

Kaposi's sarcoma complicating rheumatoid arthritis treated with corticosteroid Kaposi's sarcoma and rheumatoid arthritis

Mehmet Sahin, MD, Muharrem Keskin, MD, Sevket E. Tunc, MD, Hasan S. Coskun, MD, Nilgun Kapucuoglu, MD.

Kaposi's sarcoma (KS) is a vascular malignant tumor, although it has previously been associated with rheumatoid arthritis (RA) as well as other connective tissue diseases.¹ It may also occur in patients with lymphoid malignant disorders,² and corticosteroids, or immunosuppressive treatment receiving patients with the acquired immunodeficiency syndrome (AIDS).³ Indeed all routes of corticosteroid treatment have been suggested as etiological factors in previous case reports of RA and KS.¹⁻³ Herein, we report a man in whom Kaposi's sarcoma occurred in conjunction with RA treated with recent systemic corticosteroids.

The case was reported in a 75-year-old man with symmetric polyarthritis who has wrist, metacarpophalangeal (MCP), proximalinterphalangeal (PIP) and knee joints, malaise, and morning stiffness. One year before admission, he was diagnosed to have elderly onset RA. Since diagnosis, he has had active disease which required institution of low-moderate dose corticosteroids and sulphasalazine therapy in another hospital. His current medications included prednisolone 16 mg/day and sulphasalazine 2 g/day. There was no history of intra-articular corticosteroid use. One month before admission, multiple violaceous and maculopapular skin lesions developed on both lower extremities. He said that he had no preexisting skin lesions before treatment. Physical examination showed a cushingoid appearing man. His vital signs were normal. Swelling and tenderness on bilaterally wrists, MCP, PIP, and knees, ulnar deviation, and synovial hypertrophy were noted during the extremity examination. There was a subcutaneous rheumatoid nodule on the dorsal aspect of the right elbow. On the medioplantar aspect of the lower extremities, there was multiple small 3-5 mm round, discrete, violaceous maculopapular lesions on the skin (Figure 1). Lymphadenopathy or hepato-splenomegaly was not detected in the remaining examination. Laboratory data showed that he had normal electrolyte, renal, and liver functions and lactate dehydrogenase (LDH) level as well as blood values (complement, hemoglobin, platelet count), although white cell count was minimally elevated at 12.500/mm³ with 76% neutrophils, 18% lymphocytes, 6% monocytes, and 2% eosinophils. Erythrocyte sedimentation rate was 80 mm/h, C-reactive protein 43.8mg/l (normally <3 mg/l), rheumatoid factor 608 IU/ml (normally <15 IU/ml). Antinuclear antibodies and

anti-human immunodeficiency virus antibody results were negative. Serum protein electrophoresis showed mild gammopathy. Chest radiography was normal. A skin biopsy was performed and KS was diagnosed histologically. Immunohistochemical staining was positive for CD31 and CD34. He died 2 months later of pneumonia complicated by pulmonary insufficiency although interferon alpha treatment for the skin lesions was started with respect to management of the KS.

Kaposi's sarcoma is now recognized to have an increased prevalence in immunocompromised hosts including in patients with AIDS, and has been associated with solid organ transplants, other malignancies, autoimmune disorders, and immunosuppressive therapy.¹ Oral corticosteroids, intra-articular corticosteroids, and even captopril therapy has been shown to play a role in the development of KS in patients with RA.¹⁻³ In addition, Cohen et al⁴ reported a case of KS, associated with the initiation of tumor necrosis factor- α (TNF- α) blockade by the humanized, mouse derived monoclonal antibody, infliximab. A recent report described 2 cases of KS following low-dose corticosteroid treatment for other rheumatological disorders.⁵ The patient in the current study had RA with the subsequent development of KS during corticosteroid therapy. A dose-dependent relationship between corticosteroid treatment and the onset of KS lesions has not been reported. However, there are reports of patients developing KS after receiving corticosteroid therapy for a duration ranging from 6 weeks to 22 years.¹ The mechanism by which KS arises in patients receiving corticosteroids is not well understood. Postulated mechanisms have included a complex interaction between geographic, genetic, environmental, and immunological factors.¹ Vincent et al⁵ reported the role of corticosteroids in the development of KS as two-fold, firstly by up-regulation of Kaposi cell proliferation, and secondly by activation of the activation of latent oncoviruses (HHV-8) as a result of chronic immunosuppression. It has been reported that the number of glucocorticoid receptors increases



