PAPER

Surgical removal of brain stem cavernous malformations: surgical indications, technical considerations, and results

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Objectives: This study was undertaken to review the indications for surgical treatment of brain stem cavernomas and to develop strategies to minimise the complications of surgery.

Patients and results: Twelve patients underwent surgical resection of a brain stem cavernoma due to symptoms caused by one or more haemorrhages. Age ranged from 18 to 47 years (mean 29.2 years). Long term follow up (mean 3.7 years) included a complete neurological examination and annual MRI studies. The annual haemorrhage rate was 6.8 %/patient/year and a rate of 1.9 rehaemorrhages/patient/year was found. Surgery was performed under microsurgical conditions with endoscopic assistance, use of neuronavigation, and neurophysiological monitoring. Navigation proved to be reliable when applied in an early stage of operative procedure with minimal brain retraction. Endoscopy was a useful tool in some cases to confirm complete resection of the lesion and to ascertain haemostasis. Ten patients had a new neurological deficit in the early postoperative period, nine of these were transient. At the last follow up the neurological state was improved in five patients, unchanged in six, and worse in one compared with the preoperative conditions. The preoperative average Rankin score was 2.2 points and had improved at the last follow up by 0.6 points to 1.6 points.

Conclusions: Symptomatic brain stem cavernomas should be considered for surgical treatment after the first bleeding. Careful selection of the optimal operative approach and a meticulous microsurgical technique are mandatory. The additional use of modern tools such as neuronavigation, endoscopic assistance, and monitoring can contribute to the safety of the procedure.

Among intracranial vascular malformations the cavernous malformation is one of the rarest, with a necropsy incidence of between 0.39% and 0.53%.^{1,2} Since the introduction of MRI cavernous malformations are diagnosed more often.^{3,4} Between 10%–23% are located in the posterior fossa with most in the pons.^{5,6} If these lesions bleed they can cause severe functional disturbances or death. Correct management of these lesions is therefore vital. In this study we describe the clinical experience with 12 surgically treated brain stem cavernomas and describe the use of neuronavigation and endoscopy.

PATIENTS AND METHODS

Between 1990 and 1999 12 patients with a cavernous malformation of the brain stem were referred to our institution and treated surgically. There were six men and five women; age ranged from 18 to 47 years (mean 29.2 years), and all had experienced one or more haemorrhages. Our criteria for a haemorrhagic episode were acute onset of symptoms, manifestation of new neurological deficits, and corresponding findings in MRI demonstrating haemorrhage into the cavernous malformation or the adjacent brain stem parenchyma. The existence of haemosiderin deposits alone was not sufficient to define a haemorrhagic episode. The patient's preoperative and postoperative neurological state was classified according to the Rankin scale to achieve a grading of functional disturbances of daily life activities. The annual retrospective haemorrhage rate was calculated based on the frequency of haemorrhages and the patient's years of life. The annual risk for rehaemorrhage was evaluated based on the frequency of rehaemorrhages and the interval between the haemorrhages. Operative removal of the cavernous malformation was performed under standard microsurgical conditions, with neurophysiological monitoring, and, more recently, using neuronavigation and neuroendoscopy. Long term follow up

included a complete neurological examination of all 12 patients and annual MRI studies. The mean follow up period was 3.7 years (range 11 months–9.2 years).

RESULTS

Clinical presentation

All patients had symptoms of one or more haemorrhages. Three patients had one haemorrhage, six patients two haemorrhages, and three patients three haemorrhages. We found 24 haemorrhagic episodes in 351 patient-years of life. Thus, the annual haemorrhage rate was 6.8%/patient/year. According to 21 rehaemorrhages in nine patients during a period of 10.9 years, we calculated a rate of 1.9 rehaemorrhages/patient/year.

Acute onset of symptoms and neurological signs were characteristic for a haemorrhage. The first haemorrhage was followed in most patients by relatively mild signs and symptoms such as vertigo, headache, and haemihypaesthesia. In patients with repeated haemorrhages worsening of neurological deficits with progressive gait disturbances, cranial nerve paresis and long tract disturbances occurred.

