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Synchronous Breast Malignancy and Astrocytoma - An Unusual Case of Double Malignancy

Kafil Akhtar[1*], Ahmad Masroor Karimi[2], Rana K Sherwani[1] and Shahid A Siddiqui[2]

[1]*Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, India*

[2]*Department of Radiotherapy, Jawaharlal Nehru Medical College, Aligarh Muslim University, India*

Correspondence should be addressed to Kafil Akhtar, drkafilakhtar@gmail.com

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ABSTRACT

The incidence of double malignancy is very low. We intend to present a case of synchronous breast and brain malignancy, which was treated successfully. Breast cancer is a very common cancer in Indian women. Multicentric gliomas are uncommon lesions of the central nervous system (CNS) with an unprecise rate of occurrence that diffusely infiltrate large portions of the brain. High grade astrocytoma is the most aggressive form of gliomas and often has a distinct neuroimaging pattern with a poor prognosis. We report a case of a 40-year-old female, who presented with a left breast lump associated with clinical features of raised intracranial pressure with slurred speech, mild confusion and transient facial paralysis. Modified radical mastectomy revealed infiltrating ductal carcinoma. Our patient was prescribed Tamoxifen and Herceptin (trastuzumab) and was treated with loco-regional radiation therapy. Computed tomography and magnetic resonance imaging demonstrated a large left parietal tumor extending from the cortex to the lateral ventricle. Complete tumor removal from the brain was performed, which on histological examination revealed a high grade astrocytoma with foci of microcalcification. Immunohistochemical staining for glial fibrillar acidic protein showed strong labeling in most tumor cells. Adjuvant radiotherapy was administered to the left parietal region with concurrent temozolomide chemotherapy.

KEYWORDS

Breast Carcinoma; Astrocytoma; Double Malignancy; Histopathology

1. INTRODUCTION

Breast cancer is the most common cancer in women [1]. Multicentric gliomas are uncommon lesions of the central nervous system (CNS) with an unprecise rate of occurrence that diffusely infiltrate large portions of the brain. High grade astrocytoma is the most aggressive form of gliomas and often has a distinct neuroimaging pattern with a poor prognosis [2,3].

With the advance of medical science and the multi-modality treatment approach, long-term survival of patients suffering from malignant diseases has been dramatically improved. At the same time, second neoplasm was found to be emerging as a long term complication of treatment with radiotherapy, chemotherapy and even with autologous stem cell

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transplantation. Subsequently second neoplasms were classified as “synchronous”, defined as occurrence of the index tumor and second malignancy within 6 month of each other, and “metachronous”, defined as occurrence of the index tumor and the second malignancy separated by a period of more than 7 months [3].

2. CASE REPORT

A 40-year-old female presented to the Surgery Clinics with a left breast lump associated with clinical features of raised intracranial pressure with slurred speech, mild confusion and transient facial paralysis. A thorough physical examination revealed a lump in the left breast of approximately 3 cm × 3 cm in size. The lump was hard in consistency with irregular margins, and it was not fixed to the skin or to underlying structures. Two firm, mobile ipsilateral axillary lymph nodes with mild tenderness could be palpated. Our patient did not have any family history of breast or ovarian carcinoma. There was also no history of oral contraceptive pills or hormone replacement therapy.

Mammography showed an increased attenuating lesion in the left breast superior to the nipple, measuring approximately 24 mm in diameter. The margins of this lesion were not sharply defined, and no calcification was seen. Fine needle aspiration cytology from the lump of the left breast suggested an infiltrating ductal carcinoma (Figure 1). Histopathological analysis of the left modified radical mastectomy revealed the tumor to be an infiltrating ductal carcinoma-grade II (Figure 2). Areas of necrosis and tumor calcification were noted. No perineural infiltration and lymphovascular emboli were found. The nipple, areola, skin and base were free of tumor and all the lymph nodes were reactive. Immunohistochemistry of the breast tumor was positive for estrogen (Figure 3), progesterone receptors and positive for human epidermal growth factor receptor 2 (HER-2neu). Our patient was prescribed Tamoxifen and Herceptin (trastuzumab) and was treated with 50 Gy in 30 fractions loco-regional radiation therapy to prevent any recurrence of the carcinoma.

