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Case Report

# Giant intracranial arteriovenous malformation as the focus of epileptic seizures

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**A man in his late thirties was found in a supine position in the hallway of his house. He had been diagnosed with epilepsy at approximately 20 years old. Since stopping treatment, epileptic events occurred more frequently and his condition deteriorated in the past 2 years. Autopsy revealed that head injuries were found on the left side of his head. A fracture from the left parietal bone to the anterior cranial fossa was also detected. A subdural hemorrhage (hematoma) spanned a wide range. A subarachnoid hemorrhage was also identified in the left parietal region. His brain weighed 1603 g, was edematous, and showed right uncal herniation. In the right cerebral hemisphere, a thick, enlarged blood vessel ran from the sagittal sinus. An egg-sized tumorous lesion of blood vessels was found on the bottom of the frontal lobe. This vascular lesion had formed between the sagittal sinus and right anterior cerebral artery. Pathologically, veins and arteries were found together, and, thus, this case was diagnosed as an arteriovenous malformation (AVM). No other pathological and toxicological findings were observed. Subdural hematoma, the cause of death, occurred from the fall to the floor. An epileptic seizure may have been the cause of the fall. AVM on his brain was considered to be the focal lesion of epileptic seizures.**

**Key words:** epileptic seizure, forensic autopsy, giant intracranial arteriovenous malformation, neuropathology, traumatic subdural hemorrhage (hematoma).

## INTRODUCTION

An arteriovenous malformation (AVM) is a typical lesion of vascular malformations and the predilection site is the cerebral hemisphere, mainly the area of the middle cerebral artery.[1] Large AVM has a nidus of greater than 5 or 6 cm in diameter, and accounts for 15% of all intracranial AVM.[2] The symptoms of AVM include hemorrhage, epilepsy and headaches. Seizures are the most common presentation of unruptured AVM.[3–6] The following factors are associated with seizure presentation: being male, a younger age, AVM located in the temporal or frontal lobe, AVM nidus diameter > 3 cm, superficial or cortical location, middle cerebral artery feeders, the absence of associated aneurysms, presence of a venous varix/varices, and superficial venous drainage.[7]

We herein report a case of a large AVM on the right bottom of the frontal lobe of the brain. An adult man was found in cardiopulmonary arrest, and his death was confirmed at the hospital. A forensic autopsy was performed to investigate his cause of death. The autopsy revealed traumatic brain damage, induced by a cranial fracture, subdural hematoma, and brain edema, and was considered as his cause of death. It was also considered that his traumatic brain damage was caused by falling to the floor and hitting his head. Along with traumatic brain damage, a large AVM was observed. The AVM was considered to be the focal lesion of epileptic seizures. An epileptic seizure may have been the cause of the fall.

## CASE REPORT

A man in his late thirties was found in a supine position in the hallway of his house. He was taken to the hospital where he was pronounced dead. No clinical treatment or examination were performed except for a postmortem CT scan and blood examination.

### Past history

He had been diagnosed with epilepsy at approximately 20 years old. He visited the hospital regularly after the diagnosis, but since the cause of his epilepsy had not been determined, he stopped treatment. Ten or more years

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**Table 1** Clinical blood examination of this case

| | | | |
|---|---|---|---|
| TP | 5.9 g/dL | CRE | 1.33 mg/dL |
| ALB | 3.8 g/dL | Na | 142 mEq/L |
| AST | 965 IU/L | K | 11.5 mEq/L |
| ALT | 1430 IU/L | Cl | 100 mg/dL |
| LDH | 7644 IU/L | S-Amy | 230 IU/L |
| ALP | 220 IU/L | CK | 590 IU/L |
| γ-GTP | 11 IU/L | CK-MB | 51 U/L |
| T-Bil | 0.6 mg/dL | CRP | 5.95 mg/dL |
| T-Cho | 103 mg/dL | WBC | 13.5 × 10^3/μL |
| BUN | 14.8 mg/dL | RBC | 443 × 10^4/μL |

ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, asparatate aminotransferase; BUN, blood urea nitrogen; Cl, chlorine; CK, creatine kinase; CK-MB, creatine kinase-MB; CRE, creatinine; CRP, C-reactive protein; γ-GTP, γ-glutamyltranspeptidase; K, potassium; LDH, lactate dehydrogenase; Na, sodium; RBC, red blood cell; S-Amy, serum amylase; T-Bil, total-bilirubin; T-Cho, total-cholesterol; TP, total protein; WBC, white blood cell.

after stopping treatment, epileptic events began to occur more frequently and his condition especially deteriorated in the past 2 years. Furthermore, epileptic seizures had become severe in the past 2 or 3 months. Seizures presented at least once every 2 weeks and he hit his head on the floor. Because he had stopped treatment, there were no clinical records since more than 10 years before his death.

## Clinical blood examination

The blood examination results from the hospital are shown in Table 1. LDH, CK, CRP and WBC were all significantly elevated. Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and potassium (K) were also elevated as the result of postmortem changes.[8–11]

## Postmortem CT findings

A postmortem CT scan showed a mass lesion on the right frontal lobe with calcification, degradation of the skull on the right side of the frontal bone, subarachnoid bleeding on the occipital lobe, subdural hematoma on the parietal lobe and brain edema (Fig. 1).

## Chief autopsy findings

The decedent was 171.5 cm in height and 65 kg in weight. Discoloration, excoriation, swelling (Fig. 2a), and

