· Letter to the Editor ·

Direct approach to thrombosed superior ophthalmic vein of recalcitrant indirect carotid cavernous fistula in thrombocythemia failed with multiple conventional embolization treatment

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Dear Editor,

I am Dr. Jungyul Park from the Division of Oculoplasty, Department of Ophthalmology, Pusan National University Hospital, Busan, Korea. I am writing to present a case of direct approach to thrombosed superior ophthalmic vein of recalcitrant indirect carotid cavernous fistula which was failed to treat with multiple conventional embolization treatment. To our knowledge this is very challenging procedure to the ophthalmologist, and not well described in literatures, especially in thrombocythemia patient with thrombosed superior ophthalmic vein. The patient's symptoms were very severe to light perception on her affected eye, but well subsided after procedure. So, we now share our challenging case and operation method.

Informed consent for publication was obtained from the patient in this case report, as potentially identifying information may be included in this article. The study is adherent to the tents of Declaration of Helsinki.

Carotid-cavernous fistula is caused by abnormal arteriovenous communication between the carotid artery vascular system and cavernous sinus. It is broadly classified into direct and indirect types; according to the Barrow classification, it is generally divided into an A type direct carotid cavernous fistula and B, C, and D type indirect carotid cavernous fistulas. The indirect carotid cavernous fistula refers to the blood vessel branch of the cranial dura mater in the internal or external carotid artery, which is connected to cavernous fistula. In other words, the dural arteriovenous fistula arises in the cavernous fistula, which can be described as a type of dural arteriovenous fistula[1]. As the pressure of the cavernous fistula increases and the superior ophthalmic vein expands, various ophthalmic symptoms such as exophthalmos and hyperemia that accompany venous congestion appear[2-3]. If symptoms are mild, conservative treatment is sufficient[4]. If treatment is necessary, it usually blocks the blood flow through the embolization of the cavernous sinus *via* the femoral vein or prevents blood flow by slowing the flow of blood vessels and causing thrombus[5-6]. If pure, conventional vascular intervention is impossible due to malformations, deformation, or thrombosis of the petrosal vein or other alternative vascular pathways, embolization of the cavernous sinus through the direct superior ophthalmic vein may be attempted[7-10]. In the case of the superior ophthalmic vein, when the vessel is dilated, it is easy to secure and manipulate the blood vessel and to insert the catheter. However, in rare cases, procurement of blood vessels and insertion of a catheter are difficult or fail due to obstructions resulting from the thrombus in the superior ophthalmic vein, and it becomes too fragile to control for attempting the direct ophthalmic vein approach[11]. The authors report a case of embolization of the indirect carotid cavernous fistula through a superior ophthalmic vein with thrombosis and no response to doppler ultrasound who failed multiple traditional treatments, and we share the surgical experience.

A 78-year-old woman with hypertension complained of the sudden onset of symptoms such as severe pain in the left forehead, pain in the orbital region, and tears, and she visited the Emergency Room 3 weeks ago. Immediately following the visit, the patient underwent magnetic resonance imaging, brain magnetic resonance imaging, and blood testing. Enlargement of the left cavernous vein and the left superior ophthalmic vein was observed (Figure 1). Thus, she was diagnosed with the left carotid cavernous fistula and underwent angiography in the neurosurgery department. Preoperative angiography imaging through the affected internal carotid artery showed the ophthalmic artery in the early phase, and the arterial phase image showed cavernous sinus (Figure 2). The arterial phase image through the affected external carotid artery and the image through the external and internal carotid artery of the right side, the opposite side, showed early flow or enhancement of cavernous sinus (Figure 3). Based on this, the patient was diagnosed with an indirect carotid cavernous fistula communicating with the cavernous sinus in several branches of both external and internal carotid arteries. In addition, the platelet increases and Janus kinase-2 (JAK-2) V617F gene were detected in the blood test; as a result, essential thrombocythemia was diagnosed. The patient had bilateral corrected visual acuity of 0.8, intraocular pressure of 16 mm Hg in both the right and the left eye, with exophthalmos of 16 mm according to Hertel exophthalmometer. No conjunctival hyperemia, conjunctival edema, ptosis, incomplete palpebra closure, diplopia, ocular movement limitation, of periorbital murmur were found. There were also no abnormal or specific findings in fundus examination, visual field examination, and optical coherence tomography.