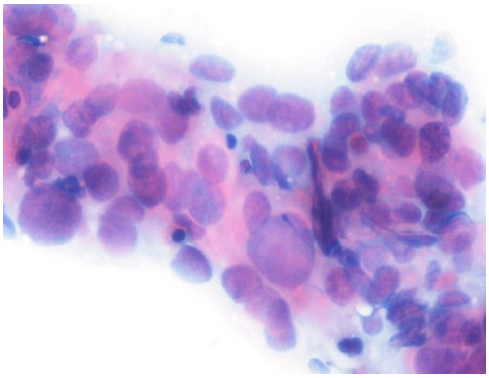

Figure 1: Fine needle aspiration cytology from the lump of the left breast showed large pleomorphic tumor cells with marked anisonucleosis and hyperchromasia, suggestive of infiltrating ductal carcinoma. Haematoxylin and Eosin × 40X.

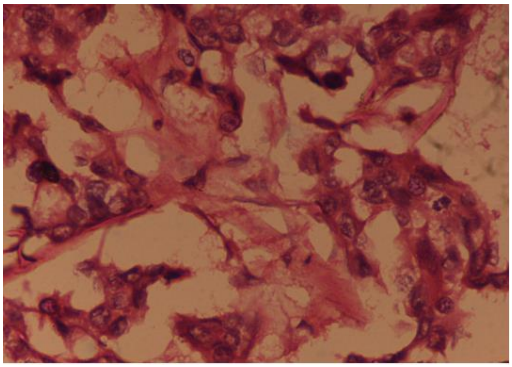

Figure 2: Histopathological sections of the left modified radical mastectomy revealed scattered and clusters of pleomorphic tumor cells with marked anisonucleosis and hyperchromasia infiltrating the stroma. Haematoxylin and Eosin × 40X.

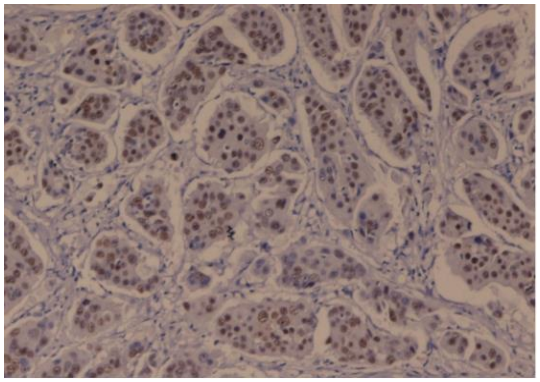

Figure 3: Immunohistochemistry of the breast tumor showed nuclear positivity for estrogen. IHC Oestrogen × 40X.

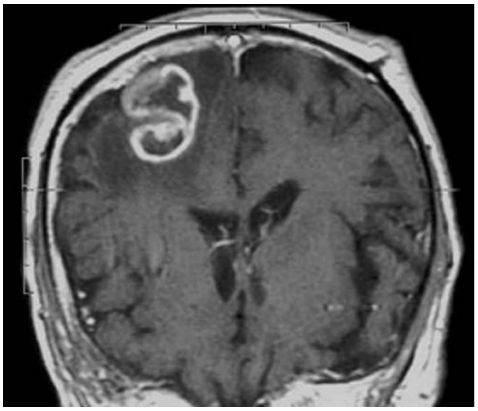

Figure 4: Computed tomography of the head demonstrated a large left frontoparietal tumor extending from the cortex to the lateral ventricle.

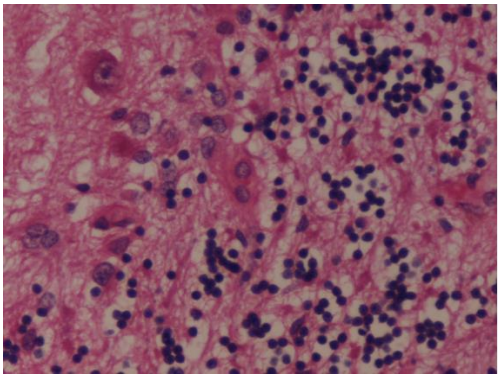

Figure 5: Histological examination of the brain tissue showed pleomorphic glial cells with marked anisonucleosis and nuclear hyperchromasia, suggestive of high grade astrocytoma. Haematoxylin and Eosin × 40X.

