Regressing anaplastic CD30-positive large-cell lymphoma of the skin

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SUMMARY

Originally believed to be of histiocytic origin, regressing primary cutaneous anaplastic large-cell lymphoma is a CD30 (Ki 1) positive T–cell lymphoma with histologic high grade malignancy, but with an often favorable clinical course with regression of individual lesions. We present a case of a 69-year-old white woman with an 8–month history of noduloulcerative lesions on her right lower leg, otherwise in good general health. The clinical, histologic, and immunohistochemical findings pointed to CD30 positive primary cutaneous anaplastic large-cell lymphoma. There were no signs of generalization, lymph node or internal organ involvement. After 2 years of activity, the disease regressed. During the 10-year follow-up period, no signs of disease reactivation were noted. Accurate recognition of this lymphoma is important to avoid unnecessary aggressive treatments.

KEY WORDS

large cell lymphoma, regressing, CD30 positive, skin

Introduction

Regressing atypical histiocytosis was first described by Flynn et al. (1) as a proliferation of atypical histiocytes confined primarily to the skin. Although histologic findings indicated a high-grade malignancy, the course was unexpectedly indolent with regression of lesions and no extracutaneous involvement. Later, the immunophenotyping of tumor cells and rearrangement of T-cell receptor genes showed that this multifocal tumor was of T-cell origin (2, 3).

The clinical picture is characterized by the abrupt onset of cutaneous noduloulcerative lesions and cyclic episodes of disease activity and spontaneous regression. It can imitate other skin diseases (4), and the diagnosis is based on histopathologic findings, immunophenotyping, and T-cell gene rearrangement analysis, as well as clinical course (2, 3, 5).

We present a case of CD30 (Ki 1) positive primary cutaneous anaplastic large-cell lymphoma with typical clinical and pathological features.

Case report

A 69-year-old white woman had an 8-month history of violaceous papules and nodules on her right

lower leg; two of them had ulcerated. The patient was in good general health.

On skin examination (September 1995) there were several violaceous papules and nodules situated in distal parts of right lower leg, measuring 1 to 4 cm in diameter (Figure 1). The biggest two lesions had a central ulceration covered with pus and infiltrated edges. Edema of that region, residual pigmented macules, and depigmented scars were also present. The lesions were not painful; lymphadenopathy and hepatosplenomegaly were not detected.

Her personal history was unremarkable except for hypertension (well controlled by nifedipine) and phlebothrombosis of the right leg 7 years earlier. Her family history was normal.

A series of investigations – routine laboratory analyses (including complete blood count, erythrocyte sedimentation rate, urinalysis, serum glucose, electrolytes, and hepatic enzymes), ultrasonography of the abdomen, and radiological examination of chest, cranium, and lower leg – were all normal. Other exams (gynecological, neurological, and hematological) revealed no abnormalities except hypertension. No extracutaneous involvement was detected.

The prominent feature on histologic examination (hematoxylin-eosin) was a dense nonepidermotropic polymorphous infiltrate consisting mainly of large cells with abundant and clear cytoplasm, and variously shaped nuclei (round, oval, kidney-shaped, and irregular), some including a nucleolus. There were also some giant cells morphologically similar to Reed-Sternberg cells (Figure 2).

Immunophenotyping (peroxidase-antiperoxidase - PAP, and alkaline phosphatase-antialkaline phosphatase - APAAP) revealed tumor cells positive for CD30 (Ki 1) (Figure 4), CD 45 RO (UCHL–1), and epithelial membrane antigen (EMA). The infiltrate was negative for CD 20, S 100, α1 antitrypsin, cytokeratin, and lysozyme.

The therapy consisted of systemic and topical antibiotics with a short course of oral corticosteroids (30 mg of prednisone daily). Despite the therapy, several new papules and nodules developed, ulcerated, and then regressed, leaving pigmented macules and/or scars (Figure 3). During the following 12 months painful nodulоulcerative lesions recurred three times on the right lower leg. During the second relapse, the patient received interferon á (6 weeks, cumulative dose 129 million IU), which had no effect on the course of the disease. Relapses and remissions lasted for 2 years, and then the disease regressed. At the last check-up (January 2006) there were no active lesions and her general health was assessed as good.

