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Dural Venous System in the Cavernous Sinus: A Literature Review and Embryological, Functional, and Endovascular Clinical Considerations

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Abstract

The cavernous sinus (CS) is one of the cranial dural venous sinuses. It differs from other dural sinuses due to its many afferent and efferent venous connections with adjacent structures. It is important to know well about its complex venous anatomy to conduct safe and effective endovascular interventions for the CS. Thus, we reviewed previous literatures concerning the morphological and functional venous anatomy and the embryology of the CS. The CS is a complex of venous channels from embryologically different origins. These venous channels have more or less retained their distinct original roles of venous drainage, even after alterations through the embryological developmental process, and can be categorized into three longitudinal venous axes based on their topological and functional features. Venous channels medial to the internal carotid artery "medial venous axis" carry venous drainage from the skull base, chondrocranium and the hypophysis, with no direct participation in cerebral drainage. Venous channels lateral to the cranial nerves "lateral venous axis" are exclusively for cerebral venous drainage. Venous channels between the internal carotid artery and cranial nerves "intermediate venous axis" contribute to all the venous drainage from adjacent structures, directly from the orbit and membranous skull, indirectly through medial and lateral venous axes from the chondrocranium, the hypophysis, and the brain. This concept of longitudinal venous axes in the CS may be useful during endovascular interventions for the CS considering our better understandings of its functions in venous drainage.

Key words: cavernous sinus, embryology, functional anatomy, arteriovenous shunt, venous sampling

Introduction

The cranial dural sinuses are venous channels situated between the two layers of dura matter that carry venous drainage from the brain. Some dural sinuses close to the cranium also participate in osseous venous drainage through the meningeal veins.[1,2] The cavernous sinus (CS) is a cranial dural sinus situated on each side of the sella turcica between the periosteum of the sphenoidal bone and the dura propria of the cerebrum. This large interperiosteodural space[3] directly continues to the extracranial spaces (orbit and nasopharynx) and is in close contact with the adjacent cranium, the hypophysis, as well as the brain. Thus, venous channels in the CS also have many afferent and efferent venous connections with these adjacent structures of different embryological origins through their tributaries. This complex venous anatomy of the CS is always a matter of interest. To conduct safe and effective endovascular interventions for the CS, it is essential to understand not only the morphological but also the functional venous anatomy around the CS. The knowledge of CS embryology will also facilitate our better understanding of CS anatomy.

The Embryological Meningeal and Venous Development around the CS

According to O'Rahilly et al.,[4] at the early embryonic stage, the primitive brain is surrounded by a loose

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mesenchyme with no discriminating features, which is referred to as the primary meninx. This primary meninx differentiates into contiguous but distinct layers. First, the pia mater develops on the surface of the brain. This is followed by the meshwork formation (future arachnoid space) in the central part of the mesenchyme adjacent to the brain, and the mesenchymal condensation (future dura mater) between the dural limiting layer and the skeletogenous layer in the peripheral mesenchyme. The cartilaginous and membranous craniums are formed within the skeletogenous layer.

Padget[5)] described in detail about the embryonic development of the cranial venous system that differentiates in a continuous but independent fashion in each layer of the meninx. In the early embryonic phase (5–8 mm of length), the primitive brain is covered by a primitive capillary plexus in the undifferentiated mesenchyme (primary meninx) and drains superficially into the venous plexus in the future dural space (the embryonic dural plexus) through numerous short venous channels traversing the future arachnoid layer, especially in the dorsolateral aspect of the primitive brain.[5,6)] The embryonic dural plexus drains into the primary head-sinus situated ventrolaterally in the dural layer on both sides of the primitive brain. The primary head-sinus drains all structures in the head region, not only the brain but also ocular and visceral structures through the primitive maxillary vein [future superior ophthalmic vein (SOV)] and the dorsal pharyngeal vein (future sphenoid emissary vein of the foramen ovale) into the anterior cardinal vein (future internal jugular vein).[5)] In the parasellar region, the primary head sinus is situated between the trigeminal nerve and the dorsal aorta [future internal carotid artery (ICA)].[5)]

Through the embryonic period, accompanying the differentiation of the meninx, numerous small venous channels in the future arachnoid layer once connecting the primitive pial and dural layers decrease in number, converging into a few elongated and augmented veins (the pia-arachnoidal veins, future bridging veins).[5)] The adult configuration of venous drainages from the brain into dural sinuses through bridging veins is established by this process of blood vessel cleavage.[7)] Due to the dorsolateral convergence of embryonic dural plexuses and the developing longitudinal anastomoses between them (formation of the superior sagittal, transverse, and sigmoid sinuses), the primary head-sinus becomes attenuated, especially in the area ventral to the otic capsule. The connections of the dural plexus to the primary head-sinus for cerebral drainage also dwindle.[5)] The remaining rostral part of the primary head-sinus under the trigeminal nerve loses the cerebral drainage role once, and is called the pro-otic sinus,[7)] that is the precursor of the CS.[5,7–9)]

At the end of the second month of gestation, accompanying the growth of the chondrocranium and membranous skull, the medial tributaries of the pro-otic sinus around the ICA and between the otic and basioccipital cartilages are newly developed. The former forms the primitive CS and the latter forms the future inferior petrosal sinus (IPS). The IPS becomes the main drainage route from the CS after the caudal part of the primary head-sinus dwindled. The intercavernous sinuses are formed as mid-line extensions of the bilateral CS.[5)] The middle meningeal vein (MMV) is also developed in the outer layer of the primitive dura as lateral tributaries of the pro-otic sinus and drains the membranous skull.[5,9)] Primary visceral venous drainage into the primary head-sinus through the primitive maxillary vein and dorsal pharyngeal vein reverse their flow direction through the development of the external jugular venous system. This forms an adult venous drainage pattern from CS to the pterygoid plexus through emissary veins traversing the foramina in the middle cranial fossa.[5)]

The dural ends of the pia-arachnoidal veins in the caudoventral part of the telencephalon, called telencephalic veins (future middle cerebral veins), form the embryonic tentorial sinus that empties into the transverse sinus. This embryonic tentorial sinus is elongated posteriorly and migrates medially in the middle cranial base as the cerebral hemisphere enlarges and anastomoses to the CS in the late fetal or postnatal period.[5)] It is noteworthy that Padget[5)] described the embryonic tentorial sinus in the primitive dura as belonging to the inner dural layer rather than the MMV that is situated in the outer dural layer. The superior petrosal sinus (SPS) is formed from a dural stem of the ventral metencephalic vein (future superior petrosal vein). The ventral metencephalic vein is the pia-arachnoidal vein that drains the ventral region of the metencephalon (future cerebellum and pons). It primarily empties laterally into the transverse sinus. Medial anastomosis to the posterior aspect of the CS is secondary in a process similar to the embryonic tentorial sinus connection to the CS in the late fatal period or after birth.[5)]

Kehrli et al.[10)] showed the embryonic meningeal differentiation of the parasellar mesenchymal space, and speculated that venous channels of different shapes and emergence times in the primitive CS might have different embryological origins, supporting the descriptions of the primitive CS by Padget.[5)] According to Hashimoto et al.,[11)] who examined the development of the CS in the fetal period based on histological sections of autopsied fetuses, many small venous channels dotting the parasellar mesenchyme around 13–15 weeks of gestation enlarge and unite to form large lumens by 28 weeks. It may also represent the developmental course of the medial tributary of the pro-otic sinus around the ICA. They also speculated that the secondary anastomoses between the embryonic tentorial sinus and the CS are one cause of this enlargement of venous channels in the primitive CS. Beautiful photographs of histological sections in their article also showed the topological contiguousness of the embryonic tentorial sinus to the inner dura matter.

