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# Hemorrhage of a Cavernous Hemangioma of the Brainstem Presenting with Fever of Unknown Origin: A Case Report

## Authors' Contribution:

Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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Conflict of interest: None declared

**Patient:** Male, 42-year-old  
**Final Diagnosis:** Brainstem cavernoma  
**Symptoms:** Headache • fever  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Neurosurgery

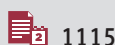
**Objective:** Unusual clinical course

**Background:** Cavernous malformations (CMs) or hemangiomas are benign vascular hamartomas of the central nervous system (CNS) that constitute 5-15% of all CNS vascular malformations. Most patients with brainstem CMs present with a sudden onset of seizures, intracranial hemorrhage, cranial nerve deficits, headache, or ataxia. Up to 20% to 50% of patients are asymptomatic, and their CMs are diagnosed incidentally on brain magnetic resonance imaging.

**Case Report:** We present a case of a 42-year-old man with a brainstem cavernous hemangioma presenting with fever of unknown origin and mild headache without meningismus. The patient underwent a midline suboccipital craniectomy and removal of a ruptured brainstem cavernous hemangioma and the surrounding thrombus. Postoperatively, the patient developed left facial nerve palsy, left abducens nerve palsy, and xerostomia. Abducens palsy and xerostomia resolved spontaneously days after the operation. At the 6-month follow-up, the patient showed stable improvement with resolution of his neurological deficits.

**Conclusions:** To our knowledge, there is no reported case of a patient with a ruptured brainstem cavernoma presenting with fever of unknown origin as the main symptom. We assume that the minimal intraventricular hemorrhage triggered the hypothalamic thermoregulating mechanism. Thus, it would be useful for physicians to raise the suspicion of a ruptured brainstem cavernous malformation with further imaging evaluation when investigating fever of unknown origin.

**Keywords:** Brain Stem Neoplasms • Fever of Unknown Origin • Hemangioma, Cavernous, Central Nervous System

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## Background

Cerebral cavernous malformations (CCMs), also known as cavernous hemangiomas, are benign vascular hamartomas of the central nervous system (CNS) that constitute 5-15% of all CNS vascular malformations [1,2]. Cavernous hemangiomas may occur at any location in the CNS. They are most frequently supratentorial (48-86%), followed by 4-35% in the brainstem and 5-10% in the basal ganglia; they rarely occur in the spinal cord [1]. Regarding brainstem hemangiomas, approximately 57% are found in the pons, 14% in the midbrain, 12% in the pontomedullary junction, and 5% in the medulla [3]. Intraventricular cavernous hemangiomas are rare and account for 2.5-10.8% of cerebral hemangiomas. Three genes are related to hemangiomas evolution (*CCM1*, *CCM2*, *CCM3*) and mutations in any one of these genes can result in multifocal CCM [4,5].

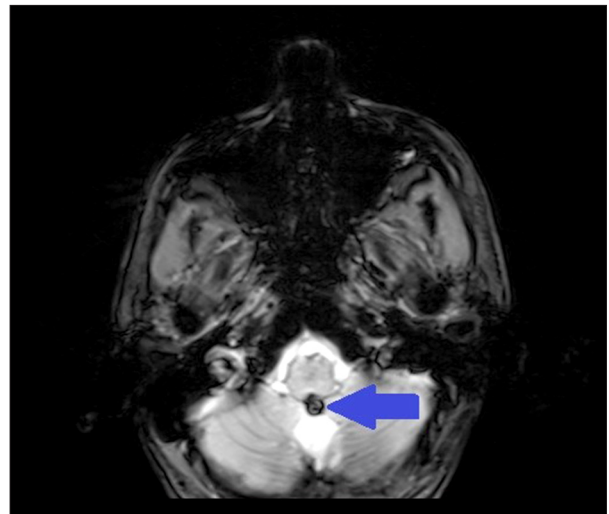
Cavernous hemangiomas are low-pressure hamartomatous berry-like vascular lesions with minimal to no intervening brain parenchyma and are usually surrounded by hemosiderin deposition and gliosis. These vessels lack muscular and elastic layers and are filled with blood at various stages of thrombosis and organization [6,7]. Sluggish blood flow through dysplastic channels results in recurrent thrombosis, calcification, and deposition of hemosiderin along the margins of the lesion [8].

Although clinical manifestations vary due to the location of cavernous hemangiomas, most patients with brainstem hemangiomas present with sudden onset of seizures, intracranial hemorrhage, cranial nerve deficits, headache, ataxia, or impairment of consciousness. Brainstem cavernous hemangiomas consistently have a higher rate of symptomatic hemorrhage in comparison with hemangiomas at other locations. Annual incidences of hemorrhage and recurrent hemorrhage are 2.8% and 32.3%, respectively [6]. Brainstem cavernous hemangiomas and first presentation with hemorrhage constitute the 2 main risk factors for rebleeding [9,10].

