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Case Report

Increased tumor marker ca-125 in multiple myeloma: a case report

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ABSTRACT

Multiple myeloma (MM) is a malignant B-cell lymphoproliferative disorder of the marrow, with plasma cells predominating. It is unlikely to encounter rising level of any tumor marker in MM patient. We present a case of 46-year-old female came to the orthopaedic clinic with chief complains of pain on her right arm, left shoulder and right hip after 5 months. The results of the bone survey of these patients showed multiple lytic lesions with a punched-out appearance in calvaria. The expansive lytic mass was seen with cortical destruction in one third proximal metaphysis to diaphysis of humerus with periosteal reaction and surrounding soft tissue mass. The basic metabolic panel (BMP) result of these patient is hipocellular with decrease of erythroid, myeloid, and megakaryocytes activity and there are 30% plasma cells with positive myeloma cells. Therefore, the patient was diagnosed with MM. The laboratory result of these patient also showed elevation of carbohydrate antigen 125 (CA-125) marker to 56 and 92 (normal range is <35). The patient reported herein showed clear signs and symptoms of MM accompanied by elevated level of CA-125 and CA-15.3 tumor markers. Elevated CA-125 values most often are associated with epithelial ovarian cancer, although levels also can be increased in other malignancies such as endometrial, fallopian tube, breast, lung, esophageal, gastric, hepatic, and pancreatic. However, there were no clear mechanism of how a malignant B-cell lymphoproliferative disorder of the marrow stimulates the production of tumor marker such as CA-125.

Keywords: Multiple myeloma, Tumor marker, CA-125

INTRODUCTION

Multiple myeloma (MM) is a malignant B-cell lymphoproliferative disorder of the marrow, with plasma cells predominating. The effects on bone are due to marrow cell proliferation and increased osteoclastic activity, resulting in osteoporosis and the appearance of discrete lytic lesions throughout the skeleton. Multiple myeloma accounts for 1% of all cancers and 10% of all haematological malignancies. Patients typically elderly which aged among 45-65 years old. The incidence in Europe is 4.5-6.0/100 000/year with a median age at diagnosis of 72 years; the mortality is 4.1/100 000/year.[1] Almost all patients with MM evolve from an asymptomatic pre-malignant stage termed monoclonal gammopathy of undetermined significance (MGUS). MGUS progresses to MM at a rate of 1% per year. In some patients, an intermediate asymptomatic but more advanced pre-malignant stage termed smouldering or indolent MM (SMM) can be recognised. SMM progresses to myeloma at a rate of 10% per year over the first 5 years following diagnosis, 3% per year over the following 5 years, and 1.5% per year thereafter.[2]

Making diagnosis of MM according to International myeloma working group (IMWG) guidelines includes history, physical examination, laboratory test and radiographic imaging. Routine testing of complete blood count with differential and peripheral blood smear review, chemistry panel including calcium and creatinine,

serum protein electrophoresis, immunofixation, nephelometric quantitation of immunoglobulins, routine urinalysis, 24 hours urine collection for proteinuria, electrophoresis and immunofixation, quantification of both urine M-component level and albuminuria.[3]

CA-125 is tumor marker commonly found in solid tumors, with extensive literature describing its correlation with ovarian tumor. It is rarely found to be elevated in MM cases with only 2 previous case reports describing this phenomenon.[4] In this paper, we would like to report our findings of MM patient with elevated level of serum CA-125.

CASE REPORT

A 46 years old female came to the orthopaedic clinic with chief complains of pain on her right arm, left shoulder and right hip after 5 months (June 2018). Patient felt pain on the right hip since last year (November 2017) after she slipped and fell down with her right hip bumping to the floor. She was not able to walk normally after she fell down. In March 2018 she slipped from the bed and her left arm bumped the wall, then she had continuous pain on her left arm. In April 2018 she also complained of pain on the right arm. Her husband was trying to lift her when suddenly there was click sound and immediate pain on her right arm.

