

Metachronous infiltration of bone marrow due to breast cancer and multiple myeloma

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ABSTRACT

Multiple primary tumors are rarely seen in clinical practice. Cases of metastatic breast cancer associated with multiple myeloma were rare in the literature. It is believed that simultaneously observed bone marrow involvement due to breast cancer and multiple myeloma is sporadic. We present a 49-year-old female patient with metastatic breast cancer who developed multiple myeloma during breast cancer treatment.

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Keywords: Bone marrow involvement, breast cancer, multiple myeloma, metachronous malignancy

Introduction

Multiple myeloma is a malignant disease of plasma cells. It is a relatively rare disease. It forms 1% of all cancer cases and 10% of all hematological malignancies [1]. Other solid organ tumors rarely accompany multiple myeloma. Breast cancer is the most frequently seen cancer in women worldwide. Its relation with colon, vulva, lung, larynx, liver, uterus cancers has been identified in the literature [2]. A case with a history of breast cancer came to internal medicine clinic offering findings remarkable for multiple myeloma.

Case Presentation

A 49-year-old female patient with no significant history except hypertension came to her physician

with a complaint of left breast mass and the patient underwent a tru-cut needle biopsy one year ago. A diagnosis of invasive ductal carcinoma exhibiting both estrogen- progesterone receptor positivity was established. PET CT demonstrated thoracic vertebral involvement. Clinically, the patient appeared to have a stage 4 breast carcinoma. She began a chemotherapeutic regimen of cyclophosphamide (600 mg/m²), epirubicin (60 mg/m²) and 5-fluorouracil (500 mg/m²). She received nine cycles of this regimen followed by the left modified radical mastectomy and lymph node dissection.

After surgery, the patient received two more cycles of chemotherapy. Since the patient stated that she had been fatigued and having palpitation, she came to internal medicine clinic in our hospital with concerns regarding these symptoms. The patient was electively admitted to our clinic for evaluation. Vital signs were blood pressure 130/85 mm/Hg, temperature 36.7°C, respiratory rate: 18/min, and heart rate: 78 beat/min.

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Cardiovascular and pulmonary examinations were within normal limits. ECG and chest x-ray were normal. Routine laboratory analyses were follows: hemoglobin 7.6 mg/dL, white blood cells 5,400/ μ L, platelet counts 234,000/ μ L, erythrocyte sedimentation rate 84 mm/h, sodium 129 mm/L, potassium 4.68 mm/L, calcium 9.5 mm/L, albumin 3.1 g/L, globulin 7.6 g/L, serum LDH 299 IU/L, serum ALP: 789 IU/L, and uric acid 6.8 mg/dL. Liver, kidney, and thyroid function tests were normal. Urine analysis revealed pH: 6, density 1,025, protein 1+, leukocyte 2+, bilirubin, and glucose (-). Peripheral smear showed hypochromia, anisocytosis, and minimal poikilocytosis without atypical cells.

Due to the reduction of albumin/globulin ratio and symptomatic anemia, serum immunoglobulin profile was requested. Serum immunoglobulin profile revealed IgG: 6,190 mg/dL, IgM: 10.2 mg/dL, IgA: 9.59 mg/dL, and IgE: 4mg/dL. Serum immunofixation test revealed monoclonal gammopathy (serum kappa light chain: 1,457 mg/dL, serum lambda light chain: 183 mg/dL). Then the patient's anamnesis was deepened, it was determined that there was a recurring back pain for the last one month in spite of analgesic treatment. Tumor invasion of the thoracic vertebra was detected in PET CT after the patient was diagnosed with breast cancer, but the lumbar vertebra was the usual appearance.

New lytic lesions that were not observed before chemotherapy was detected in a linear graph of lumbar vertebrae taken to illuminate the etiology of the patient's back pain. (L2-L4). On the initial assessment of the patient appeared to have hyponatremia, anemia, hypergammaglobulinemia, monoclonal gammopathy and lytic lesions on radiography. A full chemistry panel was significant for a prominent increase in the serum globulin and an elevated IgG. These aspects of her hyponatremia were highly suggestive for pseudohyponatremia to paraproteinemia.

Histopathologic examination of the bone marrow biopsy revealed CD138+ plasma cells with atypical morphology and tumor tissue with epithelial cells with large hyperchromatic nuclei (Figures 1-3). A presumptive diagnosis of simultaneously observed bone marrow involvement due to breast cancer and multiple myeloma was made. Hematology was consulted. A review of the pathology revealed multiple myeloma and the patient was referred to hematology clinic. The decision to treat this patient was based upon bone marrow involvement by atypical plasma cells, monoclonal gammopathy. The consultants on hematology recommended chemotherapy for multiple

myeloma. The patient underwent nine cycles of bortezomib-dexamethasone treatment. Full remission was achieved.

