Isolated bone marrow occurrence of classic hodgkin's lymphoma in an hiv-negative patient

Classic Hodgkin's Lymphoma is a disease usually characterized by lymph nodal presentation. Rare cases with extra-nodal first clinical manifestation may occur, and primary bone marrow involvement may be part of them: isolated bone marrow forms have been recently described in the context of HIV infection. We herein report a case of isolated bone marrow Hodgkin's Lymphoma occurrence in a HIV-negative, elderly patient. The impacts of such unusual Hodgkin's Lymphoma manifestation on clinical practice as well as the related diagnostic and therapeutic implications are discussed.

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Classic Hodgkin lymphoma (HL)[1] is a disease usually characterized by lymph nodal localization and contiguous spread. Bone marrow secondary involvement by HL in adult accounts for an average of 10% in the reported series.[2] Extranodal presentation of HL at diagnosis is rare.[3] HL bone marrow presentation has been described in HIV-infected patients.[4] A 64-year-old man with a previous history of arterial hypertension and prostatic hypertrophy was hospitalised four times since July 2004 for remittent fever of unknown origin treated each time with antibiotic therapy, resulting in fever reduction. Serological and microbiological tests did not show any pathogen, including HIV. In January 2005 the patient was referred to our Institution for fever occurrence, accompanied by chills and asthenia. A thorax-abdominal computerized tomography (CT) and abdominal ultrasonography did not disclosed pathological lymph nodes and abnormally structured spleen. A complete blood count showed pancytopenia (Hb 8.5 g/dL, WBC 2100/mm^3, platelets 61000/mm^3) and serum lactic dehydrogenase (LDH) of 2800 UI/L. The Bouin's fixed, paraffin embedded bone marrow biopsy confirmed multilineage dysplastic features, and showed also focal fibrotic tissue (20% of valuable areas). Within fibrotic tissue were present dilated sinusoids, small and intermediate T-lymphocytes, histiocytes, plasma cells, as well as scattered large cells with characteristics of Reed-Sternberg cells (Figure 1A) and their variants: these large cells resulted immunoreactive for CD15 (Figure 1B), CD30 (Figure 1C) and PAX-5, in part for bcl-2, while they did not react for CD45 (Leukocyte Common Antigen), CD20, CD3, OCT-2, p53, and ALK-1, as usually reported.5 Accordingly to these findings, a diagnosis of classic Hodgkin's lymphoma (HL) was made. Bone marrow aspirate revealed only bilineage dysplasia. ECOG performance status was.[3] Extensive work-up did not show additional localizations outside the bone marrow, and final staging according to Ann Arbor Classification System was IVB. The patient then received the first cycle of ABVD scheme of chemotherapy; immediately after the end of vinblastine infusion fever of 39°C, shiver and oxygen desaturation appeared. Increase in serum creatinine and LDH, elongation of PT and aPTT with increase in D-dimers developed; neutropenia worsened and Gram-negative pneumonia occurred, thus requiring antibiotic administration. Despite the therapy, acidosis and coma developed, and patient died of cardiac failure two days later. Autopsy was not performed.

Bone marrow biopsy is performed in many settings, and it is considered mandatory in cases of fever of unknown origin: in this case, core biopsy may be able to disclose underlying infections or neoplasms, including lymphomas. Bone marrow involvement by HL is usually associated with an overt clinical nodal manifestation: in this latter occurrence, if peripheral lymphadenopathy is absent, HL usually appears under the form of deeply localized pathologic lymph nodes,[6] particularly in the retroperitoneum.[7] Moreover, some cases of HL may present with bone marrow fibrosis, but the diagnosis is possible only on lymph nodes.[8] An exception to this rule is represented by some HIV-positive patients, in which bone marrow involvement may occur selectively in the absence of extra-marrow disease.[4] A recent review pointed out the rarity of isolated bone marrow involvement by HL, however without providing specific data on HIV status of those patients.[2]

The present case shows that isolated bone marrow HL may occur also in immunocompetent subjects and in an age group older than those reported so far. The bone marrow biopsy in this case represented the only diagnostic clue. In contrast, bone marrow aspirate revealed to be inadequate in diagnosing diseases like HL, as previously demonstrated.[9]

The very unfavorable outcome in this patient may be related to a combination of either this aggressive disease and the infective complications rose during chemotherapy.

In routine practice, the lymph node biopsy remains the gold standard for HL diagnosis and subtyping. Within this

Figure 1. Bone marrow biopsy involvement by Hodgkin Lymphoma: (A) Giemsa staining shows classical Reed-Sternberg cell (arrow) embedded in its proper background mainly represented by small lymphocytes, granulocytes and vessels; the neoplastic cells were immunoreactive for CD15 (B) and CD30 (C).

regard, also a random lymph node biopsy may not be able to disclose an underlying HL, as others and we previously demonstrated;[4,8] therefore this practice is not recommended for diagnosis. The awareness of the existence of such unusual forms even in patients without known risk factors may facilitate their recognition and therapeutic decisions.

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