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CD30 + cutaneous T-cell lymphoma associated with sarcoidosis *

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Abstract

We observed a 61-year-old woman, presenting with deeply infiltrating, erythemato-cyanotic, sometimes ulcerated or crusted plaques and nodules, mainly located on the lower limbs. Similar lesions had been present for more than 4 years, with a typical evolution: fast growth, followed by ulceration and necrosis, resulting in hyperpigmented, atrophic patches. The patient had had Rx-confirmed, symptomatic lung sarcoidosis for 5 years. Histological examination of skin lesions showed diffuse dermal and hypodermal lympho-histiocytic infiltrate, mainly composed of pleomorphic cells. On immunohistochemistry, the infiltrate was mainly composed of CD2 +, CD3 +, CD45RO +, CD4 +, CD30 +, CD25 − T-cells, with sparse CD1a + dendritic cells. The typical clinical evolution (relapsing, self-regressing plaques and nodules), morpho-immunological features of skin lesions, and strong expression of CD30 antigen by neoplastic T-cells suggest the possible classification of this case as CD30 + (Ki-1 +) cutaneous T-cell lymphoma. The association with systemic sarcoidosis, together with a down-regulated cell-mediated immune response, suggests the possibility that this latter may be a common denominator in the development of the two diseases.

Key words: Skin; T-cell lymphoma; CD30 antigen; Sarcoidosis

Introduction

The association of non-Hodgkin's lymphomas (NHL), with or without cutaneous involvement, and Hodgkin's lymphomas with sarcoidosis is not uncommon [1–3]. The possible (immune) mechanisms underlying the development of the two diseases, or anyhow linking them to each other, are currently obscure.

We report here the case of a 61-year-old woman with lung sarcoidosis who subsequently developed cutaneous nodular lesions characterized by indolent, self-regressing course and lasting 4 years before the diagnosis of cutaneous lymphoma was made. The clinical, histological, and immunohistochemical features of the skin lesions strongly suggest the classification of this case as CD30 +

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cutaneous T-cell lymphoma, a recently defined entity characterized by slowly progressive course and favourable prognosis.

Case report

The patient, a 61-year-old woman, was first seen in our institution in February 1991. At presentation she had several cutaneous and subcutaneous nodules (Fig. 1), deep red to violet in colour; some of these lesions were superficially ulcerated and/or crusted (Fig. 2), without any subjective symptoms. Careful clinical examination of the skin revealed some hyperpigmented, athrophic scars. No clinically enlarged lymph nodes were found in the superficial stations.

According to the clinical history, the patient was in generally good health until September 1986, when she developed intractable cough, accompanied by fever (37.5–38°C) and fatigue. Chest X-rays showed mediastinal hilar enlargement.

Specific tests (Kveim test +, ACE moderately increased) and generic evaluation of delayed-type immune response (virtually absent skin reaction to recall antigens; Multitest® Merieux, France) led to diagnosis of sarcoidosis, and corticosteroid treatment (1 mg/kg/day prednisone p.o.) was initiated.

Fig. 1. Nodules and plaques (involving skin and subcutis) and hyperpigmented, atrophic lesions on the right arm in a subject with CD30+ cutaneous T-cell lymphoma associated with sarcoidosis.

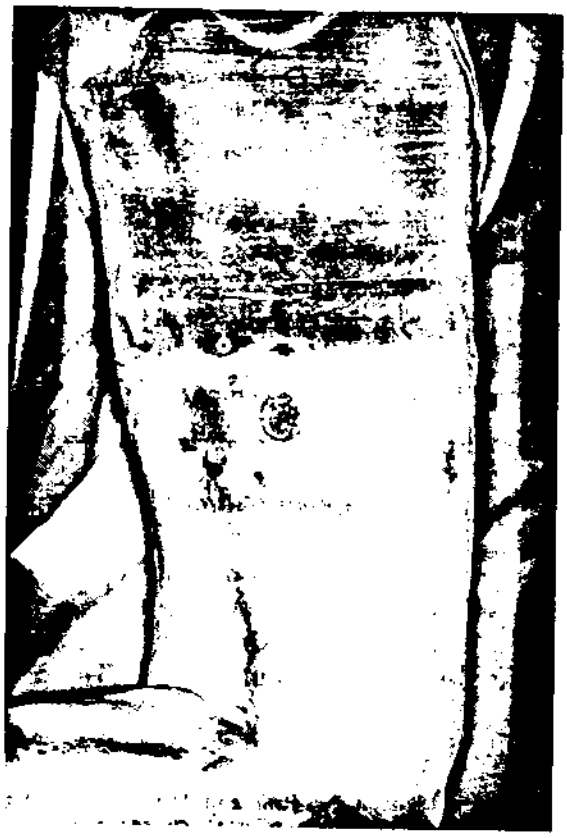

Fig. 2. Ulcerated and crusted plaque and hyperpigmented lesions on the right thigh (same subject as Fig. 1).

