Int J Clin Exp Med 2016;9(6):12153-12162
www.ijcem.com /ISSN:1940-5901/IJCEM0022787

Case Report

Bilateral carotid and vertebral rete mirabile associated with intracranial multiple hemorrhages: a case report and literature review

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Received December 27, 2015; Accepted March 18, 2016; Epub June 15, 2016; Published June 30, 2016

Abstract: Intracranial rete mirabile (RM) rarely occurs in humans, especially cases that involve both the anterior and posterior circulation (Carotid and vertebral RM, CVRM). The present study reports a rare CVRM case, which showed multiple intracranial hemorrhages during its onset, making it even rarer. The patient was a 48-year-old male; the onset included sudden headache and dizziness, and computed tomography (CT) showed subarachnoid hemorrhage, subdural hematoma and intraventricular hemorrhage. CT angiography (CTA) and digital subtraction angiography (DSA) revealed that normal structures at the cavernous segment of bilateral internal carotid artery (ICA) and at the foramen magnum of bilateral vertebral artery had disappeared and were replaced by abnormally developed vascular networks, findings that were diagnosed as CVRM. The external carotid artery system was involved in the blood supply for the RM at the cavernous segment, and the anterior spinal artery was involved in the blood supply for the RM at the foramen magnum. Additionally, two aneurysms were observed on the anterior spinal artery. The patient's multiple intracranial hemorrhages were considered to be RM bleeding or collateral circulation bleeding, which was conservatively treated. The anterior spinal artery aneurysms were followed up closely with imaging exams. In the report of this rare case, we suggest that RM cases, especially CVRM, can present as rare multiple intracranial hemorrhages and as a complication of anterior spinal artery aneurysms. We should pay more attention to RM in clinical practice.

Keywords: Rete mirabile, multiple intracranial hemorrhages, anterior spinal artery aneurysm

Introduction

Rete mirabile (RM) is a fine meshwork of anastomosing vessels that replace the parent artery [1]. This structure is relatively common in lower mammals, such as cats, sheep and pigs [2]. When it occurs in humans, RM commonly involves the carotid artery and the vertebral artery; at this time, normal continuous intracranial anatomical structures of the internal carotid artery (ICA) or the vertebral artery disappear at the skull base and are replaced by an abnormally developed transdural arterial network. In such a case, an RM can be unilateral or bilateral. Most cases of RM in humans involve only the carotid artery system, i.e., a carotid rete mirabile (CRM), while an RM that simultaneously involves the vertebral artery system, i.e., a vertebral rete mirabile (VRM), is very rare [3]. Bilateral CRM and VRM cases are called CVRM, of which there have only been approximately 10 reports worldwide [4]. The clinical manifestations of RM are very complicated; most RMs may not have symptoms and cannot be found, while those with clinical symptoms mainly show ischemia and bleeding. In such cases, the bleeding is commonly seen as subarachnoid hemorrhage (SAH) and intracerebral hematoma [5]. Simultaneous multiple intracranial hemorrhages at different locations have never been reported. The present paper reports a case report and literature review of rare bilateral CVRM characterized by hemorrhage at onset and showing multiple instances of bleeding at different locations, which are rare.

Case report

The patient (male, 48 years old) was admitted to the hospital due to "sudden headache and