Preoperative imaging included CT, MRI, and cerebral angiography in all cases. There were no pathological findings in cerebral angiography. One patient (No 12) with multiple supratentorial and infratentorial cavernous malformations was operated on supratentorial cavernous malformation for 17 years before surgery of his brain stem lesion.

Surgical treatment and MRI findings

The operative approach was selected according to two general considerations: to minimise damage of the surrounding structures and to facilitate complete resection of the lesion. An overview is given in table 1. All operations were performed under standard microsurgical conditions with monitoring of median nerve somatosensory and brain stem acoustic evoked potentials. Neuronavigation and endoscopy were used if necessary (see illustrative case No 12).

Table 1 Patients with cavernous malformations of the brain stem

Patient No	Sex	Age (y)	No of haemorrhagic events	Preoperative Rankin score	Postoperative Rankin score	Localisation	Operative approach	Follow up (months)
1	M	33	3	5	2	Pons	Retromastoidal	52
2	F	24	2	1	1	Medulla oblongata	Subcerebellar	48
3	M	25	1	0	1	Pons	Retromastoidal	110
4	M	34	2	4	4	Ponto-mesencephalic	Presigmoidal-transtentorial	70
5	F	47	3	4	3	Mesencephalon	Presigmoidal-transtentorial	44
6	M	27	3	2	1	Pontomesencephalic	Supracerebellar	21
7	F	32	2	1	1	Pons	Retromastoidal	15
8	F	28	1	2	2	Pons	Subcerebellar	16
9	M	23	2	1	0	Mesencephalon	Supracerebellar	106
10	F	24	1	1	1	Medulla oblongata	Subcerebellar	23
11	F	18	2	3	1	Crus cerebri	Fronto-orbitozygomatic	11
12	M	36	2	2	2	Pons	Retromastoidal	12

For planning of the surgical approach MRI was evaluated for the exact location of the cavernoma, its relation to the bleeding cavity, and the proximity of the lesion to the pial surface of the brain stem. In five cases MRI demonstrated that the cavernous malformation was located superficially reaching to the pial surface, whereas in the remaining seven patients the cavernous malformation was covered by some normal brain stem parenchyma. During surgery the cavernous malformation or the bleeding cavity were directly visible at the surface of the brain stem in three patients. In six patients only mild to moderate haemosiderin staining of the pial surface was detected after exposure of the brain stem. In three patients the operative field seemed normal.

In all five patients in whom MRI suggests a superficial location of the cavernous malformations the surface of the exposed brain stem was abnormal. In two of these cases the cavernous malformation was directly visible and in three cases haemosiderin staining was recognisable.

In all patients the cavernous malformation was resected completely as demonstrated by postoperative MRI.

Postoperative course and outcome

Ten of the 12 patients operated on had a new neurological deficit in the early postoperative period. In nine of these 10 patients the new deficits were transient. One patient (No 3) had persistent unilateral sixth cranial nerve dysfunction. At the last follow up all 12 patients were alive. Compared with the preoperative neurological conditions the postoperative state was improved in five patients, unchanged in six, and worse in one (No 3). The preoperative average Rankin score was 2.2 points. At the time of the last follow up the average postoperative score had improved by 0.6 points to 1.6 points. A summary is given in table 1.

Four patients underwent a second operation. One patient required evacuation of a supratentorial epidural haematoma which developed near a right frontal burr hole for a perioperative ventricular drain. In three patients a CSF shunt was inserted.

Illustrative cases

Case No 1

A 33 year old man presented with acute onset of headache associated with a left hemiparesis, gait disturbance, and lower cranial nerve disturbances. Due to two rehaemorrhages the patient's neurological condition deteriorated continuously (Rankin score 4). Eventually he was admitted for surgery. Brain MRI showed a cavernous malformation located in the pons. Repeated haemorrhages had led to a space occupying lesion of increasing size (fig 1 A-C). A suboccipital retromastoidal craniotomy was performed and the lateral aspect of the pons was exposed showing a circumscribed red-bluish area.

