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Case Report

Brain Metastases in a Patient with Ovarian Cancer

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Abstrat: Brain metastases are associated with a poor prognosis. Depending on the patient's age, functional status, extent of systemic disease, and number of metastases. We report a case of 22-year-old female who presented with 2 months history of headache and vomiting and 1 day history of not communicating, neck stiffness, and generalized body weakness. Patient has been unwell for 2 months after she had collapsed at school 2 months prior complaining of severe headache, she allegedly stroked one month prior with left sided weakness. No history of trauma and seizures but had history of falling and remaining unconscious for unspecified period of time. No history of chronic illness and no family history of malignancies. Brain CT scan and MRI documented multiple lobulated irregularly enhancing brain parenchymal mass lesions of variable sizes, patient was taken to theatre and burr hole for brain tumor biopsy was done and specimen taken for histology which confirmed metastatic carcinoma and the tumor immunoreacted negatively to TTF1 and positively to CK7. Treatment of brain metastasis has evolved over the years from WBRT only for most patients to multimodal therapy including surgical resection, if feasible, followed by Whole brain Radiotherapy (WBRT) and/or chemotherapy.

Keywords: Brain Metastases, Ovarian Cancer, Wholebrain Radiotherapy

1. Introduction

The brain, along with the bone, liver, and lung, is one of the most common sites of metastasis with about 170,000 new cases of brain metastases diagnosed each year in the USA, a figure which is 10-fold higher than that of patients diagnosed with primary brain malignancies [1, 2]

Common sources of brain metastases are lung, breast, renal and colorectal carcinoma, and malignant melanoma, and it has been estimated that up to 40% of patients with these cancers may develop brain metastasis in the course of their disease [3]

Brain metastases from ovarian cancer are rare and a late manifestation of the disease that occurs in patients with prolonged survival. [4, 5]

The incidence of brain metastases from ovarian cancer ranges from 0.29% to 5%. [6, 7]

Recently, advances in neuroimaging, such as computed tomography (CT) and magnetic resonance (MR) imaging, have allowed careful monitoring of cancer patients, which together with the increased survival of patients, has led to more frequent and earlier detection of brain metastases. Therefore, clinical reports of brain metastases from gynecological cancers have increased gradually [8].

2. Case Presentation

A 22-year-old female presented to the emergency department of our hospital with 2 months history of headache and vomiting and 1 day history of not communicating, neck stiffness, and generalized body weakness. patient has been

unwell for 2 months after she had collapsed at school 2 months prior to our consultation complaining of severe headache, she allegedly stroked one month prior with deviation of mouth to the left side and left sided weakness. She had episodes of confusion at home, no history of trauma and seizures but had history of falling and remaining unconscious for unspecified period of time. No history of chronic illness and no family history of malignancies.

On examination, ill looking patient not in respiratory distress, avoiding light,

Level of consciousness 12/15: E3, M5, V3; pupils equal and reacting to light 3mm; left sided hemiparesis, right sided facial nerve palsy,

Investigations: White cell count: 6,4; Haemoglobin: 13,1; Platelet: 267; MCV: 82,5; Sodium: 130; potassium: 4,6; urea: 3,9; creatinin: 98

Sodium was corrected and patient was taken to theatre and burr hole for brain tumour biopsy was done and specimen taken for histology, patient recovered and was sent home while waiting for histology result and futher investigations with Level of consciousness of 15/15 unfortunately patient vomited blood at home and died on the way coming back to hospital.

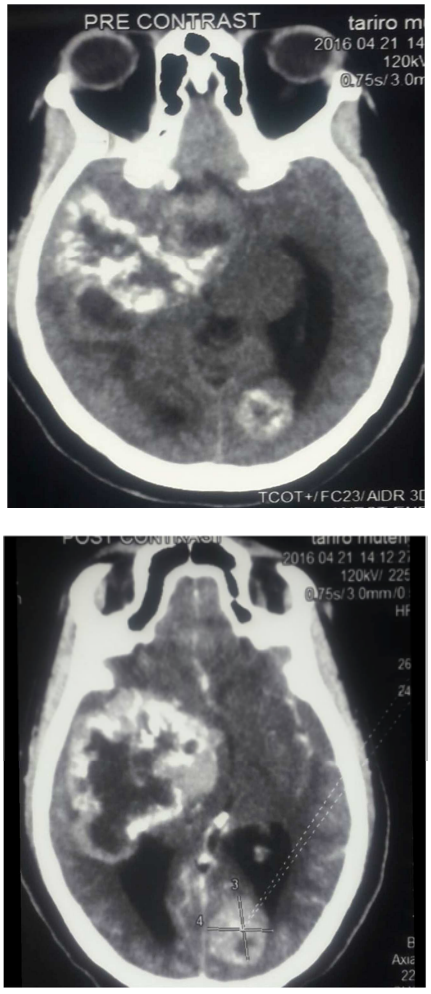

Figure 1. *Pre contrast CT scan Brain (left): heterogenous irregular calcified masses, post contrast (Right): extensive leptomeningeal enhanced plus multiple heterogenous lesions compressing the right lateral ventricle with midline shift.*

