Assessment of Therapeutic Access Routes for Endovascular Therapy of Cavernous Sinus-dural Arteriovenous Fistula

Bikei Ryu,1,2 Shinsuke Sato,1,2 Tatsuki Mochizuki,2 Shogo Shima,2 Tatsuya Inoue,2 Kentaro Kuwamoto,2 Yoshikazu Okada,2 and Yasunari Niimi1

Objective: The usefulness of endovascular treatment for cavernous sinus (CS)-dural arteriovenous fistula (dAVF) has been established. As the first choice of endovascular intervention for CS-dAVF, transvenous embolization (TVE) is generally performed, and the inferior petrosal sinus (IPS) is usually selected as the main access route to the affected CS because of its accessibility. However, the angiographical pattern of the CS varies among individuals. In some cases, it is difficult to access the affected CS via the ipsilateral IPS because of thrombosis, hypoplasia, or aplasia. Therefore, in some cases, alternative venous access routes are needed for TVE.

Methods: A retrospective study was performed with 27 patients diagnosed with intracranial dAVF who underwent endovascular embolization at our institution. Among these, the data of nine patients with CS-dAVF treated by endovascular intervention were analyzed retrospectively in this study. We reviewed the endovascular access routes for CS-dAVF treatment based on anatomical and embryological considerations.

Results: The most common complaint was diplopia, followed by exophthalmos and chemosis. There was no hemorrhagic onset. Cortical venous reflux (CVR) was recognized angiographically in six patients. The IPS on the affected side was angiographically occluded in four patients. TVE was attempted first in all patients. In five patients where the ipsilateral IPS was patent, TVE was successfully performed via the ipsilateral IPS. In four patients where the ipsilateral IPS was occluded, microcatheter access to the affected CS via the ipsilateral IPS was unsuccessful. The following alternative access routes were selected: the superficial temporal vein, facial vein, direct puncture of the superficial middle cerebral vein (SMCV), and ascending pharyngeal artery (APA) for transarterial intravenous embolization (TAIV). The CS-dAVF had disappeared in all patients at the final follow-up examination. In the case of difficult access, compartment formations of the intracavernous sinus were recognized. Compartment formation due to the anatomical and embryological differences of the intracavernous structure may have influenced the ability of the catheter to reach the affected shunted pouch.

Conclusions: In cases where the approach via the ipsilateral IPS was difficult, alternative access routes were effective for the required embolization. It is extremely important to fully understand the angioarchitecture, location of the shunted pouch, and compartments of the CS for successful endovascular treatment. Anatomical and developmental CS considerations may be useful for better access route selection.

Keywords: ascending pharyngeal artery, cavernous sinus, dural arteriovenous fistula, transarterial embolization, transvenous embolization
Introduction

The usefulness of endovascular treatment for cavernous sinus (CS)-dural arteriovenous fistula (dA VF) has been established. Transvenous embolization (TVE) is generally accepted as the first choice for endovascular intervention to treat CS-dA VF.\(^1\)–\(^8\) Furthermore, with the development of DSA, detailed diagnosis of the shunted pouch has become possible; selective TVE has also become possible in recent years.\(^9\)

In TVE for CS-dA VF, the inferior petrosal sinus (IPS) is usually selected as the initial access route to the affected CS because of its accessibility. However, the angiographical pattern of the IPS varies among individuals. Moreover, in some cases, it is difficult to access the affected CS via the ipsilateral IPS because of thrombosis, hypoplasia, or aplasia. Therefore, in such cases, it is necessary to attempt TVE using alternative venous routes. Thus, detailed preoperative examination is required for appropriate access-route selection. To date, TVE has been reported using several venous routes rather than the IPS.\(^1,3,5,6,8,10-12\) However, we sometimes encounter cases where the affected CS cannot be reached from these alternative routes at the time of actual treatment. Sinus or vein organized thrombosis and hypoplasia or aplasia may affect microcatheter advancement. Moreover, the CS structure is not simple, and some compartments may develop by partition formation. The CS is a complex of venous channels with embryologically different origins,\(^2\) and it may also affect compartmentalization.