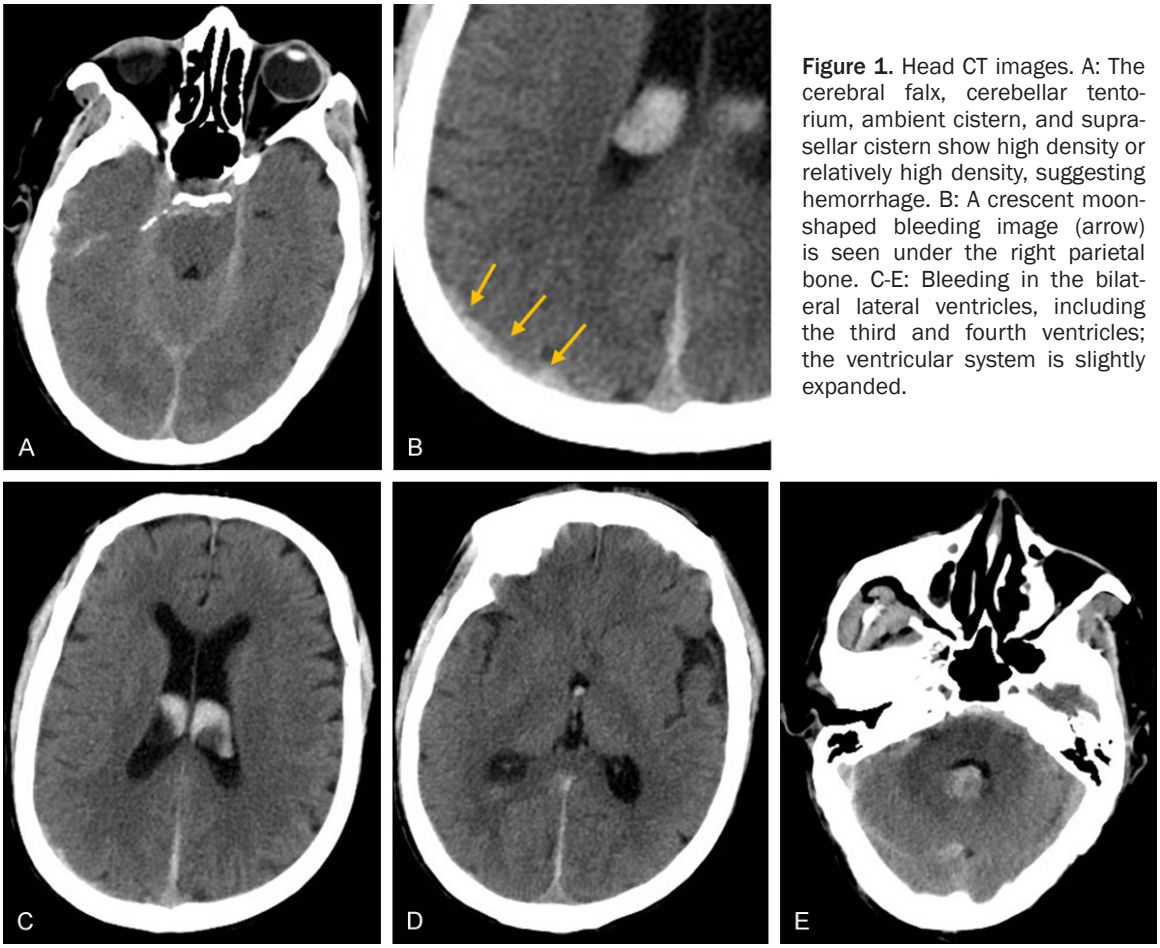

Figure 1. Head CT images. A: The cerebral falx, cerebellar tentorium, ambient cistern, and suprasellar cistern show high density or relatively high density, suggesting hemorrhage. B: A crescent moon-shaped bleeding image (arrow) is seen under the right parietal bone. C-E: Bleeding in the bilateral lateral ventricles, including the third and fourth ventricles; the ventricular system is slightly expanded.

dizziness for one hour". He was previously healthy and denied any familial history of cerebrovascular disease, hypertension and diabetes. Physical examination revealed the following: blood pressure 130/85 mmHg, conscious, answering questions accurately, flexible limb activity, neck stiffness, and positive Kernig signs. Emergency head computed tomography (CT) showed images of high-density diffuse bleeding in the cerebral falx, cerebellar tentorium, ambient cistern, and suprasellar cistern; crescent moon-shaped bleeding was observed under the right parietal bone, along with bleeding in the bilateral lateral ventricles, the third ventricle and the fourth ventricle (**Figure 1**). The symptoms suggested SAH, subdural hematoma and intraventricular hemorrhage. Initial CT angiography (CTA) examination revealed that the ophthalmic artery segment, the clinoid segment of the bilateral ICA and the communicating segment of the right ICA were not visible, and vascular networks were observed at sellar region, Additionally, fenestration of the right ophthalmic artery was observed, the bilateral vertebral arteries were slightly thinner, some tortuous vessels were seen above foramen magnum, the bilateral middle cerebral arteries were slightly thinner, and the A1 segment of the right anterior cerebral artery was not visible. Furthermore, the contours of the left anterior cerebral artery, the basilar artery, and the posterior cerebral artery were natural, the images were good, and the lumens did not show significant narrowing or expansion (**Figure 2**). A thin-layer enhanced CT scan revealed that the bilateral carotid canal and the cervical transverse foramen had developed well (**Figure 3**). Because CTA failed to clearly diagnose, further digital subtraction angiography (DSA) examination was performed, which showed that the main stem of the bilateral ICA disappeared after it reached the cavernous sinus, and it evolved into a vascular network. Angiography of the external carotid artery showed that the internal maxillary artery branches and the ascending pharyngeal artery provided a blood