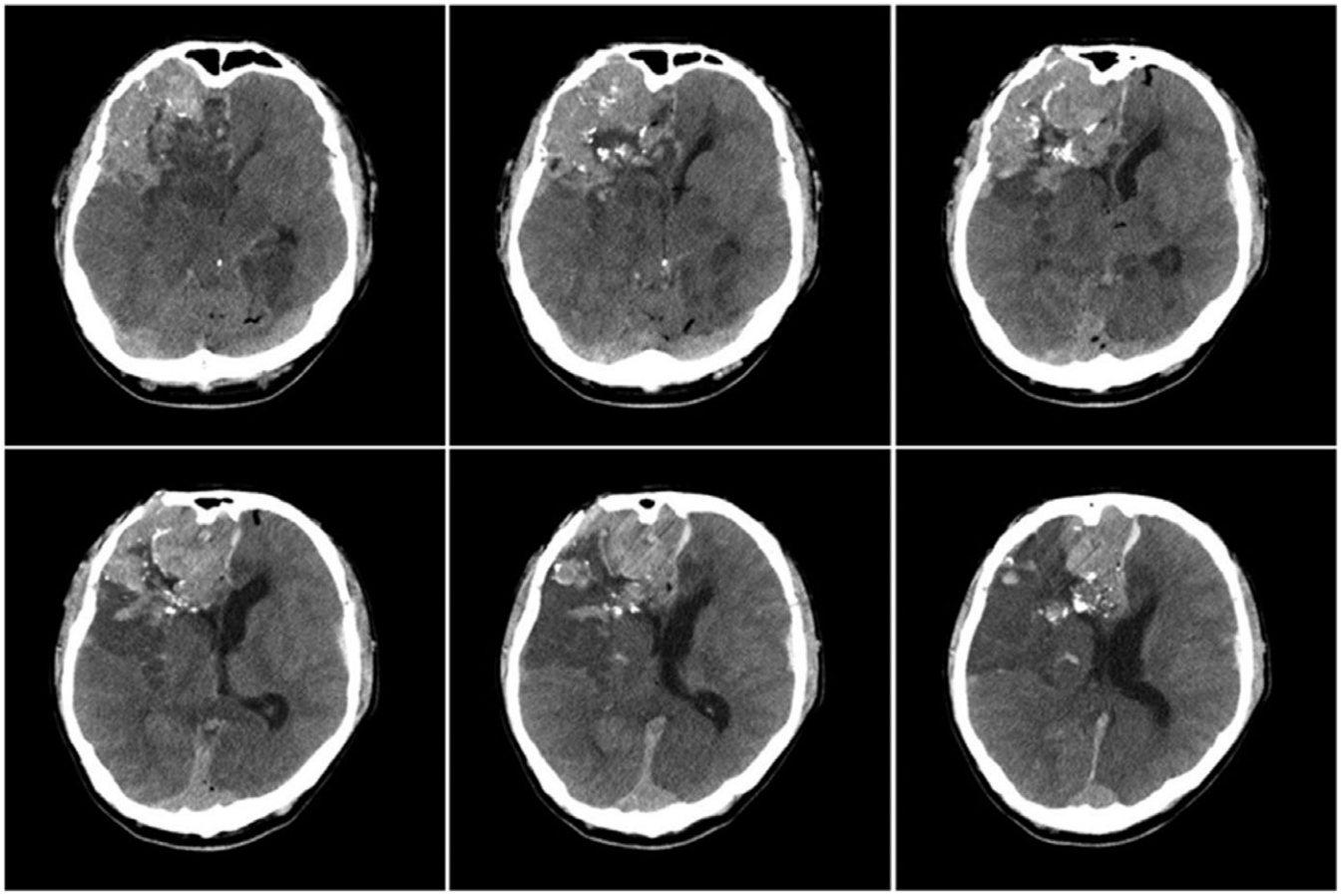

**Fig. 1** Postmortem CT findings. A tumor lesion in the right frontal lobe with calcification, brain edema, subdural hematoma and right frontal bone fracture.

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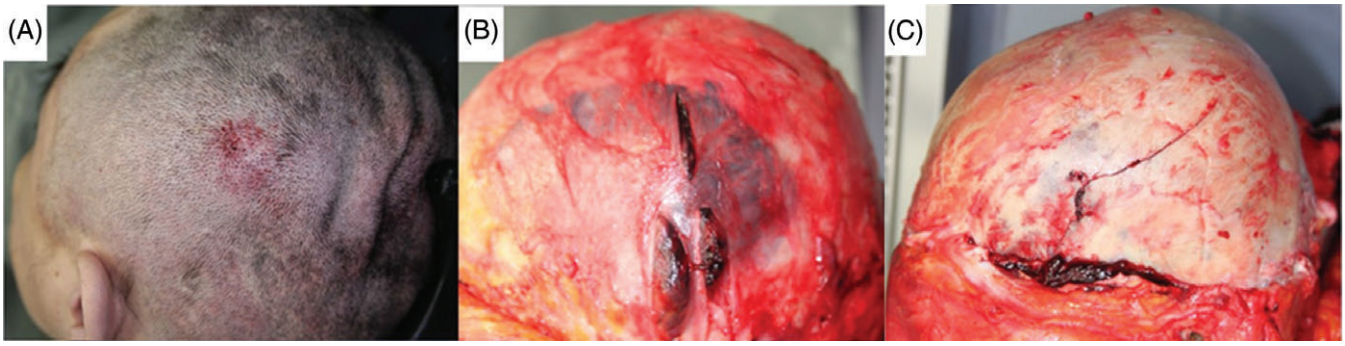


**Fig. 2** Head injuries on the left occipital region. Discoloration, excoriation and swelling (A), and subcutaneous and muscle hemorrhages (B) were found on the left side of the head. A fracture from the left parietal bone to the anterior cranial fossa was also observed (C).

subcutaneous and muscle hemorrhages (Fig. 2b) were found on the left side of his head. A fracture from the left parietal bone to the anterior cranial fossa was also observed (Fig. 2c). A fracture was also found on the right frontal bone. An enlarged blood vessel was observed in the subcutaneous scalp, and bold vascular grooves were noted on the internal surface of the cranial skull beside the vascular groove of the meningeal artery (Fig. 3b). A subdural hemorrhage (hematoma) spanned a wide range (Fig. 3a). A subarachnoid hemorrhage was also observed in the left parietal region (Fig. 3c).

