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Case Report: Hemorrhagic Central Neurocytoma

Khawand Saeed Perdawd
MBChB, Trainee at Iraqi Board of Medical Specializations-Neurosurgery
Hawler Teaching Hospital
https://orcid.org/0009-0003-8553-1627

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Abstract

Central neurocytomas are infrequent tumors, yet they represent the most common primary intraventricular neoplasm among young and middle-aged adults. Their slow growth typically results in detection during the 2nd-4th decades of life, with an even distribution between genders. Due to its rarity and similar features to more common neoplasms, misdiagnosis can pose challenges. Accurate diagnosis often involves radiological imaging, MRS, histopathology, and immunohistochemistry assessments. This was a case report of a 47-year-old man with a right lateral ventricular central neurocytoma accompanied by intraventricular hemorrhage. Surgical intervention through craniotomy resulted in partial mass removal using a transcortical approach. He was referred to the oncology team who recommended radiotherapy. Subsequent hydrocephalus led to a VP shunt placement.

Keywords: *central neurocytoma, hemorhhage*

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Introduction:

Central neurocytoma is a benign and rare tumor originating from cells in the germinal matrix located near the foramen of Monro within the septum pellucidum. It often shows a preference for the left frontal horn but can also arise in the periventricular region. These tumors account for 0.25%-0.5% of all primary brain neoplasms. They are categorized as WHO grade II lesions (1, 2). While astrocytomas, ependymomas, oligodendrogliomas, and primary cerebral neuroblastomas are potential differential diagnoses, a definitive diagnosis can be established through immunohistochemistry (3).

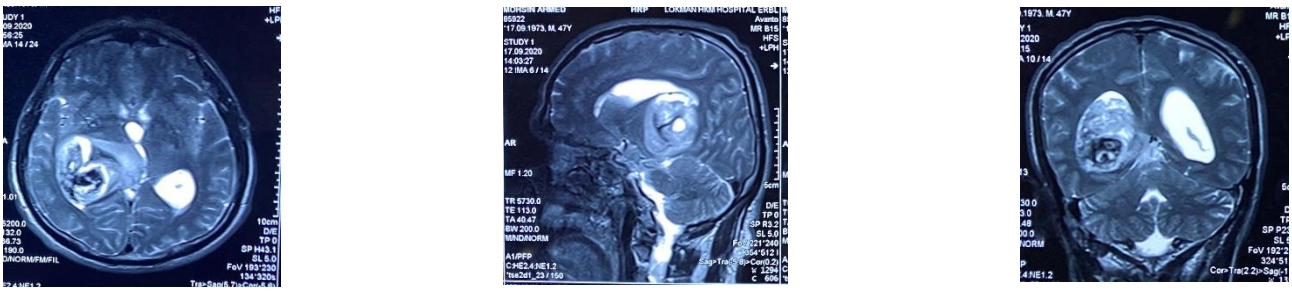
Presently, there appears to be no gender preference for central neurocytomas, although historically, it was believed that females had a higher susceptibility (1, 4). Patients typically exhibit symptoms associated with increased intracranial pressure, including frequent headaches, vomiting, and papilledema. Additionally, manifestations of mass effect like gait disturbances, seizures (in cases with extraventricular extension), or even hemiparesis may occur, albeit rarely. There are instances of abrupt onset due to intraventricular hemorrhage (4, 5).

Surgical resection is the primary treatment, offering an excellent prognosis when complete removal is achieved. In cases of incomplete excision, radiation therapy serves as an adjunctive approach (5, 6). Approaches for tumor removal can include transcortical, transcallosal, or endoscopic methods.

Case Presentation:

A 47-year-old man, without any known medical conditions, visited the neurosurgery outpatient clinic due to a one-month history of headache, vomiting, and blurred vision. Examination showed bilateral papilledema upon fundus examination.

A brain MRI with and without contrast was conducted, revealing a distinct lobulated mass located in the right occipital horn and body of the lateral ventricle. The mass extended beyond the ventricle and appeared isointense to gray matter in T1, displaying heterogeneous regions. In T2, it appeared iso to hyperintense with central hypointensity, indicative of intratumorally hemorrhage. There was slight enhancement observed after gadolinium administration. The presence of the tumor led to midline shift due to mass effect.