Computed tomography of the head demonstrated a large left frontoparietal tumor extending from the cortex to the lateral ventricle (Figure 4). A complete tumor removal from the brain was performed, which on histological examination revealed a high grade astrocytoma with micro calcifications seen focally within the tumor (Figure 5). Immunohistochemical staining for glial fibrillar acidic protein showed strong labeling in most tumor cells. Adjuvant radiotherapy was administered to the left parietal region (60 Gy in 30 fractions), and the patient received concurrent temozolomide chemotherapy. Our patient is symptom-free and doing well after one year and eight months of completion of the primary treatment. She is on routine follow up and evaluation and under the drug regimen of Tamoxifen and Herceptin for another 6 months.

3. DISCUSSION

The incidence of multiple primary cancers is rare and is reported to be between 0.3% and 4.3% [4]. The second primary lesion is identified either simultaneously with the primary lesion (synchronous) or after a period of time (metachronous). Cases of malignancy of the breast with synchronous or metachronous malignancies of the ovary, stomach, rectum and oral cavity have been reported.

The occurrence of two or more primary malignant tumours in a patient was regarded at one time as an uncommon event. Bilroth in 1889 documented several such cases and these were then considered clinical rarities. However, in recent years multiple primary malignancies have been reported with increasing frequency. Moertel in his study of 37,580 cases of malignant disease from the Mayo Clinic reported multiple primary malignant tumours in 10.6% of autopsy cases and 46.0% of surgical cases [5].

Studies of multiple primary malignancies have been useful tools for exploring risk factors by examining associations between different malignancies. An association between two cancers might suggest that those cancers share etiological risk factors. Three tumor suppressor genes common to breast and brain malignancies are p53, Rb and BRCA [6,7]. Two risk factors that are common to these two carcinomas are alcohol intake and smoking [8]. Positive association between alcohol intake and carcinoma of the breast has been consistently demonstrated. The risk appears to be linearly related to the amount of alcohol consumed. About 25% of breast carcinomas worldwide are due to obesity, according to the international agency for research on cancer [9]. Other possible explanations for such an association would be a hereditary predisposition to multiple cancers, as side effect of previous treatment for

cancer, or to a chance phenomenon. Further studies are needed to guide the treatment of such cases.

The occurrence of double or multiple primary malignancies of different organs is largely a matter of coincidence, involving mainly the most commonly encountered tumours. Its frequency is dependent on the age at first diagnosis and the length of survival after the treatment of the original tumour. Most of the cases in this series occurred in relatively young patients who have survived well over 5 years after the first treatment [10,11]. For this reason, as our treatment results improve, we could expect an increasing incidence of multiple primary malignancies.

The apparent incidence would also be expected to increase as we develop a greater awareness of this condition leading to better diagnosis. There is no reliable clinical means of distinguishing a second primary from a metastasis and diagnosis must be made by exploration and biopsy. It has been shown that in 70.0% of clinically evident multiple primary malignancies, the second tumour was the cause of death and in 70.0% no evidence of the first primary was found at autopsy [12]. Accordingly, emphasis must be placed on early diagnosis and radical management of the second primary [13].

Resection of both neoplasms frequently offers the best chance of long-term survival [14,15]. Our patient underwent surgery for both the primaries because her general condition was good and she had no other medical reasons to deny surgery. Finally, it is worthy of note that therapeutic procedures in the management of the first primary lesion may themselves exert a carcinogenic influence [16]. It is imperative, therefore that the cancer patient should be under continuous surveillance to the end of his life even if he is apparently cured [17].

4. CONCLUSIONS

The incidence of multiple primary cancers is rare. The reason why some patients are more prone to develop multiple cancers remains obscure. Synchronous double malignancies can be treated by considering the malignancy at two separate sites as independent carcinomas, taking in consideration the total dose of radiation to a critical organ and the total dose of toxic chemotherapeutic drugs.

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