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Complete Remission of a Primary Cutaneous B Cell Lymphoma Treated with Intralesional Recombinant Interferon Alpha-2a

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PRIMARY CUTANEOUS B cell lymphomas (CBCL) are rare, and closely resemble those described in 1951 by Crosti as reticulohistiocytoma [1]. Patients usually present with localised indolent nodular skin lesions with slow progression and low propensity for extracutaneous spread [2, 3]. Because of this favourable prognosis, CBCL have been considered "skin-associated lymphoid tissue" (SALT)-derived lymphoma by a parallel with the lymphomas of "mucosa-associated lymphoid tissue" (MALT) [1, 3]. Conventional therapy includes surgical excision, electron beam radiation therapy (EBRT) and systemic chemotherapy. All of these are effective, but remissions are mostly transient. To date, the optimum management for localised cutaneous lymphoma still remains controversial.

A 53-year-old man presented in 1976 with nodular skin lesions on the left side of the thorax, progressing slowly for 6 years. Histological diagnosis was not certain (lymphocytoma cutis? malignant lymphoma?). One year later, he noticed a rapid increase in the size of the nodules. Histological examination revealed findings compatible with Crosti's reticulohistiocytoma. He was treated with systemic combination chemotherapy (cyclophosphamide, doxorubicin, VM-26, prednisone) from May 1977 to December 1977, with complete response (CR). A first relapse occurred in May 1978, close to the site of onset. EBRT (32 Gy) led to prompt disappearance of lesions. Radiotherapy was followed by consolidation systemic chemotherapy (cyclophosphamide, vincristine, prednisone) from May 1978 to May 1980. Three years later, the patient developed nodules confined to a circumscribed area of the back. Histological features were compatible with Jessner and Kanof's lymphocytic infiltration. EBRT (32 Gy) was performed, with clinical CR. He relapsed in the skin outside the initial site involved (but always on the trunk), and outside the previous radiotherapy fields, in 1985, 1986 and 1989. He was re-irradiated and showed good response. He was re-admitted to the hospital in October 1991 because of papulonodular lesions, ranging in diameter from 2 to 6 cm, on the left side of the thorax and abdomen (Fig. 1). Histological examination revealed a diffuse neoplastic dermal infiltrate without epidermotropism. Electron microscope examination confirmed lymphoid cells. Referring to the working formulation for clinical usage, the lymphoma was classified as diffuse small cleaved cells (centrocytic type), intermediate grade. Immunohistochemical data confirmed the B cell nature of the infiltration. Monoclonal antibodies on paraffin sections showed MB2+ UCHL1+ LN1− LN2+ phenotype. On cryostat sections, the neoplastic cells expressed CD19+, CD20+ pan-B antigens. Pan-T antigens (CD7) and CD4, CD8 antigens were not expressed [4]. An extensive lymphoma work-up was performed and failed to show extracutaneous disease. Peripheral adenopathies and systemic B symptoms were absent. There was no evidence of infection by HTLV 1, human immunodeficiency virus (HIV) 1-2 or Epstein–Barr virus (EBV).

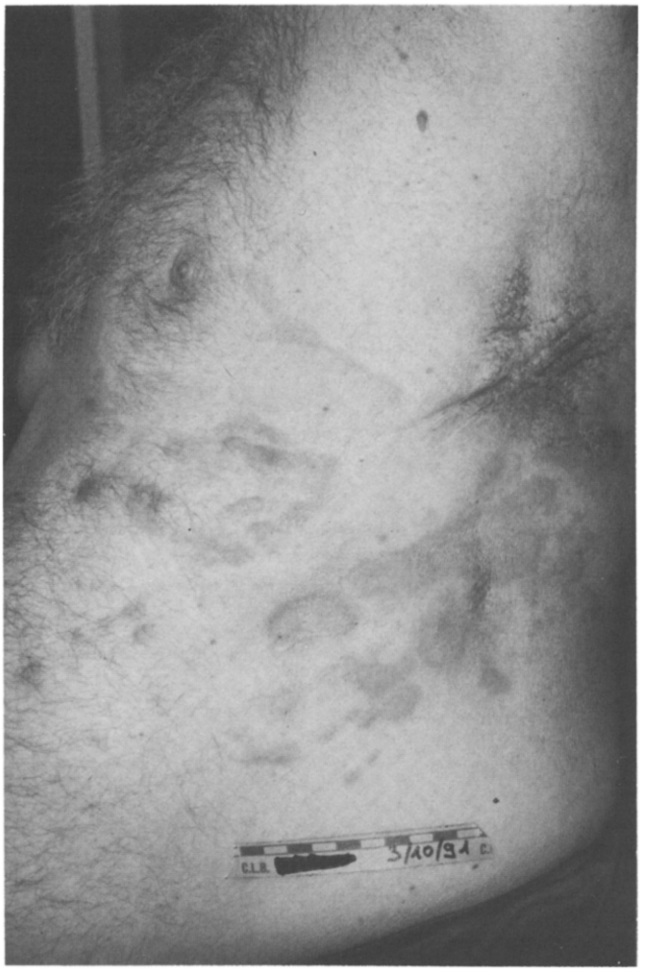

Fig. 1. Clinical presentation in October 1991, showing cutaneous nodules on the left side of the thorax and abdomen.

