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Neuro-ophthalmic manifestations of intracranial cavernous hemangiomas

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PURPOSE: *To describe the neuro-ophthalmic manifestations of patients with intracranial cavernous hemangiomas (cavernomas).*
METHODS. *A retrospective review of all patients with intracranial cavernomas with neuro-ophthalmic manifestations who were treated at the Royal Adelaide Hospital in Australia between 1994 and 2004.*
RESULTS. *There were nine patients (three men and six women), with a mean age of 39 years (range 22–61). There was one cerebellar lesion, two thalamic, four pontine, one midbrain/pontine, and one midbrain. Ophthalmic presentations included internuclear ophthalmoplegia (one patient), third cranial nerve (CN) palsy (one patient), fourth CN palsy (one patient), and sixth CN palsy (six patients). Three patients underwent extraocular muscle surgery, and six were treated medically or observed. In five patients the diplopia resolved, in three it was only mild, and in one patient no significant change was noted during the follow-up period.*
CONCLUSIONS. *Diplopia is the main neuro-ophthalmic manifestation of intracranial cavernomas. Sixth CN palsy is the most common cause. Neurosurgical or conservative treatment leads to improvement in most cases, and later use of spectacles or extraocular muscle surgery may lead to further improvement. (Eur J Ophthalmol 2006; 16: 148-52)*

KEY WORDS. *Cavernous hemangiomas, Intracranial, Cranial nerve palsy, Diplopia*

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INTRODUCTION

Intracranial cavernous hemangiomas (cavernomas) are uncommon vascular hamartomas of the central nervous system. This diagnosis has been increasing owing to advances in radiologic imaging (1-3). Subsequently, literature regarding diagnosis and appropriate management for cavernomas has also been increased, allowing a more scientific based approach to management. However, there is little literature discussing neuro-ophthalmic manifestations of cavernomas. We present our experience with nine patients who were diagnosed with neuro-ophthalmic manifestations secondary to intracranial cavernomas.

METHODS

This study includes all patients with neuro-ophthalmic manifestations secondary to intracranial cavernomas treated at the Royal Adelaide Hospital in Australia between 1994 and 2004. Patients were included only if the lesion caused ocular manifestations, and the data were retrospectively collected from a review of case notes. The details recorded included the patient's demographics, the primary diagnosis, general manifestations, ocular manifestations, radiologic features, surgical and ophthalmic management, and the follow-up period and outcome. The duration of follow-up monitoring was calculated from the first symptom caused by the cavernoma that had been brought to medical attention.

RESULTS

There were nine patients with intracranial cavernomas—three men and six women—with a mean age of 39 ± 12 years (median 37, range 22–61 years). All patients were hospitalized for initial assessment and management.

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Of the nine lesions, one was cerebellar in origin, two were thalamic, four were pontine, one midbrain/pontine, and one in the midbrain. General manifestations included headaches in five patients, ataxic gait in five patients, trigeminal or facial nerve palsy in four patients, hemiparesis in two, and decreased consciousness in two (Tab. I). The main ophthalmic complaint was diplopia (100% of cases). On neuro-ophthalmic examination, internuclear ophthalmoplegia (INO) was noted in one patient, a third cranial nerve (CN) palsy in one patient, and a fourth CN palsy in one patient. Partial or complete sixth CN palsy was noted in the other six patients: in four of them it was isolated, and in two patients it was associated with INO (one patient) or bilateral gaze palsy (one patient) (Tab. I). All patients presented with a sudden onset of symptoms attributable to an acute bleed rather than a progressive onset of symptoms secondary to a mass effect. The mean duration of ophthalmic signs and symptoms prior to presentation was 14 days (range, 2–30 days).

Five patients initially underwent a CT scan and all nine patients underwent an MRI. CT findings included a hyperdense lesion in 60% of CT scans, heterogenicity in 20%, and no abnormality was detected in the last 20%. In 5 patients (56%), the MRI scans displayed high T1- and T2-weighted signal images (Fig. 1), while in the other 4 (44%), there were mixed signals on T1- and T2-weighted images. In 6 patients (67%), MRI scans also displayed hemosiderin deposits as a surrounding ring.