On physical examination, there was a lump on proximal area of left arm with the size of 10 × 10 cm. It was tender, fixed, solid, well-defined margin, radial artery palpable, and range of motion was limited due to pain. The right arm region showed deformity and tenderness at middle third of forearm, radial artery was palpable, and range of motion was limited due to pain. The right hip showed deformity, shortening, tenderness over the hip and dorsalis pedis artery was palpable (Figure 1-3).

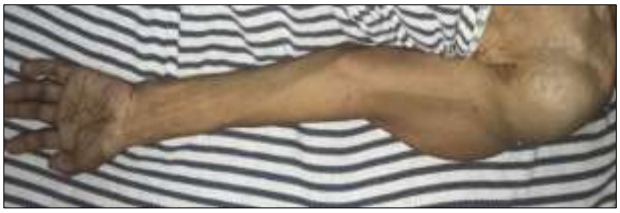

Figure 1: Left arm region.

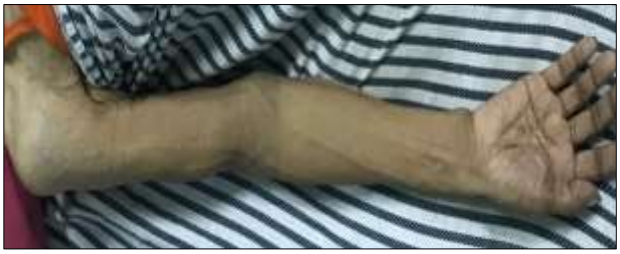

Figure 2: Right arm region.

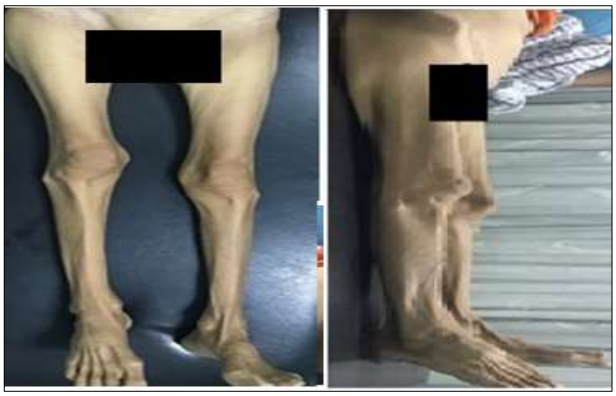

Figure 3: Leg length discrepancy.

Abnormality was found on the conventional x-ray. On the left shoulder x-ray of patient showed a pathological fracture left proximal humerus with lytic lesions. On the right arm x-ray of patient showed a pathological fracture right humerus distal third with lytic lesions. On the pelvic x-ray, showed pathological fracture right neck femur (Figure 4-6).

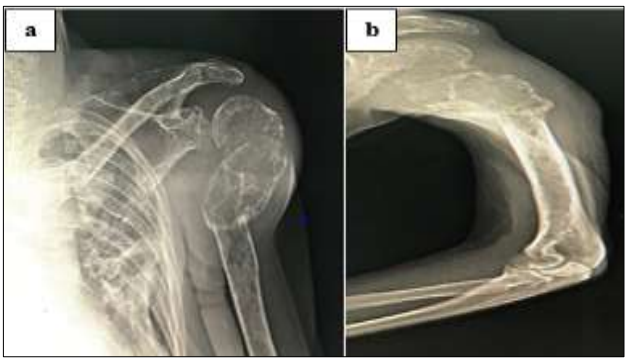

Figure 4: (a) Antero-posterior and (b) lateral view of left shoulder x-ray.

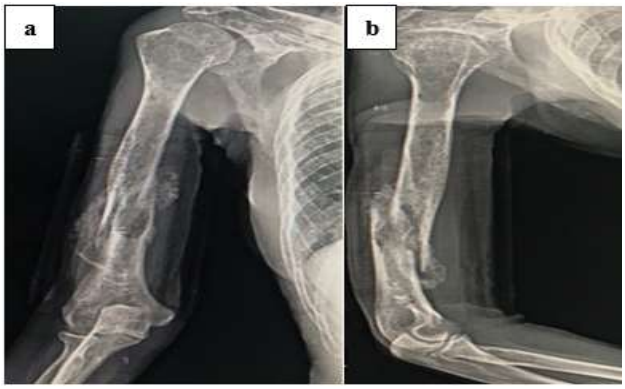

Figure 5: (a) Antero-posterior and (b) lateral view of right shoulder x-ray.