His brain weighed 1603 g, was edematous, and showed right uncal herniation. In the right cerebral hemisphere, a thick, enlarged blood vessel ran from the sagittal sinus (Fig. 3c,d). A small egg-sized tumorous lesion of blood vessels was found on the bottom of the frontal lobe

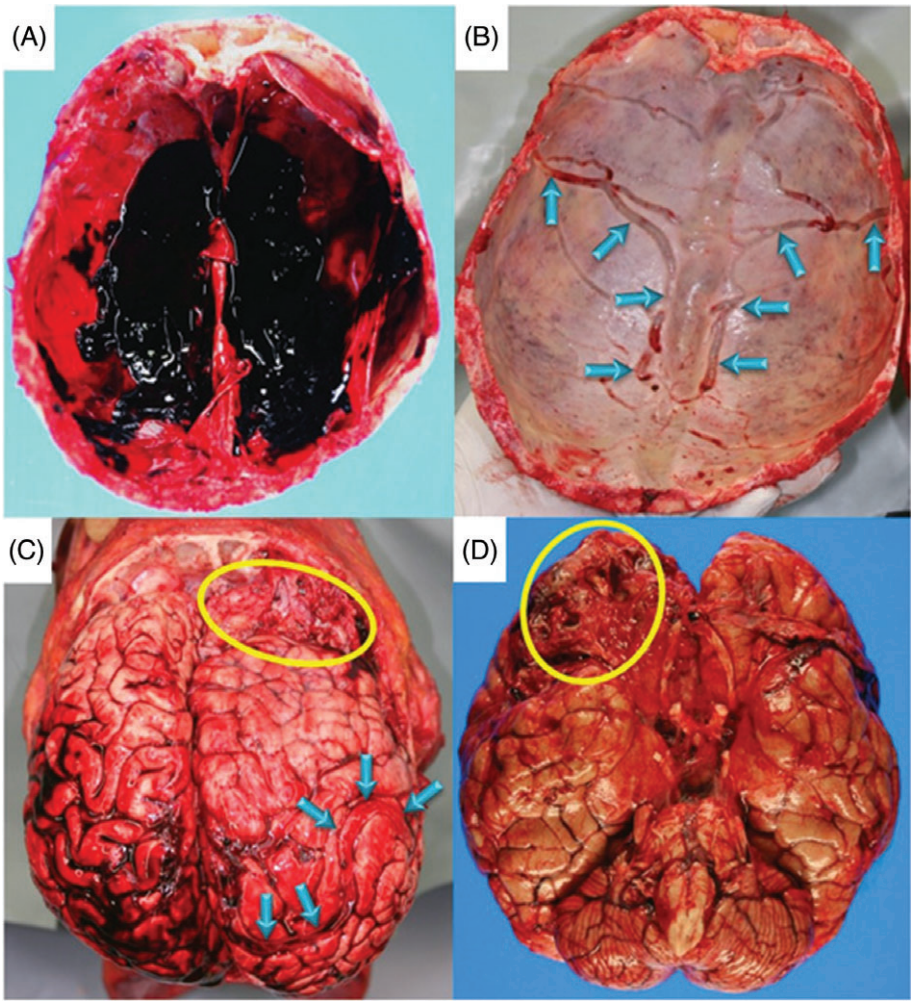


**Fig. 3** Intracranial lesions. A subdural hematoma spanned a wide range (A). A subarachnoid hemorrhage was also observed in the left parietal region (C). In the right cerebral hemisphere, a thick, enlarged blood vessel ran from the sagittal sinus (B and C; blue arrows). A small egg-sized tumorous lesion of blood vessels was found on the bottom of the frontal lobe (C and D; yellow circle).

