# Kaposi's sarcoma after alpha-interferon treatment for HIV-negative T-cell lymphoma

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**Abstract** **A 54-year-old HIV-negative patient suffering from T-cell lymphoma of Lennert's lymphoma (Lel) type was treated for 13 months with interferon α-2b. While on treatment with interferon the patient demonstrated suppression of total and CD4+ lymphocytes to levels < 0,5 and 0,2 × $10^9$/l, respectively. Although interferon was successful in controlling the lymphoma the clinical course was complicated by the rapid development of aggressive, fatal Kaposi's sarcoma shortly after cessation of interferon treatment.**

**It is suggested that the immunosuppressive effect of interferon therapy (or the T-cell lymphoma or both) may have played a role in the development of Kaposi's sarcoma as a second malignancy.**

*S Afr Med J* 1993; **83:** 430-431.

The use of interferons has led to a number of immunological disturbances, usually autoimmune in nature.[1,2] We report here the occurrence of rapidly growing Kaposi's sarcoma in a patient being treated for a T-cell lymphoma (Lennert's lymphoma) with recombinant α-interferon. Certain aspects of the apparently paradoxical effects of α-interferon action may be relevant to the pathogenesis of this condition.

## Case report

A 45-year-old woman presented in October 1982 with bitonsillar enlargement of recent onset. Biopsy disclosed a malignant lymphoma with morphological and immunohistological features consistent with a T-cell lymphoma of the Lennert's (Lel) type (Fig. 1). Initial staging revealed only localised tonsillar involvement. Treatment comprised six cycles of combination chemotherapy, which was stopped in July 1983 after the patient had shown a full clinical response.

In 1985 there was a relapse of the lymphoma with generalised lymphadenopathy together with systemic symptoms. Further chemotherapy again led to regression of nodes. After clinical response chemotherapy was again discontinued in March 1986.

A third relapse in 1987 was accompanied by retroperitoneal lymph nodes as well as a cutaneous ulcer in the sacral region. Biopsy again showed the presence of Lel, with more florid epithelioid cell reaction than before. Screening for HIV by enzyme-linked immunosorbent assay (ELISA) was negative.

In December 1987 the patient was started on treatment with interferon α-2b (Intron; Scherag) 1,5 × $10^6$ units daily by subcutaneous injection. Over the next few weeks the lymphadenopathy and systemic symptoms completely disappeared. During interferon therapy a significant decline in the total lymphocyte count, from normal levels to 0,5 × $10^9$/l, as well as moderate granulocytopenia (1,5 × $10^9$/l) were noted. This suppression persisted throughout the period of interferon treatment. CD4+ counts were consistently < 0,2 × $10^9$/l throughout the period of interferon therapy.

At restaging of the lymphoma 13 months after initiation of interferon therapy there was no evidence of residual disease. Interferon therapy was stopped but 4 weeks later the patient presented again with fever, extensive herpes labialis and oral and oesophageal candidiasis. In addition there was supraclavicular lymphadenopathy and palpable splenomegaly (4 cm below the costal margin). Laboratory studies showed a haemoglobin concentration of 9,5 g/dl, a leucocyte count of 5,1 × $10^9$/l and a thrombocyte count of 130 × $10^9$/l. Computed tomography (CT) of the abdomen again revealed retroperitoneal lymphadenopathy. Investigation for HIV by means of ELISA and Western blot assay was again negative.

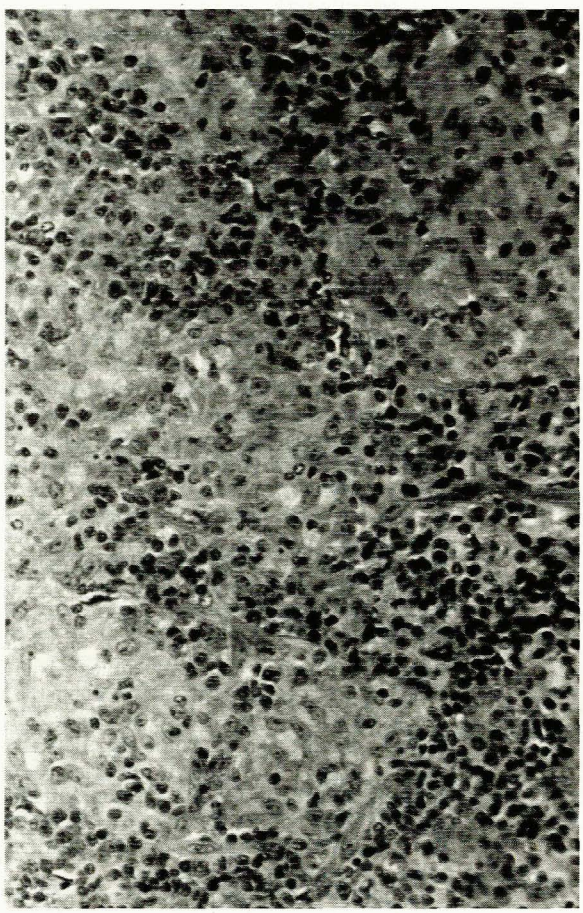

FIG. 1.
**Biopsy of the tonsil (October 1982) shows replacement of the tonsil by an abnormal infiltrate comprising small to intermediate-sized lymphoid cells with a slight irregularity to their nuclear outline. There is a florid epithelioid histiocytic response (H and E, original magnification x 400).**

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Accepted 26 Jun 1992.

