Case Report

Plasma Cell Neoplasm Mimicking Metastatic Bone Disease in a Breast Cancer Survivor: A Case Report Highlighting the Role of Serum Protein Electrophoresis

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Abstract

Breast cancer, a prevalent solid tumor, is the most common cancer among women worldwide. Hematological malignancies, such as acute myeloid leukemia, myelodysplastic syndrome, and acute lymphoblastic leukemia, are more frequent in breast cancer survivors, while plasma cell neoplasms are less common. We report the case of a 44-year-old woman with breast cancer who underwent neoadjuvant chemotherapy and surgery, presenting one year later with bone lesions and anemia. Initially suspected to be metastatic bone disease, the findings of elevated serum total protein and globulins prompted serum protein electrophoresis, which revealed a distinct M band in the gamma region, suggesting a plasma cell neoplasm. Further evaluation confirmed this diagnosis, and treatment was initiated. This case underscores the importance of considering elevated total protein, globulins, and an altered albumin-to-globulin ratio as primary bone marrow disorders, such as plasma cell neoplasms, in breast cancer patients with bone lesions.

Introduction

Plasma cell neoplasm is a systemic malignancy characterized by the uncontrolled proliferation of monoclonal plasma cells in the bone marrow, resulting in the production of nonfunctional immunoglobulins or immunoglobulin light chains, known as M-protein. Diagnosing this condition is challenging due to nonspecific symptoms, such as bone pain, fatigue, and aches at multiple sites [1]. Typically diagnosed in individuals aged 65–75 years with a male predominance [2], plasma cell neoplasms may be overlooked in younger female patients, where symptoms might be mistaken for aging or other conditions. Indications for testing include incidental findings of elevated total protein, unexplained anemia or cytopenias, hypercalcemia, renal impairment, lytic bone lesions, or unexplained osteopenia in patients with bone pain or fractures [3].

Breast cancer, the most common cancer among women globally, has seen reduced mortality rates due to advances in screening and treatment. However, its association with secondary malignancies, such as plasma cell neoplasms, is rare [4]. We present a case of a 44-year-old woman with invasive ductal carcinoma of the right breast, treated with chemotherapy, modified radical mastectomy, and radiotherapy. One-year post-treatment, she developed back pain, anemia, acute kidney injury, and bone lesions, initially suggestive of metastatic tumor deposits. Further evaluation revealed a plasma cell neoplasm, highlighting the diagnostic challenges of distinguishing between metastatic disease and primary bone disorders.

Case Report

A 44-year-old woman presented with a right breast nodule and was evaluated at our hospital. Examination revealed a retroareolar nodule with a peau d'orange appearance and enlarged right axillary lymph nodes. Biopsy confirmed grade 3 invasive ductal carcinoma, with immunohistochemistry indicating ER-negative, PR-low positive, and HER2/neu-positive status. A bone scan showed no lytic or metastatic lesions. The final diagnosis was carcinoma of the right breast, staged as cT4bN2M0. The patient received neoadjuvant chemotherapy with four cycles of Adriamycin and Cyclophosphamide, followed by four cycles of Paclitaxel. She then underwent right modified radical mastectomy and adjuvant radiotherapy over five weeks, followed by hormonal therapy with Tamoxifen.

