Case report

Osteolytic lesions as a presenting sign of acute myeloid leukemia

CARMEN S. P. LIMA 1,*, JORGE V. PINTO NETO 1, MARCELO L. DA CUNHA 2, JOSE VASSALLO 3, IZILDA A. CARDINALLI 3 and CARMINHO A. DE SOUZA 4

1 Hematology and Hemotherapy Center, State University of Campinas, Campinas, São Paulo, Brazil
2 Department of Radiology, Faculty of Medical Sciences, State University of Campinas, Campinas, São Paulo, Brazil
3 Department of Pathological Anatomy, Faculty of Medical Sciences, State University of Campinas, Campinas, São Paulo, Brazil
4 Department of Internal Medicine, Faculty of Medical Sciences, State University of Campinas, Campinas, São Paulo, Brazil

Abstract—Osteolytic lesions rarely occur in acute myeloid leukemia (AML). We reported an atypical form of the disease, with marrow fibrosis and osteolytic lesions, in a 17-year-old patient, whose main symptom was lumbar pain. Diagnosis of AML was established by bone marrow and lymph node histological analysis. Computed tomography (CT) scan and 99mTc-MDP bone scintigraphy scan revealed osteolytic lesions. After remission-induction, bone marrow aspirate and biopsy showed no evidence of leukemic infiltration, nevertheless bone abnormalities persisted on 99mTc-MDP bone scintigraphy, suggesting residual disease. Suspect bone areas were irradiated with symptomatic improvement and 99mTc-MDP bone scintigraphy showed the appearance of more condensed bone compared with the pre-radiotherapy pattern. Twelve months later he was readmitted to the hospital due to relapse of AML and died of sepsis within a few weeks. This report illustrates the usefulness of histological studies to establish diagnosis of AML in atypical cases, as well as the importance of CT scan and bone scintigraphy scan for the identification of osteolytic lesions. It also provides additional data as evidence that although osteolytic lesions indicate an adverse prognosis in AML, local irradiation results symptomatic relief.

Key words: Acute myeloid leukemia; osteolytic lesions; immunohistochemistry; computed tomography scan; bone scintigraphy scan.

*To whom all correspondence should be addressed. Dr. Carmen Silvia Passos Lima, Hematology and Hemotherapy Center—UNICAMP, Cidade Universitária Zeferino Vaz, CP: 6198, CEP 13081-970, Campinas, SP, Brazil. Fax: (55-19) 788 8750, E-mail: carmenl@obelix.unicamp.br
INTRODUCTION

Granulocytic sarcoma (GS) is a localized tumor mass composed of immature cells of the granulocytic series [1]. GS occurs in about 5 percent of acute myeloid leukemia (AML) cases and may be the initial manifestation of the disease [2, 3]. Diagnosis is particularly difficult if bone marrow is not available for cytological analysis (dry tap) [4, 5]. The poorly differentiated nature of cells, which may resemble those of large cell lymphoma [3, 6–8], constitutes a problem to pathologists. Therefore, immunohistochemistry analysis should be performed to define the myeloid origin of the tumor [7, 8].

In spite of specific tissue and organ system involvement [6, 9], osteolytic lesions constitute a rare manifestation of AML [4, 10–16]. Currently, bone osteolytic lesions have been identified using X-rays, computed tomography (CT) scan or bone scintigraphy scan [11, 14, 17]. The prognostic significance and the adequate treatment of this bone abnormality in AML have not been sufficiently established [3, 6, 7, 9, 11, 13].

We report here, an atypical case of AML in a patient whose main manifestation was osteolysis.

CASE REPORT

A previously healthy 17-year-old man was admitted to the Hospital of the State University of Campinas, with a 2-month history of weakness, fever, severe lumbar pain and weight loss. Muco-cutaneous pallor and left cervical and axillary palpable lymph nodes were the only abnormalities at physical examination.

Laboratory findings: lactate dehydrogenase 945 U/l (normal: 150–450), mucoproteins 16 mg% (normal: 1.8–3.8), hemoglobin 8.2 g/dl, hematocrit 27%, MCV 66 fl, MCH 20 pg, MCHCM 31 g/l, leukocyte count 5.9×10⁹/l, platelet count 248.0 × 10⁹/l, serum iron 88 UG/d (normal: 53–167), TIBC 247 UG/dl (normal: 242–359). Differential leukocyte count showed neutrophils, 69%; eosinophils, 2%; lymphocytes, 26%; monocytes, 3%. Peripheral smears showed anisocytosis and occasional tear-drop poikilocytosis; no blast cells were found. There were no bone abnormalities on roentgenograms, but CT scan revealed osteolytic lesions involving the sacrum and ischium. ⁹⁹ᵐTc-MDP bone scintyscan showed areas of increased activity in the right radius, ischium, femur, several ribs, skull and both humeri (Fig. 1A and B). An open biopsy of the axillary lymph node was performed and histological examination evidenced a diffuse, homogeneous growth of medium sized, round or oval cells, with scant cytoplasm and large nucleous with multiple nucleoli (Fig. 2A). Bone marrow smears could not be obtained (dry tap), but a trephine biopsy section revealed blast infiltration and fibrosis. Immunohistochemistry of both bone marrow and lymph node was performed in paraffin sections using the usual streptavidin-biotin-peroxidase technique [18]. Positivity was obtained using the antibody for common leukocyte antigen (CD45, Dako) and lysozyme (poly-
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Figure 1A. CT scan of pelvis revealed osteolytic lesions.