The results of the bone survey of these patients showed multiple lytic lesions with a punched-out appearance in calvaria. In the right and left humerus, a fracture of the right humerus with callus formation, displacement (+),

accompanied by lytic lesions of the humerus, clavicle, scapula, radius and right ulna. The expansive lytic mass was seen with cortical destruction in 1/3 proximal metaphysis to diaphysis of humerus with periosteal reaction and surrounding soft tissue mass.

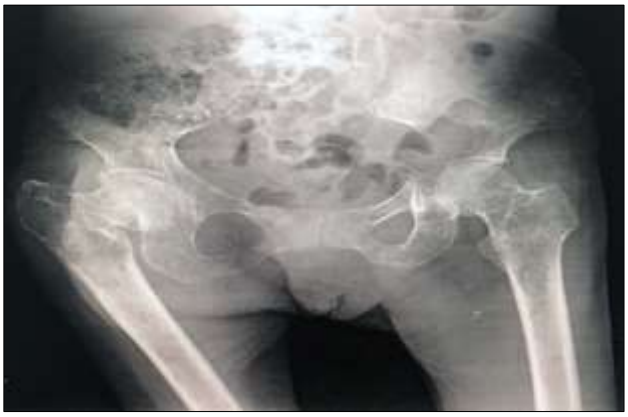

Figure 6: Antero-posterior view of pelvic x-ray.

The laboratory result of these patient, showed elevation of CA-125 marker to 56 and 92 from the normal range is <35. Because of the extremely increased serum tumor markers, the existence of a concomitant solid neoplasm was also suspected (Table 1).

Table 1: Laboratory result.

	Result	Normal
TSHs	0.45	0.27-4.20
FT4	1.38	0.93-1.70
T3	-	1.2-3.1
T4	-	5.1-14.1
CEA	1.16	3.8-5.5
AFP	1.42	5.8
CA19,9	3.6	27
CA15.3	9.42	<4
CA-125	56.92	<35
ALP	65	53-128
SGOT	11.0	11-33
SGPT	16.10	11-50
BUN	21.40	8-23
SC	0.32	0.7-1.2
CRP	40.17	0.0-5.0
LDH	295	240-480
LED	110.7	<20
Na	121	136-145
K	2.79	3.1-5.1
Ca	8.4	8.40-9.70
GDS	83	80-140
Albumin	2.20	3.4-4.8
Hematology		
WBC	5.13	4.1-11.0
HB	10.86	13.5-17.5
HCT	36.39	41.00-53.00

The BMP result of these patient is hipocellular with decrease of erythroid, myeloid, and megakaryocytes activity. And there are 30% plasma cells with positive myeloma cells. Therefore, the patient was diagnosed with MM.

DISCUSSION

Plasma cells arise from B-lymphocytes and normally produce immunoglobulins. Myeloma cells arise from post-germinal center plasma cells in lymph nodes and migrate back to the bone marrow (BM). All cases are preceded by MGUS.[5]

Patients generally present with bone pain (60%), fatigue (30%), weight loss (25%), paresthesia (5%), and recurrent infections (particularly pneumonia and urinary tract infections) with streptococcus pneumonia, *Hemophilus influenza* and *Escherichia coli* being the most common causative agents. Examination may reveal fever (0.7%), hepatomegaly (4%), splenomegaly (1%) and lymphadenopathy (1%).[7] Pulmonary and pleural involvement are rare except in advanced disease. Cardiac involvement is seen with accompanying amyloidosis. Extra-medullary plasmacytomas are seen in 7% upfront and up to 20% at relapse. Peripheral neuropathy is also rare at initial presentation and suggests amyloidosis or POEMS syndrome. Hypercalcaemia may cause symptoms such as thirst, polyuria and abdominal pain. Clinical signs (apart from a pathological fracture) are often unremarkable. Localized tenderness and restricted hip movements could be due to a plasmacytoma in the proximal femur. In late cases there may be signs of cord or nerve root compression, chronic nephritis and recurrent infection.[8]