Recombinant interferon α2a treatment (rIFN-α2a) (Roferon°) was initiated in October 1991 and consisted of 3 million U rIFN-α2a injected intralesionally, each week into a different nodule. After each injection, fever (grade 1) and mild fatigue occurred during a 24-h period. After 8 weeks of treatment, the nodules had reduced in size. Then, 5 million U rIFN-α2a were administered intralesionally once a week. Clinically, the lesions showed partial response (PR) after 4 months of treatment. Then, 10 million U rIFN-α2a were given monthly by local injections into the remaining nodules. This treatment led to a CR in September 1992 (Fig. 2). Therapy was discontinued in October 1992. The patient was in persistant complete remission in October 1993.

In the last few years, a number of studies have evaluated the role of IFN in non-Hodgkin's lymphoma. Significant responses have been observed in follicular lymphoma [5, 6]. The exact mechanism operative in the IFN-induced regression of lymphoproliferative disorders remains uncertain [7]. rIFN-α has been

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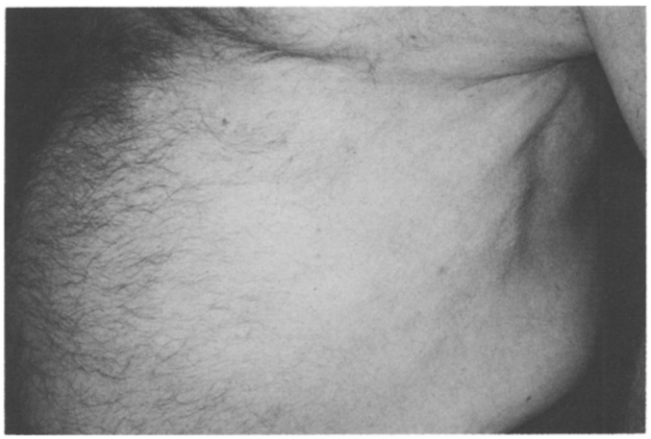

Fig. 2. Complete remission after intralesional rIFN-α2a (January 1993).

used in the treatment of cutaneous T-cell lymphomas (CTCL) systemically [5, 8]. Intralesional rIFN-α also has a beneficial effect in early plaque stage CTCL (mycosis fungoides) [8, 9]. More recently, intralesional rIFN-γ and rIL-2 have been reported to be effective in CTCL [8, 10]. B cell neoplasms are also potential targets for IFN [7], and our case demonstrates the efficacy of local rIFN-α2a in CBCL. In the study of 83 CBCL of Santucci and colleagues [3], 1 case of PR after rIFN-α2b has been reported.

Our case also illustrates the problem of differentiation between pseudolymphoma (such as lymphocytoma cutis and Jessner's lymphocytic infiltration) and malignant skin infiltrates [1, 3]. In the literature, CR of a B cell cutaneous pseudolymphoma treated with intralesional IFN-α has been reported [11].

The lack of extracutaneous spread of CBCL justifies the choice of non-aggressive therapy [2]. Remissions can usually be achieved repeatedly with local irradiation. EBRT proved to be the most suitable treatment for both initial lesions and relapse to the skin [2, 3]. Intralesional administration of rIFN-α may be given safely and can lead to a remission of CBCL in heavily pretreated patients, if local EBRT is not more possible. Large series and longer follow-up are required to confirm the precise role of IFN-α in CBCL.

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Escape Phenomenon After Successful Bromocriptine and Octreotide Treatment in Thyroid Stimulating Hormone Secreting Pituitary Adenoma Residual Tissue

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WE REPORT the case of a 63-year-old male with thyroid stimulating hormone (TSH) secreting pituitary adenoma in which bromocriptine and octreotide were temporarily effective.

The patient had a goiter and hyperthyroidism and was treated with thyrostatics from 1965 to 1979 without improvement.

In 1979, laboratory data confirmed thyrotoxicosis with radioimmuno assay (RIA) TSH levels ranging from 5.2 to 16.7 μU/ml. Skull tomography revealed a hypophyseal adenoma, with invasion of the sphenoidal area, which was removed transphenoidally.

TSH levels stabilised around 3 μU/ml but thyrotoxicosis persisted and thyroidectomy followed by radioiodine was performed. The patient was euthyroidal with oral levothyroxine (L-T4) (1.8 μg/kg/day) but TSH did not fall below 8 μU/ml. Bromocriptine was administered with success but an escape phenomenon arose after 3 months (TSH 16 μU/ml). Cranial computerised tomography (CT) (magnetic resonance imaging was impossible because of metal clips attached after surgery) revealed tissue in the sphenoidal area. A 24-h TSH assay demonstrated an absence of cyclicity with high night levels and no inhibition after triiodothyronine (T3). The α subunit/TSH ratio (10.2) was elevated. A single 0.1 mg subcutaneous (s.c.) dose of octreotide followed by TSH immunoradiometric assay (IRMA) every hour for 8 hours showed a decrease in TSH levels from 13.9 to 9.7 μU/ml. Continuous adminstration (0.1 mg s.c./8 h for 5 days) produced a decrease in TSH levels from 13.9 to 0.7 μU/ml.

After 2 months of octreotide administration IRMA TSH levels became persistently high (4 μU/ml). The voluntary suspension of therapy by the patient brought TSH levels back to the initial concentrations (23 μU/ml). We resumed octreotide therapy but the TSH levels remained high.

Euthyroidism obtained with L-T4 and no TSH suppression with T3 administration exclude elevated TSH levels as compen-

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