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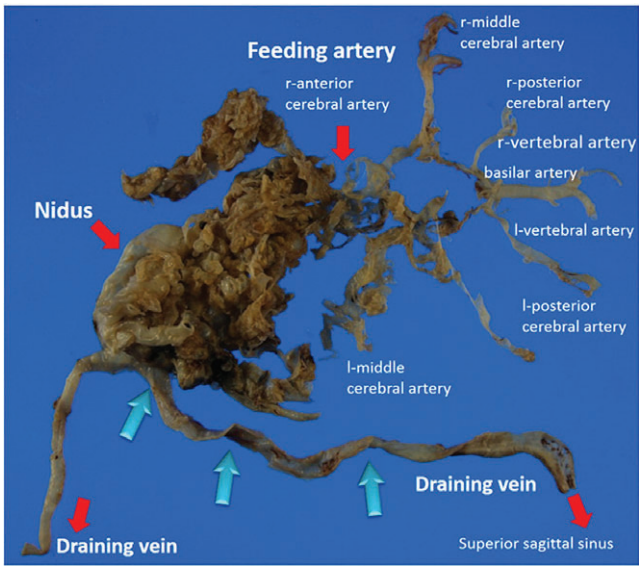


**Fig. 4** Large arteriovenous malformation (AVM), feeding artery, nidus and draining vein.

(Fig. 3d). This vascular lesion, approximately 6 cm in diameter, had formed between the sagittal sinus and right anterior cerebral artery (Fig. 4). However, there was no obvious hemorrhage around the vascular lesion. No other injuries, such as contusions, were observed.

In other organs, such as heart, lung, liver, and kidney, no significant pathological changes were observed.

## Histopathological findings

The vascular lesion was observed histopathologically with conventional staining using HE, LFB, Azan (AZ), EvG and berlin blue. There were many vessels of various sizes, shapes and wall thicknesses; these vessels shared vessel walls (Fig. 5a,b). A suspension of elastic fibers of the blood vessel wall was observed in one blood vessel wall. A difference in thickness was partially noted in the blood vessel wall (Fig. 5c,f ). In one blood vessel wall, there were parts at which elastic fibers were present, missing (Fig. 5c, d,f ), and had turned around (Fig. 5c,e).

## Toxicological examination

An ethanol analysis was performed using headspace gas chromatography with flame ionization detection (HS-GC-FID) on QP-2010Plus GC (Shimadzu, Kyoto, Japan).[12] Alcohol was not detected in blood or urine. Toxicological