Based on these findings, a microcatheter was inserted into the right femoral vein through the petrosal sinus to check the left cavernous sinus and enlarged superior ophthalmic vein and perform coil embolization in the left cavernous sinus. As a result, blood flow to the superior ophthalmic vein was significantly reduced. Thus, we expected that thrombus formation would block the flow of the blood, so we determined to finish the procedure and wait until the symptoms had subsided. However, after the procedure, the patient continued to have symptoms such as a headache, nausea, and vomiting. Brain magnetic resonance imaging showed that the superior ophthalmic vein of the patient was enlarged further. On the ophthalmologic examination, the following symptoms were observed: the visual acuity was light perception on the left eye, intraocular pressure of 20 mm Hg, exophthalmos of 21 mm, complete paralysis of the left ocular movement, complete closure of eyelid, corneal edema, pupil enlargement, iridoplegia, severe conjunctival hyperemia and conjunctival chemosis (Figure 4). After three additional coil embolization using a microcatheter through the femoral artery and vein, the patient showed the following symptoms: thrombosis in the superior ophthalmic vein and severe ophthalmic vein

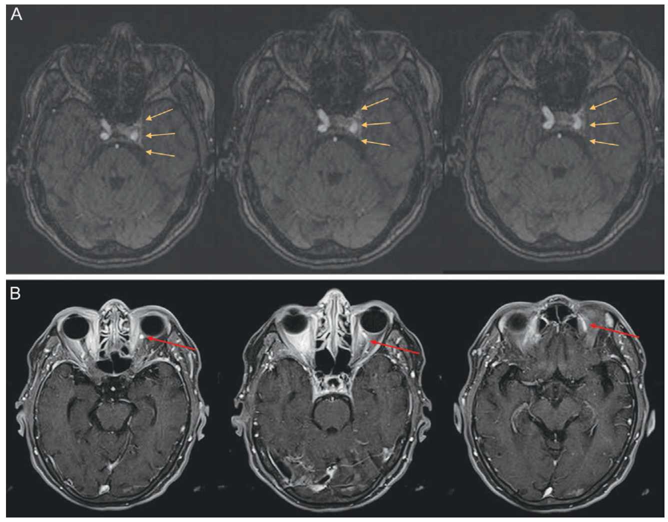

Figure 1 Magnetic resonance image demonstrating enhancement of left cavernous sinus (A) and engorgement and dilatated left superior ophthalmic vein (B).

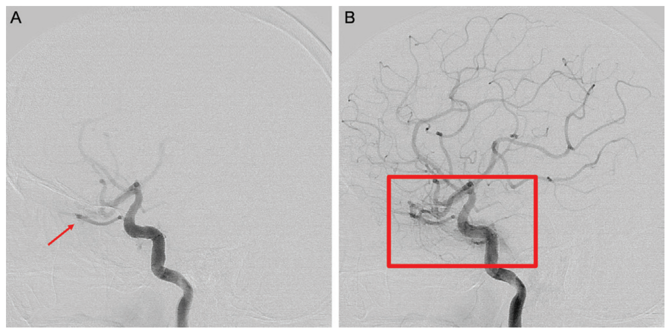

Figure 2 Angiography shows early filling of ophthalmic artery (A) and early filling of cavernous sinus on arterial phase which phase normally show no cavernous sinus filling (B).

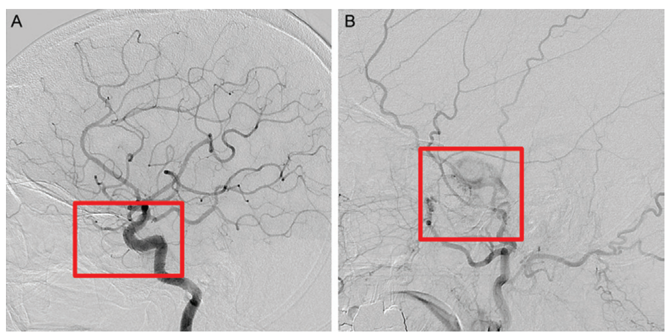

Figure 3 Contralateral (right) angiography *via* internal carotid artery (A) and external carotid artery also showed early filling of left cavernous sinus (B).