Biopsy of the supraclavicular mass revealed this to be a soft-tissue deposit, rather than a lymph node, showing histological features of Kaposi's sarcoma (Fig. 2). No lymphoma was evident in this biopsy nor at full restaging, which included bone marrow trephine biopsy. Despite treatment with broad-spectrum antibiotics, antifungal and antiviral agents as well as re-introduction of α-interferon, the patient's condition deteriorated and she died of sepsis and multi-organ failure in May 1989.

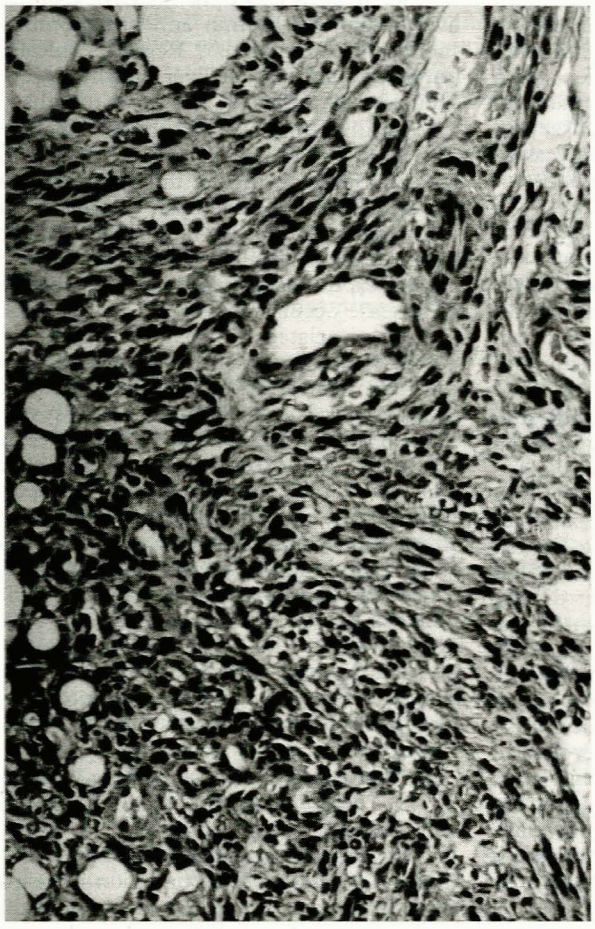

FIG. 2.
**Biopsy of soft-tissue tumour deposit showing involvement by Kaposi's sarcoma. The vascular component of the tumour is prominent (H and E, original magnification x 400).**

## Discussion

Lel has only fairly recently been recognised as a specific entity with histogenetic origin from peripheral T-lymphocytes.[3,4]

Diagnosis of the condition is complicated by the presence of a reactive cellular component presumably induced by the secretion of lymphokines by the malignant T-cells. Immunocytochemical studies are important in confirming the diagnosis. The patient described here had all the morphological and immunocytochemical features of Lennert's lymphoma.

Therapy of the peripheral T-cell lymphomas has not been well standardised. Some patients appear to achieve remission with aggressive chemotherapy but treatment failure or relapse after initial response to chemotherapy is not infrequent. This was the case in the patient described here. A therapeutic trial of interferon resulted in a good clinical response that lasted for over 13 months but within 4 weeks of the interferon treatment being stopped the clinical course was complicated by a rapidly developing, aggressive Kaposi's sarcoma.

Kaposi's sarcoma is often associated with underlying immunosuppressed states, including organ transplantation, auto-immune illnesses and AIDS.[5-7] Since interferon treatment has been the mainstay of systemic therapy of Kaposi's sarcoma in these patients the occurrence of Kaposi's sarcoma in our patient so shortly after interferon therapy would appear to be paradoxical but may be related to the diverse regulatory effects of the interferons which are both immunomodulatory as well as antiproliferative. Among the immunomodulatory activities the effect on natural killer (NK) cells has received most attention. While a number of studies have shown a significant enhancement of NK cell activity with the use of natural interferons,[8] decreased NK cell activity has also been described as well as more generalised immune suppression.[9,10] The differences observed in various studies may be dependent, among other factors, on the state of NK cell activity before treatment as well as on the dose and source of interferon and the duration of treatment.[9] The direct antiproliferative effects of interferons, which are not confined only to malignant cells but which also suppress the proliferation of normal haemopoietic precursors, causing granulocytopenia and lymphopenia with resulting immune suppression, may also be of importance.[10] Interferon therapy appears clearly to have been effective in suppressing the growth of the T-cell lymphoma in this patient. Since it appears unlikely that the Kaposi sarcoma appeared *de novo* during the 4-week interval during which interferon was discontinued, interferon treatment appears not to have prevented tumorigenesis, and indeed, by virtue of the reduction of CD4+ lymphocytes, may have contributed to the development of the Kaposi sarcoma.

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