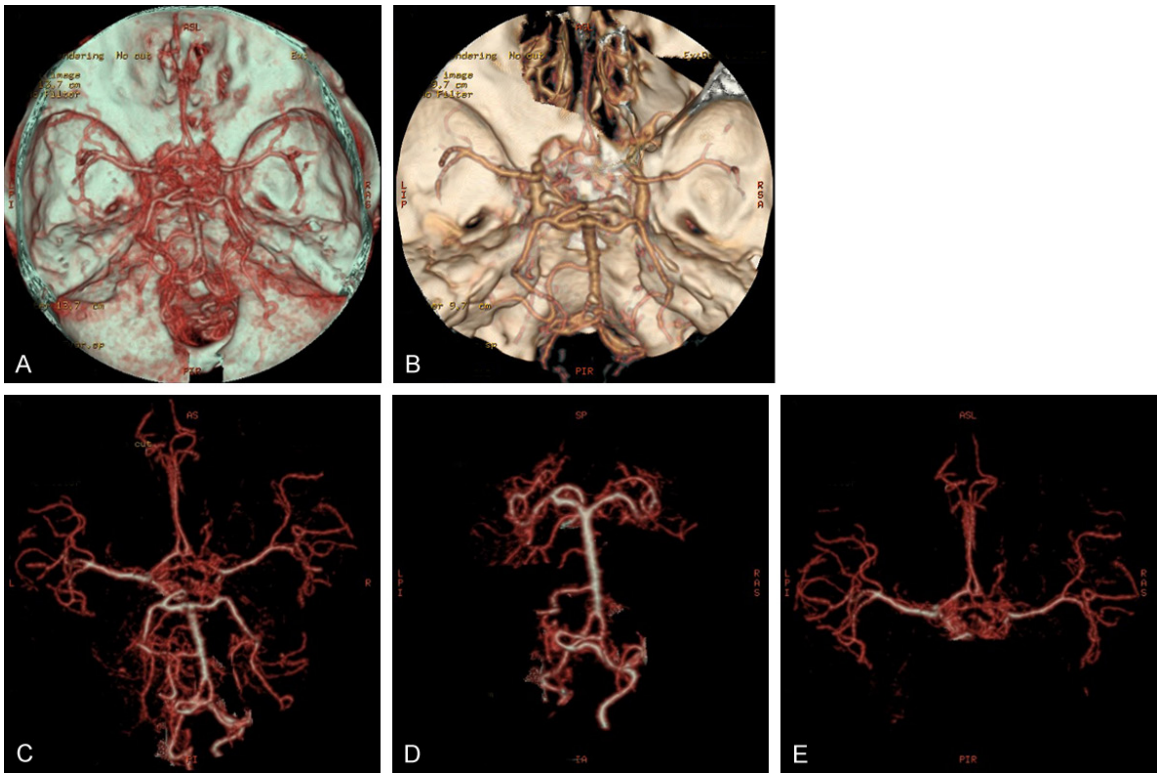

Figure 2. Head CTA images. A-E: The ophthalmic artery segment and the clinoid segment of the bilateral ICA; the communicating segment of the right ICA is not shown, and vessel networks can be observed in sellar region. Fenestration of the right ophthalmic artery is observed. The bilateral vertebral arteries are slightly thinner, and vessel networks are seen above foramen magnum. The bilateral middle cerebral arteries are slightly thinner, and the A1 segment of the right anterior cerebral artery is not shown. The contours of the left anterior cerebral artery, the basilar artery, and the posterior cerebral artery are natural, the images are good, and the lumen does not show significant narrowing or expansion.

supply to the vascular network, and intracranial arteries, such as the middle cerebral artery and the anterior cerebral artery, started from the vascular network. Angiography of the bilateral vertebral artery showed that the main stem of the bilateral vertebral artery disappeared at the foramen magnum region and also that it evolved into a vascular network; in the meantime, after the V2 segment of the bilateral vertebral arteries sent out the anterior radicular spinal artery, they continued to become tortuous and expanded into the anterior spinal artery, which traveled upwards to connect to the vascular network to participate in the blood supply. At the same time, the vertebrobasilar artery provided a blood supply to the anterior circulation through the posterior communicating artery (**Figures 4**-**6**). An expanded saccular aneurysm could be seen at the junction of the right anterior radicular spinal artery and the anterior spinal artery, and aneurysm-like changes could be seen slightly above the structure (**Figure 7**). According to the onset characteristics and the abovementioned imaging findings, this case was diagnosed as bilateral CVRM associated with intracranial multiple hemorrhages and anterior spinal artery aneurysms. We planned to use conservative treatment for the multiple intracranial hemorrhages and imaging follow-up for the anterior spinal artery aneurysms. The patient was hospitalized for 14 days and was discharged after a good recovery with any positive sings in the nervous system. We planned to employ a periodic DSA follow-up to monitor the changes in the aneurysms.

Discussion

RM mainly refers to a meshwork of multiple fine arteries or arterioles that freely intercommunicate and reconstitute the absent or hypoplastic segments of the parent artery [1]. RM means 'wonderful net' in Latin [6]. RM is commonly observed in lower mammals, such as cats,

