Unusual Presentation of Peripheral T-Cell Lymphoma

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Abstract:
Mature or peripheral T cell lymphomas (PTCL) are uncommon in most parts of the world and account for only 10-15% of all non-Hodgkin's lymphomas (NHLs). They usually occur in middle-aged to elderly patients, 68% presenting with features characterized by a disseminated disease, with systemic symptoms in nearly half of them (45%), bone marrow (BM) involvement in a quarter (25.8%), and extranodal disease in a third (37%). We report for the first time a patient with a lesion on the glans penis, an unusual site.

Key words: Cutaneous T-Cell lymphoma, penile ulcer, and Non-Hodgkin's lymphoma

Case presentation:
A 40-year-old Nepalese male, married with three children, not known to have any medical illness, presented on July 13, 2004 with a six-week history of an ulcerated lesion on the penis that was gradually increasing in size. He had not lost weight, had no fever or urethral discharge and gave no history of sexual contact.

Physical examination showed a fit-looking young male with normal vital signs. Examinations of chest, heart and abdomen were all normal with no palpable lymph nodes. Examination of his genitalia revealed an ulcerated lesion measuring 1 x 1.5 cm with an erythematous base and everted edges on the inner surface of the glans penis. Other parts of the penis and testes were normal. Chest x-ray, kidney and liver function tests were normal; lactic dehydrogenase (LDH) 238 IU/L. HIV and hepatitis serologies were negative.

A biopsy of the ulcer showed a heavy infiltration of the base by dense monotonous small to medium sized atypical lymphoid cells showing central hyperchromatic vesicular nuclei with irregular nuclear contours (Figures 1, 2). These cells were diffusely stained with CD45 and CD3 (Figure 3) and were negative for B-cell markers.

Figure 1: A low power view of the penile ulcer showing heavy infiltration of the ulcer base by monotonous small to medium sized atypical lymphoid cells (Hematoxylin & Eosin, original magnification x 84)

Figure 2: A high power view of the lymphoid infiltrate showing the cytological details of small to medium sized atypical lymphocytes with scanty cytoplasm and central irregular hyperchromatic nucleus (Hematoxylin & Eosin, original magnification x 160)
A complete blood picture was within normal limits (WBC $5 \times 10^7$/L, Hb 92g/L, platelets $273 \times 10^9$/L with a normal differential count). Bone marrow aspiration showed about eight per cent of small and medium-sized pleomorphic atypical mononuclear cells having scanty to moderate amounts of basophilic cytoplasm and clumped chromatin with some showing irregular nuclear contour. Bone marrow biopsy showed interstitial and diffuse infiltration by atypical mononuclear cells with areas of paratrabecular infiltration (Figure 4). These atypical cells stained positively with CD45, CD3 (Figure 5) and CD8 and were negative for CD30, ALK, CD4 and B markers.

Three weeks later, while waiting for the completion of staging, the patient developed weakness in both lower limbs, with neurological features of spinal cord compression at the 8th dorsal spine, confirmed by MRI examination. Radiotherapy to the dorsal spine was started, followed after a week by chemotherapy according to CHOP protocol but unfortunately the patient went into severe neutropenia, developed septicemia and died on day seven of chemotherapy.

Discussion:

Mature or peripheral T-cell lymphomas (PTCL) are uncommon in most parts of the world and account for only 10-15% of all non-Hodgkin's lymphomas (NHLs)\(^{10}\). They usually occur in middle-aged to elderly patients, 68% presenting with features characterized by a disseminated disease, with systemic symptoms in nearly half of them (45%), bone marrow (BM) involvement in a quarter (25.8%), and extranodal disease in a third (37%)\(^{22}\).

The 1999 World Health Organization (WHO) classification of the hematopoietic and lymphoid neoplasms resolved criticism about lymphoma classification and aroused new interest in PTCL\(^{13}\). At present diverse cases are lumped under the heading of PTCL not otherwise specified (PTCL-NOS) or unspecified (PTCL-U) which comprises the largest group of T-cell neoplasms in Western countries. Although a variety of morphologic subtypes has been described, no consistent immunophenotypic, genetic or clinical features have been associated with most of them\(^{40}\). PTCLs are generally aggressive neoplasms that frequently involve the skin either as a primary or secondary manifestation of the disease. In fact, the skin was found to be the second most common extranodal site involved by primary lymphomas\(^{5}\). In a retrospective study over a 19-year period, Yaqoob et al.\(^{66}\) reported that NHLs presenting as skin lesions are commonly of the B-cell phenotype followed by T-cell phenotype (NOS) and mycosis fungoides. Bekkenk et al.\(^{7}\) indicated that PTCL-U presenting in the skin has an unfavorable prognosis irrespective of the presence or absence of extracutaneous disease at the time of diagnosis, cell size and expression of CD4\(^+\) or CD8\(^+\) phenotype. The only exception in their experience was a group of primary cutaneous small or
medium sized pleomorphic cutaneous T-cell lymphomas (CTCLs) with a CD3+, CD4+, CD8 phenotype presenting with localized skin lesions. They also added that the duration of skin lesions prior to diagnosis was usually short (median six months).

In a recent Japanese experience, Kojima et al. (1987) found that survival of CD4+/CD8- cases, corresponding to cytotoxic PTCL, was significantly worse than that of CD4+/CD8-.

Primary cutaneous CD30- small/medium-sized pleomorphic T-cell lymphoma is a diagnosis by exclusion. Confronted with lesions prior to diagnosis was usually short (median six months).

Localized skin lesions. They also added that the duration of skin lesions, particularly differentiation from (tumor stage) MF and pseudo-T-cell lymphomas may be difficult and requires detailed analysis of clinical, histologic, and immunophenotypic data (19).

The influence of the immunophenotype on the outcome of aggressive NHL has long been questioned; however, in the more recent literature, most authors agree on the adverse prognostic meaning of the T-cell phenotype per se (10,11) regardless of other well-defined clinical prognostic indexes such as the International Prognostic Index (IPI).

In a recent study undertaken by Gallamini et al. (2003), a new prognostic model for PTCL-U was proposed, the PIT (Prognostic index for PTCL-U) based on four simple clinical variables: age, performance status (PS), LDH level, and bone marrow involvement. PIT seems to have an overall superior predictive capacity compared to IPI.

Following the guidelines of the Dutch Cutaneous Lymphoma Group, most patients with only solitary or localized skin lesions at presentation are treated with radiotherapy, whereas patients presenting with multifocal skin lesions or with concurrent cutaneous and extracutaneous disease are generally treated with doxorubicin-based chemotherapy (CHOP [cyclophosphamide, doxorubicin, vincristine, and prednisone] or CHOP-like courses), with additional radiotherapy in some cases. In general, a beneficial effect of radiotherapy may be expected only in the subgroup of primary cutaneous CD3+/CD4+ small/medium-sized pleomorphic CTCLs presenting with solitary or localized skin lesions. The results of doxorubicin-based chemotherapy are equally disappointing both in patients presenting with solitary skin lesions or with concurrent extracutaneous disease.

Other studies have suggested that more intensive regimens also are not effective in these PTCLs-U (10,13). It is to be emphasized that our case represents the first record in the literature of a T-cell lymphoma, CD3+, CD8+ and CD30-presenting solely as a penile ulcer and constitutes a further unusual presentation of PTCL.

References:


