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Advances in the Diagnosis and Treatment of Parasellar Cavernous Sinus Cavernous Hemangioma

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Abstract

Parasellar cavernous sinus cavernous hemangioma (CSCH) is a lesion that often originates from cavernous sinus and progresses to parasellar region outside the brain. CSCHs are often benigngenerally account for 2% to 3% of all cavernous sinus tumors. Due to abundant blood supply, surgical removal of CSCHs often causes massive intraoperative hemorrhage. CSCHs are often histologically confused with meningiomas. MRI findings of CSCHs often resemble those of the cerebrospinal fluid with slight hypointensity or isointensity to the ectocinerea on T1WI and hyperintensity on T2WI, showing marked enhancement and delayed enhancement after contrast enhancement. In addition to surgical removal, radiotherapy has shown good curative effects. This article has also reviewd the clinical manifestations, imageologic manifestations, differential diagnosis, and treatments of CSCHs in the related literatures

Keywords: Brain Tumor, Parasellar Tumor, Cavernous Hemangioma, Cavernous Sinus, Hemangioma

Abbreviations

CSCH: Cavernous Sinus Cavernous Hemangioma
CM: Cavernous Malformation
CSH: Cavernous Sinus Hemangioma
GKS: Gamma Knife Radiosurgery
SBRT: Stereotactic Body Radiation Therapy

Introduction

Cavernous hemangioma is also known as cavernous angioma. Intracranial cavernous hemangiomas are benign lesions mainly composed of cavernous vascular sinuses without muscular layers or elastic fiber layers, thus lacking the microscopic features of arteries or veins, which contain no nerve parenchyma and do not invade brain tissue [1]. Intracranial cavernous hemangiomas include intracerebral and extracerebral cavernous hemangiomas (extra-axial cavernous hemangiomas). The cerebral parenchymal type is much more commonly seen and can develop anywhere in the brain, while extra-axial cavernous hemangioma is relatively rarely seen, and it has the same histological manifestations but different imageology, treatment, and complications [2]. The most common extracerebral cavernous hemangioma is parasellar cavernous sinus cavernous hemangioma (CSCHs; accounting for 0.4% to 2% of all intracranial cavernous hemangiomas) that appears more often in female patients around their forties [3]. Among the common vascular lesions, cavernous hemangiomas have a high incidence of 10% to 15%, which is second only to developmental venous malformations.

The MRI enhancement sequences of intracerebral cavernous hemangiomas tend to differ from those of extracerebral cavernous hemangiomas in that the former has no obvious enhancement [4]. MRI of parasellar CSCHs often resemble those of the cerebrospinal fluid with slight hypointensity or isointensity to the ectocinerea on T1WI and hyperintensity on T2WI, showing marked enhancement and delayed enhancement after contrast enhancement. In contrast, meningiomas usually show isointensity to the ectocinerea on T1WI and T2WI, homogenous enhancement, and features of the meningeal tail. The unrestricted diffusion of CSCHs was assumed to be due to the slow flow within the lesion that allows free diffusion of water molecules, thus showing iso- or hypointensity on DWI [5, 6]. Besides meningiomas, lesions in the parasellar region that need to be differentiated from cavernous hemangioma include craniopharyngiomas, epidermoid cysts, and trigeminal schwannomas. CSCHs are often misdiagnosed as meningiomas due to their close resemblance in X-ray imaging and CT scans. Nevertheless, the MRI findings of the two are different and are often serve as the key to their preoperative differentiation. Due to the complex structure at the location of parasellar cavernous hemangiomas, the symptoms include headache, diplopia, sight and visual field changes, impaired eye movement functions, trigeminal neuralgia, facial nerve palsy, and hormonal changes. Although parasellar CSCHs can be surgically removed, their locations and abundant blood supply has greatly increase complexity of the operation and the risk of massive intraoperative hemorrhage. At present, radiotherapy has shown obvious efficacy for parasellar cavernous hemangiomas.

Method

Articles concerning CSCHs were located and collected by keywords searching such as parasellar, cavernous sinus, cavernous hemangioma, and hemangioma, Information on parasellar CSCHs was summarized. Discussion and analysis were made based on one patient with CSCH and relevant literature to summarize the clinical manifestations, imageologic manifestations, differential diagnosis, and treatments of CSCH.