In this study, we reviewed endovascular access routes in CS-dA VF treatments performed at our institution. Then, we analyzed cases that were difficult to approach from the ipsilateral IPS with anatomic and embryological considerations.

Materials and Methods

A retrospective study was performed with 27 patients diagnosed with intracranial dA VF who underwent endovascular embolization at St. Luke’s International Hospital, Tokyo, Japan, between February 2015 and March 2019. Among these, nine patients treated for CS-dA VF were included and their data were reviewed retrospectively. Patient information was collected from the medical records. Demographic data, past medical history, laboratory data, baseline clinical status, and imaging results, in addition to treatment results and complication details, were analyzed for all patients.

Diagnosis and treatment strategy

Based on DSA combined with MRI and MRA, the diagnosis and detailed angioarchitecture were evaluated by a neurosurgeon who was well experienced in interventional neuroradiology. A biplane angiography system (Artis zee Q, Siemens Healthcare GmbH, Forchheim, Germany) was used for the DSA. In addition to conventional DSA, 3D rotational angiography (RA) was subsequently performed. The obtained 3D data were reconstructed into thin slab-maximum intensity projection (MIP) images as well as multi-planar reconstruction images and volume rendering images. The angioarchitecture, including shunt location, feeders, drainers, and anatomy of the CS, was analyzed in detail. We retrospectively examined the access route to the affected CS, treatment strategy, and treatment results.

In principle, patients with symptoms or cortical venous reflux (CVR) were indicated for treatment under sufficient informed consent. Endovascular treatment was performed under general anesthesia in all cases. For the purpose of obliteration of the shunt by TVE, we considered the access route to the affected CS. In cases where the ipsilateral IPS was patent, TVE was attempted via the ipsilateral IPS. Even in cases where the ipsilateral IPS was occluded angiographically, we first attempted TVE via the occluded ipsilateral IPS. In cases where it was not possible to introduce the microcatheter into the affected CS, the access route was changed. Coils or n-butyl-2-cyanoacrylate (NBCA) liquid embolic material were used to obliterate the shunt.

Outcome assessment

Treatment results were evaluated as complete obliteration (no shunt), near-complete obliteration (small residual shunt with disappearance of CVR and marked reduction of the shunt), and partial obliteration. Outcome assessment was evaluated immediately after TVE and at the last follow-up. We evaluated symptom change, procedure-related complications, and other comorbidities or mortality. In addition, technical efficacy including the access route and degree of difficulty in microcatheter advancement was also evaluated. Ischemic lesions and exacerbation of edema, residual shunt, and hemorrhagic changes after the treatment were evaluated using MRI and MRA. Follow-up observation after treatment was performed by MRI and MRA.
Results

Clinical presentation and patient demographics
The details of clinical presentations and patient demographics are summarized in Table 1. In this study, nine patients diagnosed with CS-dAVF were treated by endovascular intervention. The patients’ ages ranged from 21 to 89 years (mean age: 62.2 years old). There were two men and seven women. The chief complaint was diplopia due to eye movement disorder (three patients). Exophthalmos and chemosis were observed in two patients. Headache, epilepsy, and asymptomatic onset were observed in two, one, and one patients, respectively. There was no hemorrhagic onset. Borden’s classification depending on venous drainage was as follows: Type 1, two patients; Type 2, six patients; and Type 3, one patient.

The feeding arteries to the shunted pouch of the CS were the middle meningeal artery (MMA), artery of the foramen rotundum (AFR), accessory meningeal artery, meningohypophyseal trunk (MHT), inferolateral trunk (ILT), and ascending pharyngeal artery (APA). CVR was angiographically recognized in six patients. Regarding the drainage route, retrograde reflux to the superior ophthalmic vein (SOV), superficial middle cerebral vein (SMCV), uncal vein, petrosal vein (PV), cortical veins of the cerebellum, and prepontine bridging vein was observed. The IPS on the affected side was angiographically occluded in four patients.