After evacuation of the haematoma, the cavernous malformation was identified and completely resected (fig 1 D-F). Postoperative MRI confirmed complete resection of the lesion. Last follow up at 52 months showed a residual mild left hemiparesis, whereas disturbances of the lower cranial nerves had resolved completely (Rankin score 2).

Case No 12

This 36 year old man was admitted because of sudden onset of a left hemiparesis associated with gait disturbances, nausea, and vomiting. With non-operative support his symptoms partially improved. Two weeks later the patient's condition deteriorated due to a second haemorrhagic event. Brain MRI demonstrated an acute intrinsic pontine haematoma. Additionally four supratentorial and two cerebellar cavernous malformations without signs of acute haemorrhage were detected (fig 2 A). Via a retromastoidal craniotomy the lateral brain stem was exposed. The pial surface of the brain stem showed no changes in colour or other abnormalities. Using CT guided navigation the bleeding cavity and the cavernous malformation were localised and the entry point on the pial surface of the brain stem was determined (fig 2 B and C). After complete excision of the cavernous malformation, the bleeding cavity was inspected with the neuroendoscope to exclude remaining pathological vessels and to control for sufficient haemostasis (fig 2 D). One year after surgery the neurological examination showed a residual left hemiparesis, but the patient was able to walk independently (Rankin score 2). Follow up MRI studies showed normal postoperative findings and no changes of the asymptomatic cavernous malformations.

DISCUSSION

Surgery of brain stem cavernomas has two main goals: to achieve complete resection of the lesion and to avoid additional neurological damage to the patient.

As a first step after exposure of the lesion the surrounding haematoma is removed, and the cavernous malformation exposed and dissected. Care is taken not to penetrate the cavernoma but to work around the borders of the lesion, so that bleeding is minimised and dissection facilitated. After removal of the cavernous malformation meticulous haemostasis is essential. No effort is made to remove the haemosiderin stained gliotic tissue that surrounds the cavity of the haematoma because it is unnecessary and may cause additional neurological damage.

Optimal timing of surgery is less well defined. In agreement with other authors^{7,8} we perform surgery in the subacute stage with a delay of several days or weeks after the haemorrhage, when the patient is in a stable condition. Additionally, in the subacute stage MR imaging allows better differentiation between the haematoma and the vascular malformation itself.

Figure 1 Case No 1. (A) Sagittal MR image showing a cavernous malformation of the pons after the first haemorrhage. (B) and (C) Sagittal MR images after the second and third haemorrhage shows an enlarging haematoma. (D-F) Intraoperative photographs. (D) After exposure the bulging aspect of the right lateral pons and subpial haemosiderin staining is visible (arrow). (E) The haematoma is removed and the cavernous malformation is identified. (F) After resection of the lesion the cavity is collapsed. Haemosiderin stained gliotic tissue surrounding the lesion is left behind.

Knowing the exact location of the cavernous malformation within the bleeding cavity is valuable for planning the surgical approach.

Neuronavigation

High resolution MRI is indispensable for the selection of the surgical trajectory to minimise or, if possible, completely avoid dissection through intact brain stem parenchyma.

In our experience, abnormalities of the pial surface of the brain stem will be visible intraoperatively, if MRI demonstrates a superficial location of the cavernous malformation. Thus, intraoperative findings after exposure of the brain stem will direct the surgeon to the best entry point. This was true in

nine of the 12 patients. However, in three of seven patients, where MRI demonstrated some amount of normal brain stem parenchyma covering the cavernous malformation, the surface of the brain stem seemed to be normal after operative exposure. For these patients with a deeply located cavernous malformation the use of neuronavigation is highly recommended to assist the surgeon in planning the incision (fig 2). Some concern may arise about the reliability of navigation due to intraoperative brain shift. An important point is to use navigation in the very early stage of exposure. When applied with minimal brain retraction and before larger amounts of CSF were drained, precision of neuronavigation to localise the cavernous malformation is excellent in our experience.

