Disseminated Pagetoid Reticulosis Presenting as Cytotoxic CD4/CD8 Double Negative Cutaneous T-cell Lymphoma

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Sir,

Disseminated pagetoid reticulosis (DPR) is a rare form of cutaneous T-cell lymphoma (CTCL) originally described by Ketron & Goodman in 1931 (1). This lymphoproliferative disorder usually presents as multiple erythematous, squamous patches, plaques, nodules, ulcerated skin tumours and, not infrequently, runs an aggressive course with dissemination of the lesions and progression to a fatal outcome (1, 2).

Cytotoxic cutaneous lymphomas are uncommon and usually express a CD8 and/or CD56 positive phenotype. They represent a heterogeneous group of lymphomas showing various features with regard to clinicopathologic profile, immunophenotypic features, clinical course and prognosis (3). All cytotoxic lymphocytes express a set of toxic proteins, e.g. perforins, granzymes A (GrA) and B (GrB), and the T-cell intracellular antigen-1 (TIA-1) (4), which are reliable markers of cells with activated cytotoxic function (2).

Gemcitabine is a nucleoside antimetabolite with established activity against several solid tumours showing promising results in the treatment of lymphoproliferative malignancies. Gemcitabine is a cytosine analogue that causes less myelosuppression as well as immunosuppression compared with other available nucleoside analogues (5).

We describe here a 35-year-old patient with a primary cutaneous T-cell lymphoma presenting with clinicopathologic features of DPR and showing a CD4/CD8 double negative, TIA-1/granzyme B cytotoxic positive phenotype. Furthermore, we report the efficacy of gemcitabine treatment in this aggressive lymphoproliferative disorder.

CASE REPORT

A 35-year-old man presented with a 1-year history of generalized, painful, erythematous, some ulcerated and exudative patches, plaques and nodules (Fig. 1). No hepatosplenomegaly or lymphadenopathy was detected. Past medical history and physical examination were unremarkable, and laboratory investigations were within normal limits. Staging procedures (total computed tomographic scans and bone marrow aspirate) showed no abnormalities. The patient’s serum was negative for anti-HTLV-1 and anti-EBV antibodies and the levels of sIL-2 receptor and sTNF-α were within normal limits. Biopsy specimens from lesional skin were routinely processed for formalin fixation and paraffin embedding. Histopathologic examination showed a dense intraepidermal infiltrate of medium/large neoplastic lymphoid cells with clear, abundant cytoplasm, hyperchromatic nucleus and prominent nucleoli, scattered in the basal and suprabasal layers of the epidermis (Fig. 2). A few atypical lymphoid cells were also present around the blood vessels of the papillary dermis. The phenotypic profile of the intraepidermal lymphocytes was as fol-

Fig. 1. Erythematous-violaceous plaques and nodules at time of presentation.
up or limited genotypic and/or phenotypic characterization (2, 6, 7–12). In the past, there had been debate concerning the origin of the atypical cells in pagetoid reticulosis, up until their T-lymphocytic nature was definitively established through immunophenotypic and geno-phenotypic studies (13). Another controversial aspect of DPR concerns its association with mycosis fungoides based on their clinical and histopathologic similarities. Therefore many authors consider DPR as an aggressive variant of mycosis fungoides (11). Nevertheless, there are several clinical, histopathologic and immunophenotypic features that distinguish these two entities (14). DPR seems to be an aggressive clonal CTCL with distinctive clinicopathological findings and heterogeneous immunophenotype including CD4+ T-helper, or CD8+ cytotoxic/suppressor or CD4/CD8 double-negative phenotype together with γδ or γδ TCR expression (6–8). Our patient’s neoplastic cells clearly expressed the above-mentioned cytotoxic proteins, strongly suggesting their origin from an activated cytotoxic T-cell subset, although they did not express CD8 antigen on their cell surface. Furthermore, they did not express markers characteristic of natural killer cells or γδ T cells. The negative staining for TdT and CD34 rules out their derivation from a T-lymphocyte precursor lineage. According to the EORTC classification, our patient should fit the diagnosis of CD30 negative pleomorphic large T-cell cutaneous lymphoma (15). Lack of CD8 antigen does not allow us strictly to classify our case among the so-called cytotoxic CTCLs (2), which are characterized by a distinctive combination of clinical, histopathological and immunophenotypical features (βF1+, CD3+, CD8+, CD7+, CD45RA+, TIA-1/GMP-17+) and which usually run an aggressive clinical course (2).

Our patient was unresponsive to INF-α in association with etretinate and DHAP therapies and because no effective standardized cure is available for DPR, we started treatment with gemcitabine while waiting for a bone marrow transplant. Gemcitabine led to a rapid improvement of the skin lesions in our patient, although it did not prevent relapse of the disease 3 months after the end of therapy.

In conclusion, we believe that our case could contribute to the knowledge on the relationship between DPR, cytotoxic cutaneous lymphomas and other CTCLs. Furthermore, we believe that our experience in the use of gemcitabine could contribute to new modalities in the treatment of cytotoxic cutaneous lymphomas, since aggressive therapeutical approaches are often ineffective and therefore new strategies are needed.

REFERENCES


Fig. 2. A dense intraepidermal pagetoid infiltrate of medium/large neoplastic lymphoid cells scattered in the basal and suprabasal layers of the epidermis. (Haematoxylin–eosin stain; original magnification (× 50.)

Fig. 3. The cytotoxic phenotype of the neoplastic cells is demonstrated by the expression of T-cell intracellular antigen-1. (Haematoxylin counterstain; original magnification (× 400.)
Eosinophilic Pustular Folliculitis Induced by Allopurinol and Timepidium Bromide

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Sir,
We describe a woman with numerous papules and pustules on her face and upper trunk induced by allopurinol and timepidium bromide. The histopathology showed the destruction of hair follicles and the infiltration of eosinophils, which we diagnosed as eosinophilic pustular folliculitis.

CASE REPORT
A 57-year-old Japanese woman was treated with oral allopurinol and timepidium bromide for urolithiasis since April 1998. One month later, she presented with an eruption on her face, followed by numerous rice-sized papules and pustules on her face and upper trunk, a fever and bilateral cervical lymphadenopathy were also present (Fig. 1). The woman visited our hospital for examination in June 1998. Laboratory studies revealed eosinophilia (white blood cell, 7,400/mm³; eosinophile, 25%, 1,850/mm³), mild liver dysfunction (glutamic oxaloacetic transaminase, 36 IU/ml; glutamic pyruvic transaminase, 65 IU/ml; gamma-glutamyltranspeptidase, 159 IU/ml; alkaline phosphatase, 436 IU/ml) and a strong inflammatory reaction (C-reactive protein, 8.3 mg/dl). No elevations were found in her serum viral titers (human herpes simplex virus, Epstein-Barr virus...