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Technetium-99m MDP Bone Scintigraphic Findings of Hypercalcemia in Accelerated Phase of Chronic Myelogenous Leukemia

Hypercalcemia in accelerated phase of chronic myelogenous leukemia (CML) is very rare. Its pathogenesis is considered humoral hypercalcemia of malignancies mediated by parathyroid hormone-related protein (PTHrP). In severe hypercalcemia, calcifications in kidneys, skin, vessels, heart, and stomach may occur. Our two cases were admitted because of severe hypercalcemia in accelerated phase of CML. On Tc-99m methylene diphosphonate (MDP) bone scintigraphies, a marked tracer accumulation was seen in the lung, heart, stomach and kidney. We report increased tracer accumulation of multiple organs on Tc-99m MDP bone scintigraphy in two rare hypercalcemic patients with CML.

Key Words: *Leukemia, Myeloid, Chronic; Hypercalcemia; Radionuclide Imaging*

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INTRODUCTION

Hypercalcemia is a paraneoplastic syndrome in various types of cancers, including adult T-cell leukemia (ATL) and multiple myeloma. Although very rare, hypercalcemia has also been reported in the accelerated phase of chronic myelogenous leukemia (CML) (1, 2), and parathyroid hormone-related protein (PTHrP) has been implicated in its pathogenesis (3, 4). Recently we reviewed two CML patients who developed hypercalcemia in blast crisis and performed a whole-body bone scintigraphy to evaluate bone involvement. We described the findings of bone scintigraphy.

CASE REPORT

Case 1

A 57-year-old man, diagnosed with CML in 1992, was admitted to our hospital in September 1998. He had generalized weakness and dizziness. Clinical examination revealed splenomegaly and hepatomegaly. Hemoglobin level was 8.3 g/dL, platelets 277,000/μL, leukocytes 27,500/μL with 8% blasts, 2% promyelocytes, 15.5% myelocytes, 10% metamyelocytes, 7.5% band form, 3.5% basophils, 5% lymphocytes and 10.5% monocytes. Leukocyte alkaline phosphatase (LAP) score was 13. His calcium level was 16.1 mg/dL (normal range, 8-10) and PTHrP 114.50 pmol/L (normal range, 13.8-55.3) and parathyroid hormone (PTH) 2.0 pg/mL (normal range, 12.0-72.0). Tc-99m methylene diphosphonate (MDP) whole-body bone scintigraphy was performed for evaluation of the extent of bone involvement. On the scintigraphy, an increased tracer accumulation was seen in the lung, heart, stomach, and kidneys and no skeletal-tracer accumulation (Fig. 1). He was treated conventionally with intravenous saline, diuretics, corticosteriods, calcitonin and hydroxyureas. His clinical symptoms improved and calcium levels decreased.

Case 2

A 32-year-old man, diagnosed with CML in 1992, showed generalized weakness, dizziness, and chest pain. Clinical examination revealed splenomegaly and hepatomegaly. Hemoglobin level was 14.6 g/dL, platelets 51,000/μL, leukocytes 142,600/μL with 1% blasts, 2% promyelocytes, 15% myelocytes, 2% metamyelocytes, 6.5% band form, 6.5% basophils, 15% lymphocytes and 10.5% monocytes. Leukocyte alkaline phosphatase (LAP) score was 13. His calcium level was 17.8 mg/dL and PTHrP 80.50 pmol/L and parathyroid hormone (PTH) 2.2 pg/mL. On Tc-99m MDP whole-body bone scintigraphy, an increased tracer accumulation was seen in the lung, heart, stomach and kidneys (Fig. 2). He was

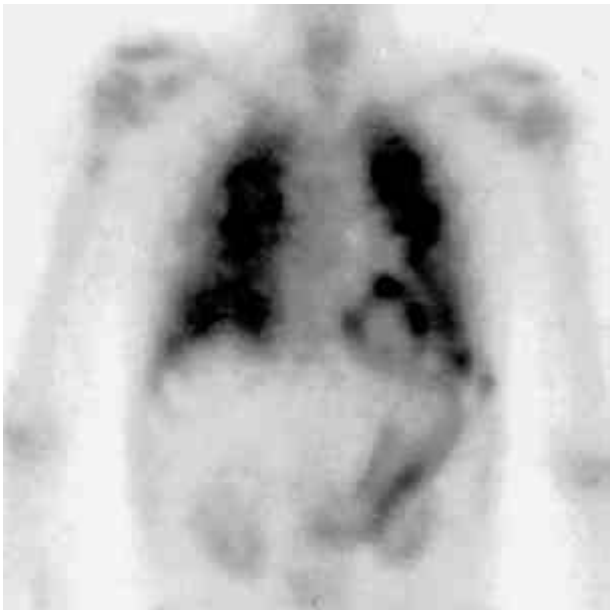

Fig. 1. Tc-99m MDP bone scintigraphy of a 57-year-old man with hypercalcemia in the accelerated phase of chronic myelogeneous leukemia shows diffusely increased uptake in both lung, heart, stomach and both kidneys.

treated conventionally with intravenous saline, diuretics, corticosteriods, calcitonin and hydroxyureas. His clinical symptoms improved.