One patient with CSCH was recently admitted to the hospital. The patient was a 72-year-old male suffering from intermittent headaches for eight years. CT scan and MRI at 2013 from other hospital suggested intrasellar cavernous hemangioma in. MRI re-examination in 2015 showed no noticeable enlargement of the lesion. The patient sensed discomfort in the left eye half a year ago in 2021 and sought advice in our hospital due to the this progress of the case.

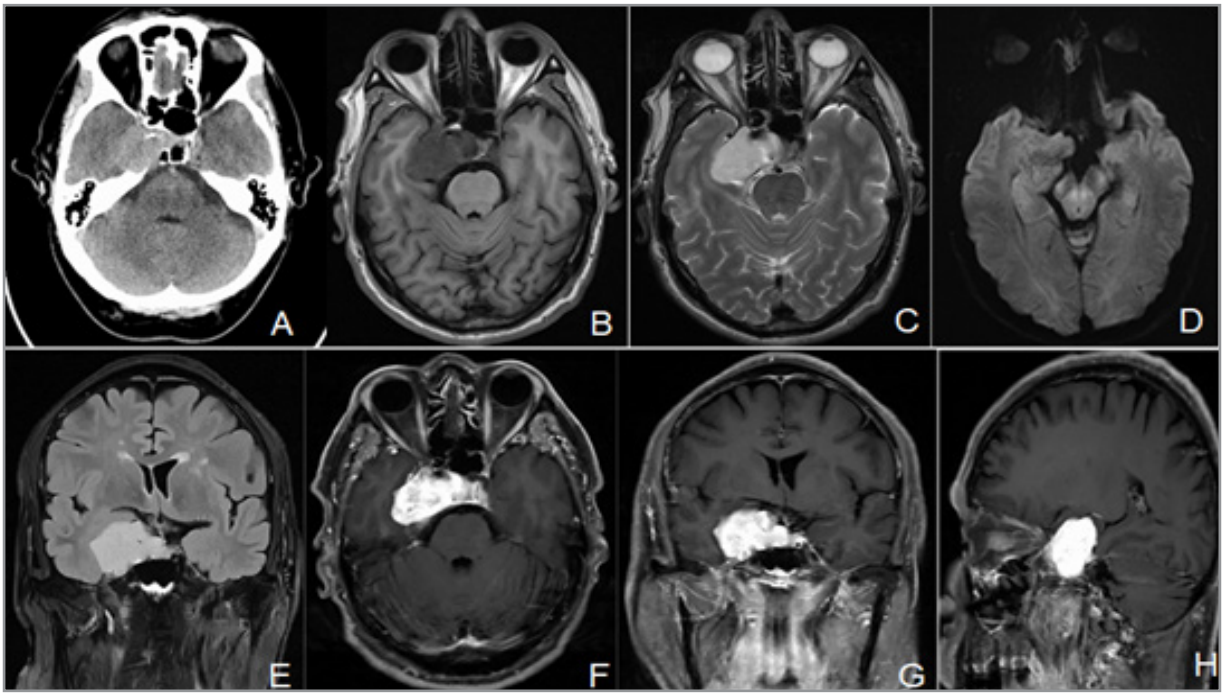

Figure 1:

A. Head CT reveals a right parasellar and intrasellar dumbbell-shaped abnormal signal with clear lobulated edges and slight hyperdensity, and no apparent damage to the basis cranii. MRI findings suggest a right parasellar and intrasellar dumbbell-shaped abnormal signal with lobulated edges and uniform signal within.

B. Hypointensity on T1WI.

C. Hyperintensity resembling the cerebrospinal fluid signal on T2WI.

D. Isointensity on DWI (b = 1000).

E. Hyperintensity on FLAIR.

F, G, and H. Early enhancement in the lesion after contrast enhancement is less uniform, the late enhancement is uniform, and no dural tail sign is observed. Part of the lesion protrudes into the suprasellar cistern and the cisterna ambiens. The right cerebral peduncle, pituitary gland, right internal carotid artery, and temporal lobe are displaced due to compression, the pituitary stalk is displaced to the left, and no visible compression is observed on the optic chiasm.

