A Case of Cerebral Cavernous Malformations Misdiagnosed as Multiple Myeloma

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Case Report

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Abstract

Cerebral cavernous malformations (CCMs) are angiographically occult cerebrovascular malformations (AOVMs) of the central nervous system. They are composed of a sponge-like abnormal vascular mass with numerous thin-walled vessels. CCM incidence rate is approximately 7% of cerebrovascular malformations. The clinical manifestations mainly include seizures, bleeding, headache, etc., with seizures being the most common first symptom, and some patients may be without clinical manifestations. MRI has been the specific diagnostic method for CCMs. This article reports the case of a patient initially diagnosed with multiple myeloma in the left temporal lobe at our hospital in September 2020. Later, the patient was confirmed to have CCMs through surgery and pathology. The main symptom was a sudden onset of cognitive dysfunction, and the patient was discharged after receiving symptomatic and surgical interventions.

Introduction

Cerebral cavernous malformations (CCMs) are congenital occult lesions and vascular malformations\(^1\). They are classified into intracranial and extracranial types\(^2\), associated with solitary lesions with a high bleeding risk in most cases. Early clinical symptoms of cavernous malformations are not evident, with a certain misdiagnosis rate. Therefore, it is necessary to distinguish them from intracranial lesions, including meningiomas, schwannomas, and metastatic tumors\(^3\). This article retrospectively analyzed a CMMs patient treated at the First People's Hospital of Lianyungang in September 2020. The clinical and imaging characteristics of CMMs were analyzed after combination with relevant literature, as reported below.

1. Patient information

1.1 History of present illness: A 61-year-old male patient was admitted due to sudden onset cognitive impairment. He could not use a mobile phone, turn on the TV, or recognize words. These symptoms persisted without relief. The patient possessed no history of head trauma, nausea, vomiting, fever, or seizures. He had good mental status, with normal appetite and sleep conditions. No abnormalities were detected in limb activity, urination, or defecation. The patient visited the Geriatric Department, where a head CT scan revealed a possible mass within the left brain hemisphere and the left frontal and temporal bone destruction.

1.2 Past medical history: The patient had undergone left orbital tumor resection 10 years ago due to left eye watering and protrusion from another hospital. The pathology report indicated a plasma cell tumor without any abnormal intracranial lesions. Thus, local radiotherapy was administered after surgery. In 2015, the patient visited our hospital and was found to present multiple bone destructions on the thoracic and lumbar MRI. Then, he was transferred to Jiangsu People's Hospital, where a "multiple myeloma" diagnosis was confirmed, and the patient underwent several inpatient chemotherapy treatments. In 2019,
the patient felt sudden chest tightness on the right side. The patient had a myocardial infarction and received coronary stent implantation. He has been regularly taking the medication since discharge.

1.3 Physical examination: The temperature of the patient was 36.3°C, the heart rate was 60 beats per minute, the respiratory rate was 17 breaths per minute, and the blood pressure was 142/71 mmHg. Cardiac, pulmonary, and abdominal examinations were negative. The patient possessed a clear consciousness but depicted decreased memory. The bilateral pupils were equally large and round, with a 3 mm diameter in both eyes. The right eye had light reflexes, while the left had no light perception. The forehead wrinkles were symmetrical, and hearing was normal in the ears. The left and right limbs had Grade 5 muscle strength with normal muscle tone. Finger-to-nose and heel-to-shin tests were normal bilaterally. The patient showed negative Babinski and Oppenheim signs. Blood tests revealed a white blood cell count of $6.79 \times 10^9$/L, with 80.7% neutrophils, a hemoglobin level of 122g/L, a platelet count of $170 \times 10^9$/L, a mean platelet volume of 8.9fL, and a red blood cell count of $3.78 \times 10^{12}$/L.