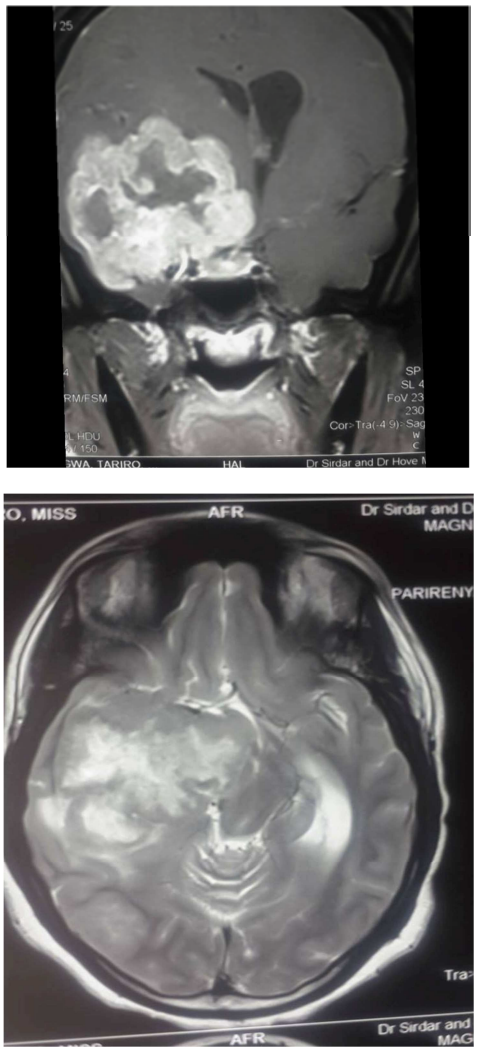

Figure 2. *MRI Scan of Brain showed multiple lobulated irregularly enhancing brain parenchymal mass lesions of variable sizes, the big mass has bright signal intensities at T1, T2 and shows aswell speckles of some calcifications within the mass.*

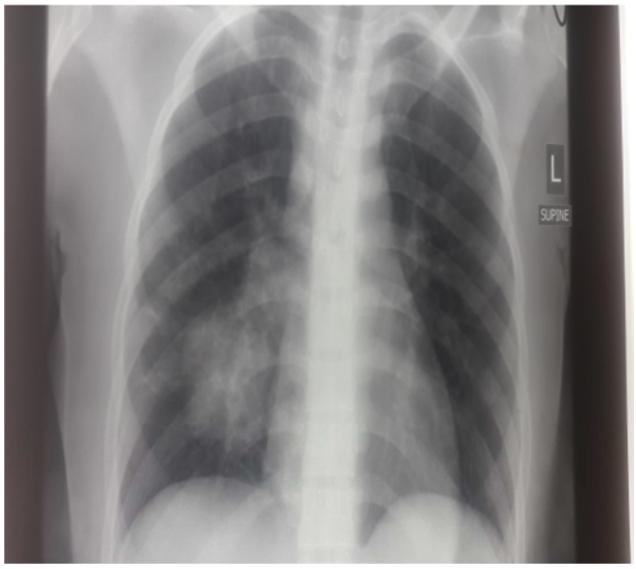

Figure 3. *Chest Xray showing a heterogeneous opacification of lower lobe of right lung.*