In summary, the CS develops from the rostral part of the primary head-sinus with its primary venous continuities to the orbit and nasopharynx, the later extensions for osseous drainage, and the late secondary anastomoses for cerebral drainage (Fig. 1).

Venous Drainage into the CS from Different Structures

1. Cerebral venous drainage into the CS

The CS carries venous drainage from the brain through bridging veins in a varied fashion. The superficial middle cerebral vein (SMCV) that drains the lateral part of the cerebral hemisphere empties into the CS directly by penetrating its lateral wall,[12–17] indirectly through the sphenoparietal sinus,[13,16,17] or through the laterocavernous sinus (LCS).[12,14,15]

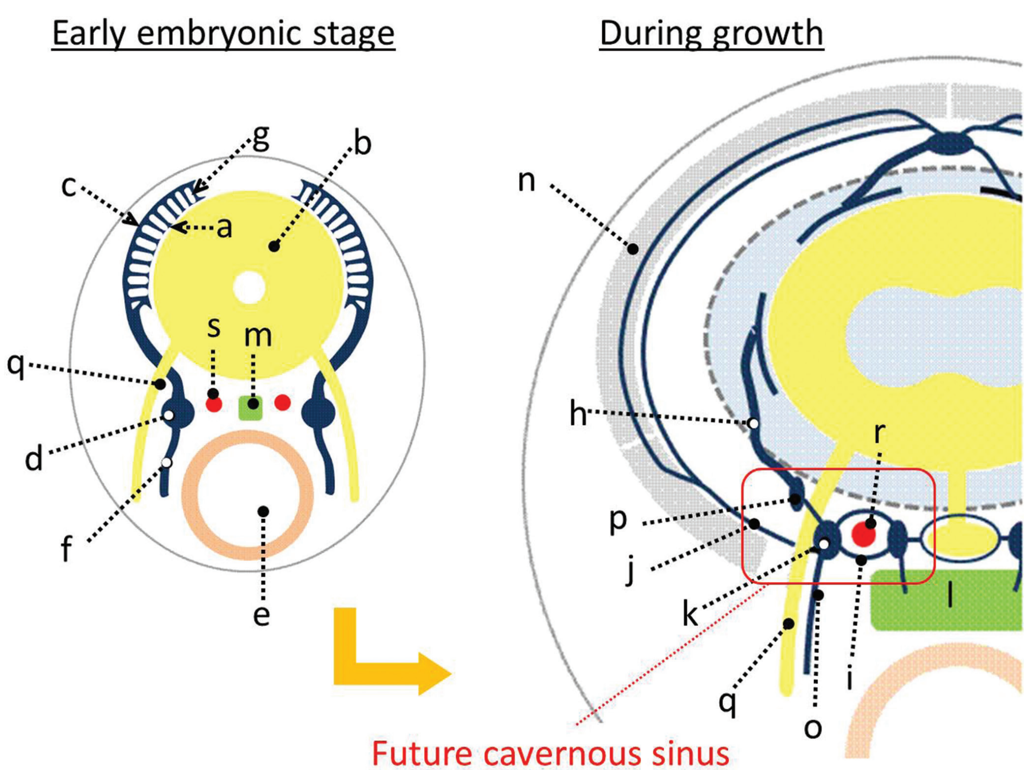

Fig. 1 Schematic drawing of the embryological venous development in the parasellar region (axial view at the level of the trigeminal nerve). At the early embryonic stage, capillary network (a) on the surface of the primitive brain (b) drains superficially into the embryonic dural plexus (c) in the primary meninx. This dural plexus empties into the primary-head sinus (d) that also receives the venous drainage anteriorly from the orbit and ventrally from the pharynx (e) through the dorsal pharyngeal vein (f). During the embryonic period, with the differentiation of the meninx, original numerous small venous channels (g) traversing the future arachnoid space decrease in number and converge into a few pia-arachnoidal veins. Superficial middle cerebral vein (SMCV) (h) is derived from one of the pia-arachnoidal veins in the ventrocaudal region of the cerebral hemisphere. In late embryonic stage, medial (i) and lateral (j) tributaries of the pro-otic sinus (k) that is the rostral remnant of the primary-head sinus (d) are newly developed, respectively, for the growing chondrocranium (l) derived from notochord (m) and membranous skull (n). The former forms a part of the future cavernous sinus, and the latter forms the future middle meningeal vein. The sphenoid emissary vein of the foramen ovale (o) is derived from the dorsal pharyngeal vein (f) with reversing its flow from afferent to efferent direction. The embryonic tentorial sinus (p) as a dural end of the SMCV secondarily connects to the cavernous sinus in late fatal or postnatal stage. q: trigeminal nerve. r: internal carotid artery derived from dorsal aorta (s).

Our general understanding of the sphenoparietal sinus is that it is a large meningeal channel that runs medially just below the lesser sphenoid wing to empty into the anterior part of the CS, usually the SMCV flows into this sinus.[2] However, Ruíz et al.[15] and Takahashi et al.[18] recently questioned this classical understanding of the sphenoparietal sinus. They described two independent venous channels (the sinus of the lesser sphenoid wing and the SMCV) that exist in this region, and they found no connections between these two venous channels. Therefore, the term "sphenoparietal sinus" may not be adequate to describe the dural continuation of the SMCV in this region. The LCS is the venous channel situated between the outer layer of the dura propria and the inner layer of loose connective tissue surrounding the cranial nerves[19,20] of the lateral wall of the CS. It was defined as one of the principal drainage pathways of the SMCV by Ruiz et al.,[12] in 1999. The SMCV empties into the LCS penetrating the outer layer of the lateral wall of the CS at its anterior part. Subsequently, the LCS flows into the SPS, the pterygoid plexus, or the CS at its posterior aspect or through the small foramina in the inner layer of the lateral wall.[12,14] When the SMCV runs more laterally to the middle cranial fossa, it forms the paracavernous sinus[13–16] in the dura of the middle cranial base. It flows into the pterygoid plexus or passes beside the emissary foramens in the middle cranial base more posteriorly to empty into the SPS or the transverse sinus.[13,14,16,21] The former variant is referred to as the sphenobasal sinus and the latter the sphenopetrosal sinus.[2] Some authors have speculated that the sphenoparietal sinus as the dural continuation of the SMCV, the LCS, and the paracavernous sinus are remnants of the embryonic tentorial sinus. Individual relative differences of the embryonic tentorial sinus migration, and the ways of secondary anastomoses to the CS may be responsible for adult variations of the SMCV drainage pattern.[5,12–14,16,17] The deep middle cerebral vein and the uncal vein also flow together with the SMCV or separately into the CS.[2,12,22–27]

