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CASE REPORT

Sudden Unexpected Death due to Brainstem Hemorrhage Associated with Cerebral Venous Malformation

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SUMMARY

Background: **Cerebral venous malformations (CVMs) generally remain silent and asymptomatic in the vast majority of cases. CVM-associated lethal intracerebral hemorrhage is extremely rare.**
Methods: **Here we presented a case with chest tightness, shortness of breath, fever and convulsive seizures. Chest and brain computed tomography, and laboratory testing were performed.**
Results: **The patient suffered a sudden cardiac arrest and expired despite aggressive resuscitation efforts. Autopsy analysis revealed a venous vascular malformation located in the pons and medulla oblongata, and brainstem hemorrhage and hematoma formation in the surrounding areas.**
Conclusions: **CVMs, though exceptionally rare, can lead to fatal hemorrhage and therefore warrant heightened clinical vigilance. Proactive measures should be implemented to mitigate potential risk factors for this severe complication. When evaluating adult patients with recurrent convulsive episodes, clinicians need to consider prompt neuroimaging to rule out life-threatening intracranial hemorrhage.**
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KEYWORDS

cerebral venous malformation, sudden death, intracerebral hemorrhage, brainstem

INTRODUCTION

Cerebral venous malformation (CVM), also known as developmental venous anomaly, is the most common type of cerebral vascular malformation [1,2]. It is generally considered to be an anatomical variation of cerebral vasculature, which presents with a benign clinical course in the vast majority of cases, and is usually found by incidental neuroimaging findings. However, CVMs are occasionally associated with acute neurological deterioration due to hemorrhagic or ischemic complications, especially in those cases with other accompanied cerebral pathologies such as cavernoma or arteriovenous malformation [3].
Though there is still controversy, it is generally accept-

ed that CVMs develop during intrauterine life, most of which remain silent and asymptomatic. With the advances of imaging techniques, fortuitous detection of CVMs happens more and more often. The estimated incidence of CVMs is 2.6 - 6.4% [4]. However, CVMs-associated lethal intracerebral hemorrhage is extremely rare. Here we presented a case of sudden death due to brainstem hemorrhage associated with CVM in a 41-year-old woman.

CASE PRESENTATION

A 41-year-old woman presented to the emergency rescue area complaining of chest tightness and shortness of breath for half an hour following an episode of anger. She had no chest pain, palpitations, hemoptysis, dizziness, loss of consciousness, cough with sputum, nausea, vomiting, abdominal pain, or diarrhea. Physical examination showed an elevated body temperature 41.6°C, respiratory rate 36 breaths/minute, blood pressure 108/51 mmHg, and oxygen saturation 97%. She was lethargic, and other examinations revealed coarse breath sounds bilaterally with no wheezes or crackles, a heart rate of 118 beats/minute with regular rhythm and no pathological murmurs, soft and flat abdomen with no tenderness, liver and spleen not palpable below the costal margin, and no edema in the lower extremities. She had been taking oseltamivir for two days due to fever prior to this consultation. The patient had a medical history of penicillin and cephalosporins allergy, breast nodule, and liver cyst, while she had no history of convulsion nor any cardiovascular-related diseases such as hypertension, diabetes mellitus, and hyperlipemia, etc. Chest computed tomography (CT) revealed bilateral bronchovascular bundle thickening, linear opacities in the right middle lobe, and a tiny nodular opacity in the right upper lobe. No significant abnormalities were detected on non-contrast brain CT scan. Initial laboratory examinations showed WBC count 7.49 x 10^9/L, C-reactive protein (CRP) level 73.68 mg/L, procalcitonin level 0.20 ng/mL, D-dimer level 0.71 mg/L, and cardiac troponin T level 20.74 pg/mL. Three hours later, the WBC count and CRP level rose to 12.75 x 10^9/L and 85.50 mg/L. Remarkably, the levels of procalcitonin and D-dimer were drastically increased to 16.60 ng/mL and 31.03 mg/L, respectively (Table 1). She experienced convulsive seizures four times within three hours, and each episode lasted one to several minutes. Diazepam and phenobarbital were administered for the rescue medication. After the last seizure, her condition became stabilized for four to five hours. The body temperature remained high above 39°C, and the heart rate maintained between 100 and 117 beats/minute, with 22 breaths/minute of respiratory rate and normal blood pressure. She continuously received supportive therapies including oxygen supplementation, antipyretic management, anti-infective treatment, and maintenance of fluid-electrolyte and acid-base balance, with close monitoring of vital signs. However, subsequently, she experienced a sudden cardiac arrest. Despite temporary restoration of spontaneous circulation following resuscitation, she suffered a recurrent cardiac arrest minutes later and succumbed despite aggressive efforts.

