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Case Report

An unusual occurrence of synchronous invasive duct carcinoma and multiple myeloma – A case report

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ABSTRACT

The cancer survival rates continue to increase with the passing day owing to advances in diagnostic modalities, therapeutic strategies and the ongoing research. Simultaneously, there is also an increase in the incidence of multiple primary cancers due to the increased survival, long term effects of chemotherapy and/or radiation therapy, higher diagnostic sensitivity and the persisting effects of behavioural and genetic risk factors.[1] Multiple Primary Malignancies (MPM) was first described in 1879 by Billroth. Multiple primary tumours are defined as synchronous or metachronous tumours presenting in the same individual. The neoplasms may be limited to a single organ or may involve multiple anatomical organs.[2] This article presents a case study of a 72-year old female, who was referred to our institute with a history of lump in the left breast and fracture of left clavicle.

1. Introduction

As per the North American Association of Central Cancer Registries (NAACCR), Multiple Primary Malignancies (MPM) can be classified into two categories: (1) Synchronous, in which the cancers occur at the same time (the Surveillance Epidemiology and End Results Programme (SEER) definition is within two months) and (2) Metachronous, in which the cancers follow in sequence, that is, atleast more than six months apart. As per the Warren Gates criteria,[3] a diagnosis of MPM can be made if (a) each tumour presents a definite picture of malignancy (b) each of the tumors is histologically distinct (c) the possibility that one tumour is metastasis of the other must be ruled out. As per the definition proposed by the Surveillance Epidemiology and End Results (SEER) project,[4] two or more primary malignancies diagnosed within a 2-month period as synchronous multiple tumors. In comparison, the International Association of Cancer Registries and International Agency for Research on Cancer (IACR/IARC) defined synchronous multiple primary malignancies as two or more primary malignancies diagnosed within a 6-month period.[5] We report a case of a 72-year old female who simultaneously presented with Invasive duct carcinoma, left breast and Multiple myeloma, left clavicle.

2. Case Report

A 72-year old female was referred to our institute with complaints of left breast lump and swelling over the left clavicular region since 5-6 months. Initial work-up done outside showed fracture of the left clavicle, therefore a detailed work-up for Plasma cell dyscrasias was initiated. Her Complete blood counts (CBC), Serum Uric acid,

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Serum Calcium and Lactate dehydrogenase (LDH) levels were within normal limits. Serum Beta-2-microglobulin was elevated (2443 ng/ml). Subsequently Serum protein electrophoresis (SPEP) was done which showed a well defined M- band (0.90 gm%) in the Gamma region and Free light chain (FLC) assay showed elevated Free Kappa (light chain) in the serum (101.8 mg/L), Free Kappa/ Lambda ratio being 7.55. Her PET/CT highlighted the lump in the left breast and showed multiple lytic lesions involving multiple bones of axial and appendicular skeleton. Fine Needle Aspiration Cytology (FNAC) and Core biopsy from the left breast lump were done. Also, core biopsy from the left clavicular lesion was done. FNAC and Core biopsy from the breast lump showed features of Invasive duct carcinoma, NST, Grade III – left breast, whereas biopsy from the left clavicular mass showed sheets of plasma cells with eccentrically placed nuclei, perinuclear hof and binucleation, suggestive of Plasma cell neoplasm. Further Immunohistochemistry (IHC) was done on the formalin fixed paraffin embedded (FFPE) blocks from both sites. Left breast biopsy showed Estrogen receptor (ER- 70%) and Progesterone receptor (PR- 70%) positivity, Her-2-neu was negative and MIB-1 labeling index was 10%, leading to a diagnosis of Luminal type-A breast carcinoma. IHC done on the core biopsy from left clavicular mass showed tumour cells which were immunoreactive for CD38, CD138 and Kappa restricted. Pan-cytokeratin (Pan-CK) and GATA-3 were added in the primary IHC panel to rule out metastasis from the breast or any other primary site, which were both negative, thereby establishing the clavicular lesion as a distinct second primary malignancy. Bone marrow aspiration was done from the left posterior superior iliac spine which showed morphologically normal marrow. Bone marrow biopsy showed 8% plasma cells which were highlighted using CD 138 and CD38. She was started on Chemotherapy – VRD regimen (Lenalidomide, Bortezomib, and Dexamethasone) along with Tamoxifen. She subsequently underwent CECT Thorax Abdomen and Pelvis along with Bilateral Digital Mammography which showed mild interval decrease in soft tissue mass in left breast in the upper central region, now measuring 2.6 x 2.1 cm (earlier 2.9 x 2.7cm) – BIRADS 6. There was no involvement of skin, nipple areola complex or chest wall. Few subcentimetric left axillary lymph nodes were seen, which were likely reactive. MRI (with contrast) both breasts corroborated the CT findings, right breast did not show any mass/ lesion. Thus, Left Modified Radical Mastectomy (MRM – Post NACT) was done which showed Residual viable Invasive duct carcinoma, Grade III without nodal involvement (0/26)- ypT2ypN0 (TNM staging as per AJCC 8^{th} edition)[6] – Residual Burden Class – II (2.062). BRCA1 and BRCA2 gene analysis was done which did not show any pathogenic variants causative of the reported phenotype. Therapy was administered further and on follow-up, Bone marrow aspiration showed only 2% plasma cells, consistent with a normal marrow and good response to therapy. Serum protein electrophoresis showed an M-band of 0.14 gm% and on FLC assay, Free Kappa levels were 30.96 mg/L and Free Kappa/ Lambda ratio was 2.47. Our patient is thus doing well on follow-up.