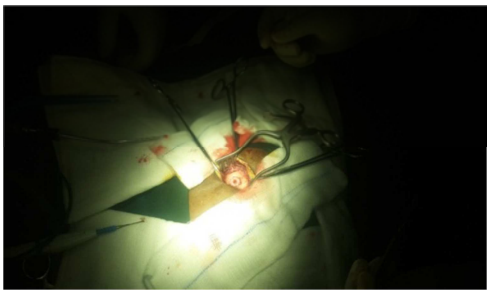

Figure 4. *Intraoperative picture.*

Histology

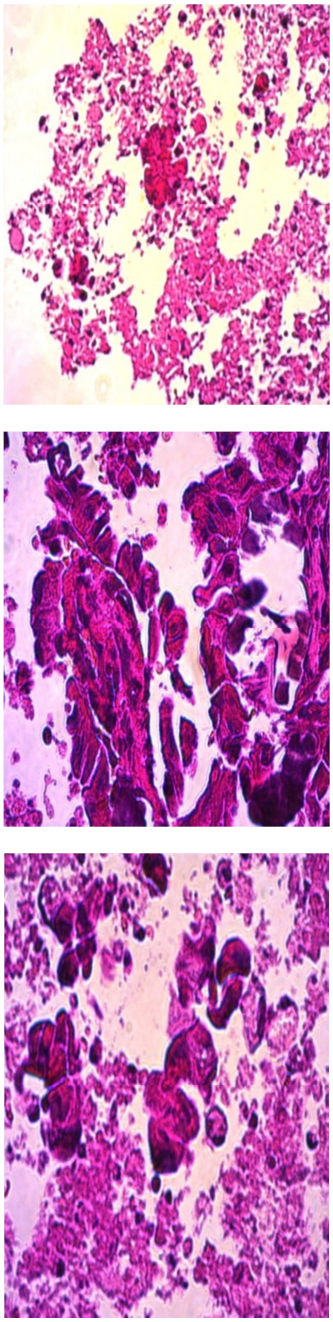

Figure 5. *The brain biopsy shows large areas of necrosis with fragments of papillary tumor. The papillae are covered by large cells with abundant eosinophilic cytoplasm and associated with psammoma bodies.*

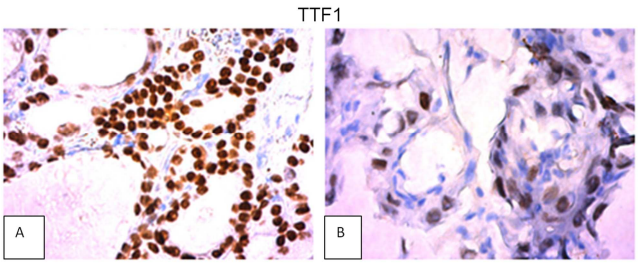

Figure 6. *The tumourimmunoreacts negatively to TTF1 A: control; B: test.*

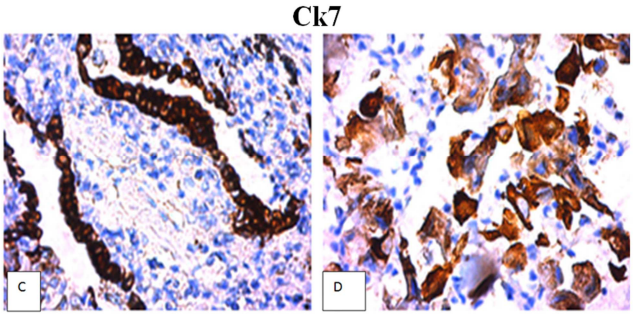

Figure 7. *The tumour immunoreacts positively to CK7; C: control; D: test.*

3. Discussion

Of the gynecological cancers, ovarian cancer is associated with the highest incidence of brain metastases. [9]

In 2011, Piura E and piura B reported 521 cases between 1978 and 2011. [10], while in 2014, Pakneshan et al. reported 591 cases between 1978 and 2013. [11] Piura and Piura determined the incidence of brain metastases from ovarian cancer to be 1.2% [10], which was twice the incidence associated with cervical [12] or endometrial cancer [13]. Pakneshan et al. reported that the incidence among the various studies ranged from 0.49 to 11.4%, with an average of 2.55% [11].

Epithelial ovarian carcinoma (EOC), which is one of the most common gynecologic malignancies, has clinical characteristics similarto those of primary peritoneal carcinoma (PPC) [14].

Endometrial adenocarcinoma is the most common gynecologic malignancy and has a low incidence of metastasis to the brain, ranging from 0.3% to 1.4% [15, 16].

The Federation of Gynecology and Obstetrics (FIGO) stage was shown to be correlated with the incidence of brain metastases. The majority of patients (>80%) with brain metastases had stage III and stage IV disease at the time of initial diagnosis. [17]

Increasing incidence of cerebral metastases may be due to a number of factors: Increasing length of survival of cancer patients as a result of improvements in treatment of systemic cancer; Enhanced ability to diagnose CNS tumors due to availability of CT and/or MRI; Many chemotherapeutic agents used systemically do not cross the blood-brain barrier (BBB) well, providing a “haven” for tumor growth there; Some chemotherapeutic agents may transiently weaken the BBB and allow CNS seeding with tumor [18].

