

## Multiple myeloma with breast masses as extra medullary plasmacytomas, A Case Report.

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### Abstract

**Background:** Breast involvement by immunolymphoproliferative disorders is rare. Primary & secondary malignant lymphomas of the breast are much more common than multiple myeloma, of which only 18 cases were reported in previous literature, till the year 2000.

**Case presentation:** We report a young female patient presented simultaneously with bilateral multiple breast masses & pathological fracture in right humerus that proved later on via histopathological examination to be a case of multiple myeloma associated with

extramedullary plasmacytoma involving breasts.

**Discussion and Conclusion:** There were diagnostic difficulties caused by the lack of specific radiological & sonographic features that differentiate between primary or secondary breast tumor & breast infiltration by immunolymphoproliferative disorders.

**Key words:** Plasma cell diseases, plasmacytoma, multiple myeloma, breast mass

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### Introduction

Breast involvement in multiple myeloma & solitary extramedullary plasmacytoma is very unusual. In most cases, the manifestation of this disease is usually systemic<sup>(1)</sup>.

Multiple myeloma is a neoplastic plasma cell dyscrasia characterized by clonal proliferation of plasma cells & overproduction of paraprotein<sup>(2)</sup>.

It is the most common plasma cell disorder representing 1% of all types of cancers<sup>(2)</sup>.

Incidence is 4.5/100 000 /year in US. It increases progressively with age.

The mean age at diagnosis of multiple myeloma is 65-70 years, while the onset before 40 years is very rare<sup>(2)</sup>.

Impaired hemopoiesis, renal insufficiency, osteolytic bone lesions, recurrent infections, hypercalcemia are the most common systemic manifestation of the disease.

Extra medullary myeloma (plasmacytoma) is defined as malignant proliferations of plasma cells with or without bone involvement<sup>(2)</sup>. When occur in the soft tissue, it usually involves the upper respiratory tract & oral cavity. Plasmacytoma of breast is very rare<sup>(3)</sup>.

This report describes a young female patient with bilateral breast masses with pathological fracture that proved to be part of manifestation of multiple myeloma with extra medullary plasmacytoma involving both breasts.

### Case presentation

Thirty four years old, an engineer, female patient presented with thirst lethargy & diffuse bone pain with difficulty in walking of 3 weeks duration. Two months ago she sustained right upper limb pain after a trivial trauma, which proved to be, later on, due to pathological fracture of

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the upper end of right humerus by open biopsy ( Figure 1), (pieces of bone at that site were sent for histopathological examination & immune histochemical staining) . Blurred vision & headache were reported but no fainting attacks or other system complaint. Menstrual history is normal. She had negative past medical & surgical history.

There is negative family history for breast cancer or other chronic or malignant diseases. She is a mother of one boy, 3 years old, with no use of any contraception or other medications. There is no history of smoking.

On examination, a young female patient ill looking with limited mobility & a POP splint over right upper limb. She is pale dehydrated, afebrile & not jaundiced. Tachycardia 112 beats per minute regular normal volume, blood pressure 100/65 mmHg. There is generalized bone tenderness especially over the limbs. There were no palpable lymph nodes any where. Abdomen, chest & cardiovascular examination were normal.

Breasts examination revealed the presence of 2 masses in the left breast (at upper inner quadrant), largest one around 2.5 x2.5 cm, and another mass in the right breast with no palpable axillary lymph nodes.

After admission a thorough evaluation performed including the basic hematological & biochemical investigations as follows;

PCV 24%, hemoglobin 76 g/l, white blood cell  $4.9 \times 10^9/l$  (Neutrophil. 51%, Lymphocyte 44%, Monocyte 3%) ESR 130 mm/hr

Blood film revealed normochromic normocytic with excess rouleaux, no abnormal leucocytes and adequate platelet

Blood sugar 110 mg/dl, urea. 36 mg /dl, creatinine 1.2 mg/dl, uric acid 6.5 mg /dl

Total serum protein 11g/dl, S. Ca (serum calcium) 11.5 mg/dl, S. ALP (alkaline phosphatase) 128.8 IU/L & S. LDH (lactate dehydrogenases) 200 IU/ L.

