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ORIGINAL ARTICLE

A retrospective and consecutive analysis of the epidemiology and management of spinal cavernomas over the last 20 years in a single center

Ardeshir Ardeshiri[1,2] · Neriman Özkan[1] · Bixia Chen[1] · Klaus-Peter Stein[1,3] · Dorothea Miller[1] · Bernd-Otto Hütter[1] · Ibrahim Erol Sandalcioglu[1,3] · Ulrich Sure[1]

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Abstract Spinal cavernous malformations (SCM) are rare lesions often presenting with acute onset of symptoms and progressive neurological deterioration due to hemorrhage into the spinal cord. With the aid of modern techniques, their surgical removal became much safer. The present study was undertaken to analyze the outcome of our series of surgically and conservatively treated patients with SCM. Over a period of 20 years, 20 surgically treated and 5 conservatively managed patients with spinal cavernous malformations were identified and enrolled into this analysis. Demographic data, clinical symptoms, localization and extension of the cavernoma, as well as pre- and postoperative neurological status were obtained. The clinical status was assessed using the Frankel score. Patients were followed up clinically and by MRI. Before surgery, 90 % (18/20) of our surgical patients were classified as Frankel D (93.8 %), whereas two patients (10 %) were graded C. None of the patients had a worse Frankel score at the time of discharge. Eighty percent of them (16 cases) remained unchanged, and 20 % (4 patients) improved during the first follow-up (*mean 6.3 months*, *range 2–17 months*). All improved patients had a superficially located SCM and were operated early (≤3 months). No worsening was observed during extended follow-up (range 9–134 months, mean 44.7 months). Five nonsurgically treated patients showed no significant clinical deterioration over a period of 6.7 years (mean, range 2.9–8 years). SCM localization and number of involved segments had no influence on outcome. Our data show that SCM can be resected with favorable neurological outcome *by using intraoperative neuromonitoring*. Within the follow-up period, patients treated conservatively remained in a stable neurological condition.

Keywords Cavernous malformations · Intramedullary spinal cord tumor · Spinal cavernomas · Spinal surgery

Introduction

Vascular lesions in the spinal cord account for about 6–7 % of all spinal tumors and [1–3]. Only 5–12 % of these vascular abnormalities are spinal cavernous malformations (SCM) [4–6].

Clinically, SCM may remain asymptomatic; however, if they become symptomatic, acute onset of neurological symptoms can occur with recurrent and progressive neurological deficits due to bleeding from the SCM. Sensory or motor symptoms are most frequent (about 60 % of the cases respectively) followed by pain (34 %) and bladder/bowel dysfunction (24 %) [7]. In contrast to the sporadic form, patients suffering from a familial syndrome or genetic alteration are at an increased risk for the development of both cerebral cavernous malformations as well as SCM [8–15].

Since recent introduction of ultra-high resolution MRI techniques and the development of modern sequences like

Ardeshir Ardeshiri and Neriman Özkan contributed equally to this work.

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✉ Ardeshir Ardeshiri
aardeshiri@aol.com

[1] Department of Neurosurgery, University Hospital Essen, University Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany

[2] Present address: Department for Trauma Surgery and Orthopedics, Klinikum Itzehoe, Itzehoe, Germany

[3] Present address: Department for Neurosurgery, Klinikum Nordstadt Hannover, Hannover, Germany

susceptibility-weighted imaging (SWI) (Fig. 1), SCM can be diagnosed more accurately [16]. Surgical tools such as routine use of the microscope and intraoperative neuromonitoring (somatosensory/motor evoked potentials (SEP/MEP) and D-wave) make surgery of these lesions much safer [17]. Since SCM are rare, the number of patients included in *published* studies is relatively small. In the excellent meta-analysis of Badhiwala et al. [7], 40 studies on spinal cavernomas were included with a total of 632 patients. Two of the main statements were favorable neurological outcomes for patients with surgery within 3 months and for gross-total resection. The authors recommended surgery for symptomatic SCM.