Discussion

Primary CD30 (Ki 1) positive cutaneous T-cell lymphomas include a group of non-Hodgkin lymphomas with two main entities: large-cell lymphoma and lymphomatoid papulosis (6–9). In addition to sharing the same antigen, they also share a benign clinical course with possible spontaneous regression. The mechanisms of regression are unclear; recent data suggest that a selective increase in CD30 ligand expression and activation of the CD30 signaling pathway might play a major role (10, 11). Clarke et al. (12) confirmed that indolent forms of CD30 positive lymphoproliferative disorders have significantly higher expression of apoptotic markers – activated FADD (Fas-associated with death domain) and cleaved caspase 3 – than biologically aggressive ones. This observation led to the conclusion that death receptor-mediated apoptosis may be responsible for spontaneous regression.

Epithelial membrane antigen (EMA) is a high-molecular-weight transmembrane protein usually expressed on the luminal surface membranes of epithelial tissues, although EMA is also expressed in lymphoid cells and in malignancies, especially plasma cell neoplasms and T/null-cell anaplastic large-cell lymphomas. On the basis of a MEDLINE search, we conclude that our patient is one of the few cases of EMA positive primary cutaneous anaplastic large-cell lymphoma (13–15).

Primary cutaneous CD30 positive large-cell lymphomas are uncommon; only a few hundred cases have been reported so far. During the 15-year period from 1991 to 2005, 104 new cases of mycosis fungoides have been registered at our Department and only 1 case of this kind of lymphoma, which further emphasizes the rarity of the disease. A favorable outcome despite worrying clinical and histologic findings is a unique feature of these lymphomas. The 5-year survival rate is high in these patients (91–96%) (16), and there is a high proportion of spontaneous remissions (16). Thus, therapy is reserved only for cases with generalized involvement of the skin or nodal involvement. A wide variety of therapeutic modalities, including radiotherapy, PUVA, and various polychemotherapy protocols, have been proposed. Recent data suggest that some patients can benefit from oral retinoids (bexarotene) (17) and topical imiquimod (18).

In our patient, a therapeutic attempt with interferon α was not successful. Spontaneous regression took place in 2 years, leading to a complete remission. It is important to know the clinical, histological, and immunopathological characteristics of this kind of lymphoma because overtreatment with aggressive remedies can be harmful to the patient.

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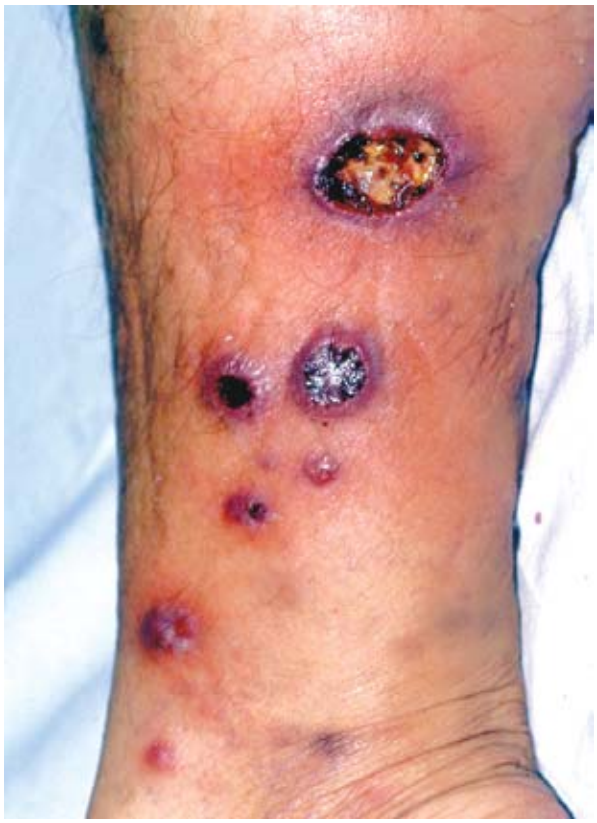