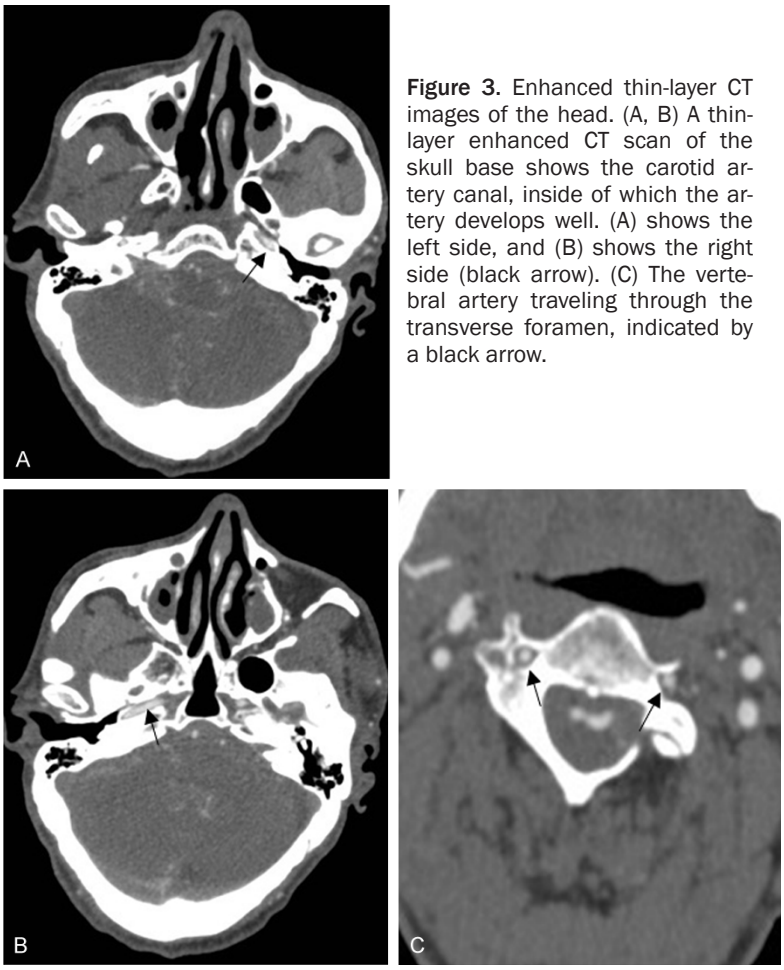

Figure 3. Enhanced thin-layer CT images of the head. (A, B) A thin-layer enhanced CT scan of the skull base shows the carotid artery canal, inside of which the artery develops well. (A) shows the left side, and (B) shows the right side (black arrow). (C) The vertebral artery traveling through the transverse foramen, indicated by a black arrow.

sheep, goats, oxen and pigs. From an embryonic development point of view, in the early embryonic stages, the continuity of the ICA or vertebral artery exists; however, in the late embryonic stage, the ICA or the vertebral artery degenerates under secondary atrophy, and a vascular network forms at this location. This type of vascular network is called RM [2]. The exact cause for RM in humans is unclear. It is speculated that RM is caused by the degeneration of the ICA or the vertebral artery during a late embryonic stage or an early neonatal stage, similar to RM in lower mammals. At these times, normal continuous intracranial anatomical structures of the ICA or the vertebral artery disappear at the skull base and are replaced by an abnormally developed transdural arterial network. Blood vessels are sent out from the vascular network to provide a blood supply to intradural arteries, such as the anterior cerebral artery or the middle cerebral artery. CRM can have a blood supply from the ICA, and the ophthalmic artery can also sometimes send out branches to provide a blood supply. In the meantime, the many branches of the external carotid artery can also participate in CRM blood supply, such as the branches of the internal maxillary artery, the middle meningeal artery, the accessory meningeal artery, and the artery of the foramen rotundum or the ascending pharyngeal artery; at this time, the RM has a function similar to the circle of Wilis [7]. The CRM of the carotid artery system occurs at the cavernous sinus at the skull base; in addition, some RM occurs at the petrous segment, which involves a smaller area [8]. However, Aburto-Murrieta et al. reported a case of CRM in 2011 that involved a larger area of the petrous ICA [9]. VRMs that occur at the vertebral artery often involve the vertebral artery at the foramen magnum, and some studies in the literature have reported that extremely rare cases could affect the lower segment of the basilar artery. For example, in 2010, Sahin et al. reported an RM that involved the bilateral CRM and the lower segment of the basilar artery [10].

RM often affects the carotid artery system (CRM) alone. However, RM will not affect the vertebral artery system (VRM) alone. When the vertebral artery system is involved, it is always combined with CRM; therefore, this type of RM is called CVRM [3]. RM is a rare vascular disease; there have only been approximately 30 case reports as of 2015, of which there are only approximately 10 reports of CVRM cases worldwide. Additionally, the condition frequently occurs in Asians [4]. The present paper reports a rare CVRM case. During the disease onset, it presented simultaneous multiple intracranial hemorrhages at several locations and included SAH, subdural hematoma and intraventricular hemorrhage. After reviewing relevant cases of simultaneous multiple intracranial hemorrhage in the literature, we suggest that the cause of