The present study was undertaken (1) to analyze the clinical outcome of surgically treated and conservatively managed patients with a SCM and, based on these results, (2) to develop a treatment algorithm.

Patients and methods

Patient data

Medical records of patients with SCM who were admitted to our department from August 1994 to July 2013 were reviewed and followed up. A total of 25 patients with SCM who were managed either surgically or conservatively were identified and included into this study. Among these, 20 patients were treated surgically and 5 conservatively. *Gender was quite equally distributed* (14 male and 11 female) with a mean age of 46 years, ranging from 17 to 72 years. The localization of the lesion was categorized into cervical/cervicothoracic or thoracic/thoracolumbar including the medullar conus, while SCM extension was classified into one or more than one involved segment. Basic demographic data, clinical presentation, and radiological examinations were reviewed retrospectively for each patient (Table 1).

Fig. 1 SWI-sequence of the cavernoma at C4 of patient 9 showing the hemosiderin ring

Surgery

An osteoplastic laminotomy with reconstruction of the posterior spinal column was the surgical approach to access the SCM. However, in earlier cases or in biomechanical stable regions (thoracic and thoracolumbar region), a laminectomy was performed as reported earlier [18]. The SCM were resected under microsurgical conditions with continuous observation of the intraoperative somatosensory (SEP) and motor evoked potentials (MEP; introduced in 2008). All patients treated surgically underwent postoperative MRI to determine complete resection of the SCM, which was performed routinely within 3 days after surgery and 3 months postoperatively.

Outcome and follow-up

Patients' neurological state was classified according to the Frankel scale in order to achieve a functional grading of impaired daily life activities and gait disturbances [19]. Functional outcome was correlated with respect to localization and involved segments of the SCM. Patients were followed up clinically and by MRI examinations 3 and 6 months postoperatively and then by yearly follow-up intervals.

Statistical analysis

Functional outcome was analyzed in terms of localization, involved segments of the SCM, and timing of the operation. Regarding the small sample size and the respective small cell numbers, respectively, we applicated for statistical confirmation of possible differences in the improvement ratio in respect to deep vs. superficial localization of the cavernoma a special nonparametric procedure. This algorithm is adequate for one single sample rate and proportions and robustness in the case of small sample size and/or small cell numbers including empty cells. For this purpose, we used the procedure Estimation of the Binominal Parameter PI provided by the software Cytel Studio version 9.0.0 (program package StatXact from Cytel software). Because of the weakness of the data, it is not appropriate to test directed hypotheses on numerical differences between groups. Therefore, the algorithm used tests unspecifically if a possible distribution shift is not statistically different from random binominal distribution (null hypothesis) or if this shift over cells is nonrandom (H_1). Thus, we also calculated only the two-sided p value for the statistical significance of the

Table 1 Basic demographic data with regard to SCM localization and functional outcome

Pat.	Sex	Age	Loc.	Involved seg.	TOS	FG pre-OP	FG post-OP	FG last FU	Last FU mon.
1	f	48	CT	2	*1*	C	D	D	47
2	m	52	TL	2	*1*	D	D	D	58
3	f	68	CT	1	*1*	D	D	D	2
4	f	46	CT	1	*1*	D	D	D	31
5	m	44	TL	1	*2*	D	D	D	38
6	m	62	TL	1	*1*	D	D	E	17
7	m	72	TL	2	*1*	D	D	D	4
8	m	37	TL	2	*1*	D	D	E	43
9	f	49	CT	1	*2*	D	D	D	14
10	f	17	TL	2	*1*	D	D	D	134
11	f	37	TL	2	*1*	D	D	D	3
12	m	59	CT	1	*1*	D	D	D	9
13	m	28	CT	1	*1*	D	D	D	4
14	f	48	CT	2	*2*	D	D	D	8
15	m	64	TL	2	*1*	D	D	D	15
16	f	24	CT	2	*2*	D	D	D	14
17	f	29	TL	1	*1*	D	D	D	6
18	m	46	CT	2	*1*	D	D	D	66
19	m	28	CT	2	*1*	C	D	D	53
20	m	70	TL	2	*2*	D	D	D	2
21	m	36	TL	1				D	96
22	f	38	TL	1				D	96
23	m	54	TL	2				D	35
24	f	49	TL	2				D	96
25	m	65	CT	2				D	78

