Abstract:
Intracranial neoplasms usually produce an insidious onset focal neurological deficit, though a sudden onset is not uncommon and is due to hemorrhage within a tumour, tumour embolism, or an embolism from non thrombotic endocarditis. A similar presentation was seen in a 27 year old female with 40 days amenorrhoea who presented with new onset simple partial seizures involving right upper limb and acute onset right facio-brachial monoplegia followed by bleeding per vaginum. She had attained menarche at 17 years of age and had a history of termination of pregnancy 4 months back after a period of 4 months amenorrhoea details of which were not available at the time of presentation. She had no history suggestive of rheumatological or hematological disorders. Her menstrual cycles were normal since menarche. Complete hemogram, Renal function test, Bleeding time, Clotting time, PT, APTT were within normal limits. Chest X ray, ultrasonogram abdomen were found to be normal. CT brain showed multiple intraparenchymal hemorrhage with surrounding edema in left parietal region. MRI brain showed ill defined areas of T1 hyperintensity in left frontoparietal region, areas of T2 hypointensity, blooming on gradient sequences, and not suppressed in FLAIR sequences with a normal MRA and MRV.ANA, Protein C, Protein S, S.Homocysteine were found to be normal. HIV ELISA, VDRL, HbsAg, Anti HCV were found to be negative. A review of obstetric history with previous records after two days which suggested a previous hydatiform mole and a raised serum Beta HCG found subsequently suggested the possibility of choriocarcinoma with brain metastasis. CSF Beta hCG was raised indicating possible brain metastasis. She was treated with chemotherapy (EMA-CO regimen) and radiotherapy for brain metastases along with intrathecal Methotrexate which was followed by remission. This case is presented due to the uncommon nature of presentation of choriocarcinoma and due to the rare occurrence of brain metastasis without lung secondaries.
Keyword: Simple partial seizures, Intracerebral hemorrhage, Choriocarcinoma, Metastasis

CASE REPORT:
A 27 year old female who had a history of 40 days amenorrhoea came with complaints of

- Involuntary movements involving right upper limb of 2 days duration
- Weakness of right upper limb of 2 days duration
- Deviation of angle of mouth to the left side of 2 days duration
- Bleeding per vaginum for past 1 day

Pregnancy was confirmed at 38 days amenorrhoea by urine gravindex test. The involuntary movements and weakness were of sudden onset with no loss of consciousness. She had headache involving both hemicranium, intermittent, throbbing not interfering with sleep. She did not have sensory disturbances, bowel and bladder disturbances.

She had a history of termination of pregnancy 4 months back after a period of 4 months amenorrhoea, details of which were not available at the time of presentation. She had attained menarche at 17 years of age and menstrual cycles used to be regular.

On examination, her vitals were stable with Pulse rate of 82/min and Blood Pressure of 130/80 mm Hg. Cardiovascular system, Respiratory system and per abdomen examination were normal. She had mild bleeding PV. Central nervous system examination showed right UMN type of VII nerve palsy and right upper limb monoparesis. Fundus examination was normal.

She was started on anti cerebral edema measures and antiepileptics. Complete hemogram, Renal function tests, Liver function tests, Chest X ray, ECG in all leads, Echocardiogram, Peripheral smear study, Bleeding Time, Clotting Time, Prothrombin Time, Activated Partial Thromboplastin Time were found to be within normal limits. Ultrasonogram abdomen showed echogenic contents in endometrial cavity suggestive of either clots or retained products of conception. A repeat ultrasonogram

The provisional diagnosis was Recurrent abortion, Acute cerebrovascular accident, Right Faciobrachial monoparesis, Simple partial seizures

Fig 1: CT Brain
done after a day was found to be normal. HIV ELISA, VDRL, HbsAg and anti HCV were negative. ANA, Protein C, Protein S, S.Homocysteine were within normal limits.

MRI Brain showed ill defined areas of T1 hypointensity in left frontoparietal region, areas of T2 hypointensity. Blooming on gradient sequences, not suppressed in FLAIR sequences with normal MRA and MRV suggesting the possibility of hemorrhagic metastasis.

When the past obstetric history was reviewed with previous records, USG abdomen done after 4 months amenorrhoea revealed a vascular mass with multiple cystic areas in endometrial cavity suggestive of hydatiform mole. Histopathology was also consistent with hydatiform mole. Based on this history serum beta HCG was done which was 27616.68 mIU/ml (normal range in non pregnant is <10mIU/ml). CSF beta HCG was 1021.12mIU/ml. So the revised diagnosis was Gestational Trophoblastic Neoplasia, Choriocarcinoma with Brain metastasis. Steroids were added in the form of intravenous Dexamethasone. CT Chest and CT Abdomen done as a part of treatment. She was given WBRT 10 doses of 300 cGy over 2 weeks and was started on Chemotherapy with EMA-CO regimen consisting of Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide and Vincristine along with Intrathecal methotrexate and Folinic acid. She showed clinical improvement of weakness, subsidence of seizures and her serum beta HCG levels dropped to 1178.24 mIU/ml and 51.7 mIU/ml following successive courses of chemotherapy indicating remission. A repeat screening MRI showed resolution of hemorrhage.