After the diagnosis was determined, two patients (Patients 1 and 3, with a thalamic or midbrain tumor) required urgent ventro-peritoneal (VP) shunts for obstructive hydrocephalus, secondary to pressure on the third ventricle or aqueduct. Another three patients were assessed to be suitable candidates for surgical excision of their cavernomas, one of which was done during the initial admission on day 25, and the other two were carried out at 3 and 6 months post presentation, as elective procedures. The two patients requiring VP shunts and one other who was not initially considered for surgical excision experienced re-bleeds at 30 months, 3 years, and 4 years after original presentation, respectively. They subsequently underwent surgical excision with one requiring a second procedure due to incomplete excision. The last three patients were managed conservatively, and as yet none has been found to experience any further bleeds during the follow-up period (Tab. I). Following discharge, all nine patients were followed up regularly in the neuro-ophthalmic clinic (mean follow-up length was 36 months; range, 1 to 108 months). Ophthalmic intervention was offered in six patients; three were considered surgical candidates and underwent

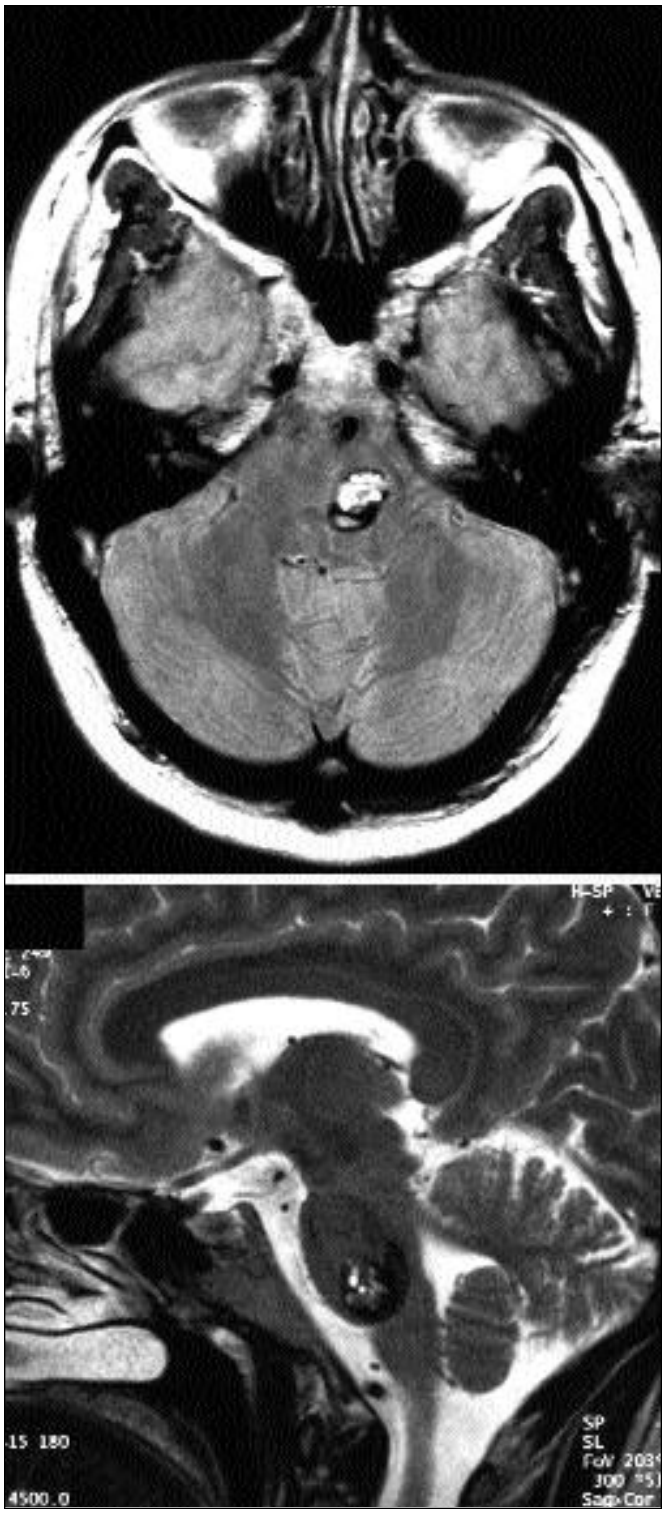

Fig. 1 - *Magnetic resonance images (MRI) of Patient 9. (Top) T1-weighted axial MRI section demonstrating a left pontine lesion with multiple high signal foci producing a popcorn-like appearance. (Bottom) T2-weighted sagittal MRI section demonstrating the same lesion with a low signal peripherally and a high signal centrally.*