Figure 2 Case No 12. (A) Axial MR image showing an acute pontine haemorrhage. A second cavernoma without signs of acute bleeding is visible in the right cerebellar hemisphere. (B) Three dimensional model for neuronavigation. (C) Intraoperative photograph showing the pontine haematoma outlined in the operating microscope by the navigation device (yellow dotted line). (D) Intraoperative photograph showing the endoscopic view of the haematoma cavity. Complete resection of the lesion and sufficient haemostasis were confirmed. Note the enhanced close up view provided by the endoscope.

Neuroendoscopy

The importance of a complete resection of the cavernous malformations is underscored by two cases reported in the literature in which remnants of the cavernous malformation caused fatal haemorrhage postoperatively.^{7,9} Incomplete resection of the cavernous malformation may occur when vision of the operative field is restricted due to bleeding or due to a deep location of the lesion in a large haematoma cavity. In these cases endoscopic assistance is valuable. As the incision into the brain stem is kept as small as possible to avoid additional damage a keyhole is created in the depth of the operative field. The type of "deep keyhole" decreases the field of vision through the microscope significantly. Under these conditions a complete inspection of the resection cavity through the microscope is hardly achieved. With the endoscope near the keyhole using a 3 mm rigid wide angle lensscope a complete and detailed view of the entire cavity is obtained (fig 2 D). Residual cavernous malformations or small bleeding points are easily identified with this technique.

Operative morbidity

The published outcome of surgically treated patients with brain stem cavernous malformation is generally good. In larger series surgical results were unchanged or improved in 69% to 91%.^{5,7,10,11} Furthermore, there are several case reports of surgically treated brain stem cavernous malformations with excellent or good results.^{5,8,9,12-16} Whereas most authors had no surgical deaths, Porter *et al*¹⁷ reported a surgical mortality of 3.5%. Two of their patients died of cardiopulmonary arrest and one of a haemorrhagic venous cerebellar infarction. Our results compare favourable with the literature.

Indications for surgery

There is general agreement that patients with incidentally detected cavernous malformations are not surgically treated as long as the lesion produces no neurological symptoms by haemorrhage. However, if a first haemorrhage occurs surgical

treatment in our opinion has to be considered even if only mild neurological symptoms are present.

Some authors stated that patients with a previous haemorrhage are more likely to have a repeated haemorrhage.^{10,17-20} Porter¹⁷ reported a rehaemorrhage rate of 30%/person/year and Fritsch *et al*¹⁰ reported in their meta-analysis an average rebleeding rate of 21%/year/lesion. In accordance with these studies we found a significantly higher risk of haemorrhage when the cavernous malformations already had caused symptoms by a previous haemorrhage. In our series the annual haemorrhage rate was 6.8% with a rate of 1.9 rehaemorrhages/patient/year. Furthermore, the literature and the findings in this series suggest that neurological deficits are more severe in repeated haemorrhages.

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NEUROLOGICAL STAMP.....

Karl Landsteiner (1868-1943)

In 1902 Landsteiner, an Austrian born American immunologist, announced one of the major medical discoveries of the century, that of the ABO blood group system. His work permitted successful blood transfusion, and the saving of so many lives. He was over 70 when in 1940 he announced the discovery of the rhesus (Rh) factor, then responsible for the serious illness or death of 1 in 200 white babies.

Landsteiner also introduced dark field microscopy for the diagnosis of primary syphilis and with several associates worked on the characteristics of *Spirochaeta pallida*. They were able to describe the mechanism that resulted in the Wassermann reaction. Together with Ernest Finger and others he discovered that the antigen, previously extracted from a syphilitic human, could be replaced with an extract prepared from ox hearts for this test.

For more than a decade between 1908 and 1922 Landsteiner performed research in poliomyelitis. He injected a preparation of brain and spinal cord tissue obtained from a polio victim into a Rhesus monkey, which later developed paralysis. Further work led him to conclude that a virus caused the disease. Later, in cooperation with the Pasteur Institute he developed a serological test for the diagnoses of the disorder.

Landsteiner received the Nobel Prize in physiology or medicine in 1930 for his discovery of human blood groups. Austria honoured him philatelically in 1968 on the 100th anniversary of his birth (Stanley Gibbons 1525, Scott 813).

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