Regarding venous drainage from the posterior fossa, the CS is connected to the medial part of the SPS and receives venous blood from the anterior part of the cerebellum and brain stem through the superior petrosal vein.[24,25] As mentioned previously, the SPS is derived from the dural end of the ventral metencephalic vein (future superior petrosal vein) that essentially carries venous drainage from the primitive metencephalon.[5] Matsushima et al.[28] described the presence of bridging veins from the anterior pontomesencephalic or transverse pontine veins to the posterior part of the CS or adjoining part of the IPS just below the Meckel's cave. Kiyosue et al.[29] also reported that bridging veins connecting the anterior pontomesencephalic venous system to the posterior part of the CS or the IPS normally exist.

Thus, the CS has a direct and large contribution to venous drainage from the brain through these bridging veins, usually from the lateral aspect of the sinus. These bridging veins may become routes for leptomeningeal venous reflux in arteriovenous shunts harbored in the CS or neighboring dural sinuses.[24,28–34]

2. Orbital venous drainage into the CS

Venous drainage of the orbital contents including the retina, lacrimal gland, and ocular muscles is carried by the SOV and inferior ophthalmic vein (IOV).[35] The SOV that drains the superomedial part of the orbit crosses above the optic nerve to reach the lateral part of the superior orbital fissure. It is commonly joined by the IOV that drains the inferolateral part of the orbit. This common stem of the SOV runs below the ophthalmic nerve (the first division of the trigeminal nerve) to enter the anterior part of the CS.[36] The distal part of the SOV anastomoses to the supraorbital and angular veins at the anterior margin of the orbit. These can be transvenous access routes to the CS via facial veins or by direct puncture of the SOV.[37–39] Spector et al.[40] described a detailed venous anatomy at the junction of the orbit and the CS, and the close continuation of the lateral wall of the SOV stem to the inner layer of the CS lateral wall. It suggests the topographic relations of the SOV to the anterior CS that is situated between cranial nerves and the ICA. Photographs of a stepwise dissection of the CS in articles by Spektor et al.[40] and Rhoton et al.[41] also clearly demonstrate the direct continuation of the SOV to the anterior CS, crossing beneath the first division of the trigeminal nerve. This anatomical setting is consistent with the embryonic development of the SOV. It is derived from the stem of the primitive maxillary vein that is situated in the maxillary process of the first branchial arch, and flows into the primary head-sinus medial to the trigeminal nerve roots from where the CS is derived.[5]

3. Venous drainage from the hypophysis into the CS

Both CSs are connected with each other by dural venous channels cross the sella turcica, which are generally called intercavernous sinuses. The anterior intercavernous sinus lies transverse on the anterosuperior margin of the sellar and empties into medial venous channels of the CS. The posterior intercavernous sinus extends across in front of the posterior clinoid plate and drains into the posterosuperior part of medial venous channels of the CS. The inferior intercavernous sinus extends across the floor of the sella and drains into the inferior venous channels of the CS.[41–44] Xuereb et al.[45] described several sinusoids of the hypophysis that join together to form small short veins emptying into each side of the CS and intercavernous sinuses, more commonly in the lateral aspects of the hypophysis. A detailed investigation using cadavers by Green[46] demonstrated that numerous hypophyseal veins drain the hypophysis to the medial or inferior part of the CS directly or indirectly through intercavernous sinuses or the plexiform venous network that is close to the surface of the pituitary gland. Sato et al.[47] reported on the swelling of the pituitary gland in cavernous dural arteriovenous fistulas (DAVFs). Shigematsu et al.[48] reported on the delayed perfusion in the pituitary gland in cavernous DAVFs using dynamic magnetic resonance imaging. These authors[47,48] speculated that venous hypertension due to DAVFs may be the cause of swelling or delayed perfusion of the pituitary gland.

In summary, venous blood from the hypophysis empties into the medial or inferior parts of the CS via many hypophyseal veins directly or indirectly through intercavernous sinuses.

4. Venous drainage from the osseous structures into the CS

The sinus of the lesser sphenoid wing situated beneath the sphenoid ridge runs medially to empty into the anterosuperior aspect of the CS after crossing medially over the SOV.[15] It drains diploic veins from the orbital roof and the greater sphenoid wing without venous connection to the SMCV.[15,17,18] The CS has connections medially to the opposite side of the CS through intercavernous sinuses. Green[46] described that anterior and posterior intercavernous sinuses receive some osseous veins from the lateral part of the posterior clinoid plate. The inferior intercavernous sinus also receives large osseous veins that drain the posterolateral parts of the sella turcica, in addition to venous blood from the hypophysis. Another, and usually the largest venous connection between both sides of the CS is the basilar plexus. It is a plexiform dural venous channel that covers the cranial surface of the clivus. They connect bilaterally to the medial aspects of the CS and IPS at multiple levels.[1,49] Tubbs et al.[49] found no venous connections between the anterior brain stem and the basilar plexus in 20 cadaver dissections. It occasionally has a connection with the cranial part of the anterior internal vertebral plexus.[49,50] Schnitzlein et al.[51] reported that the diploic venous channel in the dorsum sellae (the sinus of the dorsum sellae) connects laterally to the posteromedial part of the CS. They suggested that it was comparable with the basivertebral vein of the spine. The presence of osseous canals on the cranial surface of the clivus has been reported.[52–54] Tubbs et al.[54] elucidated from cadaver dissections that the content of this clival canal was a vein. We may also easily suppose that the vein in the clival canal and the basilar plexus are respective homologs of the basivertebral vein and the anterior internal vertebral venous plexus of the spine.

The MMV that drains the membranous skull and the greater sphenoid wing empties superiorly into the venous lacuna and the superior sagittal sinus, and inferiorly into the CS or the pterygoid plexus through the sphenoid emissary vein of the foramen ovale.[2,6] Embryologically, the MMV is derived from the pro-otic sinus (future lateral wing of the CS) as its lateral tributaries in the outer layer of the dura, accompanying the development of the membranous skull.[5,9] Thus, one of the primary drainage routes of the MMV must be to the lateral wing of the CS. García-González et al.[55] described that the frontal and anterior temporal diploic veins also drain into the CS via the MMVs and the sphenoparietal sinus (the sinus of the lesser sphenoid wing), based on cadaver dissections.