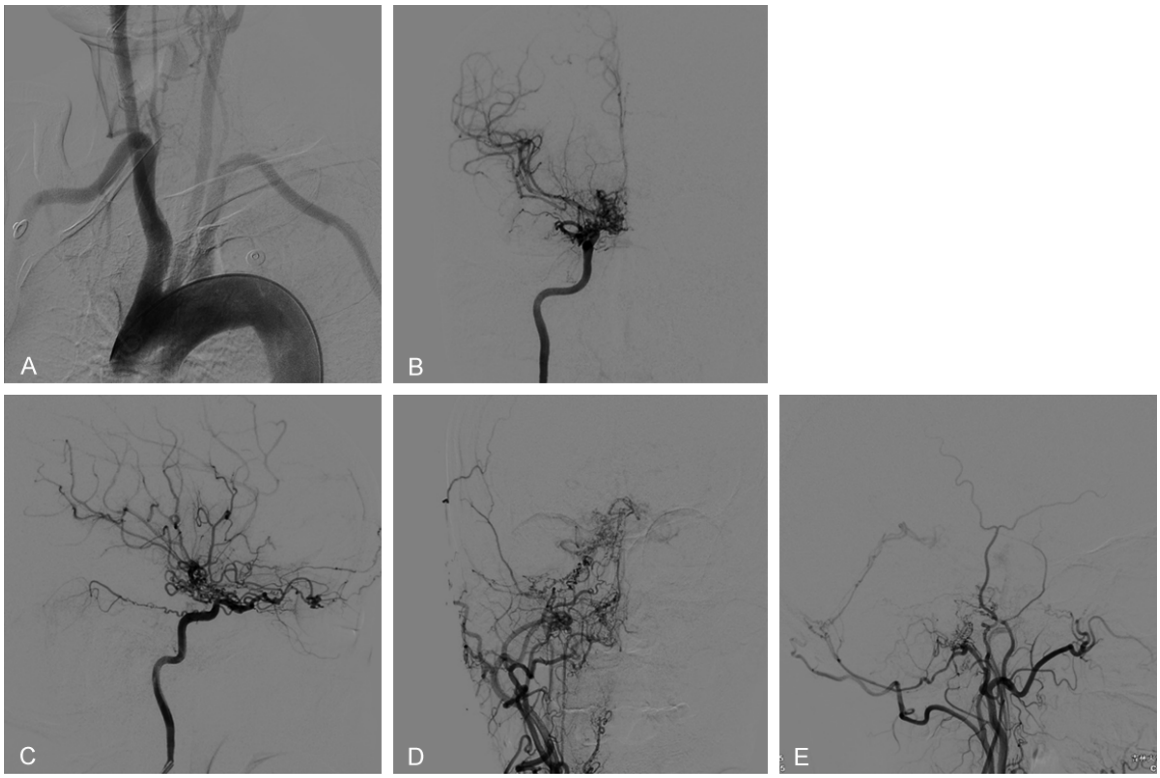

Figure 4. Head DSA images. A: The course of the aortic arch is normal, and no abnormalities are seen in the traveling of each branch. B, C: Lateral image of the right ICA, showing internal carotid arteries extending at the cavernous sinus to become the ophthalmic artery. The ICA and the ophthalmic artery form an abundant vascular network near the cavernous sinus. The anterior cerebral artery and the middle cerebral artery start from the vascular network, and the posterior extension of the meningeal pituitary stem can be seen. D, E: Lateral image of the external carotid artery, showing the ascending pharyngeal artery and the internal maxillary artery sending out branches to participate in the vascular network blood supply. The ascending pharyngeal artery sends out branches to continue to become the meningeal artery and participates in lateral circulation near the cerebellar tentorium.

hemorrhage may be the bleeding of a fragile RM blood vessel or an anastomotic branch, which induces a transient increase of blood pressure, thereby causing other locations to bleed simultaneously [11]. Although RM is rare, it still has important clinical significance. Because the abnormal vascular network and the formed lateral circulation in RM are fragile, the condition is prone to ischemic and hemorrhagic symptoms; therefore, it has certain clinical significance [12]. Because it is rare, RM tends to be misdiagnosed, especially in VRM that includes participation of the anterior spinal artery, and the expanded tortuous anterior spinal artery tends to be misdiagnosed as spinal dural arteriovenous fistula [13]. Moreover, the abnormally proliferated blood vessels also have imaging similarities to moyamoya disease [14]. In fact, RM has its own diagnosis criteria and is diagnosed according to the criteria that will least likely lead to misdiagnosis.

Intracranial RM has the following diagnosis criteria: 1) hypoplastic ICA; 2) arterial plexus between the maxillary artery and the cavernous portion of the ICA; 3) dilated ophthalmic artery; 4) non-hypoplastic supraclinoid ICA that is fed by the arterial plexus and the ophthalmic artery; 5) bilateral lesions; and 6) no abnormal vessels, such as moyamoya vessels in the intradural circulation [12]. Although meeting the above criteria can accurately diagnose RM, the condition sometimes needs to be distinguished from other types of congenital vascular agenesis or dysplasia. In these congenital diseases, a carotid canal or a transverse foramen may not develop or may be narrow, which are criteria that do not exist in RM [12, 15]. After a clear diagnosis of RM, attention should be paid to determine whether RM is simultaneously combined with other diseases, including aneurysms, arteriovenous malformations, carotid-cavernous fistulas, pseudoxanthoma elasti-

