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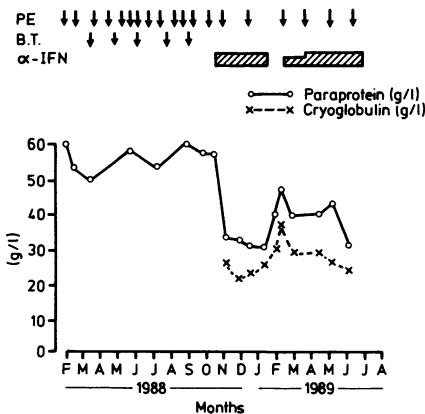
Treatment of Waldenström's macroglobulinaemia with α interferon

Alpha interferon has been shown to have some activity against B cell non-Hodgkin's lymphomas, primarily the low grade histological types.¹ It has also been used in Waldenström's macroglobulinaemia, but its activity in this disorder is not very well documented.² We report a patient with Waldenström's macroglobulinaemia and cryoglobulinaemia, who derived considerable benefit from treatment with α interferon.

A 68 year old Caucasian woman presented in November 1985 with a six month history of recurrent epistaxis, night sweats, and severe Raynaud's disease. She also complained of blurring of vision. On examination the fingers were blue, there was no lymphadenopathy, and the spleen was just palpable. Fundal examination showed typical changes of hyperviscosity. A full blood count showed: haemoglobin concentration of 10.7 g/dl, white cell count of $8.7 \times 10^9/l$ with a normal differential, and a platelet count of $360 \times 10^9/l$. Urea and electrolytes and liver function tests were normal, but the total protein was raised at 126 g/l, with the presence of an IgM λ paraprotein band. There was minimal immune suppression and Bence-Jones protein was absent. The paraprotein band was quantitated at 55 g/l, of which 40 g was a cryoglobulin. The bone marrow findings were consistent with a diagnosis of Waldenström's macroglobulinaemia.

She had urgent plasmapheresis with good resolution of her symptoms, but as Bence-Jones protein became detectable within the next few months, she was started on a course of chlorambucil, 10 mg daily for seven days, repeated every four weeks. As there was no change in the paraprotein concentration, this was discontinued. She continued to have plasma exchanges every four to six weeks and remained quite well. In early 1988, however, her condition began to deteriorate and she was given cyclophosphamide, 1 g intravenously, at monthly intervals. This was discontinued after six months as the paraprotein concentration had not changed. Moreover, she was requiring regular blood transfusions.

By October 1988, despite three weekly plasma exchanges, her general condition continued to deteriorate. She had excessive gum bleeding, her visual disturbance worsened, and she had several episodes of loss of consciousness. She was therefore given α interferon (Intron A), 3 megaunits three times weekly. The figure shows the striking response of the paraprotein and cryoglobulin concentrations to treatment with α interferon. In particular, she required no further blood transfusion and needed only one plasma exchange in the ensuing three months. She experienced severe side effects from α interferon, however, and it was temporarily discontinued. The paraprotein concentration increased, with reappearance of her symp-



Response of paraprotein and cryoglobulin concentrations to treatment with α interferon. PE = plasma exchange; BT = blood transfusion.

toms, necessitating an urgent plasma exchange. She was given another preparation of α interferon (Roferon A) at a lower dose (3 megaunits twice weekly), without much improvement in her symptoms. When the interferon was increased to 3 megaunits three times weekly, the cryoglobulin concentration fell to around 25 g/l and her symptoms disappeared. She remains well and has not required any further plasma exchange since June 1989.

This case shows that α interferon may be useful in the treatment of refractory Waldenström's macroglobulinaemia, especially in association with cryoglobulinaemia. It may also be worth exploring its use in cases of cryoglobulinaemia from other causes.

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Apoptotic cell death during renal transplant rejection

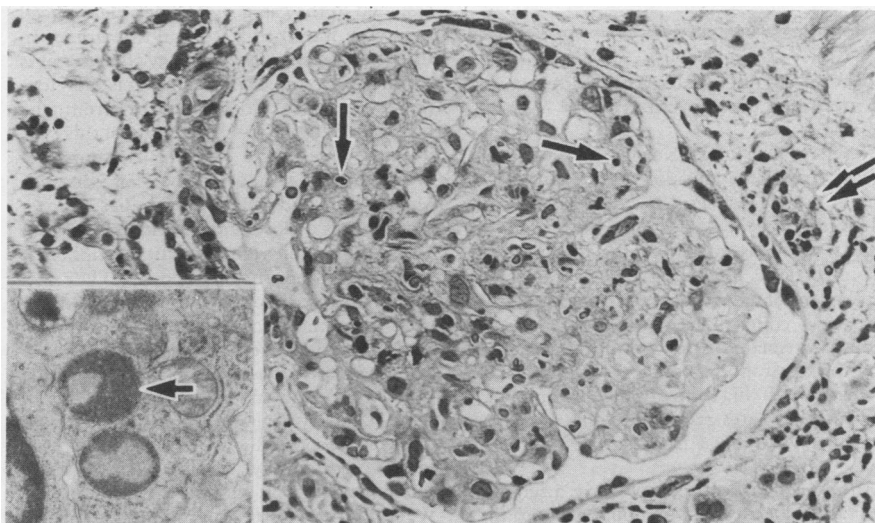
Apoptosis is a form of intrinsically programmed cell death described in a wide range of physiological and pathological states.¹ Its occurrence has been documented in several renal disorders.² Acute rejection of renal transplants produces widespread damage, principally in tubules and vasculature, but glomerular abnormalities have been reported.³ Although well described, the pathogenesis of much of this damage is unclear. We describe a case of acute renal transplant rejection in which cell death by apoptosis was striking within the glomeruli and tubules.

A 45 year old woman who had had a functioning renal transplant for nine months presented with a pronounced decline in renal function. Rejection was clinically confirmed by biopsy and the patient responded slowly to increased doses of immunosuppressive drugs. A second biopsy specimen two and a half weeks later showed diminished but continuing active rejection which eventually responded to immunosuppression. Four and a half months after that, however, a further decline in renal function occurred with a third biopsy specimen showing chronic rejection.

The first biopsy specimen showed acute rejection with a prominent interstitial lymphocytic infiltrate and a "tubulitis" with tubular necrosis. Endothelial swelling, foam cells, lymphocytic infiltration and oedema were present in the intima of medium and large sized arteries. A variable expansion in mesangial matrix was seen, but striking cell death by apoptosis was identified, principally in endothelial cells but also in the mesangium (figure). Review of the tubular damage showed, focally, a similar mode of cell death. Electron microscopic examination showed characteristic apoptotic nuclear fragments with condensed, featureless chromatin. Some had been phagocytosed by other cells (figure; inset).

The second biopsy specimen was similar but the rejection process was milder. Apoptotic cell death persisted in the glomeruli. Arterial narrowing, tubular atrophy, and interstitial fibrosis typical of chronic vascular rejection were seen in the third biopsy specimen.

As far as we know, this is the first description of apoptosis during acute renal trans-



Glomerulus with prominent apoptotic bodies in characteristic scattered distribution (single arrow). Interstitial infiltration and tubulitis are also seen (double arrow) (Haematoxylin and eosin). Inset: apoptotic body in tubular epithelial cell.