extraocular muscle surgery once their visual disturbances had stabilized (Patients 4, 5, and 6; Tab. I). The other six patients were treated medically with spectacles in two patients and patching in one. Another three patients were observed regularly and no intervention was required. Overall, five of our patients (56%) did not complain of diplopia, and in three patients (33%), there was only mild diplopia in the extremes of gaze by the end of follow-up. The last patient was assessed to have only mild improvement in his ophthalmic symptoms after conservative management, but this was attributable to the overall poor outcome following his intracranial hemorrhage, and no further treatment was offered.

DISCUSSION

The exact incidence and prevalence of intracranial cavernomas in the general population is not known. Estimations vary and range between 0.4 and 0.9% of the popu-

TABLE I - CLINICAL CHARACTERISTICS OF PATIENTS WITH CEREBRAL CAVERNOUS HEMANGIOMAS

Patient Age, yr/sex	Anatomic location	General manifestations	Neuro-ophthalmic symptoms	Neuro-ophthalmic diagnosis	Neuro imaging	Ophthalmic management	Ventriculo-peritoneal shunt	Follow-up, mo
1 30/M	Thalamus	Headaches, decreased consciousness	Diplopia	Partial R sixth CN palsy	CT: hyperdense lesion MRI: high T1 & T2 signals	Glasses	Yes	72
2 61/M	Pons/ midbrain	Headaches, ataxic gait	Diplopia	L INO and partial sixth CN palsy	MRI: mixed T1 & T2 signals	Conservative	No	6
3 37/F	Midbrain	Headaches, decreased consciousness	Diplopia	Bilateral fourth CN palsies	CT: heterogenic lesion MRI: mixed T1 & T2 signals	Conservative	Yes	72
4 36/F	Pons	L hemiparesis, ataxic gait, partial seventh CN palsy	Diplopia	R sixth CN palsy, bilateral gaze palsy	MRI: mixed T1 & T2 signals	Accommodative lenses, R. Jensen's procedure + R & L MRM recession	No	108
5 35/F	Pons	Headaches, R partial fifth CN palsy	Diplopia	L sixth CN palsy	MRI: high T1 & T2 signals	L MRM recession and L LRM resection	No	18
6 53/F	Cerebellum	Ataxic gait, L partial seventh CN palsy	Diplopia	L partial sixth CN palsy	CT: hyperdense lesion MRI: high T1 & T2 signals	L MRM recession and L LRM resection	No	25
7 22/F	Thalamus	R hemiparesis, ataxic gait	Diplopia	R third CN palsy	MRI: mixed T1 & T2 signals	Glasses	No	25
8 44/M	Pons	Ataxic gait, L fifth CN palsy	Diplopia	L partial sixth CN palsy	MRI: high T1 & T2 signals	Conservative	No	1
9 38/F	Pons	Headaches, dizziness	Diplopia	INO	CT: hyperdense lesion MRI: high T1 & T2 signals	Eye patching	No	5

CN = Cranial nerve; CT = Computed tomography; MRI = Magnetic resonance imaging; INO = Internuclear ophthalmoplegia; MRM = Medial rectus muscle; LRM = Lateral rectus muscle

lation (4). They occur with equal frequency in males and females (5-7) and the majority of patients are diagnosed between the third and fourth decades of life (3, 7, 8). Similar findings were found in our series where the mean age was 39 years. The ratio of females to males in our series was 2:1, and this can be attributed to the small sample size of our study. Although a familial form of intracranial cavernomas exists (9), none of the patients in our series had a relevant family history.

It is generally accepted that most cavernomas (60 to 80%) are located supratentorially (1, 5, 10-12). This is consistent with other studies which have found that approximately 18 to 35% of cavernomas are located in the brainstem (13, 14) and 2.5 to 10.8% in the ventricles (15). The clinical presentation varies greatly according to the anatomic location. Possible symptoms include headaches, visual and sensory disturbances, and ataxia. Nevertheless, some may be asymptomatic, and are only detected as an incidental finding on brain imaging for other reasons (7, 8). Large studies have shown that seizures are the most common clinical presentation for all cavernomas (1, 4, 6). This is more frequently noted in supratentorial tumors rather than infratentorial cavernomas, which tend to present with progressive neurologic deficits (6, 8). The annual bleeding rate for brainstem cavernomas is about 2.5%, with recurrent hemorrhage rates ranging from 5 to 21% in several studies (8, 13, 16). On the other hand, the annual bleeding rate of supratentorial lesion is only 0.25 to 1.1% (6, 8, 12), thus the natural history of brainstem lesions is probably worse than that of lesions in other areas.