Treatments and outcomes
Treatments and outcomes are summarized in Table 1. In all patients, TVE was attempted first and endovascular treatment for shunt obliteration with approved devices was performed under general anesthesia. All patients were heparinized during the procedure. All procedures were performed using the transfemoral approach. In five patients where the ipsilateral IPS was patent, the ipsilateral IPS was used as the access route for the TVE. In four patients where the ipsilateral IPS was occluded, microwire access to the affected CS via the ipsilateral IPS was difficult. Therefore, the following alternative approach routes that were clearly visualized angiographically were selected after unsuccessful penetrations using a 0.035-inch guidewire: the superficial temporal vein (STV), facial vein (FV), SMCV with direct puncture via craniotomy (Case 2), and APA (Case 1). In two cases (Cases 1 and 2), the CS compartment was recognized where the shunted pouch was localized.

Coils were used in all cases as embolic material. In Case 1, NBCA was injected in the shunted venous pouch

<table>
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<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Symptom</th>
<th>Borden type</th>
<th>IPS patency (Ipsi/Contra)</th>
<th>Treatment</th>
<th>Approach route</th>
<th>Embolic material</th>
<th>Immediate result</th>
<th>Final result</th>
<th>Symptom outcome</th>
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<td>APA/Coil</td>
<td>NBCA/Coil</td>
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<td>Improved</td>
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<td>Occluded/Patent</td>
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<td>Improved</td>
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<td>TVE</td>
<td>STV</td>
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<td>TVE</td>
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<td>IPS/IPS</td>
<td>Improved</td>
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<td>F</td>
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<td>1</td>
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<td>TVE</td>
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<td>Patent/Patent/Occluded</td>
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APA: ascending pharyngeal artery; CO: complete occlusion; Contra: contralateral; F: female; FV: facial vein; PV: petrosal vein; IPS: inferior petrosal sinus; Ips: ipsilateral; M: male; NBCA: n-butyl-2-cyanoacrylate (Cryobeads); SMCV: superficial middle cerebral vein; TVE: transvenous embolization; Va: vertebral artery; V2: second cervical vertebra; V3: third cervical vertebra.
for transarterial intravenous embolization (TAIV). Complete obliteration immediately after the procedure was achieved in seven patients. The CS-dAVF had disappeared in all patients at the final follow-up examination. Symptoms improved in six of the eight patients who were symptomatic before the treatment. In two patients, symptoms persisted (oculomotor nerve palsy) or were aggravated (abducens nerve palsy) after treatment.

**Illustrative cases**

Case 1. A 54-year-old man was admitted to our hospital for treatment of asymptomatic CS-dAVF (Borden type 2). DSA showed dAVF involving the left CS draining into the SMCV, uncav vein, SPS, PV, and cortical vein of the cerebellum. Remarkable CVR with a pseudophlebitic pattern was recognized. The dural shunt to the affected CS was supplied by the MMA, AFR, MHT, ILT, and APA. The shunt point was localized at the posterior medial side of the CS (Fig. 1A–1F). The ipsilateral IPS was angiographically occluded (Fig. 1G). First, TVE was planned via the ipsilateral occluded IPS. The occluded IPS was reopened by a Headway17 microcatheter (MicroVention TERUMO, Tustin, CA, USA), and the microcatheter was introduced to the posterior side of the CS (Fig. 1H). Selective angiography showed the posterior compartment of the CS and the draining route into the SPS, PV, and cortical vein of the cerebellum (Fig. 2A and 2B). The anterior side of the CS was not visualized. In this case, although the thin slab-MIP image revealed a very thin connection between the anterior and posterior compartments of the CS (Fig. 2C and 2D), the microcatheter could not reach the shunted pouch. Consequently, we changed the access route to the contralateral clival branch of the APA (Fig. 2E and 2F). A Marathon microcatheter (Medtronic, Irvine, CA, USA) was advanced to the posterior medial side of the CS via TAIV (Fig. 3A and 3B) where the shunts were localized. After blocking the reflux to the SMCV with a coil (Fig. 3C and 3D), 25% NBCA was injected in the shunted pouch (Fig. 3E and 3F). The shunt was completely obliterated without any complication (Fig. 3G and 3H).

