Abstract. – Hypercalcemia is a rare metabolic disorder in course of B cell lymphoma. The mechanism of hypercalcemia in patients with malignancy may include the increased extrarenal production of vitamin D from tumoral cells or neighboring macrophages, i-PTH or PTHrP from tumoral cells. In this case we reported a 34 years old caucasian woman with acute renal failure and hypercalcemia as onset of splenic lymphoma in absence of abnormal levels of serum vitamin D and PTHrP. Because of dramatic recovery of renal function and hypercalcemia after splenectomy, we can speculate that main mechanism of hypercalcemia is related to vitamin D production from neighboring lymphoma macrophages.

Key Words: Hypercalcaemia, Parathyroid hormone-related peptide, Renal failure, Vitamin D, Splenic lymphoma.

Introduction

Hypercalcemia is common in patients with multiple myeloma and T cell non Hodgkin lymphoma while is rare in B-cell lymphoma. The hypercalcemia in course of hematologic malignancies could be related to osteolytic mechanism, synthesis of parathyroid hormone-related protein and abnormal 1,25 dihydroxyvitamin D (1,25(OH)2D3) production from tumoral cells or neighboring macrophages. It is also well known that hypercalcemia is a manifestation of advances disease and some studies revealed a correlation with a poor prognosis and an early diagnosis is necessary in these cases for a better outcome.

Case Report

A 34 years old Caucasian woman with general malaise, abdominal fullness and nausea was admitted to our Department. A blood sample revealed microcytic hypochromic anemia (haemoglobin 8.5 g/dL) with erythrocyte sedimentation rate 30 mm/hr.

Biochemistry tests showed acute renal failure with serum creatinine of 1.9 mg/dl (normal range 0.6-1.4 mg/dL) and creatinine clearance of 39 ml/min, hypercalcemia (Ca++ 13.5 mg/dL, normal range 8.6-10.2 mg/dL) in association with normal phosphate levels; LDH was 933 UI/L (normal range 285-540). Urinalysis showed mild proteinuria (216 mg/24h) with increased urinary excretion of calcium (565 mg/24 h with normal range 100-321 mg/24 h).

Her history reported a 3 kg weight loss during the previous 4 months. Blood tests (hepatic, renal function and hemochrome) performed about 6 months before were in normal limits. She denied recent infectious diseases and use of drugs. Her family history was unremarkable.

Serologic tests for hepatitis C virus was positive with normal liver function; serology was negative for hepatitis B virus, Cytomegalovirus and Epstein Barr virus.

The physical examination was normal except for marked splenomegaly.

The patient was treated with hydration and furosemide for hypercalcemia without improvement of symptoms and renal function over the next few days.

Biochemistry tests revealed mild decrease of serum intact PTH (i-PTH) (9.3 pg/ml) compared to normal ranges (11-54 pg/ml) while serum 1,25(OH)2D3, thyroid hormones and bone alkaline phosphatase levels were in normal range. Parathyroid hormone related protein (PTHrP) levels were negative.

Abdominal ultrasound showed a vascularized no well-defined mass (13 cm in diameter), with hypoechoic density between spleen and left kidney.
A total body computed tomography (CT) confirmed an irregular lesion (DM 13 cm) in relation to the spleen with several calcifications and fibrosis; this lesion did not enhanced after an injection of contrast medium (Figure 1). Moreover, the CT revealed a lymphadenopathy in the para-aortic area of 28 mm in diameter.

Bone marrow examination was negative for blasts or mononuclear cell infiltration.

Because spleen neoplasia was suspected, a splenectomy was performed. Histological examination of the spleen showed neoplastic proliferation with diffuse large B-cell components. The diagnosis was high grade non-Hodgkin’s lymphoma large B-cell (B-NHL) (Figure 2). Immunohistochemistry was positive for CD20 and negative for Bcl-2 and CD3.

After splenectomy, laboratory analysis showed hypocalcemia (Ca++ 7.1 mg/dl) and impairment of renal function (creatinine 0.7 mg/dl) within 24 h. Then she started chemotherapy for B-NHL with favourable outcome.

In this case we reported acute renal failure and hypercalcemia as onset in splenic lymphoma.

**Discussion**

Hypercalcemia of malignancy (HM) is a syndrome that occurs in the absence of bone metastases.

Hypercalcemia is a relatively frequent metabolic disorder recognized in tumors such as breast cancer, multiple myeloma, adult T-cell leukemia, renal cell carcinoma and non small cell lung.

In contrast to solid tumor disease and T-cell malignancies HM is less common in B cell lymphoma.

The mechanism of hypercalcemia in patients with malignancy may include the increased extrarenal production of 1,25(OH)2D3 from tumoral cells or neighboring macrophages, i-PTH or PTHrP from tumoral cells. Vitamin D-dependent hypercalcemia is due to increased calcium and phosphate absorption from the intestine and to decreased excretion of calcium.

PTHrP have a similar activity to PTH; this is secreted by the cancer cells and promotes osteoclastic bone resorption causing hypercalcemia.

Generally high serum calcium levels in patients with B-cell lymphoma are dependent to the secretion of 1,25(OH)2D3 from lymphoma adjacent macrophages as often revealed by immunohistochemistry.

In fact, while an increased production of 1,25(OH)2D3 is demonstrated both in non-Hodgkin’s and Hodgkin’s lymphoma, PTHrP related hypercalcemia is usually observed in patient with HTLV-1 related adult T leukemia and lymphoma.

Because of dramatic recovery of renal function and hypercalcemia after splenectomy, we can speculate that main mechanism of hypercalcemia is related to vitamin D production from neighboring lymphoma macrophages.

Finally, some reports showed pre-existing HCV infection before the onset of diffuse large B-cell lymphomaB-cell in our patient. However, this infection not appear to influence the outcome of therapy.
References