Pre-op

Figure 1: MRI T2 (Axial – Sagittal – Coronal)

Hence, the patient underwent craniotomy for tumor removal via right parieto-occipital transcortical approach. The cortex was exposed in the right parieto-occipital region, followed by dissection through the white matter until reaching the tumor situated within the occipital horn and posterior section of the right lateral ventricle. The tumor lacked a distinct capsule and displayed a soft consistency. Its color ranged from grayish to brown, showing signs of invading the brain tissue with unclear boundaries between brain and tumor. Numerous thrombosed veins were visible, along with many vessels traversing through the deepest areas and the presence of hematoma. Substantial removal of the mass was performed, and the dura mater was meticulously closed.

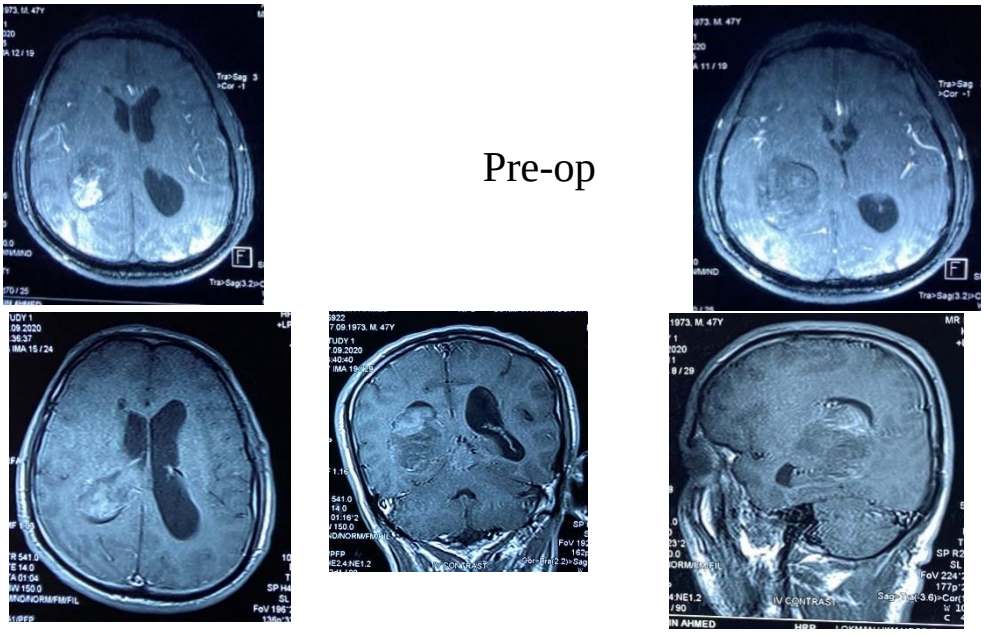


Figure 2: MRI T1 (Axial – upper images)
T1 with contrast (Lower images)

After the surgery, the patient was gradually taken off the ventilator. He spent the night in the ICU and was subsequently moved to a regular ward. Upon examination, no abnormalities were detected, and he was discharged home after 3 days. The excised tumor was sent for histopathological analysis. Under the microscope, the tumor displayed sheets of uniform and unremarkable glial cells with perinuclear halos, arranged within a vascularized fibrillary matrix. Additionally, a few calcospherites were observed, along with inconspicuous mitotic activity. However, no microvascular proliferation or areas of necrosis were evident. Immunohistochemistry revealed widespread synaptophysin expression in the tumor cells, while they tested negative for GFAP. The Ki67 labeling index was found to be less than 2%. Based on these findings, the final pathological diagnosis indicated a Central Neurocytoma classified as WHO grade II.

Ten days post-surgery, the patient underwent an examination, during which the stitches were removed. Notably, he was no longer experiencing headaches or vomiting, and his vision had returned to normal.

Given the partial removal of the mass, the patient was subsequently referred to the oncology department for further treatment. The proposed adjuvant therapy includes options such as radiation and/or chemotherapy to complement the surgical procedure.

