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Iatrogenic Kaposi's sarcoma following immunosuppressive therapy for systemic lupus erythematosus

Sir,

Kaposi's sarcoma (KS) is a rare malignant tumour (incidence 0.01%) of endothelial and vascular smooth muscle cells. Four types of KS have been described: classic KS, which is an indolent disease predominently affecting the Ashkenazi Jews; African endemic KS; HIV-related KS; and iatrogenic KS appearing as a result of immunosuppressive therapy (1, 2). Recently, human herpesvirus 8 (HHV-8) was identified as the causative agent in almost all the cases of KS (3, 4).

A 39-year-old woman of Berber origin was admitted in our department for acute polyarthritis affecting the small joints of the hands and inferior legs oedema. Biological exams showed ESR 68 mm/h,CRP 26 mg/l, normal cells blood count, positive antinuclear antibodies (1/360), positive anti-DNA antibodies (1/160), negative rheumatoid factor. Urine proteins were 3.5 g/d and serum albumin 25 g/l. Serum urea and creatinine were in normal range. The diagnosis of SLE was made. Kidney biopsy showed proliferative glomerulonephritis. Treatment was started: monthly pulses (1 g) of cyclophosphamide with prednisone 60 mg/d for 6 weeks followed by gradual dose reduction to 20 mg after 12 weeks. There was a marked clinical improvement associated with a fall in her ESR to 10 mm/h and normal renal tests within the second month. One week after the fourth cyclophosphamide pulse, she developed severe genital herpes infection which quickly disapeared after high doses of acyclovir (200 mg x 5/d). Two months later, she developed disseminated large purple nodules on the face, the dorsum of the forearm, the hands and the lower legs (Fig. 1). A skin biopsy showed typical KS lesions and blood investigations showed high-titre of IgG antibodies to Herpesvirus 1,2 (1/3500) and HHV-8 (1/5600). Prednisone was decreased gradually to 5 mg/d. Skin lesions showed partial regression but inflammatory markers and proteinuria raised once again. Three months later, The renal function tests worsned dramatically and the patient died suddenly after cardiac dysarythmia secondary to hypokaliemia.

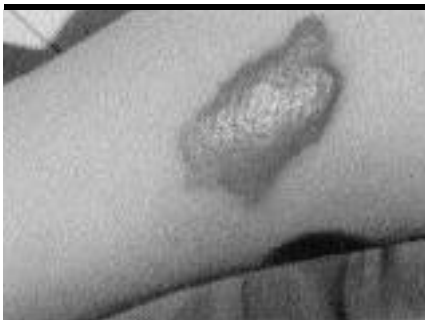

Fig. 1. Typical cutaneous lesions of Kaposi's sarcoma affecting the forearm.

Iatrogenic KS was first described among post-transplant patients on high-dose immunosuppressive therapy (5). It has also been observed in patients receiving immunosuppressive therapy for autoimmune diseases, including pemphigus vulgaris, dermatomyositis, polymyalgia rheumatica, rheumatoid arthritis, Sjögren syndrome, temporal arteritis, Crohn's disease, and SLE. Most of these patients were treated by steroids alone or in combination with cytotoxic drugs (e.g. cyclophosphamide, azathioprin and cyclosporin A). The first case of KS in SLE was reported by Klein *et al.* in 1974 (6) and since that, only 2 other cases were reported (7, 8). In 1994 Chang *et al*. (3) described a novel herpesvirus from a KS lesion which was named HHV-8. It was subsequently isolated from all types of KS lesions. Prior infection with HHV-8 is a requisite for the development of disease and it is likely in our case that infection was acquired by sexual route in the same time of the herpes infection. The question arises as to how immunosuppressive treatment can lead to the emergence of KS. Recent in vitro evidence supports the hypothesis that steroids have a direct role in stimulating tumour development and growth (9, 10).

Interrupting immunosuppressive therapy usually improves the KS lesions but can be followed by a flare of the underlying disease. Some kind of treatment without immunosuppressive effects and active on the underlying disease would be the best solution. Recently, Kötter and coll. (1) used interferon a in a iatrogenic KS during treatment of a severe ocular Behçet's disease and obtained complete remission of both disorders. The use of intravenous immunoglobulins would have been a possible alternative in our case. Our observation also suggest that clinicians should think to screeen patients for HHV-8 in autoimmune diseases when hign doses of immunosuppressive therapy are required.

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