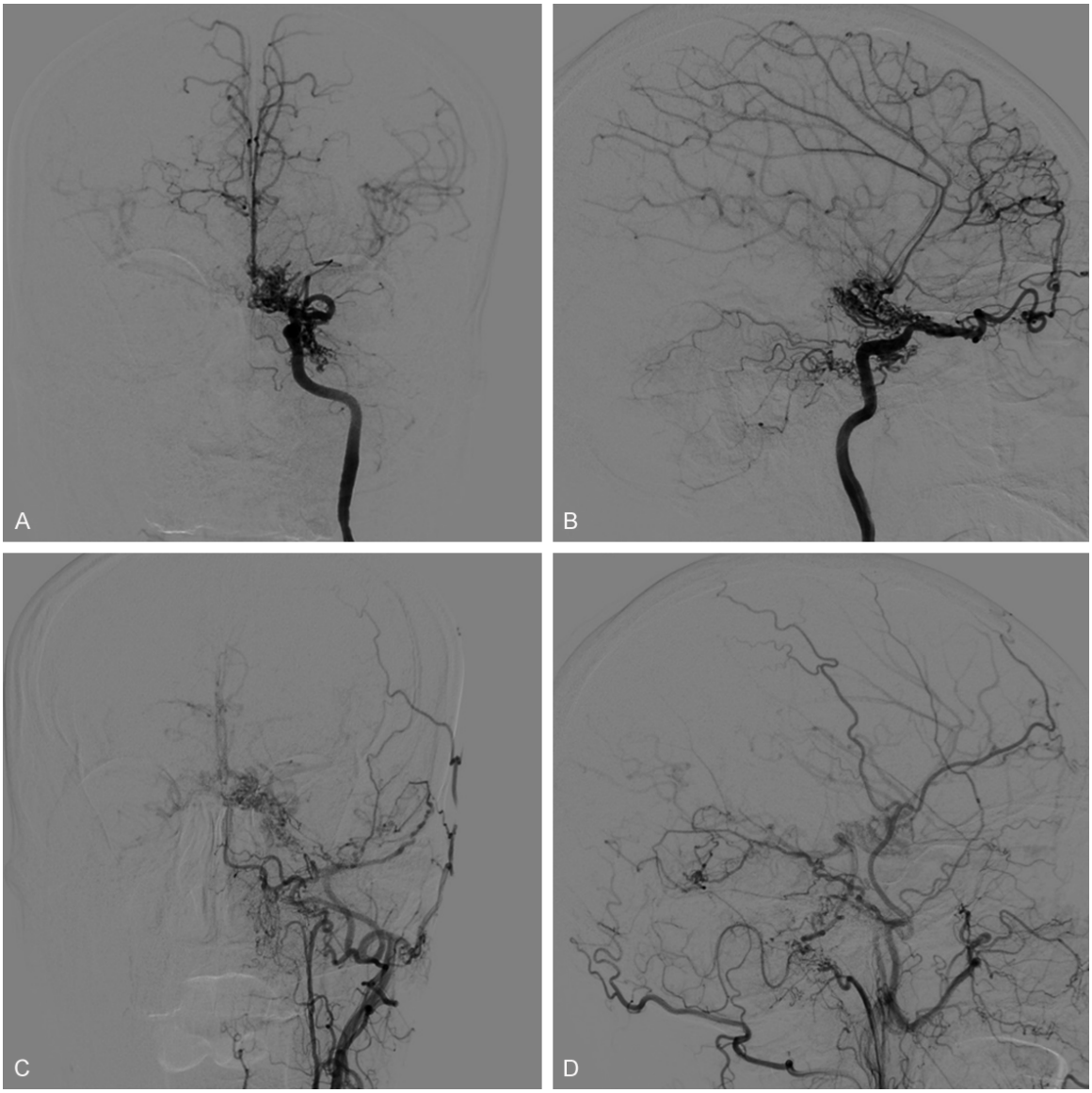

Figure 5. Head DSA images. A, B: Lateral image of the left carotid artery, showing the forward extension of the ICA at the cavernous sinus to become the ophthalmic artery. The ICA and the ophthalmic artery form an abundant vascular network near the cavernous sinus. The anterior cerebral artery and the middle cerebral artery start from the vascular network, and the posterior extension of the meningeal pituitary stem participating in the cerebellum blood supply can be seen. C, D: Lateral image of the external carotid artery, showing the ascending pharyngeal artery and the internal maxillary artery sending out branches to participate in the vascular network blood supply.

cum, and Dieulafoy's lesion [10]. In addition, it has been reported that RM can be combined with concomitant aortic arch deformity [16]. There has also been a report of the simultaneous combination RM and Galen aneurysmal malformation [17]. Of these complications, the combination with pseudoxanthoma elasticum (PXE) is particularly special. For example, in a 2012 report, Del Zotto et al. suggested that CRM development may be one of the mechanisms leading to an ischemic stroke in young adults affected by PXE. Furthermore, in patients with CRM, clinical features of PXE should be carefully examined, and ATP-binding cassette sub-family C member 6 (ABCC6) gene screening should be considered [18]. In 2011, Vasseur et al. reported a similar study, and they also mentioned that PXE is related to RM [19]. The CVRM case reported in the present paper meets all of the above criteria, the diagnosis is

