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CLINICAL ARTICLE

Solitary fibrous tumor of the central nervous system: a clinicopathologic study of 24 cases

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Abstract
Objective Solitary fibrous tumor is a rare, spindle-cell benign mesenchymal neoplasm and has a high recurrence rate. In this study, we reviewed our experience in the diagnosis and treatment of 24 patients with central nervous system solitary fibrous tumors.
Methods Clinical data were retrieved from the medical records. Prognosis was assessed by clinic service and telephone interview. The specimens were stained with hematoxylin and eosin. Immunohistochemistry for CD34, CD99, EMA, HMB-45, Bcl-2, vimentin, GFAP, S-100, MBP, CK and MIB-1 was performed in all cases. Distributions of time to progression and recurrence were estimated using the KaplanM eier method and compared using the log-rank test.
Results The 24 patients included 13 men and 11 women with a median age of 49.0 years. The most frequent initial symptoms were headache, dizziness, unstable walk and hearing loss. The most common location was cerebellar pontine angle (n=6). Surgery reached gross total removal for 18 patients but subtotal removal for six patients on initial operation. Histopathologic examination showed spindle to oval cells were disposed in wavy fascicles between prominent, eosinophilic bands of collagen. Dense bands of collagen appeared in cross section as minute nodules that separated individual tumor cells. Cellular areas with a partial hemangiopericytoma pattern were noted in six cases. Atypical presentations were shown on initial operation in three cases. CD34, CD99 and vimentin were 100% positive; but EMA, CK, MBP, HBM-45 and GRAP were 100% negative. The positive in Bcl-2, RF and S-100 was 89%, 85% and 26%, respectively. Follow-up information was available for 23 patients. The median follow-up period was 36.0 months. Nine patients recurred and one patient died from the progression. Incomplete surgical resection was significantly associated with recurrence (p=0.010). MIB-1 labeling index in recurrence was higher than in no recurrence (6.0% versus 3.4%, p=0.029). All treated with subtotal removal only had subsequent tumor recurrence or progression; however, the two patients who were administered adjuvant radiosurgery after subtotal removal did not recur or progress. Adjuvant radiosurgery seemed to improve the prognosis (p=0.028).
Conclusions Solitary fibrous tumor is a rare mesenchymal tumor with a propensity to recur. The most affected area is the cerebellopontine angle. Immunohistochemistry should be used to differentiate solitary fibrous tumor from other tumors. The extent of resection, MIB-1 labeling index and some anaplastic features might be predictive for recurrence. Postoperative radiosurgery might be an option in incompletely resected solitary fibrous tumor. Regular and long-term follow-up remains mandatory to monitor recurrence.

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Keywords Solitary fibrous tumor · Spindle cell neoplasm · Immunohistochemistry · CD34 · MIB-1 labeling index · Prognosis

Introduction

Solitary fibrous tumor (SFT) is a rare, spindle-cell, benign mesenchymal neoplasm, which was first described as a tumor arising from the pleural cavity by Klemperer and Rabin in 1931 [10]. Since then, it has been described in many extrapleural sites, including soft tissues, nasal cavities, upper respiratory tract, lung, pericardium, mediastinum, peritoneum, and liver [3, 14, 25]. In 1996, Carneiro et al. [1] reported the first case of meningeal SFT. To our knowledge, about 100 cases of central nervous system (CNS) SFT have been reported in the English literature to date. Most of them are described as isolated case reports, except for several series of cases [2, 6, 8, 15, 21–23]. The diagnosis of SFT is difficult because of the broad range of morphologic characteristics and its resemblance to various other lesions. The clinical course, cytogenetics, prognosis, and treatment protocol for CNS SFT are still unknown. To the best of our knowledge, this is the largest series of CNS SFT in the existing literature, where we study clinical and histopathologic features of 24 cases and review the relevant literature.

Materials and methods

Search methods and case definition

All patients were operated on and treated at our institute from January 2002 to December 2010. All tumors were reviewed by two neuropathologists (H.C. and Y.W.), who had no prior knowledge of the clinical status of the patients by re-examination of the tumor samples using the 2007 WHO classification to confirm the diagnosis [12]. Patient charts were retrospectively reviewed and clinical data, including age, sex, clinical presentation, duration of symptoms, tumor location, tumor size, neuroradiological data, extent of surgery, and adjuvant treatment were collected.

