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Case Report

Meningioma or dural-based metastasis: ^{68}Ga DOTA-TOC PET/CT as a problem-solving tool

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Abstract: - Positron emission tomography/computed tomography (PET/CT) using 68Ga-DOTA-conjugated peptides (68Gallium DOTA-(Tyr3)-octreotide) is a non-invasive diagnostic technique to assess tumors with a high affinity for somatostatin receptors (SST). Besides neuroendocrine tumors, several other tumors express SST; meningioma being one of them. We report the case of a 35-year-old female, diagnosed with choriocarcinoma, and detected to have an intracranial space occupying lesion at the time of staging investigations. The patient underwent both 18F-2-fluoro-2-deoxy-D glucose (18F-FDG) and 68Ga-DOTA-TOC PET/CT scans, which showed reduced uptake on 18F-FDG and intense uptake in the lesion on the 68Ga-DOTA-TOC PET/CT scan. The radiological picture was suggestive of meningioma. The patient was treated with combination chemotherapy for choriocarcinoma to a state of complete serological remission, without the need to biopsy the space occupying lesion and spared the patient of escalated doses of chemotherapy. Surgical excision of the brain lesion confirmed the diagnosis of Meningioma (Grade II)

Keywords: Choriocarcinoma; Gallium Radioisotopes; Meningioma; Positron-Emission Tomography

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Introduction:

Choriocarcinoma is an aggressive tumour of the gestational trophoblast of the placenta. It is a highly vascular tumour and shows rapid hematogenous metastases.[1] The site of metastasis includes lungs (80%), vagina (30%), pelvis (20%) and liver (10%). Brain

metastases are reported in 10% of patients.[2] Brain metastases are usually accompanied by lung and vaginal metastases.[3] Presence of cerebral metastases is considered a poor prognostic factor, and the presence of tumour mass and hemorrhage can lead to death. Treatment of cerebral metastases includes surgery, radiotherapy and/or chemotherapy and timely management can improve survival in these patients.[1.]

Meningiomas are the most common dura-based tumour.[4] Meningiomas can be further classified as either typical: grade I (most common, and benign), atypical; grade II and malignant: Grade III, which are more aggressive tumors. [5] Although biopsy is the standard of care for diagnosis, it is not always possible or desirable.

Differentiating meningioma from dura-based metastases on conventional CT scan or MRI is challenging, as meningioma and metastatic deposits have overlapping radiological features.[6]

PET/CT with radiotracer ^{18}F-FDG is widely used for assessing metabolic activity of tumour tissue. It has the ability of whole-body coverage in one examination and is widely used to diagnose metastatic sites. However, its role in detecting either meningioma or brain metastases is limited, due to high physiological brain uptake. In addition, high FDG uptake may also be seen in inflammatory conditions, which can lead to further diagnostic dilemma[5,7.]

PET/CT using highly specific radiotracer ^{68}Ga-DOTA-conjugated peptides (DOTA-NOC/DOTA-TOC/DOTATATE) is a non-invasive diagnostic technique to assess neuroendocrine tumors due to the high affinity of these compounds for SST receptors. The primary role of ^{68}Ga-DOTA-conjugated peptide PET/CT is staging, follow up, and selection of candidates for radionuclide therapy in patients with neuroendocrine tumors. Meningiomas are known to overexpress SST receptor, subtype-2.[8] Due to the high receptor binding and high tumour-to-background ratio, ^{68}Ga-DOTA-conjugated peptide PET/CT scan offers an excellent imaging modality for diagnosis of meningioma. ^{68}Ga-DOTA-conjugated peptides also provides additional information on tumour delineation, tumour growth rate and treatment planning.[9] The present article reports a case of intracranial SOL in a patient of choriocarcinoma, which on ^{68}Ga-DOTA-TOC PET/CT was suggestive of meningioma and later proved to be meningioma on biopsy.