**DISCUSSION:**

It is known that primary and metastatic intracranial neoplasms can sometimes cause intracerebral haemorrhage, which in about half of the cases may be the first manifestation of tumour.[1] However, on general basis, metastatic tumours bleed more often than primary CNS neoplasms. Choriocarcinoma, bronchial carcinoma, melanoma and renal cell carcinoma have been reported to be the metastatic tumours more often responsible for intracerebral haemorrhage,[2] apart from lymphoreticular malignancy. Gestational choriocarcinoma is a rare tumour in the West, but its incidence is
Choriocarcinoma is a malignant tumour of cytotrophoblasts and syncytiotrophoblasts, which can arise in any type of gestation and the types of preceding pregnancy includes most often hydatiform mole followed by normal pregnancy, spontaneous abortion or ectopic pregnancy. Primary placental choriocarcinoma can easily be missed due to their small size. Choriocarcinoma is known to spread by the vascular route and often metastasises to the central nervous system (CNS). The incidence of CNS metastasis from gestational choriocarcinoma has been reported to range from 3% to 28%\[^3\]. This wide range of incidence is probably due to varying referral and follow up patterns at different centres. Despite the fact that prognosis of primary disease has improved greatly with effective chemotherapeutic agents, presence of metastasis in the CNS is considered an adverse prognostic factor. Choriocarcinoma is suspected when there is persistent or irregular uterine haemorrhage, following abortion or hydatidiform mole. Rapid growth and haemorrhage make the tumour a medical emergency. The most common sites of metastasis are the lungs (in 80% of patients), vagina (30%), pelvis (20%) and liver (10%). Cerebral metastases occur in about 10% of the cases. \[^4\]\[^5\] The central nervous system is seldom involved in the absence of pulmonary metastasis \[^6\]. Ishizuka et al\[^6\] reported pulmonary metastasis in 27 out of 28 patients with brain metastasis in patients with gestational choriocarcinoma. However, metastatic cerebral choriocarcinoma without pulmonary metastasis has been reported in literature. \[^7\]\[^8\] Metastatic disease occurs in 4% of patients after local management of hydatidiform mole and very rarely after term pregnancies or abortions. Radioimmunoassay of beta human chorionic gonadotrophin (hCG) should be used to confirm the diagnosis. The diagnosis is usually based on a rising human chorionic gonadotropin level or a plateau in the level that persists for more than three weeks. \[^9\]\[^10\] It is estimated that serum : CSF ratio of less than 60:1 is a sensitive indicator of metastasis in the brain. The prognosis of choriocarcinoma with cerebral metastasis has improved considerably with time. Earlier, only about one third of cases presenting early with CNS presentation survived and none with late CNS presentation. After 1974, intrathecal prophylaxis with methotrexate given in high risk patients has improved the overall survival to 80% in the CNS presentation group and 25% in the late CNS group. \[^10\]\[^11\] Difficulties in the diagnosis and management of unsuspected gestational choriocarcinoma presenting with intra cerebral haemorrhages continue. Differential diagnosis in such a clinical scenario include cerebral venous thrombosis (CVT), tumour, haematoma and arterio venous malformation (AVM) with bleed. In an unsuspected case, heparin therapy with a clinical diagnosis of cerebral venous thrombosis in post partum period may lead to catastrophic haemorrhage. Measurement of hCG in CSF and serum further helps to implement early therapy and effective management of these patients. Histopathological examination of the surgically removed blood clots remains the corner stone for accurate diagnosis. The management is typically chemotherapy, although surgery can play an important role for disease that is persistently isolated in the uterus (especially if childbearing is complete) or to control haemorrhage. For women wishing to maintain fertility or with metastatic disease, the preferred treatment is chemotherapy. Chemotherapy is guided by the hCG level, which typically drops to
undetectable levels with effective therapy. Single-agent treatment with methotrexate, or actinomycin D 90% cures of women with low-risk disease. Patients with high-risk disease (high hCG levels, presentation 4 or more months after pregnancy, brain or liver metastases, failure of methotrexate therapy) are typically treated with multi-agent chemotherapy [e.g., etoposide, methotrexate, and actinomycin D alternating with cyclophosphamide and vincristine (EMA-CO)], which is typically curative even in those women with extensive metastatic disease. Cisplatin, bleomycin, and either etoposide or vinblastine are also active combinations. Survival in high-risk disease exceeds 80%. Cured women may get pregnant again without evidence of increased fetal or maternal complications. Surgical treatment is the method of choice for brain metastasis in patients displaying rapidly deteriorating signs. A better prognosis will be achieved by a combination of surgical removal, chemotherapy and irradiation.[11]

CONCLUSION:
A circumscribed haemorrhagic lesion with perilesional oedema in young women of reproductive age group should raise the suspicion of metastatic choriocarcinoma. Measurement of hCG in CSF and serum further helps to implement early therapy and effective management of these patients. Histopathological examination of the surgically removed blood clots remains the corner stone for accurate diagnosis. This case also illustrates the need to consider the diagnosis of metastatic cerebral choriocarcinoma even if pulmonary examination is negative.

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