The oncology team suggested initiating radiation therapy, and consequently, the patient underwent a series of radiotherapy sessions as part of their treatment plan.

One month post-surgery, the patient began experiencing weakness on the left side of his body. During examination, it was found that the power of the left upper limb was graded at 3/5, and the left lower limb at 2/5. Alongside these symptoms, the patient also complained of headaches, vomiting, and visual issues.

A brain MRI conducted with gadolinium contrast indicated that the remaining tumor was exerting pressure on the cerebrospinal fluid (CSF) pathway, leading to hydrocephalus and resulting in periventricular edema.

Consequently, Ventriculoperitoneal shunt (VP) was performed to the patient. After the shunting procedure, the patient's symptoms of headache and vomiting improved. However, the weakness in the left side of the body worsened compared to the condition prior to shunting. The power of the left upper limb decreased to 2 out of 5, and the left lower limb's power dropped to 1 out of 5.

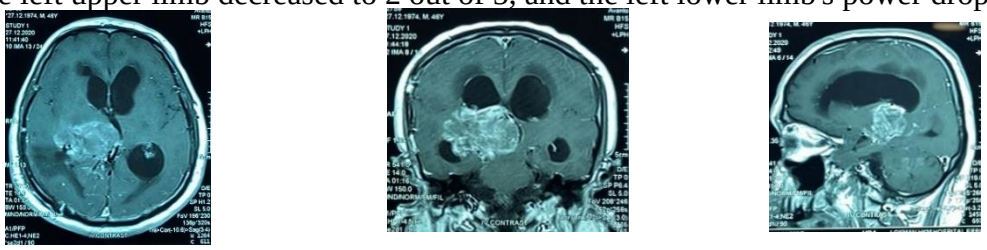


Figure 3: Post-Op MRI T1 with contrast (Hydrocephalus)

Regrettably, two days following the VP shunt surgery while still hospitalized, the patient experienced sudden and severe chest pain along with shortness of breath. An ECG revealed an extensive myocardial infarction (STEMI). Despite efforts at cardiopulmonary resuscitation, the patient's condition deteriorated, and he passed away.

Discussion:

Central neurocytomas are uncommon yet well-differentiated tumors thought to originate from ectodermal neurons (7, 8). They constitute less than 1% of primary CNS tumors. Spontaneous intraventricular hemorrhage is extremely rare (9, 10). While most literature indicates no sex predilection (13, 14), some studies suggest a slightly higher prevalence in men, although one study showed a female predominance (11). These tumors typically affect individuals between 20-40 years old, with the peak occurrence in the third decade of life (9-13).

In terms of location, central neurocytomas are primarily situated deeply in the midline, often near the foramen of Monro in the frontal horn of the lateral ventricle. They can attach to the septum pellucidum, leading to extension into the third ventricle (11, 13, 15). However, they can also be

found in other areas such as the third and fourth ventricles (14, 16), brain parenchyma, or even the spinal cord (11, 13, 14). Generally benign, central neurocytomas have a favorable prognosis with appropriate treatment, although more aggressive and atypical malignant forms have been identified (7, 11, 14).

CLINICAL PRESENTATION:

Central neurocytomas typically have a gradual onset, ranging from a few days to several years, but they commonly become apparent within 3 to 6 months (14, 17). Due to elevated intracranial pressure, often with secondary obstructive hydrocephalus, patients often experience symptoms like headaches (most common), nausea, vomiting, visual disturbances, and vertigo. On examination, papilledema and ataxia are frequently observed signs (14, 18).

Additionally, atypical presentations can include seizures, memory problems, cognitive changes, and numbness or weakness in the limbs (13, 14, 17). Although rare, cases of sudden hemorrhage into the ventricle or brain parenchyma have been documented (9, 17, 19, 20).

A retrospective study indicated that 7.9% of 69 patients had hemorrhagic central neurocytomas. Additionally, Gunawat et al. reported two cases of central neurocytomas with intraventricular hemorrhage, both presenting with sudden headache and vomiting (19)

The exact cause of hemorrhage remains uncertain (9, 20), but potential factors include thrombocytopenia, hypertensive heart disease, aneurysms on feeding vessels, and the fragile nature of tumor vessels (9, 19, 20). This intra-tumoral hemorrhage can serve as a distinguishing factor between central neurocytomas and other intraventricular masses that are less likely to bleed.