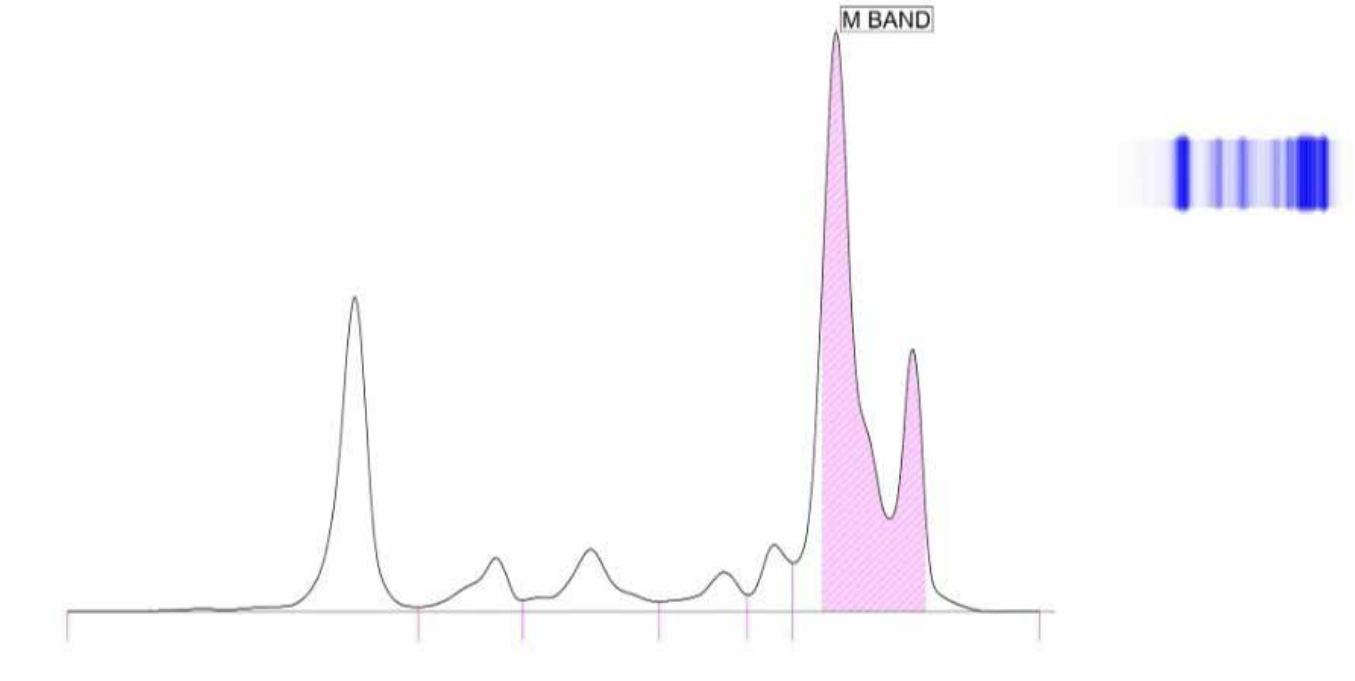
One year later, the patient presented with lower back pain, vomiting, and constipation, managed with supportive care. Routine investigations revealed severe normocytic normochromic anemia, treated with blood transfusion and hematinics. One month later, she was readmitted for persistent anemia. Abdominal ultrasound showed bilateral bulky kidneys with increased cortical echogenicity, prompting kidney function, liver function, and electrolyte tests. These revealed acute kidney injury and hypokalemia. High-resolution CT of the chest and MRI of the lumbar spine identified multiple lytic lesions in the axial and appendicular skeleton, initially suggestive of metastatic bone disease.

Table 1: Investigations Performed During the First Visit and One Year Later.

Investigations	Initial Findings	One Year Later	Biological Reference Interval
Serum Creatinine (µmol/L)	41.5	176.8	45.9–91.9
Total Bilirubin (µmol/L)	5.1	11.9	3.42–22.2
Total Protein (g/L)	79	119	63–82
Serum Albumin (g/L)	40	35	35–50
Serum Globulin (g/L)	39	84	19–37
Albumin/Globulin Ratio	1	0.4	1.0–2.5
Aspartate Transaminase (AST) (U/L)	30	23	14–36
Alanine Transaminase (ALT) (U/L)	17	11	0–35
Alkaline Phosphatase (ALP) (U/L)	101	105	38–126
Serum Sodium (mmol/L)	141	145	137–145
Serum Potassium (mmol/L)	4.1	3	3.5–5.1
Serum Chloride (mmol/L)	108	104	98–107
Hemoglobin (g/L)	117	67	120–160

Given the elevated total protein, globulins, and altered albumin-to-globulin ratio, serum protein electrophoresis (SPE) was performed using the Sebia Minicap system. The electrophoretogram (Figure 1) revealed a distinct M band in the gamma region and reduced albumin levels.

Figure 1: The electrophoretogram revealed a distinct M band in the gamma region and reduced albumin levels.



This finding prompted further evaluation for plasma cell neoplasm, including serum free light chain estimation, bone marrow aspiration and biopsy, and serum calcium measurement. Results are shown in Table 2.

Table 2: Investigations for Plasma Cell Neoplasm Evaluation.