All nine lesions in our series of patients were infratentorial in origin, six of which were in the brainstem, two in the thalamus, and one in the cerebellum. All patients presented with neurologic deficits of at least one or more cranial nerve, in keeping with the literature, and none experienced seizures. The re-bleeding rate in our series was 33%, which is higher than that mentioned in the literature.

As mentioned previously, there is an increase in the rate of diagnosis of intracranial cavernomas, and this can be directly attributed to improved imaging techniques. Angiography and CT scans had been used previously to aid in making the diagnosis, but it is now widely accepted that MR imaging is the gold standard for diagnosing cavernomas (1, 2, 10, 17). Acciarri et al (1) found MRI to be highly specific for cavernomas, providing a typical picture in 88.6% of cases. This is in stark contrast to CT and angiography, which identified only 43.2% and 4% of cases, respectively. Zabramski et al (18) described four possible patterns of MRI findings: Type I lesions are hyperintense on T1- and T2-weighted images and indicate subacute hemorrhage. Type II lesions show a mixed signal intensity on T1- and T2-weighted images, with a surrounding hemosiderin ring. Type III lesions are hypo- to isointense, whereas Type IV lesions are poorly visualized except on gradient echo sequences (18). Our MRI findings were similar to Type I or II lesions described in the literature. Five of our patients displayed high T1- and T2-weighted signal images (Fig. 1), and four displayed mixed T1- and T2-weighted signals.

Neurosurgical treatment of cavernomas is dependent on the presentation of the patient. Asymptomatic patients are managed by clinical observation and repeated imaging, irrespective of location (4, 7). Indications for surgical resection of accessible symptomatic lesions include progressive neurologic deficits, intractable epilepsy, and recurrent hemorrhages (1, 7). Patients with inaccessible symptomatic cavernomas are usually observed despite the poor natural history associated with untreated brainstem and thalamic lesions (7). Stereotactic radiosurgery has been suggested by some for the treatment of inaccessible areas (18) but this treatment remains controversial and is not recommended by many (1, 4, 19, 20). The treatment of our patients followed the guidelines that have been established in the literature. Our patients were all symptomatic and therefore managed under the neurosurgical unit. Three patients were offered primary excision, and underwent surgery between 1 and 6 months post presentation. Another three patients underwent surgical excision after recurrent hemorrhages, whereas the last three patients were managed conservatively for their inaccessible symptomatic cavernomas.

There is very little literature available on the ophthalmic manifestations of intracranial cavernomas. Kupersmith et al (8) presented a series of 37 patients with brainstem cavernomas, and found that diplopia was the most common clinical feature, presenting in 51% of cases. Similarly, Bertalanffy et al (4), in their subseries of 24 patients with brainstem cavernomas, showed that diplopia was a common clinical feature, presenting in 42% of cases. Shimura et al (21) reported a case of bilateral gaze palsy secondary to a pontine cavernoma.

We found that the primary ophthalmic complaint in all our patients was diplopia secondary to a third, fourth, or sixth CN palsy, or INO. Initial management of these patients should be in accordance with documented neu-

rosurgical opinions. We found that regardless of the neurosurgical management decision, whether conservative or surgical, there was at least some degree of improvement in the patient's ophthalmic symptoms over time. This occurred gradually and often stabilized at around 12 months post hemorrhage. At this stage, patients were offered further management, including extraocular muscle surgery or spectacles, if deemed appropriate. Following this approach we found that in 8 (89%) of our patients there was complete or partial resolution of diplopia by the end of follow-up.

In conclusion, intracranial cavernomas are rare lesions. The main neuro-ophthalmic symptom is diplopia secondary to a CN palsy or INO. The appropriate treatment for cavernomas, whether neurosurgical or conservative, may lead to some degree of improvement in visual symptoms in the majority of cases. Once this improvement plateaus, further benefits can often be obtained by extraocular muscle surgery or the use of spectacles.

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