RADIOLOGY:

Central neurocytomas typically present as well-defined, lobulated masses within the lateral ventricles, often attached to the septum pellucidum. On CT scans, they exhibit mixed density, with hypodense regions indicating cystic degeneration. Calcification, found in 20-50% of cases, can appear as patchy, globular, coarse, or clumped areas. Hemorrhagic changes are occasionally visible. Mild to moderate enhancement is observed after contrast administration.

On MRI, central neurocytomas show a heterogeneous iso to hypointense appearance in T1-weighted images, while T2-weighted images display an iso to hyperintense, soap-bubble-like multi-lobulated aspect. After gadolinium injection, variable enhancement is common, often displaying moderate enhancement. Hypointensities or patches in both T1 and T2 MRI images suggest the presence of hemorrhage, calcification, or cysts. In the pre-operative stage, the list of differential diagnoses included central neurocytoma, ependymoma, oligodendroglioma, and choroid plexus papilloma. Choroid plexus papillomas are primarily located in the posterior fossa in adults, while ependymomas typically lack cysts and rarely exhibit calcification.

Central neurocytomas (CNs) are predominantly situated within the supratentorial ventricular system. They extend into the third ventricle in around 26% of cases, and in rare instances, they can even extend outside of the ventricles (22).

SURGERY:

Total excision, through transcallosal, transcortical, or endoscopic approach, is the gold standard treatment (24, 25). In only 30-50% of the cases it was resected totally (2, 8, 13), most likely because it is vascular and adherent to adjacent structures (2). 5-year survival rate after total resection was 99% while subtotal excision resulted in 86% 5-year survival rate (8, 13). However, there should be a consideration of a balance between benefits and risks of the surgery since severe neurological deficits and deterioration may result from insisting of tumor resection excessively and aggressively (21).

Based on a systematic review, the complication rate was found to be 31% after gross total excision of CN. In contrast, the complication rate after achieving the maximum safe excision followed by radiotherapy was 24% (25).

Indeed, the primary goals of the surgery are to achieve the utmost removal of the mass while minimizing neurological aftereffects, obtaining a representative sample for accurate histopathological diagnosis, and restoring cerebrospinal fluid flow (14). The choice of surgical approach is influenced by the tumor's location as well as the surgeon's personal expertise and practice (2, 15). Excising CN can be difficult due to its large size, deep positioning near crucial structures, and occasional high vascularity (21). Therefore, for a tumor in the 3rd ventricle or both lateral ventricles without dilatation and to avoid cortical injury, the transcallosal approach is mainly chosen and performed (2,10,15, 21, 25). For easily reaching the lateral ventricle tumor, to minimize the risk of injury to the parasagittal veins and fornix, to avoid incising the corpus callosum, and to operate on large tumors transcortical approach is preferred (2, 8, 15, 25) . Absolutely, when selecting the approach, it's crucial to take complications into account. The transcallosal approach has been linked to complications such as memory deficit, hemiparesis, aphasia, mutism, and disconnection syndromes. Conversely, the transcortical approach is associated with convulsions, memory loss, confusion, mutism, and aphasia (2)

Interestingly, despite these considerations, a retrospective study involving 63 patients didn't show significant differences in terms of neurological complications and extent of excision when comparing different surgical approaches (15, 25). Complication rates were similar between these approaches (2). To mitigate complications associated with open surgery, endoscopic tumor removal procedures have been utilized (25)

In a study by Cheng et al., endoscopic surgery exhibited lower mortality and morbidity rates compared to open surgery for intraventricular tumor resection (24). Three patients underwent endoscopic tumor resection without major complications, confirmed radiologically (24). Another

retrospective study involving 86 patients indicated a 3.5% incidence of hemorrhagic complications following endoscopic intraventricular tumor resection (24)

Neuronavigation system was deployed for safety and accuracy purposes as image-guided for neurosurgical operations to localize and delineate brain lesions, thus, ensuing maximum safe excision. However, brain shift intra-operatively may limit its accuracy (26). Therefore, intraoperative ultrasound has been used as fast and a real-time image which gives a correlation between the images obtained intraoperatively and preoperative images which are embedded in neuronavigation system (26, 27). It also helps in identification of challenges intraoperatively, such as CSF deliquoration, rapid visualization of hematoma, poor distinct microscopic boundaries and blood clot and tumor residual detection in chambers of the ventricles and surgical cavities (27).

