

A Case of Glioblastoma Multiforme in a Known Case of Breast Carcinoma

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Abstract :

Introduction : Glioblastoma multiforme, also known as grade IV astrocytoma, is a fast growing, aggressive type of central nervous system tumor that forms on the supportive tissue of brain. These tumors contain various cell types, hence the name multiforme, the most common being astrocytes. The literature reports many cases of primary breast carcinoma having coexisting glioblastoma multiforme either at the time of diagnosis of breast carcinoma or later. This association may not be due to chance but rather to genetic changes in hormone status and in particular to sex hormones. Another important point of view is represented by the chemotherapy treatment of breast cancer, which could have a carcinogenic effect and explain the growth of glioblastoma. This consideration, in our opinion, is important, because more effort should be made to understand the pathogenesis of glioblastoma multiforme and to improve the therapeutic approaches.

Key words : Astrocytoma, Breast carcinoma, Glioblastoma Multiforme

Introduction :

Breast cancer is the most common type of cancer and the second leading cause of cancer death in women. The age-adjusted incidence rate is 124 per 100,000 women per year. High-grade gliomas are, however, relatively rare (incidence: ~4/100,000 person-years).⁽¹⁾ Breast cancer is one of the most common origins of metastatic lesions in the central nervous system. Many patients with a breast cancer and concurrent brain tumor(s) were diagnosed to have a metastatic lesion or lesions in the brain. It is, however, possible that a different pathology such as primary brain malignancy may occur in such patients with an already known malignancy. We, herein, report a 66 year-old female patient who suffered from Glioblastoma Multiforme (WHO grade IV) 1 year after her diagnosis of breast cancer.

Case Report :

An old female patient, aged 66 years, came to outpatient department with complain of forgetfulness since 1 month and right upper limb weakness since 2 days. She had undergone modified radical mastectomy

1 year ago for invasive ductal carcinoma (not otherwise specified) grade II of right breast followed by neoadjuvant chemotherapy and hormonal therapy. Thorough clinical examination showed weak right hand grip, Brocca's aphasia and MMSE (Mini Mental Status Examination) score of 15/30 suggestive of moderate dementia. The MRI of her brain showed heterogeneously enhancing mass lesion in left temporo-parietal region with moderate surrounding edema causing midline shift. She was operated with left parieto-temporal craniotomy, tumor was excised and sent for histopathological examination. Specimen received consisted grossly of multiple whitish brownish soft tissue portions measuring 5x5cm in aggregate. On cut section it was whitish. Microscopic examination revealed tumor to be composed of round to ovoid cells and fibrillary cells having pleomorphic, hyperchromatic nuclei with mitosis. Extensive necrosis and vascular proliferation with prominent endothelial cells were seen. Perinecrotic pseudopalisading was also present. And the diagnosis of GLIOBLASTOMA MULTIFORME (WHO grade IV) was made.

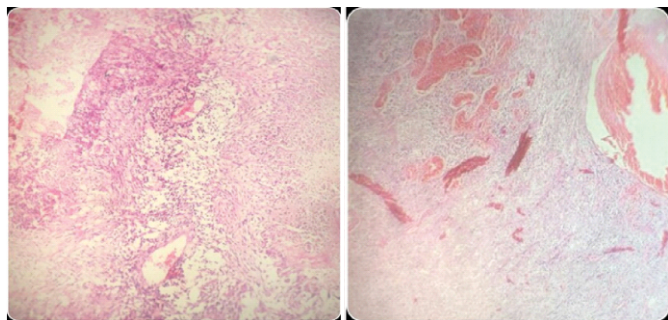
Figure 1(a) & 1(b): Histology of Glioblastoma Multiforme (WHO Grade IV)

Discussion :

Glioblastomas represent 15% of all primary intracranial neoplasms. The vast majority of glioblastomas (90%) develop rapidly de novo (primary glioblastomas). Secondary glioblastomas progress from low grade diffuse astrocytoma or anaplastic astrocytoma. The

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Figure 1(a) & 1(b) : Histology of Glioblastoma Multiforme (WHO Grade IV)



cause of most cases is unclear. Risk factors include genetic factors such as neurofibromatosis and Li-Fraumeni syndrome, previous radiation therapy.

Initially, signs and symptom of glioblastoma are non-specific including headache, nausea. Varying degree of dementia soon follows. The diagnosis is made by radiological and histopathological findings. CT and MRI findings are suggestive of space occupying lesion. On histopathology, glioblastoma multiforme are characterized by areas of necrosis and anaplastic cells with high degree of mitosis. There is also presence of marked vascular proliferation.

Treatment is mainly palliative and the recurrence rate is very high. The most common length of survival following diagnosis is 12 to 15 months.

A study was conducted by Piccirilli M. in 2005 on 11 cases of diagnosed breast carcinoma who developed glioblastoma multiforme after interval of approximately 18 years which concluded that study of genetic substratum is important to demonstrate association between Breast carcinoma and GBM.⁽²⁾ The most important genes predisposing breast carcinoma are BRCA1, BRCA2 and p53. Germline mutations in BRCA-1 and BRCA-2 significantly increase the risk of developing breast and ovarian cancers, and are also associated with an increased incidence of primary cancers at other sites.⁽³⁾ However, study conducted by Merium Boukerroucha in 2015 suggested no role of BRCA1 mutation in development of GBM in patient of breast carcinoma.⁽⁴⁾

p53 mutations generally predispose to the Li-Fraumeni syndrome, specific of children and young adults, in which there is association between breast, brain, adrenocortical, haematological cancers and sarcomas.

Another important tumor suppressor gene, located on the 10q23 chromosomal region is PTEN. PTEN mutations are responsible for Cowden's disease, a dominantly inherited syndrome characterized by an increased risk of breast and thyroid cancer and multiple hamartomas of the skin. However, PTEN mutations have also been found in glioblastomas and to a lesser extent in meningiomas and medulloblastomas in a study conducted by Feng Han in 2016.⁽⁵⁾

The other important aspect that could explain the association between breast carcinoma and GBM is endocrinological. A California Cancer Registry Population Based-Analysis suggested that the risk of developing GBM among women with breast cancer is elevated moderately relative to their peers, but that the risk is substantially elevated in women who develop breast cancer before the age of 45, when the level of estrogen is presumed to be higher before menopause.⁽⁶⁾ Another study by Rahim Ahmadi concluded that Progesterone is also involved in regulation of the growth of brain tumors. High dose of progesterone have cytotoxic effects on brain tumor cells in cell culture.⁽⁷⁾ Our patient's immunohistochemistry showed 90% ER positive cells as well as 90% PR positive cells.

Conclusion:

The association between Breast Carcinoma and Glioblastoma Multiforme cannot easily be explained as a coincidence. The genetic substratum is important for predisposition to Breast Carcinoma and Glioblastoma Multiforme. Hormone status and, most importantly, sex hormones are important in the growth of Breast Carcinoma and are also important to determine the development of Glioblastoma Multiforme.⁽⁶⁾ Another important aspect is the chemotherapeutic treatment of prior malignancies, in this case Breast Carcinoma. Adjuvant chemotherapy could play an important role, even though it has not been clarified, in the genesis of a new malignant neoplasm such as glioblastoma. Tumors are usually considered and treated independently in the setting of two distinct neoplasms,⁽⁸⁾ which lead to overtreatment. Hence, long-term epidemiological studies of larger cohorts are needed to confirm the association and to establish the common risk factors, pathogenetic mechanisms and better treatment options for both tumors.

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