Bone marrow testing with obtaining an aspirate plus trephine biopsy with testing for cytogenetics, fluorescent in situ hybridization (FISH) and immunophenotyping. And also imaging such as bone survey including spine, pelvis, skull, humerus and femurs, magnetic resonance imaging of the axial skeleton is very informative if available/feasible, but is not mandatory, whole-body PET-Scan imaging is also not mandatory, but can be used to confirm MGUS (positron emission tomography negative) or exclude unsuspected and/or extramedullary myeloma (positron emission tomography positive), infection, and/or an associated second malignancy.[4]

The main concern is pain control and, if necessary, treatment of pathological fractures. General supportive measures include correction of fluid balance and (in some cases) hypercalcaemia. Limb fractures are best managed by internal fixation and packing of cavities with methyl methacrylate cement (which also helps to staunch the profuse bleeding that sometimes occurs). Perioperative antibiotic prophylaxis is important as there is a higher than usual risk of infection and wound breakdown. Risk of spinal cord compression because of spinal fracture need immediate stabilization either by effective bracing or by internal fixation. Unrelieved cord pressure may

need decompression. Solitary plasmacytomas can be treated by radiotherapy. Specific therapy is with alkylating cytotoxic agents (e.g. melphalan). Corticosteroids are also used especially if bone pain is marked but this probably does not alter the course of the disease. Treatment should be carried out in a specialized unit where dosages and response parameters can be properly monitored. The prognosis in established cases is poor, with a median survival of between 2 and 5 years.[6]

On the other hand, CA-125 is a glycoprotein normally expressed in coelomic epithelium during fetal development. This epithelium lines body cavities and envelopes the ovaries. Elevated CA-125 values most often are associated with epithelial ovarian cancer, although level OF CA-125 also can be increased in other malignancies such as endometrial, fallopian tube, breast, lung, esophageal, gastric, hepatic, and pancreatic. CA-125 levels are elevated in about 85 percent of women with ovarian cancer, but only 50 percent of those with stage I disease. Higher levels are associated with increasing stages of the disease and the highest in tumors with non-mucinous histology. Multiple benign disorders also are associated with CA-125 elevations, presumably by stimulation of the serosal surfaces.[9]

Wang et al found extremely high level of CA-125 in a patient with IgE myeloma. Even though there were no abdominal involvement and serosal effusion, the CA-125 level was extremely high on admission and dramatically decreased to normal limits after chemotherapy and never increased to higher than reference limits again. They hypothesized that some cytokines abnormally synthesized by plasma cells stimulated the mesothelial cells to increase the secretion of CA-125 or that plasma cells themselves abnormally synthesized CA-125. The decrease of CA-125 level after treatment as seen in their patient could possibly be used to confirm response to specific treatments and elevating CA-125 level to signal recurrence.

De Larrea et al also reported their finding of increased CA-125 level in one patient with plasma cell leukemia. They concluded that the increase in the number of peripheral blood plasma cell count along with the simultaneous increase in the tumor markers of CA-125 and CA-15.3 and the dramatic decrease of both after treatment with cyclophosphamide and dexamethasone, strongly suggests that a plasma cell proliferation by itself can result in high levels of these tumor markers.

Our finding agrees with both previous reports. However, there were no clear mechanism of how a malignant B-cell lymphoproliferative disorder of the marrow stimulates the production of tumor marker such as CA-125. We do not recommend this examination to be made into standard procedure of MM diagnostic due to its low specificity, yet to acknowledge the possibility of such occurrence.[1]

CONCLUSION

This paper reports a patient with MM who had high level of CA-125. There were no clear mechanism of how a malignant B-cell lymphoproliferative disorder of the marrow stimulates the production of tumor marker such as CA-125. We do not recommend this examination to be made into standard procedure of MM diagnostic due to its low specificity, yet to acknowledge the possibility of such occurrence.

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