After 2 months of full-dose schedule, the dosage was gradually diminished (0.1 mg/kg/week) to discontinuation at the end of January, 1987. Systemic symptoms, chest X-rays, and laboratory tests were noticeably modified by the treatment, although complete remission was not achieved. In March, 1987, the patient developed several cutaneous and subcutaneous nodular lesions of the abdominal wall. According to the patient the lesions had developed subcutaneously, rapidly later involving the skin, ulcerating, crusting and, eventually, self-healing with hyperpigmentation, atrophy and scarring.

During the following 4 years new lesions developed on the trunk and limbs with very similar features: fast growth, ulceration, crusting and self-healing with atrophic scarring. No correlation with possible exacerbation of sarcoidosis or with steroid treatment

TABLE 1

Panel of monoclonal antibodies used for histological examination of a cutaneous T-cell lymphoma lesion

Antibody	Cluster designation	Source
B1	CD20	CC
Leu-14	CD22	BD
T11	CD2	CC
T3	CD3	CC
UCHL-1 [a]	CD45RO	DP
OKT4	CD4	OD
OKT8	CD8	OD
Leu-1	CD5	BD
OKT6	CD1a	OD
Leu-8	NA	BD
IL-2 r.	CD25	BD
HLA-DR	NA	BD
C3b r. [a]	CD35	DP
Ki-1	CD30	DP
Ber-H2 [b]	CD30	DP
J5	CD10	BD
Leu-M3	CD14	BD
Leu-M5	CD11c	BD
OKM1	CD11b	OD
OKT9	CD71	OD
Ki-67	NA	DP
L26 [b]	CD20	BI
MB2 [b]	NA	BI
LN1 [b]	CDw75	BI
LN2 [b]	CD74	BI
MT1 [b]	CD43	BI
MT2 [b]	NA	BI
LN3 [b]	NA	BI
anti-κ	NA	BD
anti-λ	NA	BD
anti-γ	NA	BD
anti-μ	NA	DP
anti-δ	NA	DP

[a] Tested on both frozen and paraffin sections.
[b] Tested on paraffin sections only.
BD, Becton & Dickinson, Mountain View, CA, USA; CC, Coulter Clone, Sheffield, UK; OD, Ortho Diagnostic Systems, Raritan, NJ, USA; DP, Dakopatts, Copenhagen, Denmark; BI, Biotest AG, Dreieich, Germany.
For predominant immunoreactivity see ref. 4.

Fig. 3. Histological picture of CD30+ cutaneous T-cell lymphoma lesion: dense, diffuse mononuclear cell infiltrate involves the dermis (and hypoderma), with a quite distinct subepidermal Grenz zone. (H&E, ×230.)

was established. Three biopsies were taken in that period (March and December, 1987; September, 1988). The histological diagnosis was 'pseudolymphoma with focal granuloma formation' in the first two biopsies and 'necrotizing vasculitis with granuloma formation' in the third.

At presentation, we took a new biopsy from a fully developed lesion of the right thigh. Half of the specimen was formalin-fixed and routinely processed for light microscopic histology, and the other half was snap frozen in liquid nitrogen, embedded in OCT, and stored at −70°C until sectioned. Cryostat sections (6 μm thick) were tested with a large panel of monoclonal antibodies [4] (see Table 1), using the alkaline phosphatase anti-alkaline phosphatase method [5]. The histological examination evidenced a dense, diffuse mononuclear cell infiltration involving the whole thickness of the dermis (with a distinct subepidermal Grenz-zone) and subcutaneous fat. The infiltrate (Figs. 3 & 4) was mainly composed of pleomorphic lymphoid cells (medium to large cells, showing a great variability in nuclear size and shape), large blast cells, occasional cerebriform cells, rare Sternberg-like cells with bizarre shape, and small lymphocytes clustered with 'histiocytic' cells. The immunohistochemical examination revealed a striking prevalence of CD45RO +, CD2 +, CD3 +, CD4 +, CD8