Patients 1–20: surgical group, patients 21–25: nonsurgical group. For the surgically treated patients, age is given for date of surgery. For the conservatively treated patients, age is given at time point of diagnosis, and only the last follow-up is mentioned as there was no worsening during follow-up in these patients

Pat. patient, *Loc*. localization, *segm* segments, *TOS* time of surgery after onset or worsening of symptoms, *pre-/postop* pre-/postoperative, *mon*. months, *f* female, *m* male, *CT* cervical/cervicothoracal, *TL* thoracic/thoracolumbar, *1* one involved segment, *2* >1 segment involved, *TOS 1* ≤3 months, *TOS 2* >3 months, *A-E* Frankel grades (*FG*) preoperative and postoperative and during follow-up (*FU*)

estimation of the binominal parameter computed by the algorithm applied in the present data analysis.

Results

Clinical and radiological presentation

Symptoms in the surgical group were sensory deficits (n=17), motor deficits (n=12), pain (n=9), myelopathy (n=7), para-/tetraparesis (n=5), and bladder/bowel dysfunction (n=3). One patient presented with acute symptoms, 16 patients had subacute or progressive symptoms, and 3 patients had recurrent symptoms. Four out of 16 patients with progressive clinical presentation showed an acute worsening before admission to our hospital. All nonsurgically treated patients were in a good neurological condition (grade D). All of them suffered from sensory deficits. Motoric deficits and pain were present in 4 patients. Myelopathy and bladder/bowel dysfunction was seen in one case. Time point of surgery was less ≤3 months in 15 patients and > 3 months in 5 cases after onset or worsening of symptoms.

Eleven SCM were located either in the cervical/cervicothoracic region (Fig. 2) and 14 in the thoracic/thoracolumbar (Fig. 3) region. In 10 patients (40 %), the SCM and its bleeding cavity involved only one segment, while in 15 cases (60 %), more than one spinal segment. The exact localization was categorized into superficial or deep. Furthermore, both these groups were subdivided into ventral, dorsal, or lateral position. In the superficial group (n=15, 75 %), eight cavernomas were dorsal and six lateral (in one case, exact localization not

Fig. 2 T1-weighted contrast-enhanced MRI images preoperatively (**a**, **b**) and postoperatively (**c**, **d**) of patient 9 (49-year-old female) with an SCM at C4. The patient presented with pain, sensory, and motor deficits of the right side of her body. Surgery was performed via a laminoplasty C3–5 and complete SCM resection was achieved (**c**, **d**)