To determine the exact cause of the patient's death, the family members consented to an autopsy. Gross autopsy of the brain tissue showed brainstem hemorrhage and hematoma formation. Histopathological analysis revealed the following findings: Multiple dilated thin-walled venous vessels with enlarged lumens were observed in the parenchyma of the pons and medulla oblongata, exhibiting varying calibers. Extensive hemorrhage and hematoma formation were noted in the surrounding areas (Figure 1a). Within one venous lumen, a thrombus was identified, containing scattered lymphocytic infiltration (Figure 1b, 1c). Reactive gliosis and compressive atrophy of adjacent brain tissue were evident. Based on the integration of clinical history, gross autopsy and histopathological findings, the deceased was diagnosed with brainstem venous vascular malformation during life. Rupture of the malformed vessel led to hematoma formation, which exerted compressive effect on the respiratory and circulatory centers located within the brainstem, resulting in dysfunction of the central nervous system. This ultimately culminated in respiratory and circulatory failure leading to death.

DISCUSSION

The risk of intracerebral hemorrhage truly related to CVMs was reported to be 0.22 - 0.68% per year in previous studies [5,6]. Here we described an extremely rare case of sudden unexpected death due to brainstem hemorrhage associated with CVM in a 41-year-old woman, and reviewed relevant literature in order to provide clinical alerts and practice guidance.

Clinical presentations in patients with CVMs are generally attributed to other accompanied cerebral pathologies. The main complaints were headache, dizziness, ataxia, nausea/vomiting, seizures and focal neurological deficits [7,8]. Our patient presented with convulsive seizures during the consultation, which were complicated with persistent high fever. In addition, marked increase of D-dimer and procalcitonin levels within three hours indicated clinical deterioration of her condition, yet these findings might inadvertently lead clinicians to focus on exacerbated inflammation and adverse outcomes of convulsive seizures while overlooking potential thrombus formation and/or hemorrhage. Histologically, CVMs are composed of dilated venous channels that are interspersed in the white matter, with simple or complex variations in venous architecture and drainage patterns [3]. Histopathological analysis of the present case revealed multiple dilated thin-walled venous vessels with enlarged lumens in the parenchyma of the pons and medulla oblongata, consistent with the histological characteristics of CVMs. Meanwhile, thrombus formation was

Table 1. Changes of laboratory examination results during a period of three hours.

	Initial results	Results three hours later	Reference range
WBC (/L)	7.49 x 10^9	12.75 x 10^9	3.50 - 9.50
CRP (mg/L)	73.68	85.50	≤ 10.00
Procalcitonin (ng/mL)	0.20	16.60	< 0.05
D-dimer (mg/L)	0.71	31.03	0.00 - 0.55
Cardiac troponin T (pg/mL)	20.74	NA	≤ 14.00
NT-ProBNP (pg/mL)	NA	264.85	< 125.00

WBC white blood cell, CRP C-reactive protein, NA not applicable.