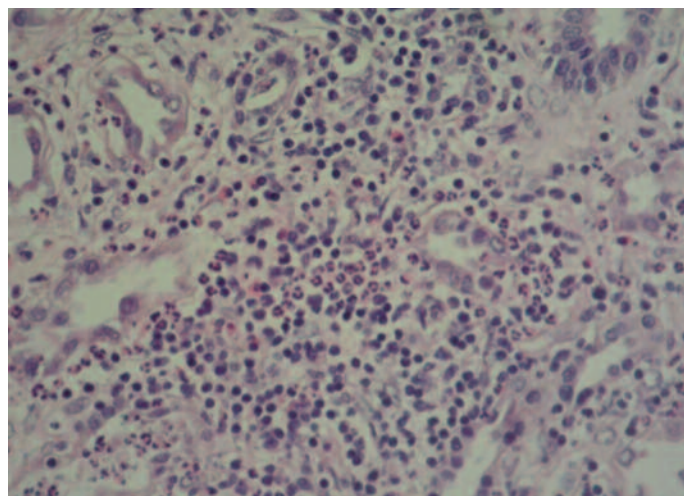


Figure 1. Areas of carcinoma in bone marrow by immunohistochemical test

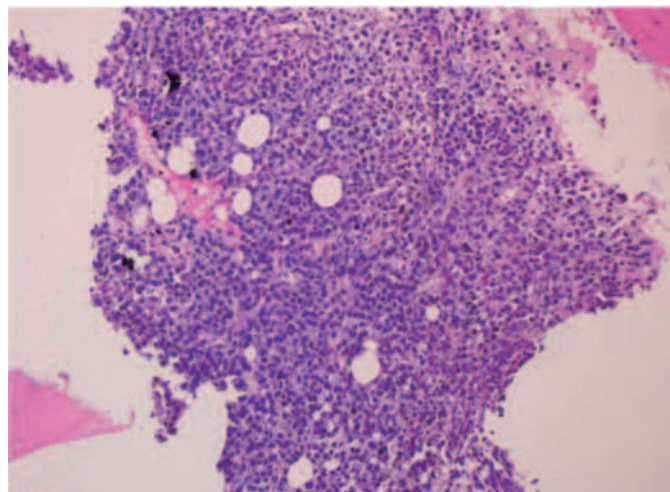


Figure 2. Plasma cells of multiple myeloma in bone marrow. H&E \times 200

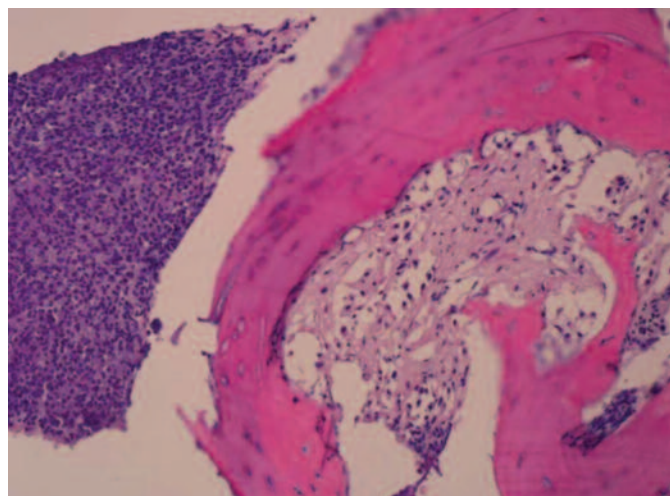


Figure 3. Plasma cells and areas of carcinoma in bone marrow. H&E \times 200

Discussion

It is a rare situation to see multiple carcinomas in the same case. It is also very rare to see bone marrow involvement due to breast cancer and multiple myeloma in the same case.

Multiple primary carcinoma descriptions are provided with the following criteria: each malignant tumor must bear histological features; they must be different from each other histologically; exclusion must be done as they are not metastasis of each other [3].

The synchronous tumor is a situation when the diagnosis of a second tumor is established at the same time or in the following six months. If this rule is not provided, the second tumor is called as metachronous [4]. In our case also offered these three criteria, in addition to this, we evaluated as metachronous tumors in our study because multiple myeloma occurred one year after the diagnosis of breast cancer. Family history, genetic predisposition, previous chemotherapy and radiotherapy history are essential factors for various tumor developments [5]. We did not detect family history, radiotherapy history or a genetic mutation. She had received a chemotherapeutic regimen of cyclophosphamide, epirubicin, and 5-fluorouracil. She received 11 cycles of this regimen. Plasma cell dyscrasia after chemotherapeutic regimen with alkylating chemotherapeutic agents especially like cyclophosphamide has been reported in the literature [6].

Multiple primary carcinoma cases were detected in 2.4% of 19,252 patients diagnosed with breast cancer in a study conducted in Italy [7]. Kılıksız *et al.* [8] identified 297 primary tumor cases (1.47%) among 20,290 cancer patients. This ratio was 1.74% in breast cancer cases (38/2,186). It was reported that breast cancer could be associated with colon, vulva, lung, larynx, liver, and cancer of the cervix [2]. Although differences in the cases of breast cancer, multiple primary tumors are often seen in the elderly. Various primary tumors accompanying breast cancer are mostly seen in young ages and this rate decreases over 65 years of age [9]. Our patient was 49 years old, is compatible with this situation. Some previous case reports are showing the simultaneous existence of a solid tumor and multiple myeloma. The simultaneous presence of a solid tumor and multiple myeloma was reported as 3% by Stegeman *et al.* [10]. Sakai *et al.* [11] reported an association between multiple myeloma with clear cell renal carcinoma and

emphasized the possible role of growth factors like IL-6. Kherfani *et al.* [12] reported a synchronous hormone receptor-positive breast cancer and multiple myeloma case with the involvement of thoracic and lumbar spinal cord. Sehgal *et al.* [13] reported a case of prostate adenocarcinoma and multiple myeloma with synchronous infiltration of bone marrow. Increased release of growth factors like IL-6, IGF-1 derived from multiple myeloma has been reported to trigger other malignancies. Demir *et al.* [14] reported a case of synchronous stomach adenocarcinoma and multiple myeloma.

Conclusions

The simultaneous existence of breast cancer and multiple myeloma are rarely reported. The presence of some laboratory signs and symptoms in patients with metastatic malignancy can be stimulating regarding synchronous or metachronous malignancies. Further studies are needed to determine the underlying etiologies and genetic factors in synchronous or metachronous malignancies.

Informed consent

Written informed consent was obtained from the patient's family for the publication of this case report.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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