Figure 1 - Photograph of the right lower extremity demonstrating violaceous maculopapular lesions on the skin.

Clinical Notes

significantly in the KS tissues both in the cytoplasm and the nucleus.⁶ Our patient had received oral corticosteroids and sulphasalazine for one year, and did not receive any TNF antagonists. There was no evidence lymphoma and other malignancies. We considered that there is a relationship between RA and the development of KS in our case and imply that this occurred after corticosteroid treatment. Our patient had Kaposi's skin lesions, which is a distribution more typically seen in the "classic" form of the disease because it is confined to the skin and localized to the extremities. The skin lesions of KS can easily be mistaken for cutaneous vasculitis, particularly on corticosteroid therapy of patients with autoimmune diseases, and skin biopsy may be useful.

In conclusion, physicians should consider that KS could occur during the treatment of rheumatologic diseases with corticosteroids, although the exact mechanism of the KS due to corticosteroids treatment of rheumatologic diseases is unclear.

Received 2nd December 2006. Accepted 12th March 2007.

From the Department of Internal Medicine, Division of Rheumatology (Sabin, Keskin, Tunc), Oncology (Coskun), Pathology (Kapucuoglu), Medical School,

Suleyman Demiel University, Isparta, Turkey. Address correspondence: Dr. Mehmet Sabin, Department of Internal Medicine, Division of Rheumatology Suleyman Demiel University, Tip Fakulesi, Ic Hastaliklari Klinigi, TR-32260, Isparta, Turkey. Tel. +90 (246) 2112613. Fax. +90 (246) 2370240. E-mail: mehmet.sabin66@hotmail.com

References

1. Louthrenoo W, Kasitanon N, Mahanuphab P, Bhoopat L, Thongprasert S. Kaposi's sarcoma in rheumatic diseases. *Semin Arthritis Rheum* 2003; 32: 326-333.
2. Safai B, Mike V, Giraldo G, Beth E, Good RA. Association of Kaposi's sarcoma with second primary malignancies: Possible etiopathogenic implications. *Cancer* 1980; 45: 1472-1479.
3. Friedman-Kien AE, Laubenstein LJ. Disseminated Kaposi's sarcoma in homosexual men. *Ann Intern Med* 1982; 96: 693-700.
4. Cohen CD, Horster S, Sander CA, Bogner JR. Kaposi's sarcoma associated with tumour necrosis factor alpha neutralising therapy. *Ann Rheum Dis* 2003; 62: 684.
5. Vincent T, Moss K, Colaco B, Venables P. Kaposi's sarcoma in two patients following low-dose corticosteroid treatment for rheumatological disease. *Rheumatology* 2000; 39: 1294-1296.
6. Guo W-X, Antakly T, Cadotte M, Kachura Z, Kuukel L, Masood R, et al. Expression and cytokine regulation of glucocorticoid receptors in Kaposi's sarcoma. *Am J Pathol* 1996; 148: 1999-2008.

New Peer Reviewers

Join our team of expert peer reviewers for Saudi Medical Journal by registering through the website at http://www.smj.org.sa/_Authors/ and select "register now" or sending an enquiry and summarized CV to info@smj.org.sa. Note that SMJ reviewers, whose reviews are returned on time and are judged satisfactory by the Editors, may receive 1 CME credit per review, with a maximum of 5 credit per year, from the Saudi Council for Health Specialties.