For residual and recurrent tumors radiotherapy has been used as adjuvant therapy (14, 28). A study by Mahavadi et al. showed that recurrence rate after gross total excision with radiotherapy (GTR+RT) was 6.9% whereas 23.9% after gross total resection alone. However, GTR+RT may increase morbidity while overall survival does not look to be changed (25). Radiotherapy after subtotal resection lessens the risk of tumor progression and causes improvement in patient overall survival rate with maximum safe excision, which is 93% in al level compared to GTR (95.5%) and GTR+RT (95.3%) (25). In case of recurrence, a stereotactic radiosurgery can be used as an alternative to conventional radiotherapy as a safe and accurate option (29). A meta-analysis study on 150 patients , received radiosurgery, revealed that overall survival rate was 98% with period of follow-up ranging from 3 to 149 patients. In these patients, 25 of them underwent radiosurgery as a primary treatment while in others it was used as adjunctive therapy. The above study concluded that for tumors that are less reachable and amenable surgically stereotactic radiosurgery can be used as an effective primary treatment (23).

In our patient, because of the large size of the tumor and hemorrhage within it, transcortical approach was chosen instead of transcallosal approach and since it was hypervascular the tumor was excised subtotally.

After the surgery, the patient was referred to the oncology department which ordered to start conventional radiotherapy.

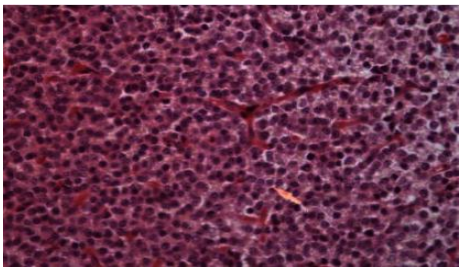
Histological:

The diagnosis of CN histopathologically is challenging since other CNS neoplasms share similar histopathological features, therefore misdiagnosis may occur.

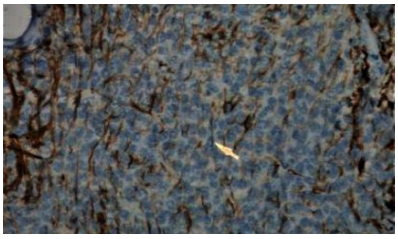
Thus, to obtain definitive diagnosis of CN, immunohistochemistry should be performed which determines the neuronal origin of the tumor.

Antibodies to synaptophysin, labeling CN in both perivascular and fibrillary areas, is the most reliable marker in immunohistochemistry. Other features of immunohistochemistry for CN include negative for glial fibrillary acidic protein and positive neuron-specific enolase (13, 14). In our case, synaptophysin in tumor cells was expressed diffusely (Figure), which are –ve for GFAP (Figure)

with Ki67 labeling index is less than 2%. In general, the histological features of central neurocytoma show uniform cells with oval or round nuclei and loose fibrillary matrix background (9).



monotonous bland neurocytoma cells



GFAP-negative neurocytoma cell expression seen in neuropil only

Figure 4: Microscopy

Conclusion:

Central neurocytoma (CN) is a slow-growing benign tumor with an excellent prognosis. However, effective local control and long-term survival are linked to total excision, the preferred treatment. Subtotal excision with residual CN, larger-sized tumors, or deeply seated tumors often requires additional adjuvant radiotherapy. In rare cases like ours, where CN presents with atypical symptoms and radiological findings, considering its slow growth and potential hemorrhagic extension into the ventricles, CN should be included in the differential diagnosis. The main goal is a complete and safe excision, resorting to subtotal resection followed by adjuvant radiotherapy if total removal isn't feasible.

Prior to sending this study for publication, a written consent was signed by the patient's son by which he agreed to use information and images of the patient.

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