Most metastases are localized to the cerebrum followed by

the cerebellum, and only rarely are leptomeningeal [19].

The primary mechanism of spread to the brain is dissemination to the lungs, then to the brain via the pulmonary vasculature [20]. Brain metastases from gynecological cancers are usually found in association with widely disseminated disease

Brain metastases are a major detrimental event in the natural history of most malignancies. In the majority of patients, the treatment of brain metastases is a palliative measure, because the primary disease is often advanced, and the general condition of these patients often is poor. Despite numerous studies designed to improve treatment outcome, the median survival is only 3–6 months. [21]

Diagnosis: Symptoms of brain metastases may be subtle initially, and may include headaches, nausea, vomiting, confusion, dizziness, decreased mental status, general or extremity weakness, urinary incontinence, gait disturbance, ataxia, visual disturbance including diplopia, photophobia, speech impairment, syncope or seizures [10, 22].

Imaging: Most brain metastases are diagnosed with a computed tomographic (CT) scan of the brain, which has been performed to investigate suspicious symptoms. The metastasis appears as a heterogeneous, contrast enhancing lesion [23].

Metastatic ovarian cancers can occasionally be calcified [24].

Contrast-enhanced magnetic resonance imaging (MRI) is the most accurate modality to image the brain [25].

Traditionally, patients with solitary metastases have undergone metastasectomy and whole brain radiotherapy (WBRT) [25]. The latter is associated with a number of late complications, including brain atrophy, necrosis, dementia, and endocrine dysfunction [26].

The current standard treatment for epithelial ovarian carcinoma (EOC) of all histological subtypes involves primary optimal debulking surgery followed by cisplatin-based chemotherapy. It is well known that almost all patients with EOC receive chemotherapy after initial diagnosis [27]. Some researchers have suggested that the increased incidence of brain metastasis in EOC is related to the effectiveness of chemotherapy [28], or that cisplatin-based chemotherapy may contribute to an increase in the incidence of CNS involvement [29, 30],

Thus, therapy of brain metastases with combination of surgery, WBRT and chemotherapy, or combination of surgery and WBRT or SRS (stereotactic radiosurgery)/GKRS (gamma-knife radiosurgery) yielded better survival results (median survival of 20, 17, and 18 months, resp.) than therapy of brain metastases with surgery alone, WBRT alone, chemotherapy alone, WBRT and chemotherapy, and no treatment (median survival of 6.7, 4.5, 7.5, 9.1, and 1.4 months, resp.). Thus, apparently, the best survival after diagnosis of brain metastases was achieved with multimodal therapy including surgical resection of the brain metastases followed by (whole brain radiotherapy) WBRT (± chemotherapy) or with SRS/GKRS [31].

The blood-brain barrier (BBB) is thought to limit delivery of large-in-size hydrophilic drugs to the brain, determining which agents and doses will be used [29] Additionally, some researchers think that improvement in the efficacy of chemotherapy delays reoccurrence in the abdominal and pelvic cavity, but that the BBB blocks water-soluble cisplatin and lowers the concentration in the CNS, increasing the incidence of brain metastasis [32].

Single metastasis: In general, surgery should be considered for patients with good prognostic factors when there is a single metastasis in an accessible location, especially if the tumor is producing mass effects [33].

Multiple metastases: The role of surgery in patients with multiple brain metastases is usually limited to resection of a large, symptomatic or life-threatening lesion or to obtain a tissue diagnosis. Retrospective trials of WBRT versus WBRT plus surgery for patients with multiple metastases have produced conflicting results that are reviewed elsewhere [33, 34].

4. Conclusion

Brain metastasis from ovarian carcinoma is uncommon, in the pre chemotherapy era, the incidence of brain metastasis among living ovarian carcinoma patients was almost nil because of the short survival of advanced-stage ovarian carcinoma patients that did not allow enough time for brain metastasis to develop. With the advent of chemotherapy for ovarian carcinoma, especially platinum-based chemotherapy, a considerable lengthening in the survival of advanced stage ovarian carcinoma patients with a median of about two years has been achieved. This prolonged survival has allowed sufficient time for brain metastases to develop and become apparent. Nevertheless, the notion expressed by some authors that the incidence of brain metastasis among ovarian carcinoma patients is continuing to rise in the post chemotherapy era and even approaching >10% is not supported by most series published in the literature that show that the incidence of brain metastases among ovarian carcinoma patients is usually within the range of 1–3% [31].

Although gynecologic cancers rarely metastasize to the brain, brain metastasis in such cases has a poor prognosis despite combined treatment modalities. Radiation therapy and surgery are effective in only partially removing masses.

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