5. Venous connections between the CS and visceral structures

The CS drains into the pterygoid plexus through emissary veins that traverse the foramina in the middle cranial fossa (foramen rotundum, ovale, or Vesalius).[1,8,11,25,41,56,57] The continuation of the CS to these emissary veins under trigeminal nerve roots is called the “lateral wing of the CS” and is a remnant of the pro-otic sinus.[5] This venous pathway is also called the “trigeminal sinus” by Henderson[58] and the “pericavernous venous plexus” by Rhoton.[41] Although these emissary veins are efferent drainage routes from the CS to the pterygoid plexus in the adult stage, precursors of these emissary veins (primitive maxillary and ventral pharyngeal veins) originally drained afferently into the primary head-sinus (primary precursor of the CS) and carried venous drainage from ventral visceral structures in the embryonic stage, as previously mentioned.[5]

Discussion

Each venous channel in the CS originally develops by providing a distinct role in venous drainage. Even after large morphological alterations during embryological developmental process (anastomoses, annexation, and dwindling), the role of each dural venous channel is still distinct. In 2008, Geibprasert et al.[59] classified the craniospinal epidural venous system into three groups based on the embryological specific of the venous drainage roles. The "ventral epidural venous space" is for bony structures derived from the notochord and the corresponding sclerotome extends from the basisphenoid (cavernous plexus) to the sacrum. The "dorsal epidural venous space" is the confluence of two different venous systems, the membranous osseous system of the cranial vault and the leptomeningeal system that drains the brain, represented by the superior sagittal sinus or the transverse sinus. The "lateral epidural venous space" is the leptomeningeal system joined by bridging veins with no direct communications with the ventral and dorsal epidural venous space. They also described the different clinical features of dural arteriovenous shunts in each epidural venous space. The ventral epidural shunt is more benign with a lower rate of cortical venous reflux. On the other hand, the lateral epidural shunt is always aggressive with cortical venous reflux. In their classification, the CS might be broadly categorized into the ventral epidural group. The CS is a peculiar dural venous sinus based on its location in the boundary between the cranial and extra-cranial structures, and in the complexity of its venous channels of different embryological origin. Therefore, it potentially contributes to the venous drainage from the brain, adjacent cranial bones, the orbit, the hypophysis and the nasopharynx.

The part of intracavernous venous channels to where the veins from those structures connect varies according to their roles of venous drainage as we reviewed in the literatures. We can and should divide the intracavernous venous channels more based on their functional and topological characteristics which can be rationally explained also by their ways of embryological development.

The intracavernous venous channels should be divided topologically in the relationships to the ICA and cranial nerves, which correspond the embryonic developmental ways of each venous channel and their original specific roles of venous drainage as showed in Fig. 1. The venous channels medial to the ICA "medial venous axis" connect anteriorly to the sinus of the lesser sphenoid wing, medially to the intercavernous sinuses, and posteriorly to the basilar plexus and the sinus of the dorsum sellae. Although in adults this medial venous axis also carries cerebral and orbital venous flow from more lateral venous axes through the venous connections between each venous axis, the original role of this venous axis is exclusively for the skull base chondrocranium and hypophysis. It probably develops from the medial tributaries of the pro-otic sinus for the chondrocranium and hypophysis. The venous channels situated laterally to the cranial nerves "lateral venous axis" are for venous drainage from the brain. The LCS and the posterolateral part of the CS are included in this lateral venous axis. The LCS derived from the embryonic tentorial sinus as a dural end of the telencephalic pia-arachnoidal veins is directly connected to the SMCV. The posterolateral part of the CS drains the SPS and also the bridging veins from the pial venous system of the brainstem. It is speculated that this posterolateral part of the CS might develop from the dural ends of the embryonic ventral metencephalic veins from which the superior petrosal vein and bridging veins from the brainstem are derived. These medial and lateral venous axes of the CS drain posteriorly into the IPS. The remaining venous channels between the cranial nerves and the ICA, including the lateral wing of the CS "intermediate venous axis" can participate in all venous drainages. This is directly from the orbit and membranous skull and indirectly from the brain, hypophysis, and skull base chondrocranium through the lateral and medial venous axes. It drains into the pterygoid plexus through emissary veins in the middle cranial fossa, or into the IPS through the posterior parts of the medial and lateral venous axes. This intermediate venous axis is indeed derived from the pro-otic sinus (rostral remnant of the primary head-sinus). Original characteristics of the primary head-sinus, including the orbital, cerebral, and visceral venous drainage, can still be seen. The superficial petrosal vein that accompanies the greater petrosal nerve in the facial hiatus empties into the emissary vein of the foramen ovale. It is the remnant of the caudal part of the primary head-sinus that dwindled in the embryonic stage.[5] Therefore, the continuity of the intermediate venous axis is theoretically from the SOV to the superficial petrosal vein through the lateral wing of the CS. Each venous axis in the CS has connections with adjoining venous axes. The medial venous axis connects with the intermediate venous axis through the spaces dorsal and ventral to the ICA. The venous connections between the lateral venous axis and the intermediate venous axis may be through the spaces between cranial nerve roots. These venous channels between nerve roots correspond to the venous drainage routes of the LCS into the CS through small foramina in the inner layer of the lateral wall described by Ruiz.[12] The IPS is the main posterior drainage pathway of the CS and is situated in the cranial surface of the petroclival fissure.[1,60] The IPS also receives venous drainage from the labyrinth through the vein of the cochlear aqueduct,[8] brainstem and inferior cerebellar surface through bridging veins from the pial venous system of the pons or the medulla oblongata.[28,29] Padget[5] described the IPS development as a medial derivative of the pro-otic sinus accompanying the growth of the skull base chondrocranium. It connects the posterior aspect of the primitive CS and the dural stem of the ventral myelencephalic vein (pia-arachnoidal vein of the primitive myelencephalon). The inferior petrosal vein (vagal vein)[28,56] that drains the medulla oblongata into the jugular bulb or inferior part of the IPS is considered to be derived from the ventral myelencephalic vein. Considering the manner of embryological development and existence of the bridging veins that empty into this sinus, the IPS should be viewed as a complex of dural venous systems of both the cerebral and osseous drainage. Thus, the IPS can theoretically drain both the medial and lateral venous axes of the CS. This concept of longitudinal venous axes in the CS is schematically shown in Fig. 2. The characteristics of the medial and lateral venous axis of the CS may respectively correspond with the ventral and lateral epidural groups advocated by Geibprasert et al.[59] We do not yet have sufficient knowledge regarding the characteristics of DAVFs that develop in each venous axes of the CS. Cavernous DAVFs is generally considered to be benign because of the low rate of intracranial hemorrhage or venous congestion by the cortical venous reflux.[25,61] However, when a DAVF develops in the lateral venous axis of the CS, it may show aggressive clinical manifestations, as DAVFs in the paracavernous sinus or the superior petrosal sinus have a tendency for aggressive manifestations with the direct cortical venous reflux.[34,62,63] The embryological origins of both the paracavernous and the superior petrosal sinuses are the same as the lateral venous axis of the CS, from the dural ends of the embryonic pia-arachnoidal veins. Ruíz et al.[64] reported a case of DAVF that developed in the LCS with a direct venous reflux into the SMCV. Ushikoshi et al.[65] reported a DAVF near the anterior clinoid process draining directly into the SMCV with the varix. These two reported cases may be considered as DAVFs that developed in the lateral venous axis of the CS.