enlargement, the pressure signs of cavernous sinus, pain, exophthalmos of 23 mm, and intraocular pressure of 25 mm Hg. In addition, choroidal detachment was observed, and the patient's symptoms worsened (Figure 5). Then, we finally decided to undergo coil embolization through exposure of the superior ophthalmic vein directly after consultation with the neurosurgery department. The procedure was as follows (Figure 6). First, the position of the superior ophthalmic vein was determined using Doppler ultrasound, and a silk suture

Figure 4 Patient showed total ophthalmoplegia, proptosis, ptosis, severe chemosis, and pupil dilatation on her left eye.

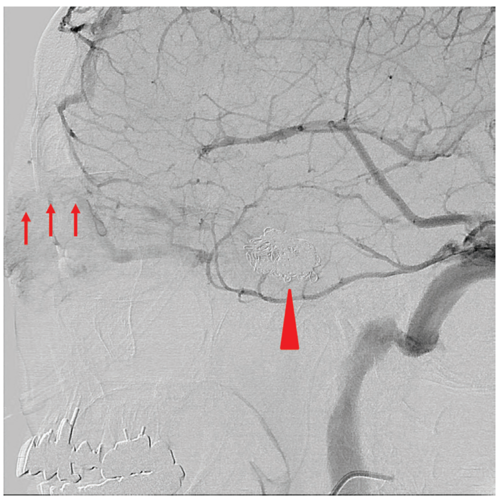

Figure 5 Angiography *via* left internal carotid artery shows previous coiling site (red arrow head), severely dilated superior ophthalmic vein and distal thromboembolic signs on her left superior ophthalmic vein (red arrows).

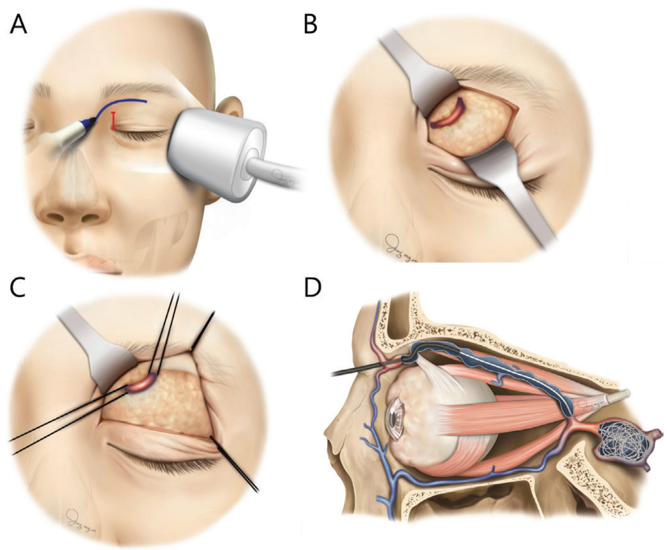

Figure 6 Surgical technique A: First check the superior ophthalmic vein with doppler ultrasound, marking the incision line along the sub-brow area; B: The incision is made on the skin, orbicularis oculi muscle and septum in order to avoid unwanted damage to the superior ophthalmic vein and surrounding tissues; C: Make traction with 4-0 silk on the distal and proximal sides of the superior ophthalmic vein to make it easy to handle and control any unexpected bleeding; D: Insert the microcatheter through the superior ophthalmic vein, and patient should show normal finally coiling embolization of cavernous sinus especially around the entrance site of the superior ophthalmic vein.