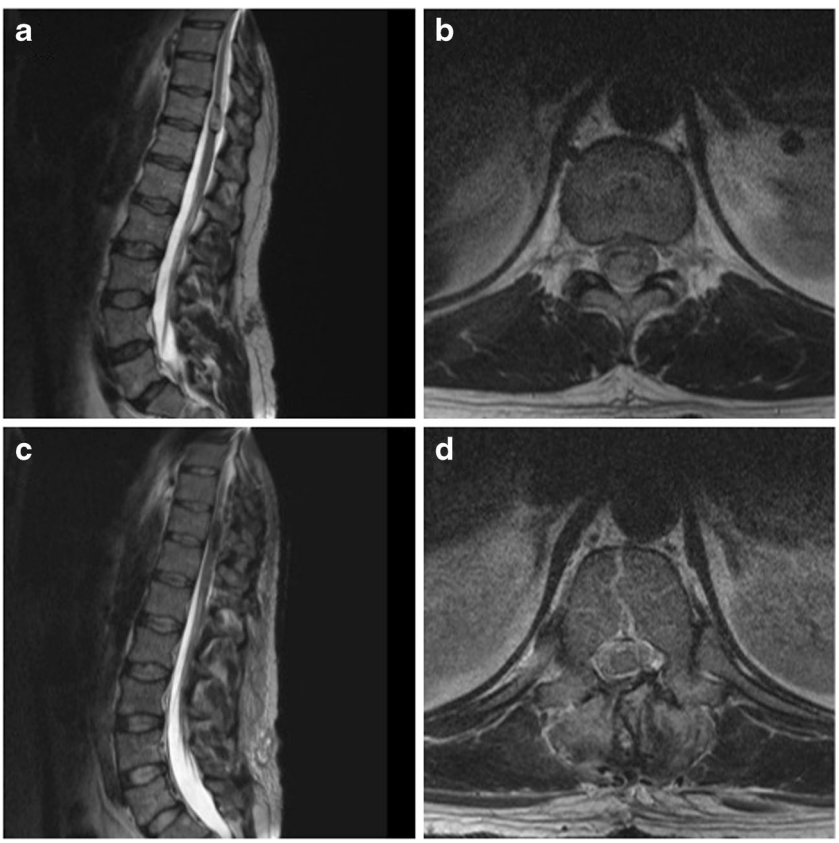

Fig. 3 T2-weighted preoperative (**a**, **b**) and postoperative (**c**, **d**) images showing a symptomatic SCM at Th11 due to local mass effect and growth (patient 5). The SCM was resected completely via an osteoplastic laminotomy as confirmed by postoperative images (**c**, **d**)

documented). Among the deep SCM (n=5, 25 %), two were dorsal, two were ventral, and one was lateral.

Surgery

The approach to the spinal cord in most cases (12 patients, 60 %) was performed by laminotomy with reconstruction of the dorsal spinal column and refixation of the laminas with miniplates. The remaining patients were operated by laminectomy or hemilaminectomy. In most cases, midline myelotomy was performed (14 cases) to assess the SCM. After surgery, complete resection of the SCM was confirmed by postoperative MRI in 19 cases, and a residual SCM was detected in one case.

Functional outcome and follow-up

Preoperative Frankel score was grade D in 18 (90 %) and grade C in 2 (10 %) patients in the surgical group. After surgery, all surgically treated patients were grade D at discharge. Thus, no functional worsening was observed after surgery, while two patients improved. Surgical patients were examined for the first follow-up after 6.3 months (mean, range 2–17 months). Eighty percent of them (16 cases) remained unchanged compared to their preoperative status, while 20 % (four patients) improved. All of these four patients had a superficially located cavernoma and were all operated early (<3 months). Thus, in the present study, the single effects of SCM location and surgical timing are completely confounded and cannot be analyzed separately. The proportion of the improved patients in the resulting single matrix showed a distribution shift in favor of the patients with superficial SCM localization and operated upon early. The estimation of the binominal parameter PI resulted in a maximum likelihood rate of PI=0.200, 95 % confidence interval (Clopper-Pearson)= 0.0573–0.4366. The exact two-sided p value is 0.0118, and so the null hypothesis that the distribution shift observed is not significantly statistically different from random binominal distribution is rejected at the 5 % significance level. Twelve patients could be assessed for a late follow-up examination (range 9–134 months, mean 44.7 months). Four (33.3 %) of them showed a better neurological state and eight (66.6 %) an unchanged condition compared to their preoperative status. SCM localization or number of involved segments had no impact on postoperative functional outcome.

A total of three patients underwent reoperation. One patient underwent complete resection of the residual SCM 17 months after initial surgery, one patient suffered from posthemorrhagic arachnopathy with syringomyelia and underwent surgery 15 months after initial SCM surgery, and another patient developed a scarring stenosis at the previously operated level and was reoperated 6 months after SCM resection.

The conservatively treated patients were followed up by clinical and radiological examination at our department and additional telephone interview for extended follow-up. Mean long-term follow-up for conservatively managed patients was 6.7 years (range 2.9–8 years). None of these patients underwent operation since none of them had a clinical and/or radiological worsening or signs for an acute bleeding during the follow-up period. All of them remained Frankel grade D during follow-up.

