Kaposi's disease and sarcoidosis

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ABSTRACT: A human immunodeficiency virus (HIV) antibody-negative 65 year old woman was treated with corticosteroids for 7 yrs because of bilateral uveitis. One year after the beginning of corticosteroid treatment, erythematous skin lesions appeared on the legs. Eight years after the diagnosis of uveitis, gastric and bronchial biopsies revealed noncaseating epithelioid cell granulomas, whilst a cutaneous biopsy showed Kaposi's disease.

Sarcoidosis-associated alteration of immune regulation and corticosteroid therapy may have promoted the development of disease.


*Sarcoma is a chronic multisystem disorder of unknown origin, characterized by accumulation of lymphocytes, mononuclear phagocytes and noncaseating epithelioid cell granulomas in affected organs. Skin anergy and depressed cellular immune processes in the peripheral blood lymphocytes have been documented, whilst an exaggerated helper T-lymphocyte immune function has been demonstrated at the sites of the disease [1–4].

Kaposi's disease (KD), also called Kaposi's sarcoma, is a multifocal skin disease that occasionally affects internal organs. It is commonly described in elderly people (both men and women) of Mediterranean origin. In addition, immunosuppression has been related to the development of the disease, since KD has been observed in patients receiving immunosuppressive therapy after organ transplantation [5], and it is frequently diagnosed in human immunodeficiency virus (HIV) antibody (Ab) seropositive patients [6]. The neoplastic nature of KD is controversial [7–11]; hence, the entity has recently been designated "Kaposi's disease" [12, 13].

We report a case of sarcoidosis associated with KD in a HIV-Ab-negative patient. Such an association has not previously been described.

Case report

A 65 year old woman was admitted to hospital in order to confirm the diagnosis of sarcoidosis. When 57 yrs of age, the patient manifested bilateral uveitis; since then, she had received corticosteroid therapy (betamethasone 4 mg daily per os every other month), until one year before admission. Ten months before admission she started to complain of painful dyspepsia, and endoscopy revealed first degree peptic oesophagitis and superficial gastritis. Gastric biopsies showed epithelioid cell granulomas in the lamina propria, associated with chronic inflammation, glandular atrophy, and intestinal metaplasia. A radiographic evaluation of the chest revealed mild lung infiltrates and left hilar enlargement, which a computed tomography scan showed to be represented by hilar, peribronchial and mediastinal adenopathies. Gallium-67 scintigraphy of the lungs demonstrated high uptake in the mediastinum and in the right lung, especially in its posterior portion; a milder uptake was detectable in the posterior portion of the left lung. Tuberculin anergy (purified protein derivative 10 U) was observed.

On admission, the patient was in fair general condition. Physical examination showed mild bilateral conjunctivitis, and crackles were audible in the left axillary area of the lung and in the lower third of the left hemithorax; mild hepatosplenomegaly was detectable. Multiple patch-lesions were evidenced on the skin of both feet and the anterior surface of the right ankle (fig. 1). Cutaneous lesions had appeared about one year after the diagnosis of uveitis, and they showed a progressive slow enlargement during the following years. The following

Fig. 1. – Patch lesions of Kaposi's disease of the right ankle skin submitted to biopsy (arrow). Similar lesions are also present on the left foot.
tests gave normal results: erythrocyte sedimentation rate (ESR); red blood cell count; haemoglobin; haematocrit; mean corpuscular volume; serum glucose; blood urea nitrogen; serum creatinine; serum electrolytes; creatine kinase; aspartate aminotransferase; alanine aminotransferase; alkaline phosphatase; gamma glutamyl transpeptidase; lactate dehydrogenase; and serum electrophoresis. Serum angiotensin-converting enzyme was 135 U·L⁻¹ (normal value <40 U·L⁻¹); white blood cell 7.0×10⁹ cells·L⁻¹, with neutrophils 72% and lymphocytes 18% (1.26×10⁹ cells·L⁻¹); total blood T-cell 0.93×10⁹ cells·L⁻¹; (normal value 1.34–2.40×10⁹ cells·L⁻¹); blood CD4+ lymphocytes 0.34×10⁹ cells·L⁻¹ (normal value 0.44–0.66 cells·L⁻¹); blood CD8+ lymphocytes 0.59×10⁹ cells·L⁻¹ (normal value 0.20–0.40×10⁹ cells·L⁻¹); CD4+/CD8+ ratio 0.58 (normal value 1–2.6); serum HIV-Ab (enzyme-linked immunosorbent assay for HIV-1) resulted negative. Lung function revealed a mild restrictive defect (transfer factor of the lung for carbon monoxide 78% of predicted normal value (% pred); total lung capacity 76% pred; and forced vital capacity 91% pred). Radiographic film of the chest disclosed interstitial opacities. Ophthalmological evaluation revealed a bilateral cataract, which was associated with bilateral iridal subatrophy, outcomes of iridocyclitis, and bilateral blepharitis; uveitis was not detected.