Normal prothrombin time & partial thromboplastin time & liver enzyme tests.

Normal general urine exam with no proteinuria. Urine for bence jones protein was negative

Serum protein electrophoresis: albumin 2.8 g/dl (3.5-5),  $\alpha-1$  0.23 g/dl (0.1-0.3),  $\alpha-2$  0.72 g/dl(0.6-1.0),  $\beta$  0.75 g/dl(0.7-1.1) &  $\gamma$  4.79 g/dl(0.8-1.6) with monoclonal band in  $\gamma$  region & marked reduction at albumin fraction.

Bone marrow aspiration revealed cellular fragment with active normoblastic erythropoiesis, active myelopoiesis sequence maturation no excess in blast. Plasma cells 5%, active megakaryopoeisis.

Bone marrow biopsy showed sections with infiltration of bone marrow by numerous clusters of immature plasma cells with normoblasts in diffuse manner.

Breast ultrasound ; Multiple ill defined complex density non homogenous masses at medial quadrant of left breast largest size 3.5x 3cm , no calcification normal skin, subcutaneous tissue & axillary region, suggestive of malignancy ,another small similar mass in right breast 2.0 x1.5 cm

FNAC (fine needle aspiration cytology) from right breast mass; sheets of lymphocytes & immature plasma cells suggestive of hemopioeitic malignancy infiltrating the breast.

Skull X ray showed 3 ill defined lytic lesions largest is 3x 0.5cm (Figure 2)

Spine X rays & pelvis X rays were normal.

Right shoulder & humerus X ray showed multiple lytic lesion over head, neck & shaft humerus with

subperiosteal reaction & pathological fracture at upper third of humerus.

Bone biopsy from site of fracture showed diffuse infiltrations of bone trabeculae by immature plasma cells (plasmablasts) with binucleated forms. Picture consists with multiple myeloma.

Immune histochemical staining of the same specimen revealed sheets of cells showing eccentric nuclei with granular cytoplasm consistent with plasma cell differentiation with frequent mitosis & abnormal nuclear pleomorphism & binucleation. These cells are positive for CD79a, CD 38, and CD 138 with kappa chain restriction. Picture consistent with malignant plasma cell disorder.

The presence of paraproteinemia & monoclonal gammopathy with skeletal lytic changes in addition to plasma cells in bone marrow biopsy are fulfilling major criteria of a diagnosis of multiple myeloma as well as the finding of related organ tissue injury (ROTI) like anemia & hypercalcemia. Breast masses are suggestive of extramedullary plasmocytoma.

After full evaluation, the treatment strategy started in form of zolderonic acid for hypercalcemia, blood

transfusion for anemia & then a specific therapy started in form of combination of thalidomide 100 mg /day orally, continuously, plus VAD protocol (vincristin 0.5 mg i.v. infusion /day, adriamycin 9 mg/mm<sup>2</sup>[16mg] i.v infusion over 24 hours & dexamethason 40 mg /day i.v. for 4 days) every 28 days.

After 4 cycles of VAD protocol with thalidomide over the whole period in addition to zolderonic acid monthly, patient improved concerning her bone pain, general condition, physical capability with healing of her fracture & removal of splint. Bilateral breast masses disappeared on clinical examination ,Her last review of investigations revealed PCV 42%, Hb. 132 g/l, WBC 5.2 x10<sup>9</sup>/l with normal differential count & normal platelet & blood film . ESR 23 mm/hr.

Total serum protein is 7.5 g/dl, Albumin 5.0 g/dl with normal serum protein electrophoresis & no M- band. Normal renal function & normal serum calcium level. Breast U/S normal no mass was seen. Skeletal bone survey showed no evidence of any new lesions. Old lesions are smaller in size & less in number.



**Figure 1: Right humerus X ray**



Figure 2:Lateral skull X ray

### Discussion

The differential diagnoses for this case is

1. Primary breast carcinoma with bony metastasis (primary synchronous multiple breast cancer).
2. Multiple plasmocytoma with extramedullary plasmocytoma involving breast.
3. Multiple myeloma with extramedullary plasmocytoma
4. Breast non Hodgkin lymphoma with bone involvement.
5. Primary osteosarcoma with breast metastasis.