Discussion

As one of the most common vascular malformations of the brain, cavernous hemangioma has an incidence of 0.6 per 100,000 adults per year [7]. Cavernous hemangioma cases account for less than 3% of all benign tumors of the cavernous sinus and 2% of all benign and malignant tumors [8]. Rosenblum published the first English case report on parasellar CSCH in 1986 [9]. Intracerebral cavernous hemangiomas are often morula-shaped with reddish-purple dilated vessels in dumbbell-like or lobulated shapes. Microscopically, cavernous hemangiomas are blood-filled, thin-walled cavernous vascular sinuses with single-layer endothelium lining and no muscular layer 5or elastic fiber layer. Within the caverns are red blood cells and dense connective tissue stroma composed of fibroblasts but no nerve parenchyma. Parasellar cavernous hemangioma often has a capsule or pseudocapsule formed from dura mater, and the lesion is semi- or fully enveloped[10-12]. Microscopic observation of the connective tissue within cavernous hemangiomas did not reveal manifestations of the previous hemorrhage. However, cavernous sinus hemangiomas can be large and contain vascular channels that lack histological evidence of thrombosis and calcification, which is consistent with their high flow rate status. Parasellar cavernous hemangiomas are classified into two types. Type A, parasellar cavernous hemangioma, consists of many thin-walled vascular sinuses with single layer capillary endothelium lining and little connective tissue between the large lumens. Completely resecting this type of parasellar cavernous hemangioma is difficult and could cause massive hemorrhage. Type B, parasellar cavernous hemangioma, often have structurally intact vasculature, sizeable parenchymal components, and dense connective tissues [13]. Compared to subtype A, subtype B has fewer sinusoidal spaces, more variable sizes, and more irregular shapes.

Hemorrhages from cavernous hemangiomas are correlated to their immature vascular proliferation, whereas the size increase of cavernous hemangiomas is correlated to repeated hemorrhages. The overall hemorrhage rate of cavernous hemangiomas ranges from 0.7% to 4.1%. Sporadic and unruptured cavernous malformations (CMs) have lower annual hemorrhage rates of 0.08-0.2% and 0.3-0.6%, respectively, with recurrence rates ranging from 3.8% to 22.9% [14]. Locations of CMs and their effects on hemorrhage rates are also controversial. Studies have shown that CMs located deeper in the thalamus, basal ganglia, and brainstem may have a higher hemorrhage rate [15]. Cerebral cavernous malformations may occur sporadically as solitary lesions or in clusters as familial diseases, whereas extra-axial parasellar cavernous sinus cavernous hemangiomas generally do not cause hemorrhages [13, 16].

Table 1. Statistics of cases in the literature

Project	Result
Sex	
Male	67 (31.5%)
Female	146 (68.5%)
Symptom	
Headache	40 (36%)
Ocular proptosis	15 (8.7%)
Blurred vision	37 (21.6%)
Diplopia	36 (21.1%)
Oculomotor nerve injury	31 (18.1%)
Abducens nerve	29 (17.0%)
Facial palsy	16 (9.4%)
Trigeminal neuralgia	14 (8.2%)
Cranial nerve injury of unspecified nerve	10 (5.8%)
Endocrine disorders	7 (4.1%)
Limb numbness	3 (1.8%)
Trochlear nerve	5 (2.9%)
Imaging studies	
CT	
Plain CT	
Low density	1 (4.3%)
Isodense	12 (52.2%)
High or slightly higher density	10 (43.5%)
Contrast-enhanced C.T.	
Significantly enhanced	31 (100%)
MRI	
T1WI	
Hypo - or isointense	38 (100%)
T2WI	
Isointense	3 (3.3%)
Hyperintense signal	89 (96.7%)
Enhancer sequence	
Significantly enhanced	84 (100%)
DWI	
Unrestricted	27 (100%)

CSCHs occur more often in females. Among the 213 patients with their genders specified in the reviewed articles, 146 (68.5%) were females, and 67 (31.5%) were males [5, 10, 17-24].

Clinical manifestations of CSCH include headache, cranial nerve changes, diplopia, facial hypoesthesia, trigeminal neuralgia, proptosis, blurred vision, hypopituitarism (amenorrhea, obesity), and galactorrhea [10, 25, 26].