The concept of intracavernous longitudinal venous axes is thought to be clinically useful, especially in catheter interventions to the CS. When treating arteriovenous shunts involving the CS, irrespective of whether it is dural or direct, the most important issue is to avoid an incomplete occlusion of the shunt and redistribution of the residual shunt flow into dangerous cerebral or ocular venous drainage routes, which might lead to cerebral hemorrhage, venous congestion,[66,67] or a deterioration of the ocular symptoms. We must also consider preserving normal cerebral venous drainage through the CS. To achieve this, obliteration of only the affected venous compartment, reported as targeted or selective embolization[68,69] seems to be the best. If this is not possible, the manner of occluding venous outflows is then important. Although it depends on the anatomical situation of each patient, using two microcatheters is desirable. One catheter is usually navigated into the intermediate venous axis to secure connections to the SOV and the lateral venous axis. The second is used to search for and occlude the fistulous compartment. If targeted embolization is not achieved, it is better to try and occlude the shunt flow by embolizing the limited parts of the intracavernous venous channels to preserve the antegrade venous drainage from the brain before making the decision of whole sinus packing. The exact positioning of catheters can be determined by their topological relations with the ICA and venograms in the sinus. Representative cases of a transvenous embolization of a cavernous DAVF and a traumatic carotid-cavernous fistula are shown in Figs. 3 and 4. In these cases, morphologically complex venous channels in the CS could be easily understood using the concept of intracavernous longitudinal venous axes. Then the antegrade cerebral venous drainage could be preserved by the selective occlusions of the venous channels in the CS.

Venous sampling in the IPS[70] or the CS[71] is generally considered useful to distinguish the adrenocorticotropin (ACTH)-producing pituitary tumor (Cushing disease) from other causes of Cushing syndrome, or to determine the preoperative lateralization of the tumor. The best sampling points in the sinus to obtain a reliable enough gradient of ACTH remains under debate.[72–75] Sampling from the medial venous axis of the CS may better reflect the ACTH secretion from the pituitary gland, because pituitary venous blood first flows into this medial axis. In other venous axes, it may be diluted by venous flows from the brain or the orbit. Although we have a limited experience with the venous sampling, one case of Cushing disease is presented in Fig. 5. In this case, sampling from the medial venous axis yielded significantly higher ACTH concentration than from the intermediate axis or the IPS. This was enough to diagnose an ACTH producing pituitary adenoma. There was no significant intercavernous ACTH gradient in this patient. Simultaneous bilateral sampling might be better to determine the lateralization of a tumor. An assessment of the flow direction between each CS through the intercavernous sinuses may also be required, if possible.

