosis patients [3]. Subcutaneous nodular lesions were first described by Darier and Roussy; they are often asymptomatic and are frequently an expression of an underlying systemic sarcoidosis. They consist of a few, 1 to 3 cm deep-seated nodules, on the trunk and extremities; rarely appearing on the face [4]. The nodules are oval, firm and elastic structures that arise deep in the dermis and subcutaneous tissue. The overlying epidermis may be slightly violaceous. Usually the lesions are asymptomatic, but 10% to 15% of patients have pruritus [4-5]. The differential diagnosis includes discoid lupus, lymphoma, pseudolymphoma, lymphocytoma cutis, lichenoid drug eruptions, granuloma annulare, necrobiosis lipoidica, cutaneous tuberculosis and leprosy. A biopsy is usually required to confirm the diagnosis of sarcoidosis. The characteristic finding is that of noncaseating granulomas composed of collections of epithelioid histiocytes, multinucleated giant cells and lymphocytes [2, 5]. The disease is generally chronic and progressive, sometimes imposing the use of combined treatments; however, spontaneous remissions are usual. The main treatment of severe forms is systemic corticosteroids. Tetracyclines (minocycline, doxycycline), effective in our case, seem to be the first alternative treatment of sarcoidosis [6]. In fact, cell-wall deficient bacteria which can infect phagocytes of the immune system have been found in tissue from patients with sarcoidosis. These bacteria may be responsible for sarcoid inflammation –

but also for other autoimmune diseases – explaining the response of these diseases to the treatment by tetracyclines [7]. Besides their anti-infectious effect, tetracyclines exhibit potent immunomodulatory (inhibition of T-cell proliferation in vitro by minocycline) and anti-inflammatory properties. Doxycycline and minocycline inhibit granuloma formation in vitro and are also efficient in treating extracutaneous lesions of sarcoidosis [11]. Tetracyclines were found useful in the treatment of other granulomatous diseases such as silicone-induced subcutaneous granulomas, granulomatous rosacea, orofacial granulomatosis, and granulomatous perioral dermatitis of children [8-11]. The remissions found in non-infectious granulomatous diseases treated with tetracyclines supports the anti-inflammatory effect of tetracyclines [11]. Other alternative therapies for sarcoidosis are sometimes required including immunosuppressive agents (methotrexate), antimalarials (hydroxychloroquine), fumaric acid esters, anticytokine agents (thalidomide), monoclonal antibody (infliximab), UVA1 phototherapy and tacrolimus [11-16].

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### داء الغرناوية العقدي تحت الجلد وانتشاره الجهازى عولج بنجاح بالدوكسيسيلين

موجز: داء الغرناوية العقدي تحت الجلد هي تظاهرة جلدية نادرة لداء الغرناوية (اللحمانيّة) الجهازى. نشير إلى حالة عند امرأة عمرها ٤٥ عاماً وفي سيرتها عقيدات تحت الجلد منذ ٧ سنوات وحدث عندها حالياً ضيق نفس. عولجت بالقشرينات الستيروئيدية ثم انتكست حين أوقف العلاج. شفيت تماماً بالمعالجة بالدوكسيسيلين ٢٠٠ ملغ يومياً. نذكر قيمة النتائج الجهازية مع المتابعة المنتظمة لمثل هذه الحالات السريرية.