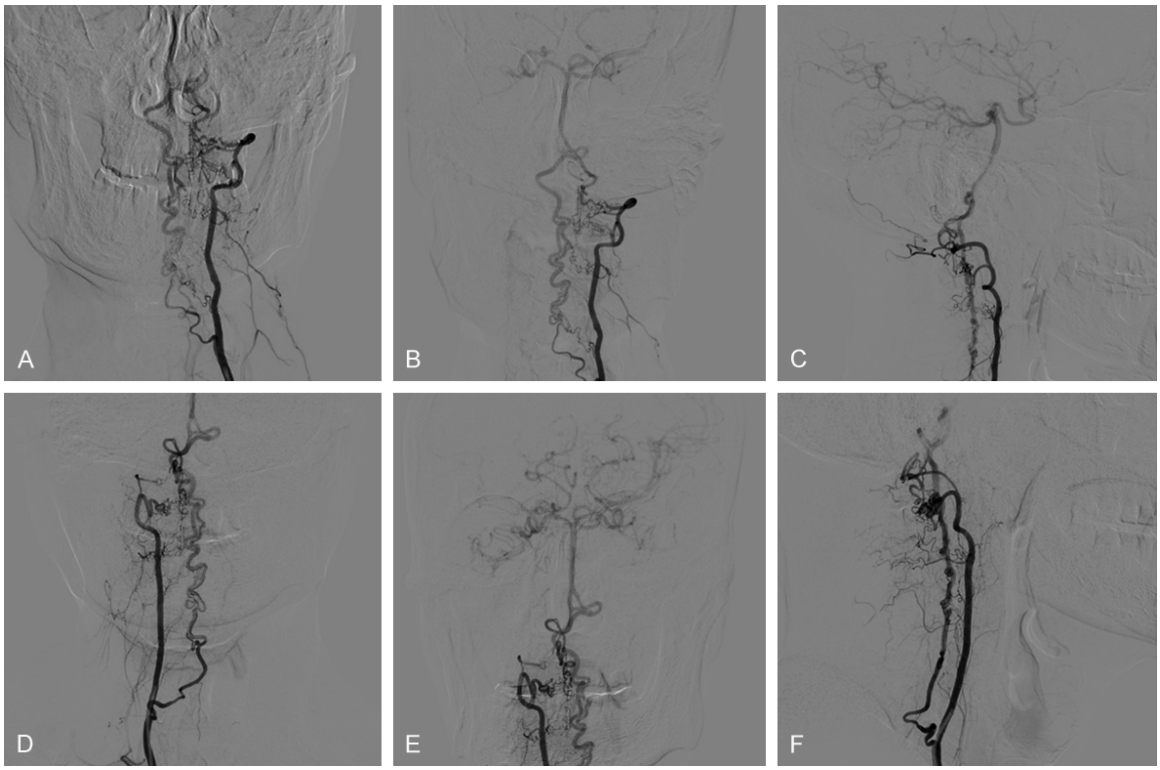

Figure 6. Angiography of the bilateral vertebral artery. The bilateral vertebral artery angiography shows that the main stem of the bilateral vertebral arteries disappears in the foramen magnum region, and the arteries also continue to become the vascular network. In the meantime, the V2 segment of the bilateral vertebral artery sends out the anterior radicular spinal artery, which continues to become an expanded tortuous anterior spinal artery, which travels to connect with the vascular network to participate in the blood supply; at the same time, the vertebrobasilar artery system provides a blood supply to the anterior circulation through the posterior communicating artery. A-C: Left vertebral artery angiography. D-F: Right vertebral artery angiography.

clear, the condition is combined with an anterior spinal artery aneurysm, and DSA examination did not detect any other diseases.

Reports of RM in addition to aneurysm are not common. But there was some reports. For example, Paschoal et al. reported that RM was complicated with ophthalmic artery aneurysms, which were treated with craniotomy and clipping [4]. In another example, Herwadkar et al. reported one case of basilar artery top aneurysm. When the aneurysm ruptured, SAH occurred, which was administered coil embolization treatment [20]. Aneurysm formation is mainly related to increased hemodynamic stress. When RM occurs, the blood flow in normal blood vessels is increased. Apart from the aneurysms at the intracranial arteries, VRM also tends to cause aneurysms at extremely rare locations, such as anterior spinal artery aneurysms. When VRM affects the posterior circulation, the anterior spinal artery will expand to increase the residual VRM blood supply. Most reported CVRMs have a combined anterior spinal artery blood supply; once the anterior spinal arteries thicken and expand, the increase in blood flow tends to cause aneurysm [21]. The case in the present study also had these similar imaging characteristics, including a saccular aneurysm on the anterior spinal artery and an aneurysm-like expansion.

RM is a complex disease. In most circumstances, whether to administer treatment is determined by clinical symptoms, of which RM can have several. Paschoal et al. reviewed previously published literature in 2015 and found 35 RM cases. The clinical symptoms of these RM cases mainly include ischemia and hemorrhage, and they have certain characteristics. For example, patients younger than 20 years old mainly presented limb movement disorders, followed by epilepsy and visual impairment, while patients older than 20 years old