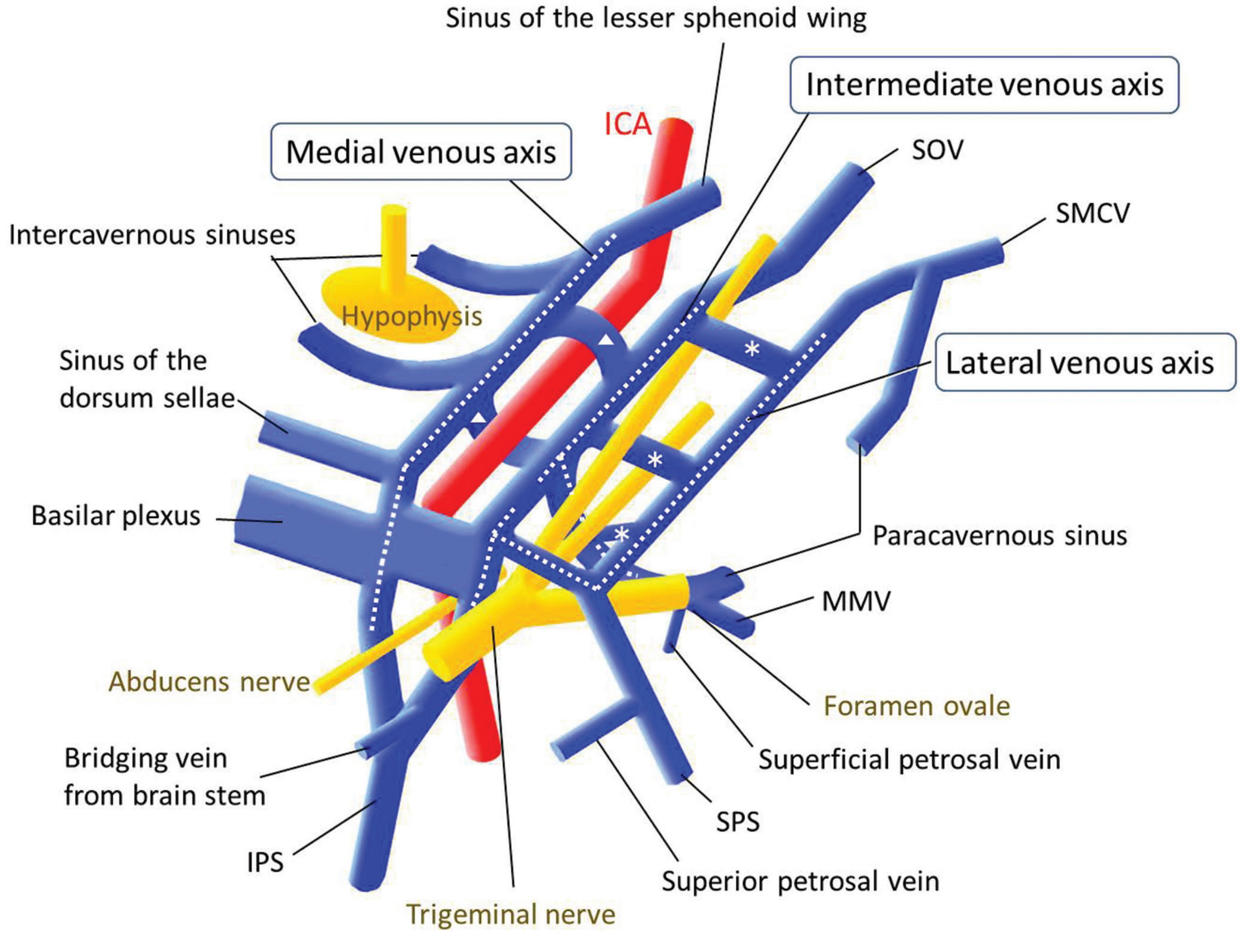

Fig. 2 Conceptual drawing of the longitudinal venous axes in the cavernous sinus (right posterolateral view). The medial venous axis is situated medial to the internal carotid artery (ICA), and receives osseous venous drainage, especially from the skull base chondrocranium through the sinus of the lesser sphenoid wing, intercavernous sinuses, the sinus of the dorsum sellae, and the basilar plexus. This medial venous axis also carries a venous drainage from the hypophysis directly or indirectly through the intercavenous sinuses. The intermediate venous axis is situated between the ICA and cranial nerves, and drains the superior ophthalmic vein (SOV) and the middle meningeal vein (MMV) into the pterygoid plexus through the emissary foramina in the middle cranial base. This intermediate venous axis also has connections with the medial venous axis through venous channels (*white triangles*) above or beneath the ICA, with the lateral venous axis through the venous channels between the cranial nerve roots (*asterisks*). The connection to the superficial petrosal vein is the embryological original course of the primary head-sinus. The lateral venous axis is situated lateral to the cranial nerves. The posterolateral part of the CS continues to the superior petrosal sinus (SPS) is also included in this venous axis. This lateral venous axis essentially carries the venous drainage from the brain through bridging veins (the SMCV, the superior petrosal vein, and the bridging vein from the brainstem). IPS: inferior petrosal sinus, SMCV: superficial middle cerebral vein.

Of course, the way of categorizing the intracavernous venous channels we propose is just conceptual and comprehensive. The degree of development of each venous channel in the CS may be individually varied. In the case of arteriovenous shunt, venous channels in and around the CS are often thrombosed. We should evaluate the individual and actual setting of the venous channels in the CS before the operation. We prefer to use coronal images of bone-subtraction computed tomography (CT) angiography as presented for the cases in Figs. 3 and 4, or contrast-enhanced coronal T_1-weighted magnetic resonance (MR) images with fat suppression as presented for the case in Fig. 5, which provide us detailed knowledge of the actual venous setting in the CS with the positional relationships to the ICA and cranial nerves. Applying this concept to the individual actual venous setting, we may easily understand the functions of the venous channels, and rationally decide the management for each venous channel in the CS.