Case 2. An 81-year-old woman was diagnosed with epileptic onset CS-dAVF (Borden type 3). DSA showed dAVF involving the right CS draining into the SMCV. Remarkable CVR with a pseudophlebitic pattern was recognized. The dural shunt to the CS was supplied by the MMA, AFR, ILT, and contralateral MHT (Fig. 4A–4C). The shunt point was localized at the lateral side of the CS. TVE was attempted via the ipsilateral IPS, although it was angiographically occluded (Fig. 4D). The occluded IPS
Fig. 2 Intraoperative findings in endovascular therapy (Case 1). Selective venography from a microcatheter placed in the left posterior compartment of the CS (A and B) shows the draining routes into the SPS, PV, and cortical vein of the cerebellum. The microcatheter tip is located in the left posterior side of the CS (arrowhead). The anterior compartment of the CS is not visualized. Axial thin slab-MIP images of rotational angiography of the left common carotid artery (C) and schematic drawing of the CS structure (D, posterior view) in Case 1 show the compartment of the intracavernous sinus. Narrow communication between the anterior and posterior CS is recognized (arrow). Selective microangiography from the clival branch of the right APA (E and F) shows the dural shunt at the left affected CS. The shunted pouch is visualized, and CVR is recognized. The asterisk indicates the shunted pouch. A-P: anterior-posterior view; APA: ascending pharyngeal artery; CS: cavernous sinus; CV: cortical vein; CVR: cortical venous reflux; IPS: inferior petrosal sinus; Lat: lateral view; PP: pterygoid plexus; PV: petrosal vein; SMCV: superficial middle cerebral vein; SOV: superior ophthalmic vein; SPS: superior petrosal sinus; UV: uncal vein.

Fig. 3 Endovascular therapy and treatment outcome (Case 1). Selective intravenousography in the shunted pouch of the CS (A and B) shows that the microcatheter is placed into the shunted pouch (arrowhead; microcatheter tip; the arrow indicates the microcatheter). Road map images (C and D) show the coils placed in the SMCV to avoid inadequate drainage change to the SMCV. Fluoroscopic images (E and F) show the casts of NBCA injected into the shunted pouch. Right and left common carotid angiography (G and H) show complete obliteration of the shunt. The asterisk indicates the shunted pouch. A-P: anterior-posterior view; CS: cavernous sinus; Lat: lateral view; NBCA: n-butyl-2-cyanoacrylate; SMCV: superficial middle cerebral vein.
was reopened by a Headway17 microcatheter. The microcatheter was advanced to the posterior side of the CS. Selective angiography showed the posterior compartment of the CS and the draining route into the SPS and pterygoid plexus (Fig. 4E). The lateral side of the CS where the shunt was localized was not visualized, and the microcatheter could not reach the shunted pouch. Next, we attempted to advance the microcatheter into the shunted pouch through the ipsilateral superficial temporal vein-angular vein-SOV route (Fig. 4F). Even using a more supportive triple coaxial system, the microcatheter could not be advanced into the CS beyond the thrombosed SOV (Fig. 5A and 5B). The thin slab-MIP image revealed that the lateral side of the CS with the shunted pouch was isolated, and no clear communication with other CS compartments was observed (Fig. 5C and 5D). With respect to transarterial embolization (TAE), TAE from the MMA was not considered out of concern for the migration of the liquid embolic material to the ophthalmic artery. TAE from other feeders (AFR, MHT, and ILT) was not considered out of concern for the migration of the liquid embolic material via dangerous anastomosis resulting in cranial nerve palsy. Therefore, direct puncture of the SMCV by craniotomy was performed under general anesthesia (Fig. 5E). The shunted pouch was selectively embolized by coils, and complete obliteration was achieved without any complication (Fig. 5E–5H). Good epilepsy control was accomplished after the treatment.