for traction was connected to the tarsal plate. Approximately 1.5 cm of incision line was made using a No.15 knife along the lower border of the eyebrows. Next, the orbicularis oculi muscle and orbital septum were carefully dissected using Westcott scissors. Then, the orbital fat was exposed and gently dissected using toothless forceps and a cotton swab. As a result, the superior ophthalmic vein was exposed at about 1.5 cm above the lacrimal caruncle, which was a position slightly deeper than the upper border of the periorbital. Then, mosquito forceps were inserted in the lower region of the superior ophthalmic vein, and the middle part of the 4-0 silk thread was held using the forceps. The mosquito forceps were then removed from the same area where it had entered. The middle part of the silk was cut, and the two thread strands were located in the distal and proximal parts of the superior ophthalmic vein, respectively, and knots were tied at each side for easy manipulation and hemostasis in case of vascular rupture. After pulling the two strands, the superior ophthalmic vein was kept in tension, and a microcatheter was inserted. The superior ophthalmic vein formed loop-like arch, so we carefully dissected the distal and proximal part of superior ophthalmic vein to verify the direction to the cavernous sinus. In addition, the positions of the catheter, superior ophthalmic vein, and cavernous sinus were identified by angiography through the femoral artery. Coil embolization was performed through the superior ophthalmic vein. Embolization was also carried out intensively on the site where the remaining blood flow was observed along with the origin of the superior ophthalmic vein. After we confirmed absolute obstruction of

Figure 7 The fistula and the symptoms of patient were dramatically resolved after coiling embolization through the superior ophthalmic vein.

the blood flow to the superior ophthalmic vein and cavernous sinus, we finished the operation. During the operation, hemostasis was achieved by minimizing the use of bipolar cautery and absorbing the cottonoid in a solution of 1: 100 000 of epinephrine and lidocaine. On the first day postoperatively, the patient's ocular edema and choroidal detachment were dramatically improved. At 2wk postoperatively, there were the following improvements: corrected visual acuity of 0.25 in the left eye; intraocular pressure of 11 mm Hg; palpebral fissure of 8 mm in the right eye and 5 mm in the left eye; and levator function of 13 mm in the right eye and 6 mm in the left eye. The ocular movement also significantly improved, but the pupil dilation and iridoplegia were not recovered. Most of the ocular movement disorder recovered at 2mo postoperatively, and the pupil dilation and iridoplegia did not recover until 5mo postoperatively (Figure 7).

Although the cavernous sinus has been considered as a large intravenous space, it was discovered by Parkinson[1] in the 1960s as a net-like structure in which veins are intricately and complexly interwoven. Located behind the optic chiasm and on both sides of the sellar, the cavernous sinus is referred to as a lateral sellar component. Understanding the venous anatomy of this structure is very important in interpreting angiography results and planning treatment. Four venous spaces were divided based on the internal carotid artery in the cavernous sinus: anterior, posterior, medial, and lateral[1]. The anterior region of the superior ophthalmic vein, the superior and inferior basilar plexus, and the posterior space of the inferior petrosal sinus form a flow after the formation of the fistula, thus becoming an important vascular flow pathway that causes various ophthalmic symptoms[12]. The flow to the anterior region passes the angular vein through the superior and inferior ophthalmic vein, thereby being connected to the facial vein. When blood flow is increased by the fistula, the superior ophthalmic vein is enlarged and becomes thick. This is accompanied by ophthalmologic symptoms such as exophthalmos and conjunctival hemorrhage, and the blood vessel is arterialized. There is no valve inside the blood vessel, and relatively smooth flow is shown, thereby becoming suitable for access through the vein. The flow to the posterior mainly passes the lower petrosal sinus and basilar plexus. If the flow of the carotid-cavernous fistula is backward [12], the ophthalmologic symptoms as shown in this patient may not appear.