1.4 Auxiliary examinations: The contrast-enhanced head CT demonstrated multiple cystic lesions with uneven wall thickness and irregular enhancement within the left frontal and temporal lobes. Some areas had solid lesions surrounded by edema with mild to moderate heterogeneous enhancement. Localized bone destruction was also observed within the left temporal and sphenoid bones (Figure 1A-1B). The left lateral ventricle was compressed, and midline structures had shifted to the right. The CT diagnosis indicated a left cerebral hemisphere space-occupying lesion and left frontal and temporal bone destruction, possibly because of multiple myeloma metastasis. The head MRI scan with contrast demonstrated irregular cystic and solid lesions within the left frontal and temporal lobes, showing enhanced cyst walls and significant heterogeneous enhancement across solid areas (Figure 2A-2C). These lesions invaded the left temporal and sphenoid bones and led to bone destruction. Large areas of edema were observed around the lesions. Moreover, the left lateral ventricle was compressed and shifted, and the midline shifted to the right. The MRI results indicated a solid-cystic lesion in the left frontal and temporal lobes, describing the possible myeloma in the left temporal and sphenoid bones involved in the left side of the brain. Based on medical history, high-grade glioma in the brain could not be ruled out.

1.5 Surgical procedures: Intraoperatively, a lesion was observed in the brain, and a soy sauce-like liquid was seen after puncturing the cystic lesion within the left temporal lobe. After the brain tissue collapsed, the left temporal lobe lesion was excised first. The lesion was purple-red and lacked a complete capsule. The tumor was approximately $2 \times 2 \times 2.5$ cm in size and was removed along the boundary of the brain tissue. The left frontal lobe lesion of approximately $2 \times 1.5 \times 1$ cm in size was excised along the normal brain tissue boundary surrounding the tumor. A connection was observed with the left lateral ventricle after lesion removal. The tumor tissue was sent for rapid pathological examination during the operation, indicating glial cell proliferation. A routine pathological test was performed on the excised tumor after the procedure.

1.6 Results: After treatment, the patient gradually regained consciousness, having equally large and round pupils and showing sensitive responses to light. Limb movements were normal. CT re-examination
revealed that most of the intracranial mass had been removed without significant bleeding in the surgical area. When the condition of the patient improved after a week of hospitalization, he was discharged with medication. Regular outpatient follow-up was conducted after discharge, and the pathological diagnosis was CMMs (Figure 3).

**Discussion**

CMMs are occult vascular malformations in the central nervous system, often occurring in the brain parenchyma. It is a benign vascular lesion due to an abnormal vascular mass (cavernous) of various thin-walled brain vessels. The lesion contains a small amount of connective tissue without brain tissue. Under the microscope, the vascular wall appears as flat collagen and endothelial cells without smooth muscle or elastic fibers. Patients with CCMs are quite prone to recurrent bleeding. The incidence of CMMs in the general population is 5%-13% [1], and approximately 80% of CMMs occur in the supratentorial region. They are most common in the deep white matter of the frontal and temporal lobes, the cortex and white matter junction, and the basal ganglia. They also occur in the cerebellum, brainstem, and spinal cord [2]. The most common clinical manifestations of CMMs involve seizures (50%), intracranial hemorrhage (25%), and focal neurological deficits without any past radiological evidence of intracranial hemorrhage (25%) [4]. Most are asymptomatic cases and discovered incidentally during autopsy. CCMs are often associated with hemosiderin deposition, causing seizures [5]. CMMs can occur sporadically or in a familial pattern. They can also be secondary to viral infection, anticoagulant therapy, trauma, surgery, vascular reaction post-bleeding, or radiation therapy [6]. Approximately 20% of cases have multiple cerebral cavernous malformations. Moreover, many patients with positive family histories depict autosomal dominant inheritance [1].

In previous reports, Mariniello et al. [11] reported a 62-year-old patient who underwent right temporal glioblastoma resection followed by radiotherapy in the surgical and surrounding brain areas. Four years later, during follow-up, a newly developed cavernous malformation could be seen in the right cerebellum. Keezer et al. [12] reported a 51-year-old male with two new cavernous malformations in the intracranial region after undergoing 17 years of intracranial irradiation for cerebellar astrocytoma. Based on the MRI features, the risk of hemorrhage in radiation-induced cavernous malformation had increased than the congenital cavernous malformation. In the present case, the patient underwent frontal plasma cell tumor surgery 10 years ago, followed by radiotherapy. The newly developed cavernous malformations are located within the same area as the previous surgery and radiotherapy, indicating that surgical and radiation treatments likely caused the disease.