Investigations	Findings	Biological Reference Interval
Free Kappa (mg/L)	113	3.3–19.4
Free Lambda (mg/L)	19.4	5.71–26.3
Kappa:Lambda Ratio	5.8	0.26–1.65
Bone Marrow Aspiration & Biopsy	80% plasma cells	Normocellular
Serum Calcium (mmol/L)	2.87	2.10–2.55

Bone Marrow Biopsy was showing increased plasma cells clusters focal admixed with myeloid cells in the available intertrabecular spaces. Bone marrow aspiration was showing particulate and hypercellular marrow with reduced trilineage hematopoiesis and replaced by sheets of plasma cells. Imprint smears were showing variable cellularity with myeloid cells and increased plasma cells.

The patient was diagnosed with IgG kappa-type multiple myeloma. Palliative radiotherapy to the pelvis provided moderate symptom relief, followed by chemotherapy with the Lenalidomide, Bortezomib, and Dexamethasone (RVD) regimen.

Discussion

Bone lesions in breast cancer patients are commonly attributed to skeletal metastases, which may present with intractable bone pain, hypercalcemia, pathological fractures, nerve compression, spinal cord compression, or bone marrow suppression [5]. In this case, the patient's back pain and bone lesions were initially suggestive of metastatic disease. However, the presence of acute kidney injury, elevated serum total protein, and globulins was atypical.

Elevated globulins are associated with acute infections, chronic inflammatory conditions, and plasma cell neoplasms [6]. As the patient had no signs of infection, SPE was performed, revealing a distinct M band (5.6 g/dL), suggestive of a plasma cell neoplasm. Further tests confirmed an altered kappa:lambda ratio (>100 mg/L kappa chains) and bone marrow with 80% plasma cells, confirming the diagnosis.

Studies, such as Mitchell et al., have reported a 4% increased detection rate of monoclonal gammopathies in patients with elevated globulins, with gamma globulins >4 g/dL associated with a 76% incidence of monoclonal gammopathies [7]. The hallmark features of multiple myeloma, encapsulated by the CRAB acronym (hypercalcemia, renal impairment, anemia, and bone lesions), were all present in this patient. Anemia occurs in ~70% of newly diagnosed myeloma cases, renal impairment in 20–40%, and lytic bone lesions in up to 80% [8].

Distinguishing between metastatic disease and plasma cell neoplasms is critical, as symptoms like hypercalcemia and

anemia overlap. The elevated globulins, altered albumin-to-globulin ratio, and M band on SPE were pivotal in identifying plasma cell neoplasm in this case. Literature reports rare coexistence of breast cancer and plasma cell neoplasms, with Levi et al. noting five cases of multiple myeloma among 443 second neoplasms in breast cancer patients [9]. A French study reported a slightly increased incidence of multiple myeloma (SIRR, 1.5; 95% CI, 1.3–1.7) among breast cancer survivors, though leukaemia and myelodysplastic syndrome were more common [10]. Clayer and Duncan identified multiple myeloma in two of four breast cancer patients with new bone lesions [11]. A case report by Timon et al had a similar finding of development of multiple myeloma in a treated breast cancer patient suggesting that clinicians should consider multiple myeloma as a cause of lytic bone lesions without extra skeletal metastases [12].

Although haematological malignancies like leukaemia and lymphoma are more frequently reported in breast cancer survivors, plasma cell neoplasms mimicking bone metastases are rare [13, 14]. The etiology of this association remains unclear, but treatment-related factors, such as chemotherapy, or genetic predispositions may contribute. Further research is needed to explore these mechanisms and the role of cumulative therapies in secondary malignancies.

Conclusion

Bone lesions in breast cancer patients are typically attributed to skeletal metastases. However, rare primary bone disorders, such as multiple myeloma, should be considered, particularly when accompanied by elevated total protein, globulins, and myeloma-defining events like CRAB symptoms. This case highlights the importance of a high index of suspicion and targeted investigations, such as serum protein electrophoresis, to differentiate plasma cell neoplasms from metastatic disease in breast cancer patients with bone lesions.

Declaration of Conflict of Interest

The authors declare no conflicts of interest that could influence the research or its findings. No financial or personal relationships with individuals or organizations that could bias this work exist.

Ethical Approval

This case report complies with the ethical principles for medical research involving human subjects as outlined in the Declaration of Helsinki. The patient provided informed consent for the use of her de-identified medical data for research and publication purposes.