Indirect carotid cavernous fistula has been reported to spontaneous improve up to 20%-50%[3,13]. If symptoms persist continuously and no natural obstruction is noted, embolization of the cavernous sinus through the femoral vein is the appropriate treatment. However, in 25%-40% of cases, access to the cavernous sinus is not easy due to venous thrombosis, structural variation, and sudden vessel bending[14-15]. In this case, access through the superior ophthalmic vein provides a direct and short path to the cavernous sinus, allowing a complete closure of the fistula[16]. Miller *et al*[17] and Quiñones *et al*[18] reported excellent outcomes of complete fistula closure in 11 out of 12 patients and 12 out of 13 patients with carotid-cavernous fistula who underwent embolization through the superior ophthalmic vein. Thus, most of the attempts through the superior ophthalmic vein show successful results, although failure is occasionally reported due to excessive bleeding or blood vessel thrombosis during the procedure. A study reported that partial thrombosis of the superior ophthalmic vein was the most problematic[11,19]. If thrombosis occurs in the proximal part of the superior ophthalmic vein, the blood vessel becomes smaller and more prone to damage, thereby making difficult to insert the catheter into the blood vessel and leading to the failure of the procedure. In this case, we attempted to confirm the blood flow using Doppler ultrasound after securing the superior ophthalmic vein connected to the angular vein and supraorbital vein, but no blood flow was observed. However, based on the anatomical structure, the superior ophthalmic vein was determined, and the catheter was inserted into the superior ophthalmic vein. Blood flow was hardly observed at the entrance of the intravascular penetration, but pulsatile blood flow was observed after the catheter passed through the area where the presence of thrombosis was suspected. During insertion of the catheter thorough the superior ophthalmic vein, we were worried about the additional thrombocytic event due to her underlying disease of essential thrombocythemia, but there weren't additional thrombocytic complications. Angiography confirmed the catheter insertion into the superior ophthalmic vein. Thrombus not only complicates the surgical approach, but also involved in worsening of ophthalmologic symptoms. The pressure of the cavernous sinus was increased, and the flow to the posterior was decreased in this patient after the first procedure. Thus, the flow to the anterior was increased, making the ophthalmologic symptoms worse. In addition, the thrombosis was developed in the proximal part of the superior ophthalmic vein, thereby further worsening the patient's ophthalmologic symptoms.

The key to successful exposure of the superior ophthalmic vein is to understand the orbital anatomical aspects of the superior ophthalmic vein and the possibility of variation. The superior ophthalmic vein plays an important role in delivering most of the orbital venous blood to the cavernous sinus and has the largest diameter[11,20-21]. It is located in the superomedial part of the orbital margin and consists of a combination of the supraorbital vein and angular vein. It extends to the posterior and lateral part of the orbit and reaches the inner boundary of the superior rectus muscle near the orbital roof. Then, it travels to the outer side of the muscle cone along the lower side of the superior rectus and passes the outer boundary of the superior rectus, the upper part of the lateral rectus muscle, and exterior of the levator palpebrae muscle, annular ligament of Zinn, and superior orbital fissure, thereby being connected to the cavernous sinus[11,21]. This understanding of the anatomical structure is significant because it enables the approach into or exposure of the vessels in a deeper position when an approach to the blood vessels in the vicinity of the palpebral skin or the blood vessel exposure fails. Thus, this possibility should be considered prior to surgery.

According to a study of the anatomical location of the superior ophthalmic vein in patients with arteriovenous fistula, the average diameter of the superior ophthalmic vein was 9 mm, and the larger the diameter of the superior ophthalmic vein, the easier the access. Therefore, some authors reported that it is better to wait for treatment until the superior ophthalmic vein is enlarged in the patients without visual problems[22]. The superior ophthalmic vein can be approached by the incision of the lower part of the eyebrow or palpebral fold, and it is located close to the orbital margin. Therefore, it is easier to expose the superior ophthalmic vein as it is closer to the cutting line of the lower part of the eyebrow, but there are cosmetic disadvantages such as scarring[17,22]. In this case, we easily confirmed the superior ophthalmic vein by incision of the lower part of the eyebrow. There were adjacent blood vessels, but we were able to approach the superior ophthalmic vein precisely by grasping the peripheral vascular structures. Unlike the report[20] that the superior ophthalmic vein was located at about 5.9 mm above the lacrimal caruncle, we found the blood vessels at about 1.5 cm.

Thrombosis makes catheter insertion difficult. In addition, catheter insertion at the deep part of the superior ophthalmic vein has a risk of uncontrolled bleeding and damage to the orbital structures. In addition, access through the superior ophthalmic vein can cause visual loss, trochlear injury, ocular damage, and other nearby tissue damage due to the development of orbital hemorrhage and hematoma behind the eyes. It may also cause infection or glaucoma[17]. However, when conventional embolization is not effective and does not respond to repeated procedures, an attempt to insert a catheter by passing through the thrombus can be carried out even if thrombus occurs in the proximal part of the superior ophthalmic vein. It is necessary to sufficiently grasp the structural variation by an accurate understanding of the anatomy through the preoperative angiography and angiography during the surgery, and the surgery should only be performed after fully explaining the risk of hemorrhage, vision loss, and stroke to patients. Effective treatment will be possible through appropriate cooperation and consultation with neurosurgeons.

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