Discussion

Clinical presentation

Spinal cavernous malformations are rare vascular lesions which may lead to symptoms such as sensory/motor deficits, myelopathy, or para-/tetraparesis [20–22]. In accordance with previous series, our patients presented mainly with progressive deterioration and sensory/motor deficits being the most common symptoms [10].

Surgical treatment

There is a general agreement that microsurgical resection of the SCM is the treatment of choice if treatment is indicated. With modern pre- and intraoperative imaging techniques like high-field MRI, even small SCM can be visualized and treatment options can be planned more accurately [16, 23]. Due to technical improvements including intraoperative electrophysiology, surgery of *intramedullary* lesions has become safer [17, 24]. In order to facilitate the intramedullary localization of the SCM, intraoperative extra- and intradural ultrasound is recommended before opening of the dura [25]. Spinal cavernomas should be removed completely while the hemosiderin rim attached to the surrounding neuronal tissue should be preserved.

Intraoperative neuromonitoring (SEP, MEP, D-wave) is crucial as it helps to avoid neurological deterioration during surgical resection. Liang et al. [26] reported in their series that four of five patients who worsened after surgery were operated in a time before intraoperative SEP and MEP monitoring. Another important issue is the complete resection of an SCM as remnants can lead to rebleeding with neurological progressive neurological symptoms. In the study of Liang et al. [26], four patients were resected incompletely and two of them showed a worsening during follow-up. In addition to the careful patient selection and the proper microsurgical technique, the routine use of intraoperative neuromonitoring proved to be helpful during surgery; thus, in almost all cases, the SCM was resected completely and in one case after reoperation without permanent morbidity.

Table 2 Comparison between patients with improvement (imp) or without neurological improvement (no imp) after surgery

	m	f	Age (years)	CT	TL	sup	deep	1 seg	>1 seg	≤3 m	>3 m
imp	3	1	43.8	2	2	4	0	1	3	4	0
no imp	8	8	47.1	8	8	11	5	7	9	11	5

Number of cases is always given, except in the category age

m male, *f* female, *y* years, *CT* cervical/cervicothoracic, *TL* thoracic/thoracolumbar, *sup* superficial, *1 seg* one segment involved, *>1 seg* more than one segment involved, *≤3 m* surgery within 3 months after onset/worsening of symptoms, *>3 m* surgery after 3 months

Prognostic factors and outcome

Our results show that age and sex could not be identified as prognostic factors with impact on outcome, which is in accordance with the literature. Shorter period of symptoms [27] and a good preoperative neurological state were reported as predictive factors for a better clinical outcome [10], whereas hemorrhages seem to have an unfavorable outcome [28]. We could not detect a localization-dependent outcome bias comparing SCM of the cervical/cervicothoracic region and SCM of the thoracic/thoracolumbar region. The same was for the number of segments involved. We noted that none of the patients with a deep cavernoma showed an improvement postoperatively while all four patients with an improvement suffered from a superficially located SCM. According to the present findings, there is a statistically underpinned tendency that patients bearing a superficially located cavernoma exhibit a better functional result. On the other hand, the effect of SCM localization is in our series completely confounded with the effect of surgical timing. However, all individuals with clinical improvement were also operated ≤3 months after onset or worsening of symptoms which is in accordance with the recommendation in the literature [7]. Table 2 summarizes the different variables in patients with or without improvement after surgery.

Liang et al. [26] reported in their large series with 96 patients an improvement of 36 %, no change in 55 %, and a worsening in 9 %. Labauge et al. [22] found the following data for long-term follow-up in 37 operated patients: improvement in 54.1 %, no change in 16.2 %, but worsening in 29.7 %. In our series, 20 % of the patients showed a better neurological condition, and 80 % remained unchanged after surgery and an improvement to 33.3 % with a better neurological state at the time of the last follow-up. In contrast to other series, our patient collectively showed no neurological deterioration either at discharge or during follow-up. Concerning conservative management of patients with SCM, meta-analyses by Badhiwala et al. showed stable conditions in 58 %, improvement in 30 %, and worsening in 11 % [7]. None of our "conservatively treated" cases showed a worsening during extended follow-up.