Routine imaging examinations for diagnosing cavernous malformations include CT and MRI. Among these modalities, MRI is the preferred choice to detect and diagnose CMMs. MRI has high sensitivity and specificity and is considered the gold standard for diagnosing CMMs [7]. Cavernous malformations appear as lesions with clear boundaries and mixed signals on conventional spin-echo sequences containing blood breakdown products from different stages and surrounded by a complete low-signal-containing
hemosiderin ring with a "popcorn" shape. Enhancement scans may or may not significantly enhance the lesion, related to forming internal blood clots and calcification. The SWI sequence more sensitively distinguishes microhemorrhages and hemosiderin than conventional sequences, and some cavernous malformations could be accompanied by bone infiltration. However, some CMMs do not possess typical imaging features. Therefore, they must be distinguished from tumor bleeding or calcification (particularly hemorrhagic metastatic tumors), high-grade gliomas, and polymorphic yellow astrocytomas.

Plasma cell tumors are classified into extramedullary plasmacytoma, multiple myeloma (MM), plasmablastic lymphoma, etc. The signal intensity of the lesion on T1WI is mostly isointense or slightly lower. In contrast, it is often isointense or somewhat higher on T2WI without prominent peritumoral edema. The enhancement scan usually depicts homogeneous enhancement and may accompany bone infiltration. In the present case, the lesion possessed a sizeable cystic component with a small solid component that appeared popcorn-like. However, there were signs of bone destruction around the lesion due to the patient’s history of multiple myeloma, causing a misdiagnosis before surgery. The lack of SWI sequence was one of the reasons for misdiagnosis in this case.

The treatment options for CMMs involve conservative and surgical treatments. Conservative treatment is preferred for asymptomatic patients, while surgical treatment is recommended for patients with prominent symptoms or high bleeding risk from lesions. However, surgical treatment may not be effective for plasma cell tumors since they are highly sensitive to radiotherapy. Therefore, imaging diagnosis is significant in determining the subsequent treatment plan and surgical approach for patients.

**Conclusion**

The accurate preoperative diagnosis of CMMs depends on imaging examinations. However, the imaging features of the lesions may not always be typical, and early-stage lesions can easily be missed due to their complex pathological and physiological changes. Therefore, differential diagnosis is crucial, particularly in patients with a history of other intracranial tumors causing misdiagnosis. Therefore, improving our understanding of CMMs is essential, particularly in patients with a history of other tumor surgeries, radiation therapies, etc. With popcorn-like characteristics observed on MRI within the local area of intracranial lesions, possible CMMs should be considered. This can improve the accuracy of preoperative imaging diagnosis and provide better comprehensive diagnostic and treatment options for clinical and surgical approaches.

**Declarations**

**Ethics approval and consent to participate:**

The case report has received ethical approval.

Consent to participate of their clinical details and clinical images was obtained from the patient.
Consent for publication

Informed consent to publish their clinical details and clinical images was obtained from the patient.

Competing interests

No conflict of interest exits in the submission of this manuscript, and manuscript is approved by all authors for publication. I would like to declare on behalf of my co-authors that the work has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed.

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Yinan Zhao: Conceptualization, Writing-Original Draft.

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Availability of Data and Materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

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Conflicts of Interest:

No conflict of interest exits in the submission of this manuscript, and manuscript is approved by all authors for publication. I would like to declare on behalf of my co-authors that the work has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed.

References


Figures

Figure 1

Reveals an enhanced CT image of the head(A), demonstrating multiple cystic lesions with uneven wall thickness and enhancement within the left temporal lobe. Solid lesions with mild to moderate heterogeneity have been observed locally, surrounded by edema. And the CT bone window image of the head(B), indicating local bone destruction in the left temporal and sphenoid bones.

Figure 2
Brain MRI scans of patient Axial T1-weighted(A), T2-weighted (B) and post-contrast T1-weighted (C) images depicts the cyst wall enhancement and significant heterogeneous enhancement of the solid portion after contrast administration, indicating a popcorn-like change.

Figure 3

Portrays the postoperative pathological image, indicating cavernous malformations possessing hemorrhagic necrosis and surrounding gliosis.

Supplementary Files

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