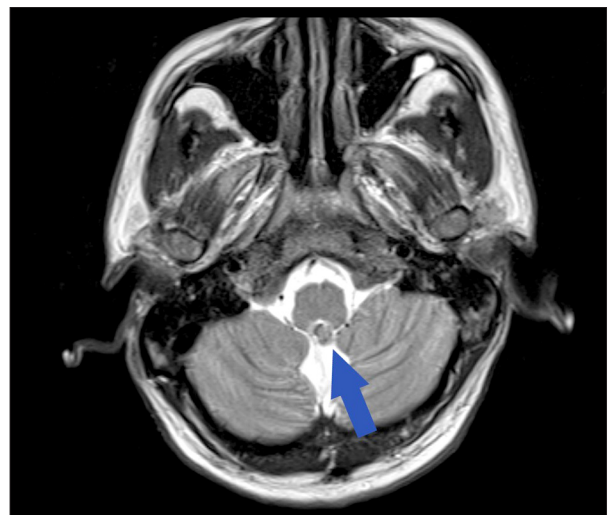
We present an unusual case of a 42-year-old man with a ruptured brainstem cavernous hemangioma, presenting with fever of unknown origin and mild headache as the only symptoms.

## Case Report

A 42-year-old man initially presented to a rural hospital with fever up to 38°C and a frontal, gradually evolving headache. Although inflammatory markers were within normal range, empirical treatment with antibiotics was instituted. After a 2-day hospitalization he was transferred to the Internal Medicine Department for further workup and investigation. During his stay, his presenting symptoms persisted, with intermittent fever up to 38°C and continuous waxing and waning headache, without

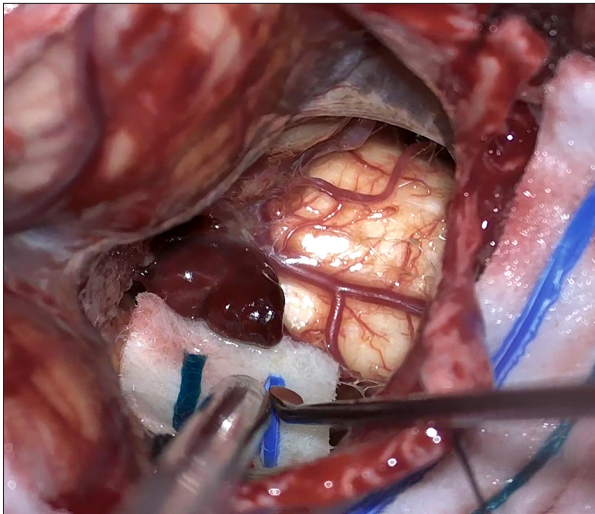


**Figure 1.** An axial gradient echo sequence magnetic resonance imaging brain scan showing the lesion (blue arrow) with a mixed-density signal indicating a bleeding of a cavernoma, extending into the fourth ventricle.

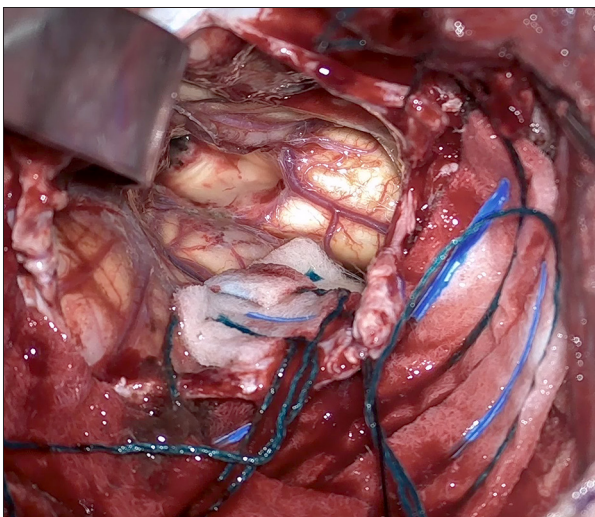


**Figure 2.** An axial T2 magnetic resonance imaging brain scan showing a well-demarcated heterogeneous signal of the pons (blue arrow), extending into the fourth ventricle.