Symptoms of 171 patients were recorded in the literature [5, 10, 17-24]. Specifically, the unspecific statistics of 60 cases indicated that the majority of the patients had the symptom of headache. Among the remaining 111 cases with definite statistics, 40 cases showed the symptom of headache, accounting for 36.04%. A to-

tal of 141 cases showed manifestations of cranial nerve injury, of which were 10 unspecified cranial nerve injuries, 36 diplopia with unspecified nerve damage, 31 definite oculomotor nerve injuries, 29 abducens nerve injuries, 5 trochlear nerve injuries, 16 facial nerve palsy, 14 trigeminal neuralgia, 71 proptosis, 37 blurred vision, 7 endocrine disorders, and 3 simple limb numbness.

Among the patients included in the literature, 31 showed manifestations of cavernous hemangioma in their CT scans, of which one showed clear hypodensity, 12 showed isodensity, 10 showed hyperdensity or mild hyperdensity, and 31 showed clear enhancement [10, 19].

In a study of 133 cavernous hemangioma cases, the authors concluded MRI features of cavernous hemangioma that include very high and uniform T2 signal intensity, dumbbell shapes, and infiltration of the sella turcica. With these three features confirmed, the sensitivity, specificity and accuracy of diagnosing cavernous sinus hemangioma (CSH) could reach 87.5%, 96.3%, and 94.7% respectively [27]. MRI findings of cavernous hemangioma show homogeneous hypointensity on T1, apparent hyperintensity on T2WI, extremely high signal intensity after T2 prolongation, which is considered to be a definite sign of cavernous hemangioma, no diffusion restriction, hyperintensity on FLAIR, and delayed enhancement after contrast enhancement, i.e., the initial inhomogeneous enhancement gradually spreads from the edge toward the center with the progress of contrast infusion [27, 28]. In a report of 15 patients suspected of cavernous hemangioma, 10 showed no diffusion restriction on DWI and almost 100% specificity for CSH [5]. If SPECT (99mTc) can be adopted, Tc-99m-labeled red blood cell imaging could furtherly improve the accuracy of cavernous hemangioma diagnosis [21].

In the reviewed articles, 38 cases showed hypointensity or isointensity on MRI T1WI, 3 cases showed isointensity on T2WI, 89 cases showed hyperintensity on T2WI, 84 cases showed homogeneous or heterogeneous enhancement, most of which were delayed enhancement, and 27 cases showed unrestricted diffusion on DWI [5, 10, 17-22]. In the articles mentioned above, the most prominent manifestations of CSCH were isointensity or hypointensity on T1WI, hyperintensity to cerebrospinal fluid signal on T2WI, and marked homogeneous or heterogeneous enhancement. CSCH could manifest as round or dumbbell-shaped clumps, marked and delayed enhancement, no dural tail sign, no apparent restriction on DWI, and predominant isointensity or hypointensity. Thorough MRI, FLAIR, DWI, enhanced sequence, and SPECT (99mTc) can significantly improve the preoperative diagnostic accuracy of CSCH.

The primary challenges for the differential diagnoses of CSH are the possibilities of cavernous sinus meningioma and schwannoma, metastases, epidermoid cysts, and invasive pituitary tumors [29]. Meningiomas often show hypo- or isointensity on T1WI and T2WI, with marked enhancement on enhancement sequences, the dural tail sign but no delayed enhancement like CSCH [18]. Metastases rarely show hyperintensity on T2. Epidermoid cysts often show hypointensity on T1, hyperintensity on FLAIR, hyperintensity to the brain parenchyma signal on T2,but no significant enhancement. Schwannomas often show hypointensity on T1WI, hyperintensity on T2WI, and heterogeneous enhancement with clear boundaries [4]. Schwannomas follow closely the nerve courses and often compress but do not envelop the internal carotid artery. The most common schwannoma is trigeminal schwannoma, often located within Meckel's cavity and cavernous sinus [29]. Pituitary tumors often show enlargement of the sellar region with an accumulation of cavernous sinuses, hypointensity on T1WI, hyperintensity on T2WI, and low enhancement signal compared with the normal pituitary gland. Pituitary tumors often envelop the internal carotid artery without causing its stenosis [31]. Functional adenomas often cause changes in hormonal indexes, and some particular pituitary tumors could cause apoplexy.

Current treatments of CSCHs include surgical removal and radiotherapy. The risk of neurovascular injury must be carefully considered before performing complete surgical resection because of the up to 40% high possibility of severe intraoperative hemorrhage Since cavernous hemangioma is richly vascularized, its surgical removal is extremely complicated and associated with the high morbidity of cranial neuropathy [27]. However, according to a recent study by Suri et al. incidence of permanent abducens nerve palsy was 14%, it's relatively infrequent. [32].