**Discussion**

TVE using coils has been widely accepted as a standard technique for the treatment of CS-dAVF. Its safety and effectiveness have already been reported, and long-term acceptable outcomes have also been achieved.3,5,6,8,14) Furthermore, selective TVE of the shunted pouch has been performed to avoid inadequate packing or overpacking of the sinus.9) As a TVE route for the treatment of CS-dAVF, the ipsilateral IPS is usually used to advance the microcatheter into the affected CS because of its accessibility. However, the ipsilateral IPS is sometimes occluded because of thrombosis organization. Although a favorable
success rate has been reported by advancing the microcatheter into the CS via the occluded IPS,\textsuperscript{1,3,14} the shunted pouch cannot be reached in some cases because of compartment formation. Thus, it is necessary to reconsider the treatment strategies and alternative access routes. In our series, TVE could be performed via the ipsilateral IPS in all cases with angiographically patent IPS. It was necessary to change to alternative routes in cases with angiographically occluded IPS.

Various routes through multiple venous channels of the CS have been considered as alternative routes to the ipsilateral IPS, and the following routes are known: the contralateral IPS through the intercavernous sinus, the facial vein, superficial temporal vein, SPS, pterygoid plexus, and direct access via the SMCV or SOV.\textsuperscript{1,3,6,7,10} Naturally, TVE is an effective treatment for CS-dAVF, but it is not always feasible to guide the microcatheter transvenously. In such cases, it is possible to approach transarterially. If access is difficult despite sufficient considerations and trials, it is necessary to perform direct puncture of the vein.\textsuperscript{11,12}

Although the development of liquid embolic material has enabled depositing embolic material to the shunted pouch rather than performing feeder occlusion, liquid embolism is not widely accepted due to the risk of embolic material migration to vessels supplying multiple cranial nerves through dangerous anastomosis in CS-dAVF. To date, several TAE techniques using the APA for dAVF have been reported, and TAE with Onyx has also been performed for CS-dAVF.\textsuperscript{3,15,16} However, glue leakage and feeder rupture were reported as complications.\textsuperscript{15} Then, as a next option to avoid the disadvantages of TAE, TAIV has been reported.\textsuperscript{17} TAIV does not involve simple TAE. The microcatheter is advanced into the shunted pouch transarterially, and embolization is performed inside the affected sinus, constituting TAIV. In our present series, we experienced a useful transarterial approach route using the APA clival branch (Case 1). Although the effectiveness of TAIV has been reported as an alternative access route,\textsuperscript{17} there is no report on TAIV using the APA in CS-dAVF. To our knowledge, the present study is the first reported case. It is possible that TAIV could be an alternative route even in CS-dAVF. As a point of caution, the risk of liquid embolic material migration may be reduced by injecting the material inside the shunted pouch beyond the feeding artery.

**Fig. 5** Intraoperative findings and outcome in endovascular therapy (Case 2). Fluoroscopic images (A and B) show the triple coaxial catheter system advanced from the STV to the SOV. The guiding catheter (unfilled arrowhead), intermediate catheter (black arrowhead), and microcatheter (white arrowhead) are located in the venous route. The microcatheter cannot be advanced into the CS via the SOV. Axial thin slab-MIP images of rotational angiography of the right common carotid artery (C) show the shunted pouch at the lateral CS. Schematic drawing of the CS structure (D, posterior view) in Case 2 shows that the shunted pouch and posterior compartment of the CS do not communicate. Intraoperative image during direct puncture of the SMCV (E). Intraoperative right external carotid angiography shows the shunted pouch at the lateral CS (F), and the shunted pouch is embolized by coils via the SMCV (G). Right common carotid angiography (H) shows complete obliteration of the shunt. The asterisk indicates the shunted pouch. A-P: anterior-posterior view; CS: cavernous sinus; ICA: internal carotid artery; IPS: inferior petrosal sinus; Lat: lateral view; MIP: maximum intensity projection; PP: petrogyoid plexus; PV: petrosal vein; SMCV: superficial middle cerebral vein; SOV: superior ophthalmic vein; STV: superficial temporal vein; UV: uncal vein.
while paying attention to the reflux of the material. Ensuring that the microcatheter tip is properly positioned inside the shunted pouch may be a prerequisite for safe liquid embolic-material injection. If the microcatheter tip is not positioned inside the shunted pouch beyond the fistula point, the possibility of liquid embolic-material migration via a dangerous anastomosis not visible on angiography remains. In such cases, the operator should hesitate to inject the liquid embolic material from that microcatheter position.

