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Letter to the Editor

Cutaneous Vasculitis Associated with Interferon

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THE TOXICITY of the interferons is being increasingly recognised [1–3] as their clinical usage grows [4, 5]. We report the occurrence of cutaneous vasculitis as a previously unrecognised complication of interferon treatment.

A 43-yr-old man with stage IIb malignant testicular teratoma (intermediate) had been treated initially with cisplatin, vinblastine and bleomycin. Transient paraesthesiae in the fingers without objective sensory neuropathy were noted during this period but Raynaud's phenomenon was never reported, even during a particularly cold winter. After partial resection of a residual abdominal mass, which contained the better differentiated component of the original tumour, he had received etoposide, actinomycin and methotrexate.

A 4-week course of treatment with human lymphoblastoid interferon (HLBI), a highly purified mixture of alpha-interferons, was commenced when metastatic disease persisted after ifosfamide. Doses of 4.5×10^6 IU HLBI (Wellcome Research Laboratories) were administered daily by intramuscular injection, and a typical mild acute reaction to the initial interferon injections with low-grade pyrexia and arthralgia was noted. This settled spontaneously and there were no injection site reactions. After 1 week the patient experienced pain in one finger-tip, increasing over the next 2 weeks until HLBI was discontinued. Ischaemic skin changes were then evident in that finger-tip together with haemorrhages in the nail-bed and beneath the free margin of that and several other finger-nails of both hands (see Fig. 1). There was no history of trauma, nor was there any evidence of peripheral vascular disease. There were no other symptoms and no other relevant findings on examination. The haemoglobin, differential white cell count, platelet count and blood film were normal and ESR 86 mm during the first hour; serum urea, electrolytes and liver function tests were normal; serum immunoglobulins were normal and cold agglutinins and cryoglobulins were not detected; antinuclear factor and rheumatoid factor were negative, LE cells were absent and the ASO titre normal. Throat swab, and blood and urine cultures were negative. Urine microscopy was normal and there was no proteinuria. Serum complement and blood viscosity were not measured. His symptoms improved over the next 2 weeks while receiving methoserpidine, and after the ischaemic skin had sloughed the finger-tip returned to normal.

The cause of this vasculitic reaction is uncertain, but local causes and systemic diseases such as the connective tissue diseases or infection were excluded by the absence of supporting features in the history, examination and investigations. A possible mechanism is the formation of immune complexes and a type III hypersensitivity reaction, despite the lack of evidence of involvement of other organs, as interferons are known to have both stimulatory and inhibitory effects on the immune system [5]. The administration of partially purified leucocyte interferon and recombinant alpha-interferon may be associated with the development of interferon antibodies [3], although this has not yet been reported with HLBI, and recently it has been reported that spontaneous antibodies to alpha-interferon have been found in a patient with SLE [6].

It is known that interferons induce a wide range of changes in cell membranes [7], and therefore an

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alternative explanation is that by affecting cell membrane rigidity, interferon could perhaps lead to an increase in blood viscosity, resulting in localised small vessel occlusion.

With the increasing use of interferons this potentially troublesome complication of treatment should be borne in mind.

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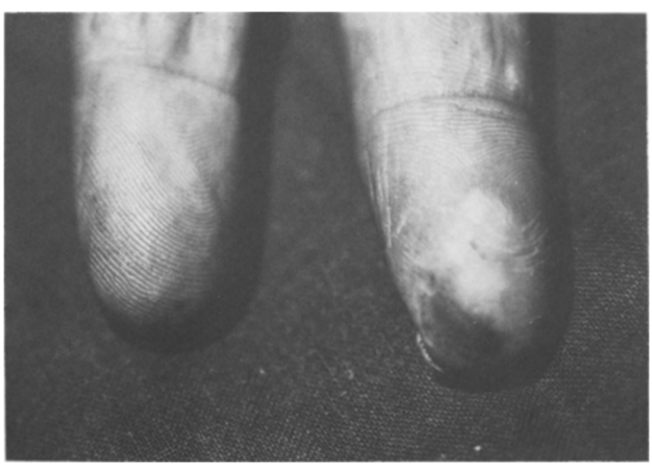

Fig. 1. *Ischaemic changes in the right middle finger-tip.*