Case Report:

A 35-year-old female, previously known to have polycystic ovarian syndrome, presented with postpartum hemorrhage, 2 weeks after intra-uterine death of the fetus. She was gravida 5, para 4. There were no other symptoms except for occasional headache for the past 2-3 years. There was no history of vertigo. On examination, the uterus was bulky. The rest of the examination of the abdomen and the chest were unremarkable, and there were no signs of cranial nerve involvement, or motor weakness in the limbs.

Recurrent vaginal bleeding was managed with uterotonics, uterine artery embolization and blood transfusion. Laboratory investigations revealed a very high β -HCG (923,100 IU/L). A computed tomography (CT) scan showed an endometrial mass measuring 12.5 cm in the long axis and 6.7 cm in transverse dimensions, and bilateral pulmonary nodules suggestive of metastases. Biopsy from the uterine mass confirmed the diagnosis of gestational trophoblastic neoplasm (choriocarcinoma) (Figure 1). Magnetic resonance imaging (MRI) of the brain showed a dura-based left frontal lobe space-occupying lesion (SOL) with significant vasogenic edema and a midline shift to the right side, suspicious for either meningioma or metastases (Figure 2A,B).

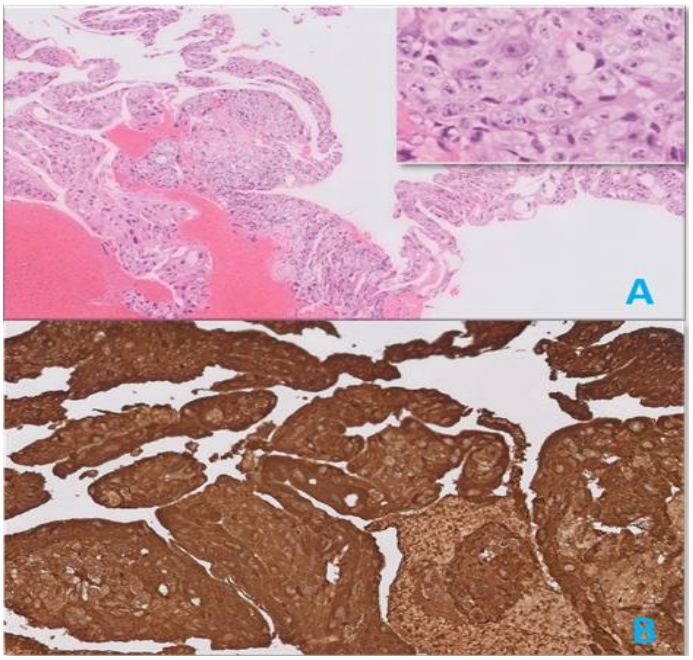

Figure 1. a) H&E, 10x, showing malignant syncytiotrophoblast & cytotrophoblasts with hemorrhage in the background with inset (H & E, 60x) highlighting large cells with pleomorphic hyperchromatic nucleus b)

IHC showing strong positive cytoplasmic staining for beta HCG

Past medical history was not significant for any illness. Family history was significant for non-Hodgkin lymphoma (brother), breast cancer (maternal cousin), and gastric cancer (maternal cousin).

Subsequent investigations revealed a 'very high-risk' gestational choriocarcinoma, (FIGO score: 15). The patient commenced on non-cross-resistant chemotherapy (EMA/EP). A significant clinical and serological improvement was observed after 2 cycles of chemotherapy and the β-HCG reduced to 37 IU/L. A CT scan of the chest, abdomen and pelvis showed a significant regression in the size of the primary disease and the pulmonary nodules. However, MRI of the brain did not show change in size or morphology of the left frontal lobe lesion. An accurate diagnosis of the SOL of the brain was crucial as it would have altered the chemotherapy plan, and the patient may have to be treated with surgery, radiotherapy, and high-dose methotrexate. The patient underwent ^{68}Ga DOTA-TOC PET/CT and ^{18}F FDG PET/CT scan. Whereas, the ^{18}F-FDG PET/CT scan showed no metabolic activity in left frontal lesion, the ^{68}Ga DOTA-TOC scan showed intense tracer uptake in the lesion, highly suggestive of meningioma. (Figure 2C,D). The patient received a full course of chemotherapy and showed complete serological and radiological remission 5 months after completion of treatment. A repeat MRI of the brain did not show change in the size or morphology of the left frontal SOL, and persistent midline shift and headache. Excision of the mass was performed, and the pathology was consistent with a diagnosis of meningioma grade II (Figure 3). The patient is doing well and continues to be in complete serological and radiological remission.