Treatment algorithm

With regard to the literature and our experience, we propose a treatment algorithm for spinal cavernomas as shown in Fig. 4. Patients with severe neurological deficits or recurrent/progressive symptoms are good candidates for surgery. On the other hand, patients without any symptoms are not

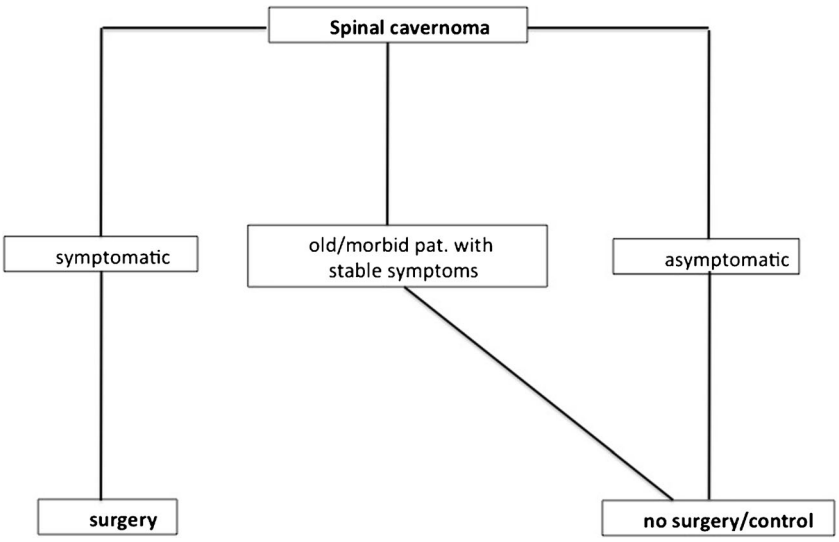

Fig. 4 Possible treatment algorithm for spinal cavernous malformations (*pat* patient)

recommended for surgery. In case of an acute deterioration, surgery should be performed. A final treatment decision is most difficult for young patients with mild symptoms. In these cases, the different options (microsurgery, conservative management, MRI controls) should be discussed clearly with the patient. In our experience, the personality and wish of the patients should be taken into consideration when a decision for surgery is made. Since surgical results are favorable [10], surgery might also be an alternative for young patients with minor symptomatic lesions that can be approached safely. Surgery in these patients may be justified as SCM tend toward clinical worsening, and preventive removal of the SCM might be more beneficial than surgery after bleeding in younger individuals [21, 28].

Summary

The treatment of SCM remains a challenge in daily neurosurgical practice. Repeated hemorrhages of cavernomas may lead to severe neurological deficits. Therefore, resection of symptomatic lesions is recommended with good results. In our series, a superficial localization of the SCM was associated with a strong tendency to better outcome. However, this effect was confounded with the timing of surgery. Therefore, definitive conclusions cannot be drawn from the present data. Rather, we need studies encompassing much larger patient samples in order to disentangle clearly the respective significance of timing of surgery and of location of the SCM on the functional result.

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Comments

Oliver Bozinov, Zurich, Switzerland

The case series of Ardeshiri et al. provides an extensive single-center experience of a rare disease and concludes favorable outcome after surgery for those patients who are symptomatic and young. The clinical results are very good. Intraoperative neuromonitoring plays a significant role nowadays for these lesions, but intraoperative imaging did not in this long-term case series. Those cases, elderly or asymptomatic, which were treated conservatively by watch-and-wait remained in a stable neurological condition. These results confirm the modern understanding and current treatment regiments for spinal cavernomas, and Fig. 4 explains perfectly in a very simple way the golden strategy for this rare disease. This experienced and well-described retrospective case series is important and adds more cases to the literature. However, it is time for a prospective multicenter randomized study or a registry for such a disease where high numbers will not be achieved by a single institute. Technically, this is a straightforward surgical procedure and does not need very few specialized centers, but active institutions should combine their patient data to one (minimum) registry and achieve hopefully one profound consensus thereby.