A transbronchial biopsy and a cutaneous biopsy of the lesion from the right ankle were performed. The microscopy examination of the bronchial mucosa showed epithelioid cell granulomas, containing occasional psammomatous calcifications and surrounded by rare lymphocytes. Necrosis was not detectable and no mycobacteria were demonstrable by appropriate histochemical stainings. These findings were consistent with chronic active sarcoidosis (fig. 2). The skin biopsy showed proliferation of lymphatic-like vessels in the superficial dermis, which dissected the collagen and formed cuffs around pre-existing venules. Areas of spindle cell proliferation were also present; lymphocytes, plasma cells and siderophages were scattered in the dermis (fig. 3). The findings were consistent with patch-stage, lymphangiomatous-like Kaposi's disease.

The woman was followed as an out-patient for 3 months; she did not receive any drugs for the two diseases. At the end of this period, hyperaemia of the skin lesions (which did not increase) appeared slightly reduced, the patient felt quite well, and in particular she did not complain of dyspnoea or dyspepsia; chest radiography was normal. Spirometry was not performed.

**Discussion**

Research of the literature did not uncover any description of KD associated with HIV-Ab-negative sarcoidosis in the past 10 yrs. Two cases of association between sarcoidosis and KD have been described in two HIV-Ab-positive patients, both homosexual males [14, 15]. The absence of description of this pathological association is surprising, considering the relatively high incidence of KD in Mediterranean countries [7], and the increased clinical suspicion and surveillance for KD. A possible explanation may be that cutaneous lesions in patients with sarcoidosis are seldom submitted to biopsy, although they should be considered in the differential diagnosis of patches, plaques and nodules of KD [7, 16, 17]. Moreover, since KD often develops in a very indolent fashion, cases of this association may have been ignored.

In the present case cutaneous lesions developed after the onset of uveitis and the beginning of steroid treatment, and, before the histological diagnosis, they had probably been interpreted as cutaneous manifestation of sarcoidosis.

Several clinicopathological variants of KD have been reported [7, 12, 18], and include: 1) classic KD in Mediterranean people; 2) endemic KD in Africa; 3) epidemic KD in patients with the acquired immune deficiency syndrome (AIDS-KD); 4) KD with immunosuppression in HIV-Ab-negative patients (organ transplantation, immunosuppressive drugs, lymphomas...); and 5) KD in homosexual HIV-Ab negative patients in the absence of immunosuppression. The classic form is rarely life-threatening and visceral involvement is unusual, thus the prognosis is generally good. The African variant is often fatal despite therapy, with rapid widespread dissemination. AIDS-KD tends to be more varied and aggressive than other forms, visceral involvement is common, and prognosis is poor; KD associated with immunosuppression in HIV-Ab-negative patients resolves in 24% of patients after reduction or cessation of immunosuppressive
therapy, and 50% of mucocutaneous lesions and 14% of visceral lesions remit following treatment. KD in homosexual HIV-Ab-negative patients, like classic form, has a favourable prognosis [7, 18].

The age and origin of the patient born in northern Italy were consistent with the epidemiological pattern described in classic KD; thus, suggesting that the development of both sarcoidosis and KD was simply coincidental.

This case is original since KD has not yet been reported in sarcoidosis, a disease not associated with complications of immunosuppression, particularly opportunistic infections, although tuberculin tests are often negative.

As both KD and sarcoidosis are relatively frequent, one may argue that there is a negative link between the two diseases, suggesting that sarcoidosis may prevent the development of KD. Alternatively, it has been suggested that impaired cellular and humoral feedback mechanisms allowing sustained proliferation of T-lymphocytes may stimulate lymphatic and endothelial cells to undergo hyperplastic or neoplastic proliferation [25]. Sarcoidosis, characterized by an exaggerated T-helper network associated to skin anergy [21, 26], may represent an alteration of immune system activation at some level may have a role in the development of KD [6, 7, 22]. KD cells are of endothelial origin [23, 24], and it has been suggested that impai-

A close surveillance of the nature of cutaneous lesions developing in patients with sarcoidosis might be helpful in clarifying the issue of the possible relationship between the two diseases, whether positive or negative.

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References