DISCUSSION

Metastatic calcification of soft tissue is a known complication of various pathologies such as chronic renal failure, secondary hyperparathyroidism (5), and malignant diseases (6, 7). Whereas metastatic calcification occurring in the absence of hypercalcemia is mainly associated with chronic renal failure (8), it is usually accompanied by hypercalcemia in other patients. Hypercalcemia is a paraneoplastic syndrome in various types of cancers. Two explanations have been considered for its pathogenesis; local osteolytic hypercalcemia caused by metastatic tumor cells and humoral hypercalcemia of malignancies mediated by PTHrP (9). Approximately 15% of hypercalcemia due to malignancy is associated with hematologic immune cell cancers. Hypercalcemia is very rare in CML, and although it may occur at any time during the disease, it mostly appears late in the course of the disease and is considered an ominous sign. PTHrP, a humoral factor responsible for hypercalcemia associated with solid tumors, lymphoma and leukemia, has been predicted to be involved in at least three polypeptides of different lengths (139, 141, and 173 amino acids). The amino-terminal portion of PTHrP has a close sequence homology to

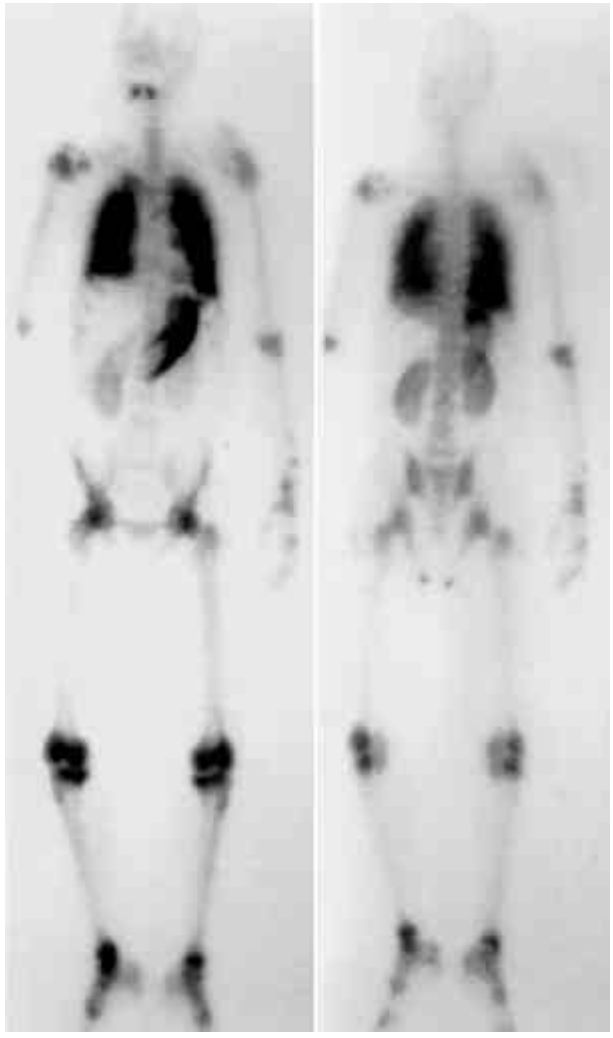

Fig. 2. Tc-99m MDP bone scintigraphy of a 32-year-old man with hypercalcemia shows diffusely increased uptake in lung, heart, stomach and both kidneys.

PTH: eight of its first 13 amino acids are identical to those of PTH (10). PTHrP induces hypercalcemia by binding and activating receptors that also bind PTH (10). Our patients had a typical history of CML, with a chronic phase of more than six years and finally resulted in blastic crisis, which was accompanied by severe hypercalcemia. PTHrP level was increased and PTH decreased. PTHrP is considered a humoral factor responsible for hypercalcemia.

In severe hypercalcemia (above 13 mg/dL), renal insufficiency and calcifications in kidneys, skin, vessels, heart, and stomach occur (11). Although underlying disease and calcium and phosphate levels may vary from patient to patient, the increased in the ion-product of calcium and phosphate appears to be an important factor in the precipitation of these substances in the soft tissues (5). A [Ca]×[P] product of 58-60 is considered the satu-

ration point of normal serum above which spontaneous precipitation may occur (12). In hypercalcemic patients, the initial visceral deposit has been shown to be brushite ($CaHPO_4 \cdot 2H_2O$), which is subsequently transformed to apatite [$Ca_{10}(PO_4)_6 \cdot (OH)_2$] (13). Tc-99m labeled phosphate or diphosphonate compounds are known to bind to hydroxyapatite crystals, probably by chemisorption (14). Tc-99m MDP bone scintigraphy of severe hypercalcemia shows diffusely increased tracer accumulation in these organs such as lung, heart, stomach, and kidneys. We thought that hypercalcemia in the acute phase of CML is a paraneoplastic syndrome mediated by PTHrP, and calcification in multiple organs may occur, which may be related in part to the high ion-product of calcium and phosphate.

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