Case report

Bone Marrow Involvement as Initial Diagnosis of Metastatic Breast Cancer

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Abstract:

Bone marrow examination is commonly used in the evaluation of hemato-oncological disorders and in patients with cancer of solid organs to detect metastases. We present a 68 years old female with anemia, high ESR, minimal axial bone pain, weight loss. These features mimic and raise suspicion of myeloma, however in this case diagnosis was done retrogradely from the bone marrow, despite her aspirate does not show much of that typical cluster of non hemopoietic, her bone marrow biopsy showed extensive fibrosis with cluster of non hemopoietic elements. So bone marrow aspiration and trephine biopsy are an effective and cheap method for evaluating metastatic bone marrow tumors.

Keywords: Bone marrow metastases; breast cancer

Introduction:

Bone marrow has played a prominent role as an indicator organ of occult tumor cell dissemination because it is easily accessible by aspiration, and it represents a relevant site of distant metastases in breast cancer

***Clinical Case*:**

68 years old female referred to Baghdad Teaching Hospital at 28th of February 2014 after she investigated and discovered that she has anemia and high ESR, when dated back to her history ,she gave a history of loss of weight., abdominal pain and for that reason she do it upper and lower scope which yielded duodenal ulcer.

When looking the cause for this ulcer it was found that it is because of abuse of non-steroidal anti-inflammatory drugs to relief bone ache which involved axial spine mainly mid and lower spine and her chest and both shoulder especially at night. She has no past medical history of any chronic illness apart with good performance statutes and do it her daily work at home.

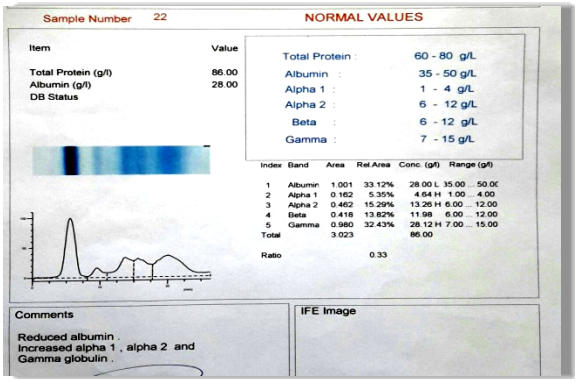
Examination: patient looks healthy, mildly anemic, no peripheral lymphadenopathy, thorough vertebral tenderness without deformity or neurological deficit in upper or lower limb

CBC at January showed the following

Date	Hemoglobin/ g/dl	WBC/m3	Platelet/m3	ESR/hr	
20.01.2014	9.6	9200	380000	120	
05.03.2014	9	11100	378000	142	Leukocytosis lymphocytosis Left shift

Her anemia, high ESR and leucoerythroblastic blood picture with her underlying bone ache raised suspicion of myeloma

Serum protein electrophoresis: Showed increase in total protein element but in form of polyclonal rather than monoclonal gammopathy as demonstrated below.



Urine for Bence-Jonce protein: was negative

Skeletal survey as part of myeloma: doesn't showed prominent lytic lesions apart from diffuse osteoporosis

Abdominal ultrasound: normal with mild to moderate hydronephrosis of the right kidney

Breast ultrasound: showed fibroglandular tissue with ductal dilatation (BIRADS II)

Complete blood picture and bone marrow:
HB 8.5g/dl, WBC 11.7X10^9, platelet 385X10^9
Differential N: 57%, L: 37%, M: 6%
With leukocytosis, lymphocytosis and tendency for rouleaux formation

The bone marrow aspirate for the first look, showed scattered cell ***resemble plasma cell*** reaching 60% of all blood element with strange morphology as shown in slides A below making diagnosis of myeloma worrisome as in Figure [1].
when they looking to the **marrow biopsy** was astonishing which showed *extensive bone marrow*

fibrosis effaced the whole architecture showing cluster of non hemopoietic elements as shown in Figure [2].

From the feedback of the biopsy and looking more precisely to aspirate showed few clustering as shown in slide B and the report of aspirate come with the marrow shows few granulocytic and erythroid precursors, with marrow infiltration *by non hemopoietic elements* in scattered and few cluster

During this time patient come back with confessional state, irritability without focal neurological deficient and the differential at that time: could be either renal, hyperviscosity or hypercalcaemia

CT brain

no abnormality have been detected

MRI brain:

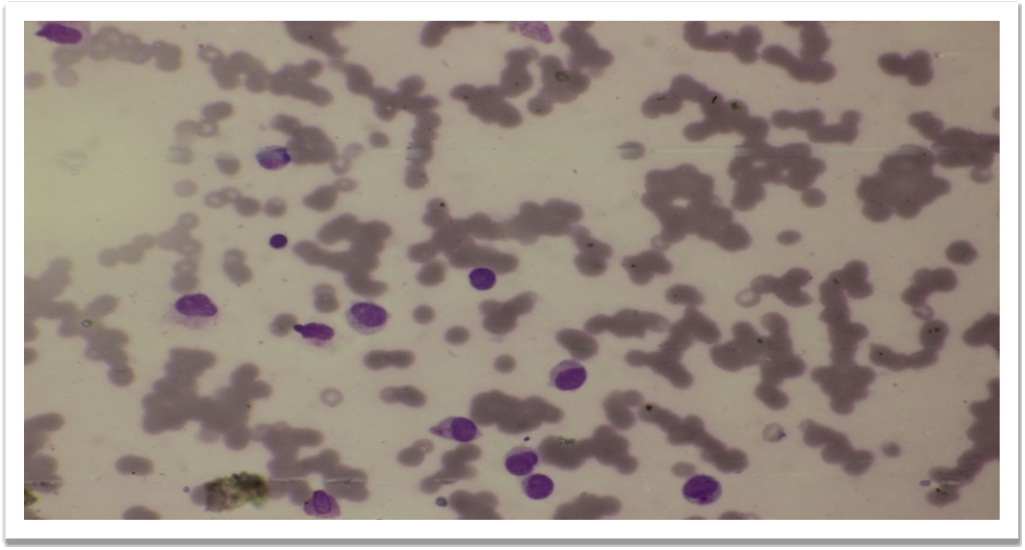
Bilateral white matter lesion in the periventricular area (picture suggest deep white matter lesion)

Laboratory investigation:

Random blood sugar 191 mg/dl
Urea 76 mg/dl
Creatinine 1.3 mg/dl
Calcium 13.9 mg/dl (8.5-10.5mg/dl)
Alkaline phosphatase 221 U/l (normal range 40-150)
ALT 104 U/L (0-55)
AST 97U/L(5-34)
Serum uric acid 12.5mg/dl **(2.6-7.2)**

After two days patient regain her consciousness with hydration, steroid therapy and zolendrinic acid

Slide A



Slide B

Figure (1): Bone marrow aspirate showed showing scattered cell *of non hemopoietic element* rather than clustering morphologically look like plasma cell especially in slide A