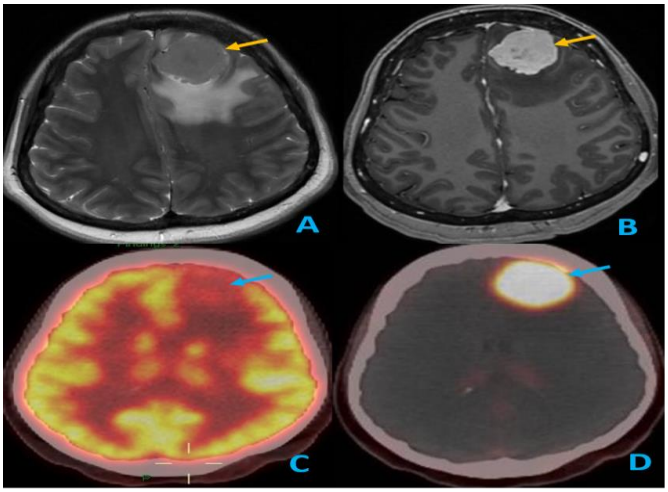

Figure 2: Space occupying left frontal lobe mass lesion; a) Axial T2W image shows a large intermediate signal intensity lobulated extraaxial soft tissue mass with perilesional vasogenic edema and mass effect b) corresponding axial T1W Fat suppressed sequence shows intense contrast enhancement c) ^{18}F-FDG PET/CT scan do not show metabolic activity d) ^{68}Ga DOTATOC scan shows intense tracer uptake in the lesion suggestive of meningioma.

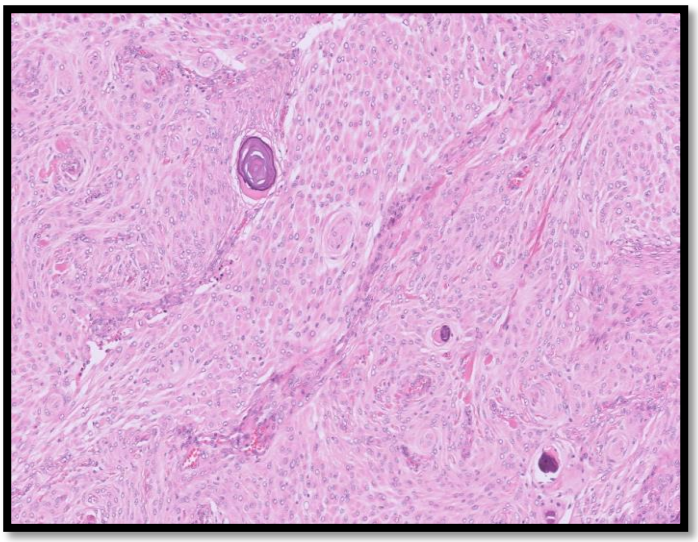

Figure 3: H& E, 10x: neoplastic meningothelial cells arranged in whorls with scattered psammoma bodies suggestive of Meningioma, grade II.

Discussion:

Choriocarcinoma is an aggressive tumour which shows brain metastases in 10% of patients.[2] Meningioma are also the most common dural based tumour[4] and co-existence of meningioma in a patient with known malignancy is often seen in clinical practice.