Credit Author Statement

The corresponding author confirms that all listed authors have reviewed and agreed upon the descriptions of their contributions. The roles of the authors are as follows:

Author 1 (Corresponding Author): Conceptualization, data collection, patient management, manuscript drafting, and final approval.

Author 2: Data analysis, laboratory investigations, and critical revision of the manuscript.

Author 3: Treatment planning, clinical follow-up, interpretation of diagnostic tests, and manuscript review.

Authors contributed to multiple roles as needed to ensure the accuracy and integrity of the case report.

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Data Availability Statement

The data supporting the findings of this case report are included within the article, specifically in Tables 1 and 2 and Figure 1. Additional de-identified patient data are available from the corresponding author upon reasonable request, subject to ethical and institutional approval.

References

1. Seesaghur A, Petruski-Ivleva N, Banks VL, Wang JR, Abbasi A, Neasham D, Ramasamy K. Clinical features and diagnosis of multiple myeloma: a population-based cohort study in primary care. BMJ Open. 2021;11(10):e052759. doi:10.1136/bmjopen-2021-052759
2. Das N, Gupta R. Risk Stratification in multiple myeloma – A review and update. Ann Natl Acad Med Sci (India). 2024;60:120–30. doi: 10.25259/ANAMS-2023-1-7-(820)
3. Houston B, Rimmer E, Zarychanski R, Sefte M. Laboratory testing in the evaluation of a monoclonal protein: a practical framework for interpretation. S Afr Med J. 2019;109:719-722. doi:10.7196/SAMJ.2019.v109i10.14314
4. Gurel A, Aygen B, Kara M, Elkiran ET. Multiple myeloma emerging after chemotherapy for breast cancer: case presentation and a brief review. Van Med J. 2015;22(3):194-196.
5. Hingmire S, Hingmire S, Baksi A, Gujral S, Badwe R, Nair R. Multiple myeloma mimicking bone metastasis in a patient with carcinoma breast. Indian J Med Paediatr Oncol. 2008;29:53-55. DOI: 10.4103/0971-5851.51446
6. Pawar NM, Hegde A. Usefulness of serum globulin levels for discriminating patients with monoclonal gammopathies/paraproteinemias. Biomedicine. 2021;41(1):31-35. doi:10.51248/.v41i1.529
7. Mitchell EB, Ali MAM, Keane P, Bienenstock J. The value of elevated gamma globulins in the diagnosis of monoclonal gammopathy and multiple myeloma. Ir J Med Sci. 1983;152(9):349-352. doi:10.1007/BF02954733
8. Eslick R, Talaulikar D. Multiple myeloma: from diagnosis to treatment. Aust Fam Physician. 2013;42(10):684-688.

PMID:24130968
9. Levi F, Te VC, Randimbison L, La Vecchia C. Cancer risk in women with previous breast cancer. Ann Oncol. 2003;14(1):71-73. DOI: 10.1093/annonc/mdg028
10. Jabagi MJ, Vey N, Goncalves A, Le Tri T, Zureik M, Dray-Spira R. Evaluation of the incidence of hematologic malignant neoplasms among breast cancer survivors in France. JAMA NEopen.2019;2(1):e187147. doi:10.1001/jamanetworkopen.2018.7147
11. Clayer M, Duncan W. Importance of biopsy of new bone lesions in patients with previous carcinoma. Clin Orthop Relat Res. 2006;451:208-211. DOI: 10.1097/01.blo.0000229296.52216.77
12. Tomono H, Fujioka S, Kato K, Yoshida K, Nimura Y. Multiple myeloma mimicking bone metastasis from breast cancer: report of a case. Surg Today. 1998;28(12):1304-6. doi: 10.1007/BF02482821. PMID: 9872555.
13. Hough B, Brufsky A, Lentzsch S. Metastatic breast cancer or multiple myeloma? Camouflage by lytic lesions. J Oncol. 2010;2010:509530. doi:10.1155/2010/509530
14. Chen PH, Tung HH, Lin CH, Huang KP, Ni YL, Lin CY. A case report of secondary synchronous diagnosis of multiple myeloma and systemic lupus erythematosus after breast cancer treatment: a CARE-compliant article. Medicine (Baltimore). 2022;101(35):e30374. DOI: 10.1097/MD.0000000000030320