Final diagnosis settled to be multiple myeloma with extramedullary plasmocytoma

Multiple myeloma is B cell lineage disseminated malignancy, due to clonal proliferation of plasma cells<sup>(4)</sup>.

Clinically apparent extraosseous manifestations are present in <5% of the cases & usually associated with more aggressive behaviour, resistance to treatment & short survival period<sup>(4)</sup>.

It is a localized growth of plasma cells. It can occur in association with bony structure (medullary) or in other area like in nasopharynx ( extra medullary) & it may occur as solitary plasmocytoma without other evidence of multiple myeloma<sup>(2)</sup>.

Clinico-pathological studies shows involvement, in 2/3 of patients, of liver, spleen & lymph nodes while rare cases report breast plasmocytoma in literatures.

Non Hodgkin lymphoma & multiple myeloma are most frequent lymphoproliferative disorders but their localization in breast is quite rare<sup>(4)</sup>.

Few cases of breast multiple myeloma are reported in literatures<sup>(4)</sup>.

Ross et al described one case & review of 10 similar records<sup>(5)</sup>.

Furthermore one case reported by Collins et al<sup>(6)</sup> & 2 cases by Mouloupoulus et al<sup>(7)</sup>. More recently Kim<sup>(8)</sup> & Ariad<sup>(9)</sup> described another 2 cases, in addition to report of 2 cases by Pasquini E. et al<sup>(4)</sup>.

The appearance of breast nodules in patients with immunoproliferative disorders makes it mandatory to differentiate between primary breast cancer & hematological malignancy<sup>(10)</sup> as well as other benign conditions that may mimic these conditions like pyogenic breast abscess, fat necrosis, lymphocytic mastitis, fibroadenoma or even synchronous breast cancer<sup>(3,11)</sup>.

Rarely multiple myeloma as a systemic disease can involve the breast as extramedullary site (Pasquini E et al reviewed only 16 cases were published in literatures yet) five of them as solitary plasmocytoma, four were synchronous with diagnosis of multiple myeloma, while one case in which breast mass precedes the diagnosis of systemic diseases. In four patients, the breast involvement followed an established diagnosis of multiple myeloma<sup>(4)</sup>.

Among these cases, distribution of breast nodules was unilateral in 9 patients & bilateral in rest of cases<sup>(4)</sup>.

Review of literatures revealed little help in the use of mammography or ultrasound examination in differentiation between myeloma involving breast & breast cancer, because multiple myeloma may give atypical appearance such as speculated mass that is difficult to be differentiated from primary carcinoma of breast by these investigations unless you have a guided core biopsy<sup>(3,5,11)</sup>.

The latest review of diagnostic criteria of multiple myeloma according to the international classification scheme as it is clinico-pathological diagnosis depends on the presence of M protein in serum or urine plus one or more of the following that must be presented which are:

1. Marrow plasmocytoma >5% in absence of underlying reactive process.
2. Tissue biopsy demonstrating replacement & distortion of normal tissue by plasma cells.

3. More than 500 plasma cells /mm<sup>2</sup> in peripheral blood.
4. Osteolytic lesions unexplained by other causes.

In case where the M protein is absent in serum & urine, it must have radiological evidence of osteolytic lesions or palpable tumors & one or more of the following that must be presented:

1. Marrow plasmacytosis >20% from 2 sites in absence of reactive process.
2. Tissue biopsy demonstrates replacement & distortion of normal tissue by plasma cells<sup>(2)</sup>.

Extramedullary plasmocytoma may represent the initial manifestation of systemic multiple myeloma or otherwise remain solitary for long time<sup>(4)</sup>.

The treatment of solitary plasmocytoma of breast should consist of local excision followed by brachiotherapy whereas when breast involvement is secondary to disseminated multiple myeloma the treatment should be treatment of the basic disease employing the most widely used schedules like VAD or melphalan based chemotherapy<sup>[4]</sup> in addition to new immunomodulating agent<sup>(2)</sup>.

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