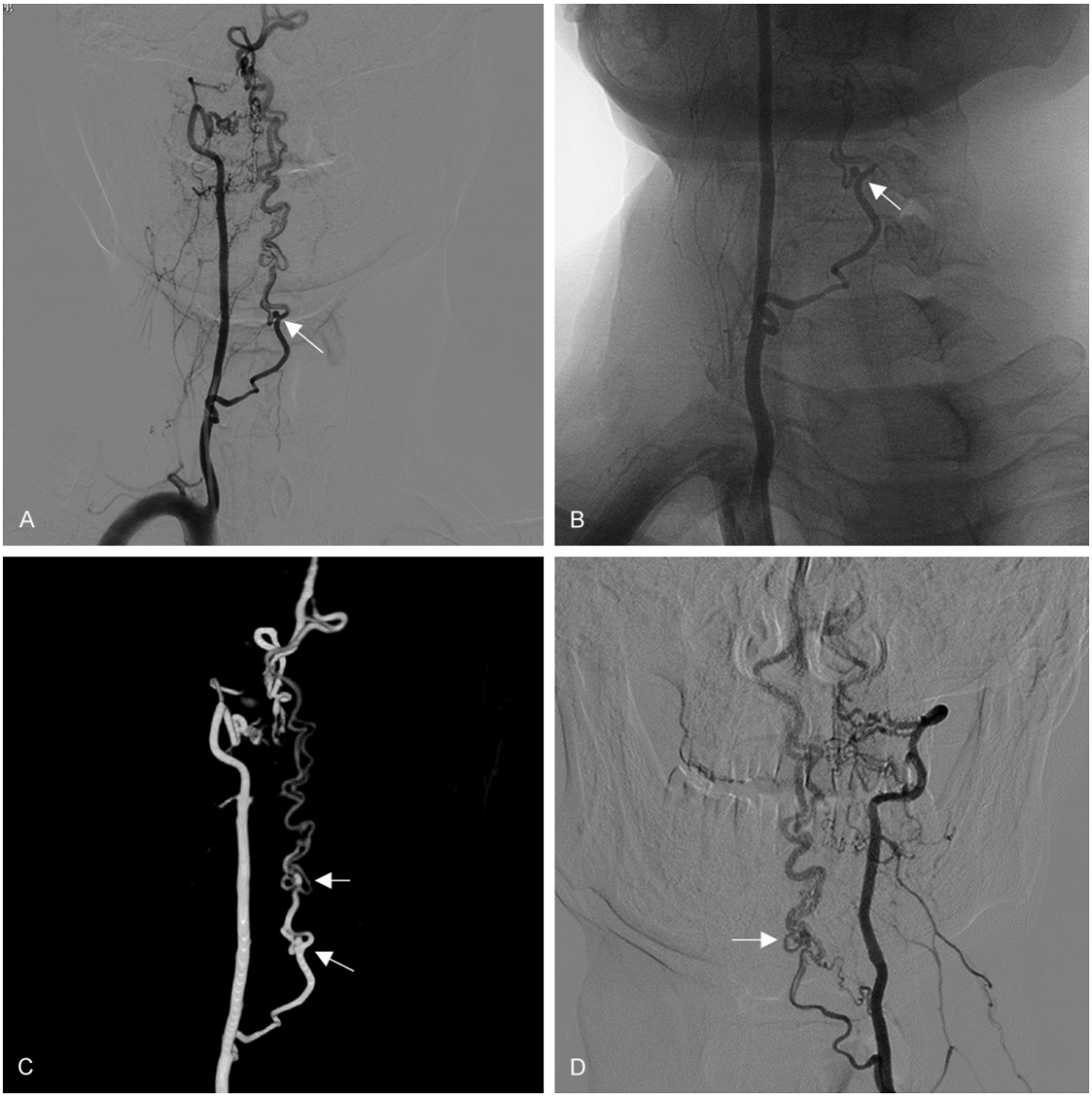

Figure 7. Bilateral vertebral artery angiography. A-C: Right vertebral artery angiography shows an expanded saccular aneurysm that can be seen at the junction of the right anterior radicular spinal artery and the anterior spinal artery, and an aneurysm-like change can be seen slightly above the structure (arrow). D: Left vertebral artery angiography can identify an aneurysm-like change above the anterior radicular spinal artery.

mainly had SAH, accounting for 40% of cases, followed by intracerebral hemorrhage [4]. The SAH/intraparenchymal bleeds are hypothesized to be due to rupture of associated aneurysms, rupture of anastomosing vessels, hemodynamic stress, or bleeding into ischemic infarcts [22]. Currently, it is suggested that RM does not require treatment if there are no symptoms, such as vascular reconstruction because most RMs can provide abundant lateral circulation. For example, Hong et al. reported that perfusion magnetic resonance imaging (MRI) was performed in a case of CRM and VRM, and no abnormalities were observed [23]. Under most conditions, RM cases are given symptomatic treatment. If the RM or the collateral circulation ruptured, most are difficult to treat. The CVRM in the present study is such a case: multiple intracranial hemorrhages were observed, DSA did not detect an aneurysms or vascular abnormalities, and the prognosis was good after conservative treatment. However, if an intracranial aneurysm occurs, treatment must be performed because the risks of a sec-

ond rupture and hemorrhage are very high, and treatment can achieve satisfactory results [4, 20]. Apart from the intracranial artery, CVRM can also cause rare anterior spinal aneurysm, which can even rupture. For example, Nagahata et al. reported one case of CVRM combined with anterior spinal artery blood supply in which rupture of the aneurysm occurred; coil embolization achieved a satisfactory result [24]. The CVRM case in the present study is combined with the anterior spinal artery. Because there was no rupture, and the surgical degree of difficulty was high; therefore, we planned imaging follow-up. If the size of the aneurysm increases or the shape is irregular, then treatment will be given. In summary, RM cases, especially CVRM cases, can present rare multiple intracranial hemorrhages and can be combined with anterior spinal artery aneurysm.

Disclosure of conflict of interest

None.

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