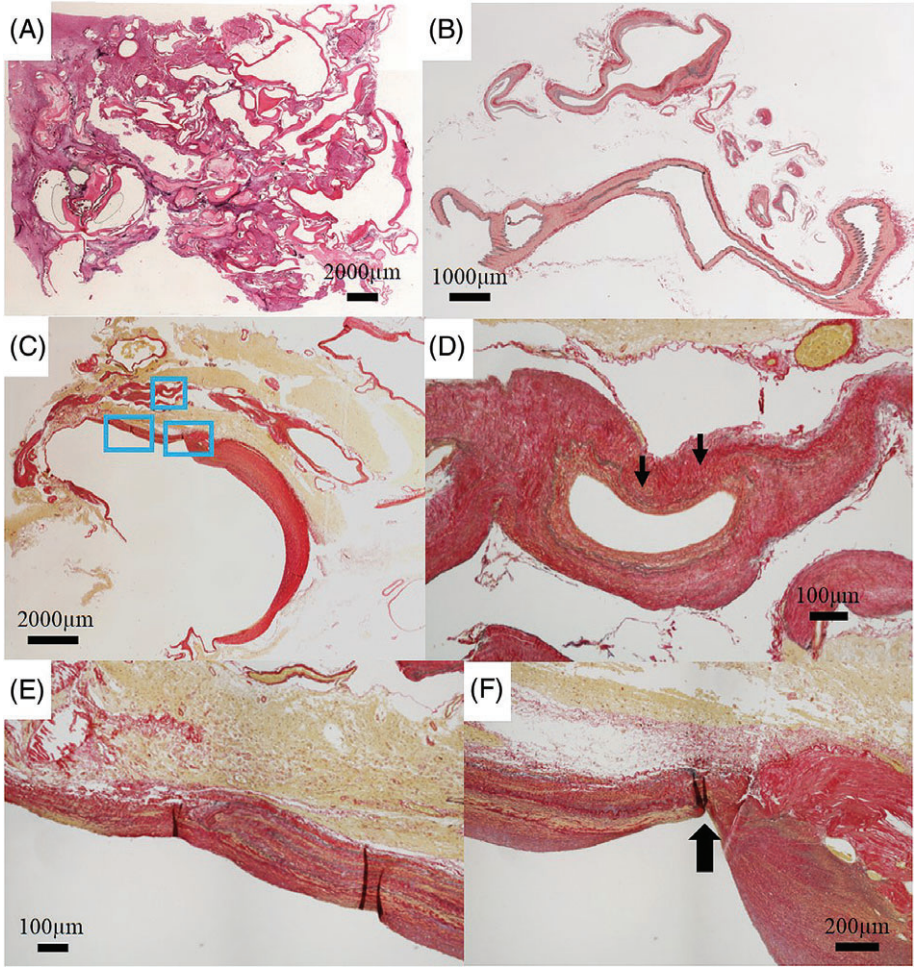


**Fig. 5** Histopathological findings of the vessel region. There were many vessels of various sizes, shapes and wall thicknesses; these vessels shared vessel walls (a and b). A difference in thickness was partially noted in the blood vessel wall (c and f ). In one blood vessel wall, there were parts at which elastic fibers were present, missing (c, d and f; arrow), and had turned around (c and e). a: HE' b–f: EvG.

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**Table 2** Features of arteriovenous malformation (AVM) in relation to this case

| |
|---|
| **Arteriovenous malformation**: **AVM** |
| **Predilection site** |
| Cerebral hemisphere, mainly in the area of the middle cerebral artery |
| **Size** |
| Increase in the natural course |
| **Large AVM**; nidus greater than 5–6 cm in diameter |
| 1) 15% of all intracranial AVM |
| 2) Onset age in the latter half of the thirties |
| 3) Primary symptoms: headaches, epilepsy and paralysis |
| **Epilepsy** frequent (18–60%) is the primary symptom in addition to intracranial bleeding |
| 1) AVM on the cortex |
| 2) The middle cerebral artery as the feeding artery |
| 3) AVM with a varix in the drainer |
| 4) Large AVM |

screening of blood and urine was performed using GC mass spectrometry (GC-MS) on QP-2010Ultra (Shimadzu, Kyoto, Japan) and a prominence liquid chromatograph (Shimadzu UFLC system, Kyoto, Japan) coupled to a TSQ Quantum Access MAX tandem mass spectrometer (LC-MS/MS) (Thermo Scientific, Waltham, MA, USA). No drugs, medical agents or chemicals were found in blood or urine.

## DISCUSSION

In this case, autopsy findings revealed that the cause of death was traumatic brain damage from brain edema, right uncal herniation and subdural hematoma. It also revealed a large vascular lesion at the bottom of the right frontal lobe, approximately 6 cm in diameter, between the sagittal sinus and right anterior cerebral artery.