clonal, Dako) (Fig. 2B), whereas pan-leukocyte-B L26 (CD20, Dako) and pan-leukocyte-T UCHL-1 (CD45RO, Dako), factor VIII: von Willebrand factor (Dako) were negative. These results were consistent with the diagnosis of AML and the osteolytic lesions were interpreted as a sarcomatous manifestation of the disease.

The patient underwent a traditional chemotherapy protocol for the treatment of AML [19]. After remission-induction, bone marrow aspirate and biopsy showed no evidence of leukemic infiltration, nevertheless bone abnormalities persisted on $^{99m}$Tc-MDP bone scintiscan in right humerus, ischium and ileum, suggesting residual disease. Suspect bone areas were irradiated with symptomatic improvement. $^{99m}$Tc-MDP bone scintiscan showed the appearance of more condensed bone compared with the preradiotherapy pattern. Intensification and maintenance chemotherapy was administered [19] and the patient presented no symptoms of the disease for twelve months. After this interval, he was readmitted to the hospital due to fever and general bone pain. The bone marrow biopsy was infiltrated by blasts, similar to those seen at diagnosis. His clinical condition rapidly deteriorated and he died of sepsis within a few weeks.
Figure 1B. $^{99m}$Tc scintyscan showed areas of increased activity in the right radius and ischium (arrows) at diagnosis of acute leukemia.

DISCUSSION

We reported here an atypical case of AML in a young patient, who presented marrow fibrosis and osteolytic lesions.

The citological analysis could not be performed because no marrow was obtained by aspiration. The diagnosis of the disease was established by lymph node and bone marrow histological analysis, including immunohistochemical reactions.

Bone osteolytic lesions were also identified as a presenting sign of the disease. This abnormality constitutes a rare manifestation of AML and is generally related to megakaryoblastic subtype [10, 11, 13, 15]. However, it can be rarely observed in other subtypes of the disease [14, 16]. In the case studied, the results of immunohistochemical studies, lysozyme positivity and factor VIII: von Willebrand factor negativity, were consistent with myeloid origin of the immature cells, according to conventional criteria [5, 7, 8, 20].

In the reported case, osteolytic bone lesions were identified only by CT and bone scintigraphy scans. Bone osteolytic lesions in the disease are generally
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Figure 2A. Lymph node infiltration by blast cells, without signs of differentiation (H & E, 600×).

Figure 2B. Positive immunostaining of atypical cells using antibody to lysozyme (IMPx-STrABC, 400×).
recognized by plain X-ray [4], but sometimes, more accurate methods, such as bone CT and scintigraphy scans are necessary for the identification of skeletal abnormalities [11, 17]. The increased skeletal uptake of radionuclides, used in $^{99m}$Tc-MDP bone scintigraphy, probably result from bone remodeling in the face of an expanded bone marrow space and may identify initial lesions [11, 17]. Residual bone disease was also identified by $^{99m}$Tc-MDP bone scintigraphy in the studied case and additional radiotherapy was administered with symptom and skeleton image improvement. Therefore, $^{99m}$Tc-MDP bone scintigraphy could be used as a non-invasive and highly sensitive identification and follow up the focal infiltrative bone lesions in this case, in good accordance with previous reports [11, 17].

The unfavourable clinical evolution of this case and the relapse of the disease with bone pain suggest that osteolytic lesions in AML represent an adverse prognostic factor. It is possibly related to the inability of chemotherapeutic agents to penetrate into bone tissue satisfactorily. The symptomatic relief achieved by local irradiation of painful lesions indicates that this palliative approach had a beneficial result in this case.

This report illustrates the usefulness of histological studies to establish diagnosis of AML in atypical cases, as well as the importance of CT scan and bone scintigraphy scan for the identification of osteolytic lesions. It also provides additional data to evidence that although osteolytic lesions indicate an adverse prognosis in AML, local irradiation may result in transient but significant symptomatic relief with improved quality of life.

REFERENCES

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