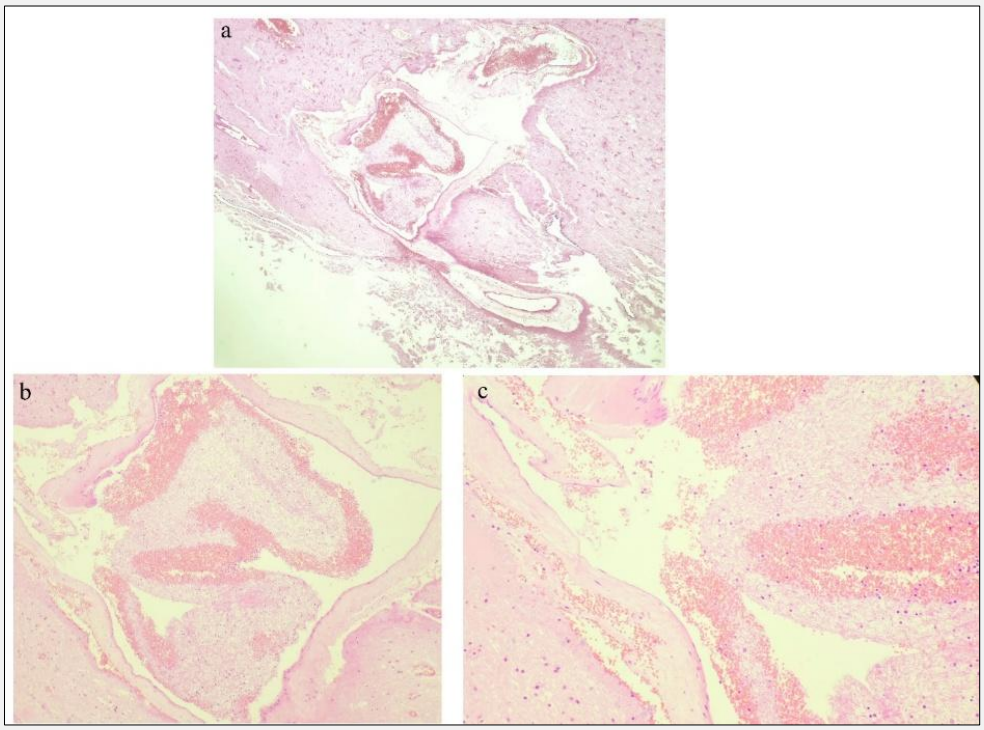

Figure 1. Histopathological findings of the brain stem parenchyma (hematoxylin and eosin staining).

A Multiple dilated thin-walled venous vessels with enlarged lumens were observed in the parenchyma of the pons and medulla oblongata (x 4 objective). B A thrombus was identified within one venous lumen (x 10 objective). C Scattered lymphocytic infiltration in the thrombus (x 20 objective).

observed within one venous lumen, and extensive hemorrhage and hematoma formation were noted in the vicinity of the CVM, leading to compression and subsequent failure of the respiratory and circulatory centers. CVMs are related to a less efficient form of the venous drainage route, with a limited number of collecting veins draining a relatively large territory of brain parenchyma. With time, the overloaded venous hemodynamics may contribute to progressive thickening and hyalinization of the venous walls of CVMs, resulting in increased resistance, decreased compliance, and venous hypertension [1]. Venous thrombosis may occur in CVMs, leading to venous ischemia or intracerebral hemorrhage. However, there is currently no solid evi-

dence to indicate that CVMs are more susceptible to thrombosis than normal cerebral veins [1]. Importantly, it is necessary for the radiologists to identify a thrombosed CVM to ensure timely management.

The morphological characteristic of a CVM is a cluster of venous radicles that converge into a large collecting vein, demonstrating a typical caput medusae appearance [9]. Neuroimaging plays a fundamental role in characterizing the angioarchitecture of a CVM and assessment of brain parenchyma surrounding the CVM [10]. Both CT and magnetic resonance imaging (MRI) can demonstrate the typical caput medusae draining into a collecting vein, allowing diagnosis of CVMs with confidence. Additionally, CT may reveal an associated hemorrhage, parenchymal calcifications, and atrophy or white matter lesions in the drainage area of CVMs. MRI is superior to CT in disclosing related parenchymal abnormalities, such as white matter lesions, and cavernous malformations [11]. Digital subtracted angiography (DSA), as the best imaging modality to observe the hemodynamic activity of CVMs, is recommended for cases with ischemic or hemorrhagic infarction, or when a cerebral vascular malformation is suspected on CT or MRI [3]. Hemorrhagic and/or ischemic infarction is the most severe complication, and early detection is crucial for timely management and good prognosis [12]. As for the present case, non-contrast brain CT scan performed after the third convulsive episode revealed no significant abnormalities, indicating that brainstem hemorrhage and thrombus formation might either have not occurred at the moment or be in its very early stage, thus remaining undetectable on CT imaging. Therefore, a repeated CT scan several hours later or CT in conjunction with MRI should be considered under certain conditions.

CONCLUSION

The patient was generally in good health, and she had no medical history of convulsion and any cardiovascular-related diseases. A retrospective analysis of the patient's clinical course and manifestations may provide some critical insights. Under exceedingly rare circumstances, brainstem CVMs, though exceptionally rare, can lead to fatal hemorrhage and therefore warrant heightened clinical vigilance. Preventive measures need to be taken to mitigate potential risk factors for this severe complication. When evaluating adult patients with recurrent convulsive episodes like the present case, clinicians should keep vigilant and consider prompt neuroimaging (CT/MRI) to rule out life-threatening intracranial hemorrhage.

Informed Consent:
Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images.

Data Availability:
The datasets used and analyzed in the current study are available from the corresponding author on reasonable request.

Declaration of Interest:
The authors have no conflicts of interest to declare.

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