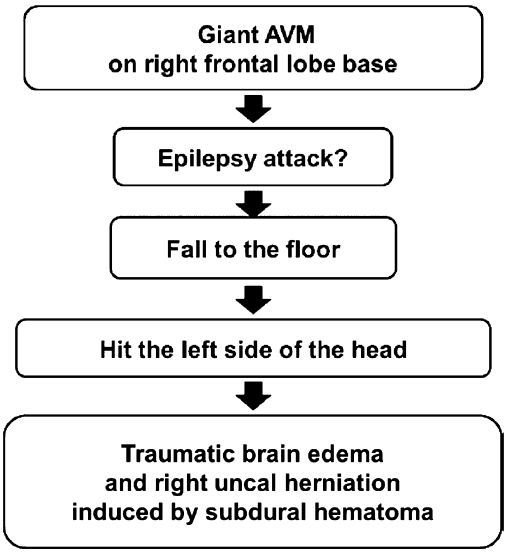


**Fig. 6** The cause of death in this case.

The arterial circle of Willis was separated by using a routine technique. The enlarged vein connected to the sagittal sinus was pulled away until the vascular lesion was revealed. The lesion had pushed against the brain, but it did not include the brain tissue, so separation from the brain was possible with comparative ease. The lesion was connected to the right anterior cerebral artery. This vascular lesion was suspected to be the AVM.

AVM have three components: feeding arteries, a nidus, and draining veins. In this case: (i) the feeding artery was the right anterior cerebral artery; (ii) the nidus was greater than 6 cm in diameter; the vascular lesion, veins, arteries, and abnormal vessels were found together; and (iii) the draining vein was the superior sagittal sinus (Fig. 4). This vascular lesion was diagnosed as AVM based on its histopathological features.

AVM is a typical lesion of vascular malformations. The prevalence of brain AVM is <1% and its incidence is between 0.01 and 0.001%.[13] The incidence of AVM per 100 000 person-years is 1.1–1.4.[14–18] Seventeen percent of patients present in the first two decades of life, while 20% present in the seventh and eighth decades.[16] AVM occurs in all parts of the CNS, whereas intracranial lesions are generally located in the supratentorial compartment. The predilection site is the cerebral hemisphere and mainly the area of the middle cerebral artery.[1] The size of AVM increases with its natural course. A nidus greater than 5–6 cm in diameter is called large AVM. Large AVM account for 15% of all intracranial AVM.[2] More than 50% of large AVM in the supratentorial region are located in the area of the middle cerebral artery.[1] Our AVM was considered to be a large AVM because of the size of the nidus, approximately 6 cm in diameter. It was also found in the supratentorial region, but was located in the area of the anterior cerebral artery instead of the middle cerebral artery.

The onset age of AVM is in the latter half of the thirties and its primary symptoms are headaches, epilepsy and paralysis. Hemorrhage is the most common presentation form of posterior fossa AVM.[19,20] In a population-based study in Sweden, hemorrhage was the initial presenting symptom of AVM in 69.6% of cases.[16] Epilepsy is the primary symptom in addition to intracranial bleeding and its frequency is 18–60%.[7,21–27] The following four parameters were predictive of epilepsy: AVM on the cortex, the middle cerebral artery as the feeding artery, AVM with a varix in the drainer, and large AVM (Table 2). Our reported AVM also had some parameters of epilepsy. Therefore, an epileptic seizure may have been the cause of the fall. In the present case, the deceased hit the left side of his head, which resulted in traumatic brain edema and right uncal herniation induced by subdural hematoma. The results of the blood examination, such as LDH, CK

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and CRP, might be a reflection of the traumatic brain edema. AVM on the brain was considered to be the focal lesion of epileptic seizures.

## CONCLUSION

The cause of death was traumatic brain damage from brain edema, right uncal herniation and subdural hematoma. A large vascular lesion at the bottom of the right frontal lobe, approximately 6 cm in diameter, was found between the sagittal sinus and right anterior cerebral artery. Histopathologically, it was diagnosed as AVM. AVM on the brain was considered to be the focal lesion of epileptic seizures. An epileptic seizure may have been the cause of the fall. In the present case, the deceased hit the left side of his head, resulting in traumatic brain damage as the cause of death (Fig. 6).

## ACKNOWLEDGMENTS

A part of this case report won a poster prize award at the 95th General Congress of the German Society of Legal Medicine, held in Heidelberg in 2016.

## DISCLOSURE

The authors declare that they have no conflict of interest.

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