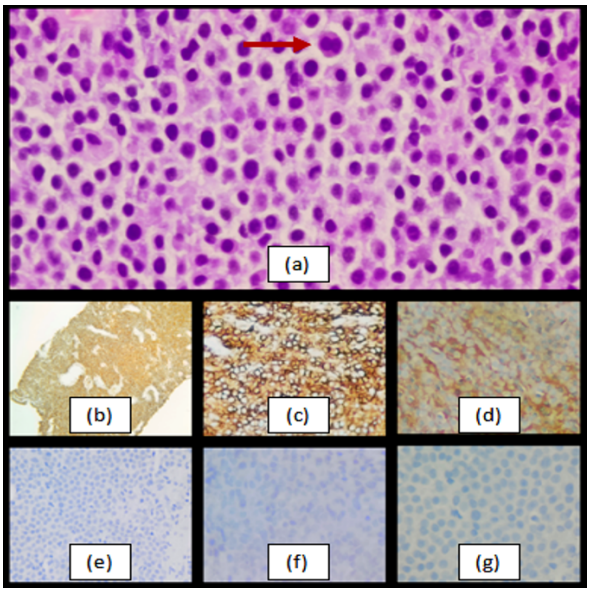

Fig. 1: Core biopsy from the left clavicular lesion; (**a**) Sheets of plasma cells with eccentrically placed nuclei and occasional binucleation (indicated with red arrow) H&E 400x; (**b**) Tumour cells show immunoreactivity for CD-38 – membranous strong and diffuse 100x; (**c**) Tumour cells show immunoreactivity for CD-138 – membranous strong and diffuse 400x; (**d**) Tumour cells show immunoreactivity for Kappa – Kappa restricted 100x, 1; (**e**) Tumour cells are immunonegative for Lambda-100x; (**f**) Tumour cells are immunonegative for Pan-CK -100x; (**g**) Tumour cells are immunonegative for GATA-3 – 100x.

3. Discussion

Multiple primary malignancies are not uncommon in cancer patients, and they may involve diverse risk factors and associations like genetics, viral infection, smoking, tobacco chewing, along with environmental or treatment-related factors. The frequency of multiple primary malignancies in the same or different organ systems ranges from roughly around 2% to 17%. In the literature reported so far, this is one of the very few case reports studying the co-occurence of Multiple myeloma and Invasive duct carcinoma in two different anatomical sites, presenting synchronously. A study by Al- Said Ali et al[7] (2009) and another case report by A. Venepureddy et al[8] (2016) had similar presentations as our patient. In our case the complete blood counts were within normal limits, however in the study by A. Venepureddy et al,[8] the patient in addition presented with B-cell monoclonal lymphocytosis and was thus monitored for

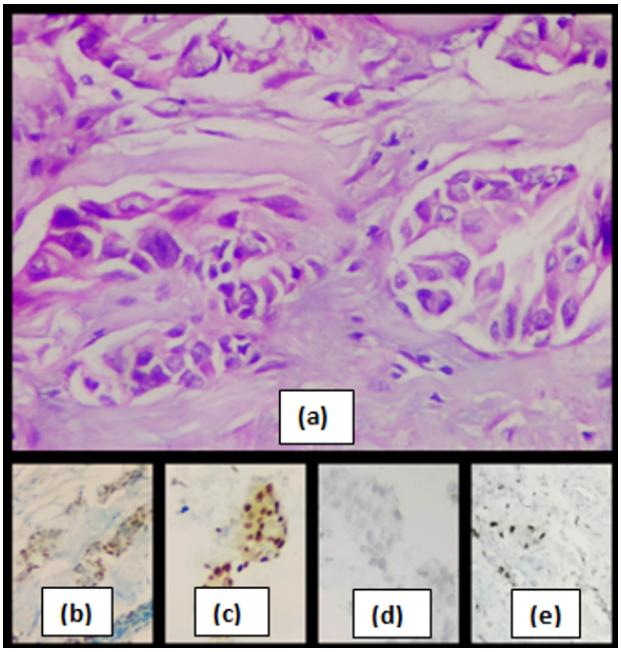

Fig. 2: Core biopsy from the left breast lump ; (**a**) Infiltrating duct carcinoma, Grade III – H&E 400x; (**b**) Estrogen receptor positivity – 70%; (**c**) Progesterone receptor positivity – 70%; (**d**) Her-2-neu– Negative; (**e**) MIB-1 labeling index – 10% in highest proliferative area

the development of CLL. In the report by Cao et al[9] (2009), the patient presented with Synchronous Infiltrating ductal carcinoma and Primary Extramedullary Plasmacytoma of the breast. Kherfani et al[10] (2014) reported a case with spinal cord compression due to concurrent involvement by multiple myeloma and metastatic breast carcinoma in the same vertebra. Khalbuss et al[11] (2006) reported the first case of simultaneous occurrence of breast carcinoma with plasmacytoid morphology and multiple myeloma in a 74-year old female, which posed a diagnostic challenge on FNAC of the breast.

4. Conclusion

In the present case study, our patient presented simultaneously with left breast lump and multiple bony lytic lesions, leading to diagnoses of synchronous Invasive Duct Carcinoma and Multiple Myeloma. The challenge we were posed with was to accurately diagnose both the conditions and stage the diseases in order to optimize and customize the therapeutic regimen, in order to achieve complete metabolic remission and cure. This study emphasises the role of an interdisciplinary patient- oriented approach to such diagnostically challenging and difficult cases, thereby facilitating timely diagnosis, appropriate management and overall prognosis.

5. Source of Funding

None.

6. Conflict of Interest

None.

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