The patient presented with a SOL in left frontal lobe, and in presence of a very high β –HCG, suggested the diagnosis of metastasis to brain. However, the MRI showed a dura-based lesion raising the possibility of a variety of differential diagnosis including metastases, primary neoplastic lesion, granuloma, meningioma etc. Although biopsy is the standard of care for diagnosis, it was not possible or desirable, because of rapidly progressive metastatic choriocarcinoma, and the need to initiate systemic treatment urgently.

Radiological imaging including CT and MRI are standard modality for assessment of brain lesions. On CT scan typical meningioma are hyperdense to isodense to the cortex and some of them show calcification and

adjacent bone hyperostosis. On MRI meningioma are isointense to cortex and perilesional edema is seen in half of the cases. Strong enhancement with dural tail sign is seen in post contrast MRI images. However, these imaging features are not pathognomonic, and many mimics demonstrate overlapping imaging features. High perfusion as seen in meningioma, can also be seen in hypervascular metastases.[4] The dural tail sign described for meningioma is not specific to meningioma.[10] Dural metastases can be seen in primary tumors of the breast, prostate, lung, bowel and germ cell tumours. Radiologically they show dural thickening and vasogenic edema. These metastases show strong enhancement with presence of dural tail in half of them mimicking meningioma. In addition, the lesion is sometimes obscured due to presence of associated haemorrhage, making its characterization difficult.[4] Many case reports in literature have described brain metastases diagnosed as meningioma on CT scan and MRI and *vice versa*. For example, EL Mehdi *et al*, reported a case of dural metastases from thyroid follicular carcinoma, misdiagnosed as meningioma. A definitive diagnosis was established only with histopathological analysis. [11] Similarly, brain metastases from various tumors including prostate, Ewing sarcoma/peripheral primitive neuroectodermal tumor, breast cancer, renal cell carcinoma, and lung cancer, mimicking meningioma has been reported.[12, 13, 14, 15, 16] Our case showed similar dilemma with differential of meningioma versus dural metastases on MRI.

PET/CT with ^{18}F-FDG is routinely used for staging various cancers. Due to slow growing tumour, FDG uptake in meningioma is usually moderately elevated [5] and its limited role in assessment of brain tumors is well known.

PET/CT with ^{68}Ga-DOTA-conjugated peptides is an excellent modality for assessment of meningioma due to overexpression of SSTR. It has high ability to detect meningioma, including the smaller lesions. It is especially useful when MRI results are equivocal, and biopsy is not possible or difficult. It can be used to confirm MRI diagnosis of meningioma as well.[8]

Published studies have shown a role of ^{68}Ga-DOTA-conjugated peptides in differentiating meningioma from metastases. For example, Purandare *et al* showed that ^{68}Ga DOTA peptides can differentiate dura-based metastases from meningioma. [17] Similarly, Unterrainer reported a case of breast cancer with 2 dura-based lesions, which were labelled as either metastases or meningioma. ^{68}Ga DOTA PET/CT scan showed high uptake in one of the lesion and was subsequently proven to be meningioma on biopsy. The other lesion which had only a bare uptake on ^{68}Ga DOTA PET/CT scan proved to be metastasis on histopathology after excision.[18]

The case presented here highlights the use of ^{68}Ga-DOTA PET/CT in differentiating meningioma from brain metastases in a patient with choriocarcinoma. Differentiating dural metastasis from meningioma non-invasively resulted in a significant impact on the management, by sparing the patient of the need for biopsy, unnecessary dose escalation of chemotherapy, or the use of radiotherapy.

In conclusion, we report the case of a young lady diagnosed to have metastatic choriocarcinoma, and a SOL in brain. ^{68} Ga DOTA-TOC PET/CT scan helped to differentiate meningioma from dural metastases non-invasively. Knowledge of tumors expressing various peptides may help to choose the correct isotope for the PET/CT scan and the timely utilization of these modalities lead to significant improvement in patient management.

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