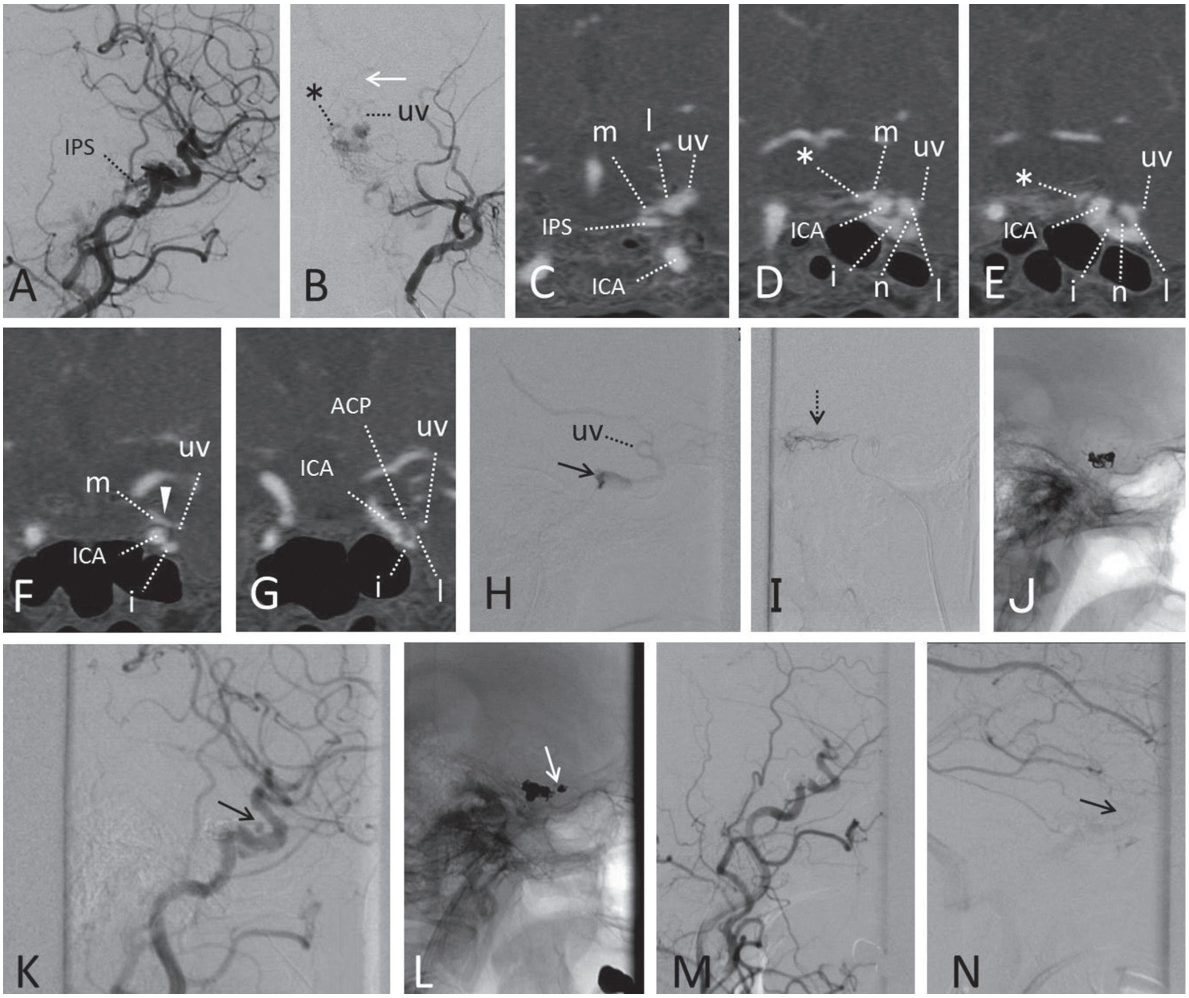

Fig. 3 Cavernous dural arteriovenous fistula. A 62-year-old female presented with left abducens nerve palsy. A: Left carotid angiogram (lateral view) showed a dural arteriovenous fistula on the left cavernous sinus (CS) draining posteriorly into the inferior petrosal sinus (IPS). B: Left external carotid angiogram (A-P view) showed fine feeding arteries converging into the medial part (*asterisk*) of the CS, and reflux into the basal vein of Rosenthal (*white arrow*) through the uncal vein (uv). C–G: Preoperative coronal bone-subtraction computed tomography angiograms, from posterior (C) to anterior (G). C: The cross-section at the level of the petrous apex showed the left IPS connected to posterior parts of the medial (m) and the lateral (l) venous axes. The uv emptied into the lateral venous axis. D, E: A small venous pouch (*asterisks*) in the dorsum sellae connected to the medial venous axis (m) was considered to be the fistulous portion. The lateral venous axis (l) connected to the intermediate venous axis (i) crossing beneath the cranial nerves (n). F, G: The intermediate venous axis (i) connected to the anterior part of the medial venous axis (m) through the anterior part of the lateral venous axis (l) and the venous channel (*arrowhead*) beyond the ICA near the anterior clinoid process (ACP). Thus, before the operation, two access routes to the medial venous axis where the fistulous compartment might exist could be identified, the one was from behind directly through the IPS, and the other is through the lateral and intermediate venous axis, and the venous channel beyond the ICA. H: Venogram (lateral view) during the transvenous coil embolization through the IPS showed the lateral venous axis (*arrow*) with a connection to the uv. This lateral venous axis was secured with the one microcatheter. I: Another catheter was introduced into the fistulous compartment situated in the posteromedial part of the CS from the posterior aspect of the medial venous axis, confirming the retrograde opacifying of the feeding arteries (*dotted arrow*) with the venogram (A-P view). J: The fistulous compartment with the posterior part of the medial venous axis was embolized. K: Left carotid angiogram showed that a faint shunt flow remained (*arrow*) in the anterior part of the medial venous axis. L: The microcatheter was navigated into this anterior part of the medial venous axis through the intermediate and lateral venous axes, and the venous channel beyond the ICA, and embolization was added (*white arrow*). M: Complete obliteration was achieved without embolizing the intermediate and lateral venous axes. N: The antegrade venous flow of the uv (*arrow*) into the IPS through the lateral venous axis was preserved. A-P: anteroposterior, ICA: internal carotid artery.

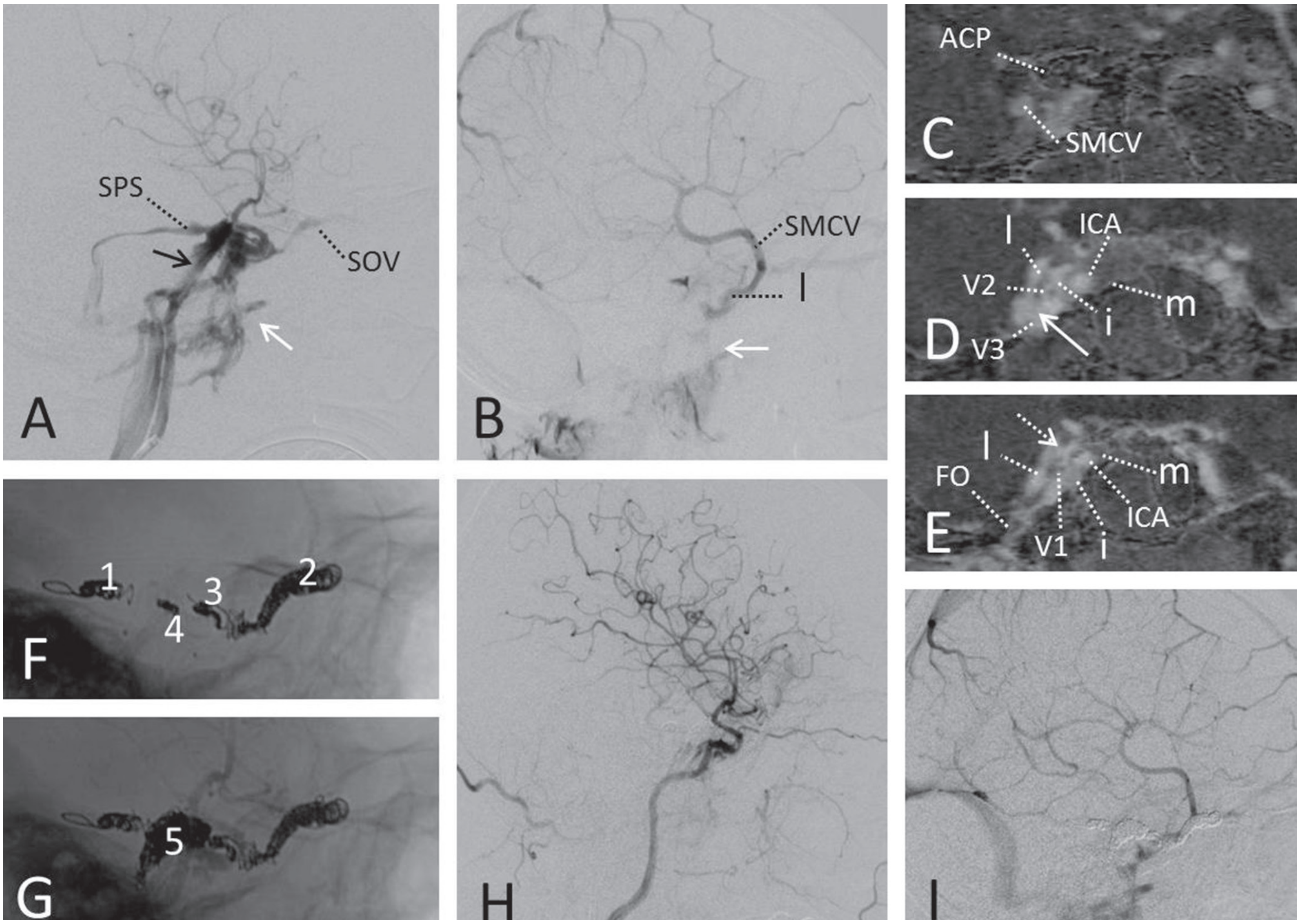

Fig. 4 Traumatic carotid-cavernous fistula (CCF). A 54-year-old male presented with exophthalmos and visual loss on the right side after serious head trauma. A: Right carotid angiogram (lateral view) showed a direct CCF at the posterior genu of the right internal carotid artery (ICA) draining antegradely into the inferior petrosal sinus (*arrow*) and the pterygoid plexus (*white arrow*), retrogradely into the superior ophthalmic vein (SOV) and the superior petrosal sinus (SPS). B: Venous phase of the angiogram showing that the antegrade venous drainage of the superficial middle cerebral vein (SMCV) into the pterygoid plexus (*white arrow*) through the lateral venous axis (l) was still preserved. C–E: Preoperative coronal bone-subtraction computed tomography angiograms, anterior (C) to posterior (E). C: The cross-section at the level of anterior clinoid process (ACP) showed the SMCV, which posteriorly connected to the lateral venous axis. D, E: There were two venous pathways connecting the lateral venous axis (l) to the intermediate venous axis (i). The one (*white arrow*) was through the aperture between the 2nd division (V2) and the 3rd division (V3) of the trigeminal nerve. The other (*white dotted arrow*) was beyond the 1st division (V1) of the trigeminal nerve. The medial venous axis (m) was thrombosed on the right side due to the trauma. F, G: Fluorographic images during transvenous embolization through the inferior petrosal sinus. Connections to the SPS (1), the SOV with the part of the intermediate axis anterior to the venous connection between V2 and V3 (2), the extension of the intermediate axis posterior to the venous connection with the emissary vein of the foramen ovale (3), and the posterior part of the lateral axis with the venous connection to the intermediate venous axis beyond V1 (4) were embolized. With these embolizations, the antegrade drainage pathway of the SMCV was completely isolated from the shunt flow. Finally, the fistulous-dilated compartment beyond the posterior genu of the ICA (5) was embolized. H: After the embolization, almost all the shunt flow had stopped without any cortical venous reflux, I: The antegrade flow of the SMCV was preserved through the anterior part of the lateral venous axis, the venous channel between V2 and V3, the remaining middle part of the intermediate venous axis, and the emissary vein of the foramen ovale into the pterygoid plexus. ICA: internal carotid artery. FO: foramen ovale.