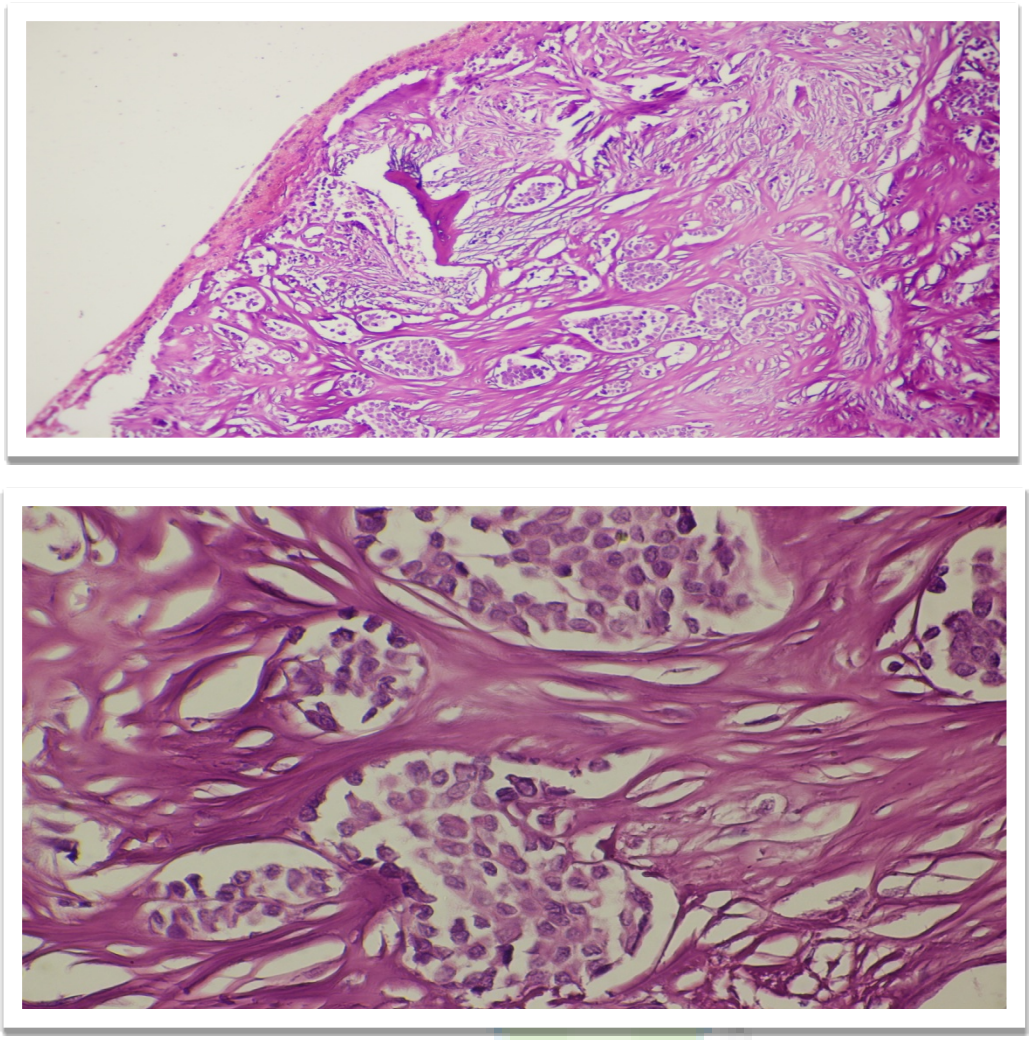


Figure (2): extensive bone marrow fibrosis effaced the whole architecture showing cluster of non hemopoietic elements

Looking for the primary source

Colonoscopy: This was normal up to splenic flexure because patient was not well prepared

CT-chest and abdomen:

Speculated irregular nodule (21X11.5 mm) seen in upper medial part of right breast.

Generalized mixed metastatic bony lesion predominantly lytic involved entire skeleton

Bilateral pleural effusion with thickening and dependent atelectasis with right subpleural nodule

Tumors marker:

CEA	more than	200 (up to 10 ng/ml)
CA 125	more than	600 (up to 35 u/ml)
Serum CA 15.3		300 (up to 25 iu/ml)
AFP		1.96 (up to 2u/ml)

Immune histochemical stain of the bone marrow biopsy:

With the looking for the primary source , bone marrow biopsy sent for histochemical stain which yield that neoplastic cell ***showed positive immunostaining*** for ***mammaglobin, cytokeratin 7, ER score(5/7), PR score (7/8), and Her2/neu (score 1+)*** While ***negative for GCDFP-15,and cytokeratin 20 marker, these*** finding go with metastic breast cancer

Discussion:

Marrow aspirates and trephine biopsies are sensitive and cheap techniques for detecting solid tumors metastatic to bone marrow.

Such investigations are indicated when there is significant probability of bone marrow metastases and when knowledge of their presence would affect the choice of primary treatment.

Trephine biopsy is more sensitive than bone marrow aspiration and sensitivity is increased by performing bilateral biopsies or by obtaining a single large biopsy and therefore these two procedures should be regarded as complementary [1].

The detection of tumor cells in a trephine biopsy when none are demonstrable in smears of an aspirate is not uncommon.

However, occasionally tumor cells are seen in aspirate smears when trephine biopsy is normal [2,3].

Marrow infiltration by metastatic tumor may be focal or diffuse. Reticulin and collagen fibrosis are commonly present and are most marked in those cases with greater degrees of marrow infiltration. Marked fibrosis is most common in carcinomas of the breast, stomach, prostate and lung [4,5,6].

The two primary sites whose identification is most important because of their sensitivity to hormonal therapy are breast and prostate. In patients with relapsed or metastatic breast cancer, the finding of bone marrow metastases is reported in 3-52% of patients [7,8,9].

The presence of bone marrow metastases may be helpful in detecting hormonal receptors in patients who have not had the determination done on the primary tumor [10].

By conventional histopathological techniques, the likelihood for the identification of isolated breast cancer cells in bone marrow is as low as 4% [11]..*Redding et al*. used an antiserum against epithelial membrane antigen (EMA) and detected breast cancer cells in bone marrow at the time of primary surgery in 28% of females without overt metastases [12].

Although this marker is known to be rather nonspecific

There was no statistical correlation between the extent of bone marrow involvement and the degree or number of cytopenias or survival after biopsy, which was a median of 13.5 months. Most of these patients present with bicytopenia or pancytopenia, and most biopsy results showed extensive metastatic involvement of the bone marrow. So many patients have been reported with first presentation as cytopenias, anemia and multiple lytic skeletal lesions, anemia of an unknown cause or isolated low platelet count[13] .

On the basis of these findings, Dr. Zhou recommends that pathologists search even routine bone marrow biopsy specimens for the presence of metastatic carcinoma.

Reference:

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