While effective embolization was possible using these routes, advancement of the microcatheter was challenging due to the intracavernous structure. The shunted pouch is defined as a tubular or elliptical vascular structure that is separated from the main sinus lumen into which multiple feeding arteries converge and continue to the CS.19) In an analysis of CS-dAVF angioarchitecture, the shunted pouches were much more frequently localized posteromedially to the CS.14) However, the relationship between the shunted pouch and CS compartment has not been elucidated. It is necessary to know preoperatively whether the microcatheter can be advanced to the shunted pouch in the CS. Then, for the preprocedural evaluation and visualization of the occluded sinus, the effectiveness of image analysis using 3D Fast Field Echo T1 gadolinium and T1 Volumetric Isotropic TSE Acquisition Black Blood MR imaging was reported.19) Furthermore, detailed analysis with thin-slab MIP images based on 3D-RA is also essential as a preoperative prediction method for CS compartment formation or thrombosis.

In addition, with proper consideration and thorough knowledge of the anatomy and embryology of the CS, better predictions can be made on whether the selected venous route is accessible or not. The CS is a complex of venous channels with embryologically different origins, and these venous channels have retained their distinct original roles of venous drainage.20) Mitsuhashi et al. divided the intracavernous venous channels into three longitudinal venous axes based on their embryological development and functional characteristics: the “lateral venous axis,” “medial venous axis,” and “intermediate venous axis.”20) The axes are linked through the venous connections between them. The lateral venous axis is responsible for venous drainage of the brain via the middle cerebral vein, SPS, and bridging vein from the brainstem. The medial venous axis carries venous drainage not only from the skull base, chondrocranium, and hypophysis but also from the lateral venous axis. The drainage from the SOV to the SPS is theoretically associated with the intermediate venous axis, which is responsible for drainage directly from the orbit and membranous skull and indirectly from the brain. The medial and lateral venous axes of the CS drain posteriorly into the IPS.20)

This concept of intracavernous longitudinal venous axes may contribute to clinical practice, especially in catheter advancement into the CS. Considering our cases based on this concept, in Case 1, the affected CS with the shunted pouch was on the lateral venous axis to which the SMCV belongs. The IPS and SOV, through which it was difficult to advance the microcatheter, were on the medial venous axis and the intermediate venous axis (Fig. 2C and 2D). Similarly, in Case 2, the affected CS with CVR to the SMCV was on the lateral axis. The ipsilateral IPS, which was difficult to reach, was associated with the medial and intermediate axes (Fig. 5C and 5D). Thus, the venous structure that we attempted to use as an access route and the actual target shunted pouch for embolization were on different axes. By considering and understanding the concept of intracavernous longitudinal venous axes, the connection of intracavernous venous drainage routes and compartment formation could be predicted preoperatively. However, this rule does not apply to all cases. It is possible that the septum can be penetrated on different axes and that the microcatheter can be guided via a thin anastomosis between the axes. Finally, we cannot know without advancement of the catheter whether the shunted pouch can be reached.

In this study, we reviewed and analyzed the access routes in endovascular treatment for CS-dAVF. Although the microcatheter could be advanced into the CS transvenously, it may be difficult to guide the catheter to the shunted pouch due to compartment formation or organized thrombosis in some CS-dAVF cases. By understanding the embryological origin of the CS, it may be possible to consider the alternative access route preoperatively. TAIV, which transarterially advances the microcatheter into the shunted pouch for embolization, may also be a viable option. When these various endovascular approaches have been exhausted, direct puncture of the veins represents a viable means of accessing the shunted pouch and of achieving curative embolization.

Conclusion

We reviewed endovascular access routes for CS-dAVF treatment. In cases where the approach from the ipsilateral IPS was difficult, embolization of the shunted pouch was possible using various alternative routes.
It is extremely important to fully understand the angiographic architecture, location of the shunted pouch, and compartments of the CS for successful endovascular treatment. Thorough knowledge of the anatomy and embryology of the CS may be useful for better access route selection.

Acknowledgment

We would like to thank our radiological technologist for the technical assistance. We would like to thank Editage (www.editage.jp) for English language editing.

Disclosure Statement

The authors declare that they have no conflict of interest.

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