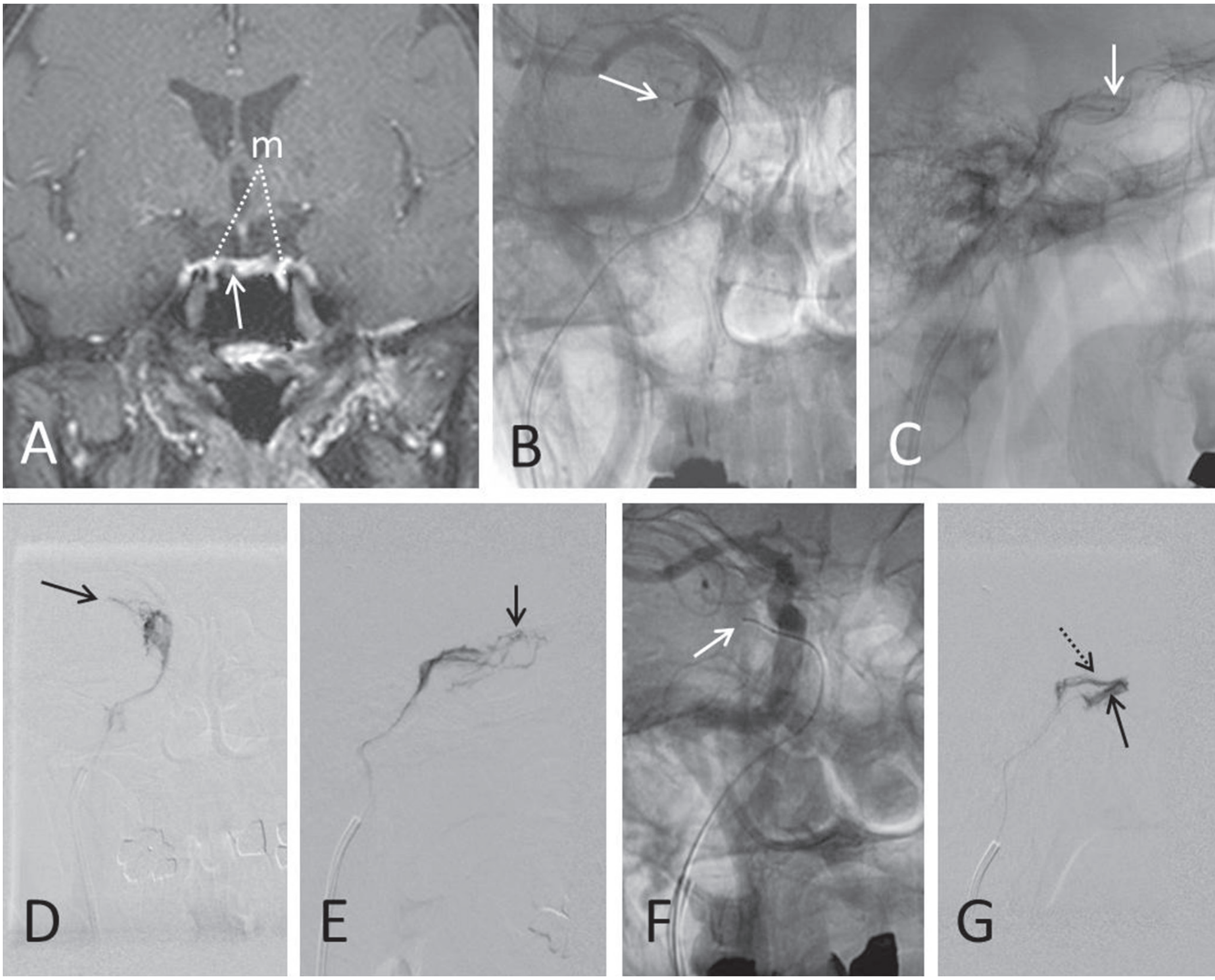

Fig. 5 Adrenocorticotropin (ACTH)-producing pituitary tumor (Cushing disease). A 70-year-old female was clinically suspected of having Cushing disease. A: Contrast-enhanced coronal T_1-weighted magnetic resonance image with fat suppression showed the small mass lesion (*white arrow*) in the right side of the pituitary gland. The medial venous axes (m) were well developed on both sides. Venous sampling without corticotropin-releasing hormone was performed to confirm the diagnosis. B: The microcatheter was introduced into the anterosuperior part (*white arrow*) of the right cavernous sinus through the inferior petrosal sinus (IPS) and the medial venous axis, using the internal carotid artery (ICA) as a landmark. C: The catheter was withdrawn into the middle part of the medial venous axis (*white arrow*). The venogram (D: anteroposterior view. E: lateral view) at this point showed the sinus of the lesser sphenoid wing (*arrow*), confirming that the catheter was in the medial venous axis. Sampling was performed at this point. F: Subsequently the catheter was introduced into the middle part of the intermediate axis (*white arrow*) through the venous channel beneath the ICA to take a sample at this point. G: The venogram (lateral view) at this point showed the intermediate venous axis (*arrow*) flowing into the medial venous axis (*dotted arrow*) through the connection beyond the ICA. Venous sampling was also performed at the middle part of the IPS and the femoral vein. Subsequent venous sampling on the left side was conducted in the same way. On the right side, the ACTH levels at the medial venous axis, the intermediate venous axis, and the IPS were 3,980 pg/mL, 9.7 pg/mL, and 52 pg/mL, respectively. On the left side, the ACTH levels at the medial venous axis, the intermediate venous axis, and the IPS were 3,080 pg/mL, 335 pg/mL, and 129 pg/mL, respectively. The ACTH level sampled from the right femoral vein was 13.8 pg/mL. With a sufficient central to peripheral ACTH gradient, the patient was diagnosed with Cushing disease and underwent a surgical tumor resection.

Conclusion

The CS is a complex of venous channels with different embryological venous drainage roles. It is situated in the parasellar region of the mesenchymal space that surrounds not only the brain but also cranial bones and visceral structures. The role of venous drainage of each venous channel in the CS remains distinct, even after alterations through embryological development. The concept of intracavernous longitudinal venous axes based on the functions of venous drainage of each venous channel may be useful to do safe and effective endovascular procedures for the CS with a simplified and better understanding of the complex venous anatomy of the CS.

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Conflicts of Interest Disclosure

The authors have no conflicts of interest with regard to the manuscript. The authors who are members of the Japan Neurological Society (JNS) have registered on line Self-reported COI Disclosure Statement Forms through the website for JNS members.

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