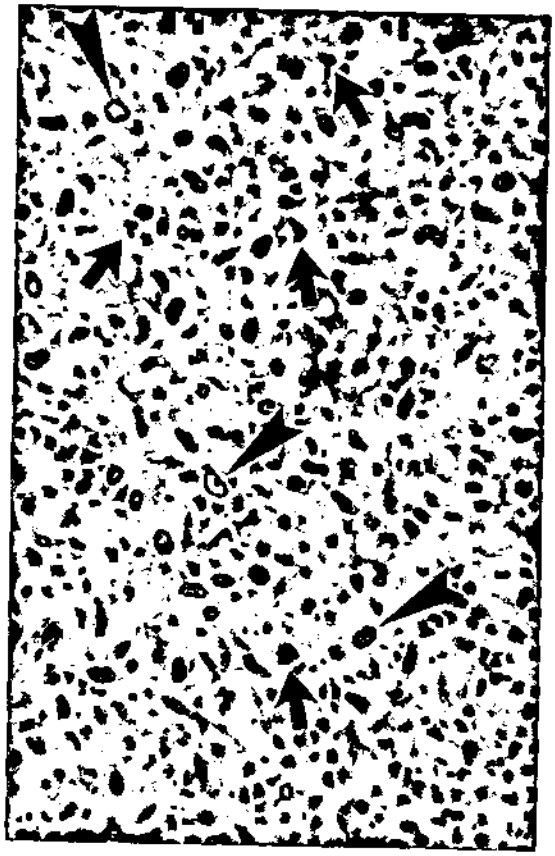

Fig. 4. Histological picture of CD30+ cutaneous T-cell lymphoma lesion: the infiltrate is mainly composed of pleomorphic cells (arrows) and large blasts (arrowheads), with occasional cerebriform cells and a number of small lymphocytes. (H&E, ×920.)

Fig. 5. Most infiltrating cells (>80%) are stained by anti-CD30 (Ki-1) monoclonal antibody. (APAAP, frozen tissue, ×230.)

– T-cells, with sparse CD1a + dendritic cells. More than 80% of T-cells expressed CD30 antigen (Fig. 5), while less than 10% expressed CD25 (IL-2r) antigen. The immuno-histochemical analysis of paraffin sections showed findings in complete agreement with those obtained in cryostat sections, i.e., pleomorphic and blast cells were constantly CD45RO (UCHL-1) +, and most (> 75%) were also CD30 (Ber-H2) +.

The patient was carefully staged and, due to the absence of detectable extracutaneous lesions, we established the diagnosis of CD30 + primary cutaneous T-cell lymphoma associated with sarcoidosis.

Discussion

The patient reported, presented sarcoidosis followed by onset of cutaneous T-cell lymphoma (CTCL). This latter was classified as CD30 + CTCL according to clinico-prognostic, histological and immunological criteria recently proposed by Belijaards et al. [6]. CD30 + CTCL is characterized by the presence of cutaneous nodules or tumors, isolated (more often) or disseminated (more rarely), and possibly self-regressing, with negative staging at presentation, and a quite favourable clinical course [6–8]. The clinico-pathological features of our case fit with those described as typical of subgroup III of CD30 + CTCL, i.e., multiple nodular lesions, self-healing and relapsing, with a histological picture resembling that of lymphomatoid papulosis [9]. This latter is characterized histologically by an infiltration of pleomorphic T-cells (small to medium-sized) and sparse large, blast-like cells, sometimes resembling Reed-Stenberg cells, while the typical CD30 + CTCL (type I) is characterized clinically by isolated nodules or tumors and histologically by a monotonous, diffuse proliferation of large CD30 + cells, irrespective of their anaplastic shape. This latter defines the large anaplastic (Ki-1 +) subgroup of peripheral T-cell lymphoma in the updated Kiel classification [10]; due to absence of differences in clinical behaviour related to the pure morphology of neoplastic T-cells, it is reasonable to suggest CD30 + CTCL is a single type of CTCL [9].

The association between NHL and sarcoidosis, not uncommon according to data in the literature [1,2] suggests speculations concerning the possible existence of an underlying immune deficiency. In fact, sarcoidosis is a chronic granulomatous process characterized by clear-cut impairment of T-cell mediated immune responses, as suggested by the strongly reduced cutaneous delayed-type reaction to recall antigens. This defect, possibly accompanied by an imbalance of immunoregulatory T-cells, might favour the selection and clonal expansion of neoplastic lymphoid cells. On the other hand, the possibility of a retroviral infection as a common etiological factor associating the two diseases is suggested by the recent finding of HTLV-I proviral sequences in a series of cutaneous CD30 + large T-cell lymphomas [11]. In this regard, the association between sarcoidosis and CD30 + CTCL cannot be considered surprising.

Speculation apart, it is important to be aware of the possible association of sarcoidosis and cutaneous lymphoma and to evaluate very prudently the therapeutic choices, to avoid exaggerated or incorrect treatment.

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