nausea/vomiting or signs of meningeal irritation. The antibiotic regimen was broadened and antiviral agents were added. The patient underwent repeated lumbar punctures, all of which had bloody appearance and featured red blood cells and increased white blood cells, which was attributed to traumatic tap (and was not xanthochromic). Initial computed tomography scan featured a small round hypodense mass attached to the floor of the fourth ventricle. The patient subsequently underwent a magnetic resonance imaging scan, and the lesion was subsequently characterized as a thrombus. Due to the persistence of the patient's symptoms, serial computed tomography scans



**Figure 3.** Intraoperative photograph showing the blood clot filling the fourth ventricle and the underlying medulla.



**Figure 4.** Intraoperative photograph showing the removal of the blood clot, the removal of the cavernoma, and the coagulated floor of the fourth ventricle.

were performed and a gradual increase in the lesion's size was noted. The patient was thus transferred to the Neurosurgical Ward for further evaluation and treatment in a good neurological state (Glasgow coma scale 15/15). Cerebral digital subtraction angiography was performed without abnormal findings. A second magnetic resonance imaging scan (including gradient echo sequence) showed further increase in the lesion's size with a clot protrusion into the fourth ventricle, leading to suspicion of bleeding of an underlying cavernous hemangioma located on the floor of the brainstem (Figures 1, 2). Owing to the high risk for further bleeding, the patient underwent a mid-line suboccipital craniectomy and removal of a ruptured brainstem cavernoma with surrounding thrombus. The blood clot filled all the area of the fourth ventricle, and the hemangioma

was located adjacent to the medial eminence and the left facial colliculus (Figures 3, 4). Postoperatively, the patient developed left facial nerve palsy, left abducens palsy, and xerostomia. Abducens palsy and xerostomia resolved spontaneously 2 days after the operation. The patient remained afebrile postoperatively and was discharged with left-sided facial nerve palsy; he had no further neurologic deficit and was afebrile and without headache. At the 6-month follow-up, the patient showed stable improvement with resolution of his neurological deficits.

## Discussion

Brainstem cavernous hemangiomas are known to present with sudden onset of seizures, intracranial hemorrhage, cranial nerve deficits, headache, ataxia, or impairment of consciousness. Symptoms can usually be attributed to hemorrhage inside or outside the margins of the lesion and mass effect [5]. Surgery is the treatment of choice for hemangiomas that have bled [4]. Brainstem cavernous hemangiomas consistently have a higher rate of symptomatic hemorrhage in comparison with hemangiomas at other locations. Annual incidences of hemorrhage and recurrent hemorrhage are 2.8% and 32.3%, respectively [6]. Stereotactic radiosurgery may be considered as a therapeutic alternative for lesions that are surgically inaccessible [11,12] because it is highly accurate and allows targeted delivery of high-dose radiation with sparing of adjacent, healthy brain parenchyma. The ventricular region surgery is considered a challenge due to the deep location and the intimate association of the cerebral ventricles with critical areas of the brainstem [13]. Hyperthermia of central origin has been described in various hemorrhagic conditions of the CNS, usually presenting with acute neurologic deficits or meningismus; its pathophysiology usually involving the preoptic area of the hypothalamus [14]. The preoptic area GABAergic neurons that play a role in thermoregulation are located within subregions such as the median preoptic subnucleus, the medial subnuclei, the dorsomedial hypothalamus, the paraventricular nucleus, and the perifornical area of the lateral hypothalamus [15]. These neurons have the EP3 subtype of the receptor for prostaglandin E<sub>2</sub>, which acts as a powerful endogenous pyrogenic mediator in the preoptic area [16]. We speculate that alterations in the local micro-environment (blood) that trigger warm-sensitive neurons of the brainstem and actions of prostaglandin E<sub>2</sub> may evoke the mechanism of thermoregulation [15,17]. However, to our knowledge, there is no reported case of a patient with a ruptured brainstem hemangioma with fever of unknown origin as the main presenting symptom. We assume that the minimal intraventricular hemorrhage triggered the hypothalamic thermoregulating mechanism. Thus, it would be useful for physicians to raise the suspicion of a ruptured brainstem cavernous hemangioma with further imaging evaluation when investigating fever of unknown origin.

## Conclusions

Here, we describe a case of a 42-year-old man with a ruptured brainstem cavernous hemangioma presenting with fever of unknown origin and mild headache as the only symptoms. Our hypothesis lies in the stimulation of the preoptic area of the hypothalamus due to prostaglandin stimulus resulting in fever of central origin. Nevertheless, more research needs to be conducted to further evaluate possible relative mechanisms between central fever and intracerebral hemorrhage. We hope that this case contributes to inclusion of brainstem cavernous hemangiomas (hemorrhagic neurosurgical conditions) in the differential diagnosis of fever of unknown origin.

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## Conflict of Interest

None.