CSCHs can be resected by the frontotemporal approach, orbital zygomatic approach, and subtemporal approach. Smaller tumors can also be resected under transsphenoidal endoscopes by the transorbital approach on the upper eyelid and the far lateral approach [21, 32, 33]. The extradural and intradural approaches are most commonly used for CSCHs resection, both can facilitate total resection. All approaches can be applied according to the specific tumor. Piecemeal resection could be the key to a successful operation considering the blood supply artery of the tumor, the management of the middle meningeal artery, the internal carotid artery in the cavernous sinus region, and the exposure of the nerves [33-34]. Intraoperative injuries to the internal carotid artery and the vital nerves in the cavernous sinus, such as the third, fourth, and sixth cranial nerves, should be avoided. Intraoperative electrophysiological detection could assist in locating the nerves. With the improved understanding of the anatomy of the cavernous sinus, tumor resection rate is higher currently than before. Patients with subtotal resection can be treated with radiotherapy postoperatively for further efficacy.

With a rich blood supply surgical removal and interventional embolization can be combined to treat cavernous hemangiomas. For example, preoperative embolization of the middle meningeal artery supplying blood to the tumor can significantly reduce blood supply and intraoperative hemorrhage [20].

Stereotactic radiosurgery can be used alone as a treatment or an adjuvant therapy after subtotal resection. Since the first successful treatment reported by Iwai et al. in 1999, gamma knife radiosurgery (GKS) has been proved effective for significantly reducingthe size of tumors and alleviate some neurological symptoms of CSH [24, 35-38]. Currently, GKS is used in management of idiopathic CSH and the postoperative management of CSH patients and has achieved good treatment outcomes [39, 40]. Stereotactic radiotherapy mechanisms are postulated to reduce endothelial proliferation, vessel wall hyalinization, and toxic radiation effects on microvessels and tumor cells, thus leading to vessel occlusion and limiting the growth of cavernous hemangioma [41]. Wang et al. reported in a 2012 systematic review on 59 patients with tumors ranging from 1.5 to 51.4 cm3

(averaging 9.6 cm3) who received stereotactic body radiation therapy (SBRT). Specifically, 55 of the patients had tumors covered by 50% to 60% isodose with a surrounding mean dosage of 13.83 Gy (ranging from 10.0 to 19.0 Gy). The remaining 2 patients were treated with staged stereotactic body therapy, one with cyberknife and the other with tumor basal radiotherapy. The mean follow-up was 49.2 months (ranging from 6 to 156 months). According to re-examination, the tumors showed remarkable shrinkage in 40 cases (67.8%), partial shrinkage in 15 cases (25.4%), and no change in 4 cases (6.8%). The volume reduction after radiotherapy was not significantly correlated with the size of the tumor but the radiation dosage. Among the 59 patients, 37 had partial surgical tumor resection before stereotactic radiotherapy, and 22 had stereotactic therapy alone. Finally, 18 of the stereotactic group (81.8%) had significantly smaller tumors. Therefore, the efficacy of radiotherapy is not significantly correlated with prior surgical resection [23]. Tang et al. (2015) reported on 53 patients who received GKS treatment. The tumors were 13.2 cm3 on average (ranging from 1.0 to 41.0 cm3) with an average diameter of 35 mm (ranging from 16 to 58 mm). A total of 34 patients had tumors larger than 30 mm. The maximum dosage to the tumor was 16.3 to 28.8 Gy with an average central dosage of 25.1 Gy and an average peripheral radiation dosage of 13.3 Gy (ranging from 8 to 15 Gy), pointing to the 49% to 64% isodose line (averaging 53%). During the 24.5-month follow-up, the tumor volume decreased by 79.1% on average, and the volume decreases were over 80% in 29 cases. The tumors did not enlarge after the treatment [17]. Therefore, the efficacy of radiotherapy for cavernous hemangioma is significant.

Conclusion and Outlook

CSCHs are rare intracranial extracerebral cavernous hemangiomas with abundant blood supply and compression on the cavernous sinus and parasellar tissues. Thoroughly clarifying the nature of the tumor via preoperative symptoms and imageological characteristics can help reduce the risk of massive intraoperative hemorrhage. In addition, current radiotherapy is effective for cavernous hemangioma, and the prognosis is good.

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