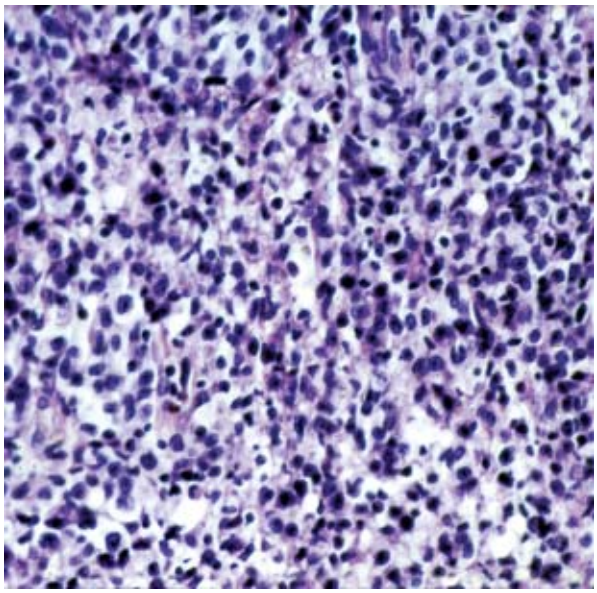
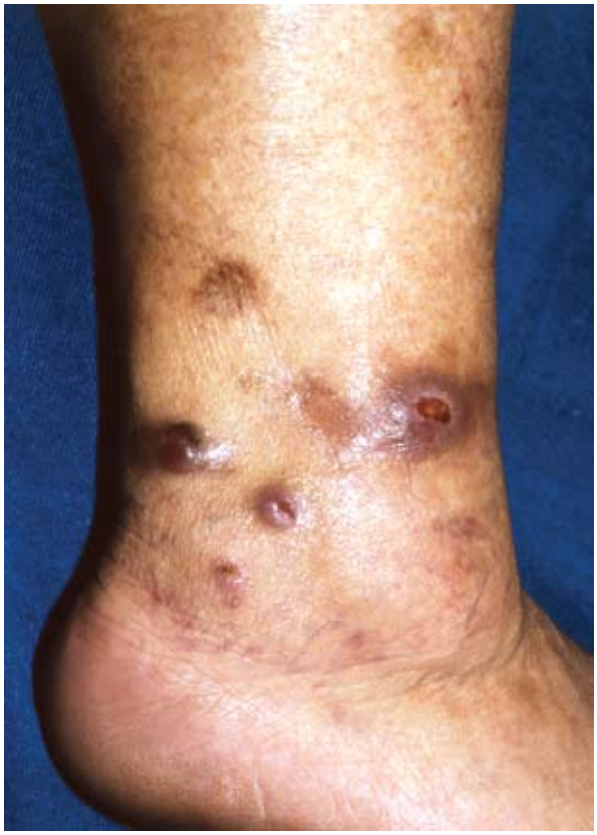


Figure 1. Multiple ulcerated papules and nodules (distal part, right lower leg)

Figure 2. Prominent pleomorphism, the most worrisome histological feature (H-E, 192x).



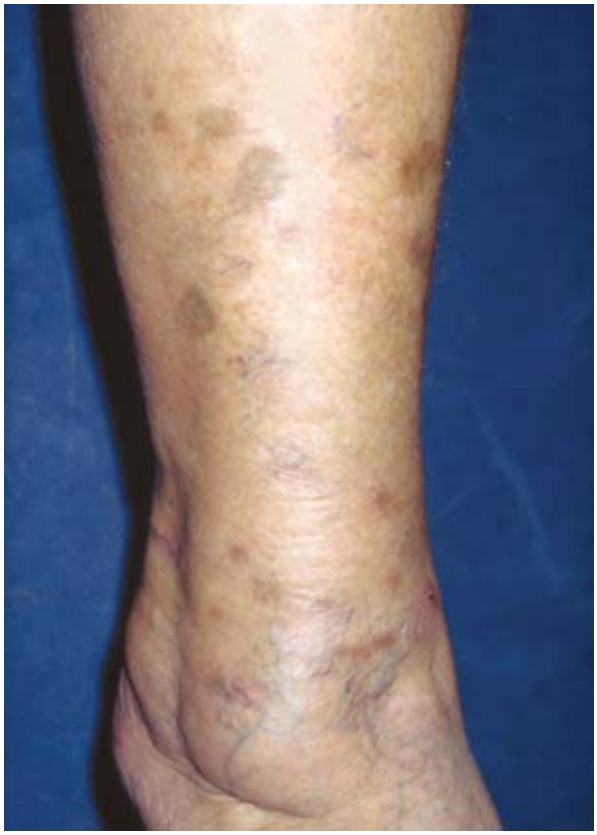


Figure 3. Noduloulcerative lesions on the lateral side of the right lower leg.

Figure 4. Residual pigmented macules and scars after regression of noduloulcerative lesions.

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