Histological re-examination and immunostaining

All the surgical specimens were fixed in 10% neutral-buffered formaldehyde solution and were embedded in paraffin wax. Routine hematoxylin-eosin-stained and reticulin fiber (RF) sections were generated, which were cut to 3 μm thick.

Immunohistochemical staining was done by the Envision technique, using monoclonal antibodies to CD34 (1: 100), CD99 (1:50), epithelial membrane antigen (EMA) (1:50), HMB-45 (1:100), B-cell lymphoma 2 (Bcl-2) (1:50), vimentin (1:100), glial fibrillary acidic protein (GFAP) (1:100), myelin basic protein (MBP) (1:100), S-100 (1:400), CK (1:50) and MIB-1 (1:100). All antibodies were obtained from M/S Dako Patts, Denmark. The MIB-1 labeling index (MIB-1 LI) was calculated in regions of maximal activity and expressed as percentage of nuclear area stained. The mitotic index was defined as the maximal number of mitoses observed in any ten consecutive high-power fields (HPFs) (one HPF=0.16 mm^2).

Follow-up and ethical committee approval

The patient's prognosis was attained by clinic service and telephone interview. The surgical procedures were conducted under guidelines and the terms of all relevant local legislation.

Statistical analysis

Student's *t*-test was used to compare the difference of MIB-1 LI among the SFT patients with or without recurrence. Fisher's exact test was used to compare the recurrence rate between patients undergoing STR plus radiotherapy and patients undergoing sole STR without radiotherapy. Distributions of time to progression and recurrence were estimated using the KaplanM eier method and compared using the log-rank test. Data were presented as median or mean, and the accepted significance was considered at 0.05. All these analysis were performed using Statistical Package for Social Sciences (SPSS, USA).

Results

During the period from January 2002 to December 2010, 28 patients with SFTs (four in the orbit, two in the cranio-orbit, two in the spine and 20 in the intracalvarium) were diagnosed at the Department of Neuropathology, Huashan Hospital Group, Fudan University. During the same period, 183 CNS hemangiopericytomas and 6,700 cases of CNS meningiomas were also diagnosed. Thus, the frequency of SFT was less than 15.3% that of hemangiopericytomas and 0.42% that of meningiomas. Intraorbital SFT had some special clinical features, so we excluded the four intraorbital cases in the study.

Clinical features

The essential clinical information of all 24 cases is summarized in Table 1. This series included 13 men and

Table 1 Characteristic of study gruop and clinical profile

Case no.	Age/gender (yr)	Tumor size (mm)	Localization	Symptoms	Clinical history	Dura attachment	Treatment	Recurrence/ progression	Treatment at recurrence	Status, follow-up (mo)
1a	43/M	—	Spinal (T11-12)	Lower extremity weakness	2 mo	Yes	GTR	Yes, 174 mo	Rachitomy	Alive, 176 mo
1b	—	30 × 20 × 20	Local recurrence	—	—	Yes	GTR	No, 2 mo	—	—
2	47/F	40 × 40 × 20	Left CPA	Headache, dizziness, unstable walk	36 mo	Yes	GTR	No, 66 mo	—	Alive, 66 mo
3a	55/M	40 × 30 × 30	Left cerebellar tentorium	Dizziness	6 mo	Yes	GTR	Yes, 36 mo	Craniotomy	Alive, 58 mo
3b	—	20 × 15 × 10	Local recurrence	—	—	Yes	GTR	No, 22 mo	—	—
4	24/F	50 × 50 × 40	Left CPA	Dizziness, unstable walk	4 mo	Yes	GTR	No, 57 mo	—	Alive, 57 mo
5a	55/M	40 × 40 × 30	Left cavernous sinus	Headache, diplopia	3 mo	No	STR	Yes, 18 mo	Craniotomy	Alive, 52 mo
5b	—	30 × 15 × 10	Local recurrence	—	—	No	STR+RS	No, 34 mo	—	—
6a	60/F	—	Left CPA	Hearing loss	3 mo	No	STR	Yes, 25 mo	Craniotomy	Alive, 42 mo
6b	—	—	Local recurrence	—	—	No	STR	Yes, 8 mo	Craniotomy	—
6c	—	40 × 30 × 20	Local recurrence	—	—	No	GTR	No, 9 mo	—	—
7	49/F	40 × 30 × 30	Right cranio-orbital	Vision loss	96 mo	No	STR	Yes, 33 mo	Follow-up	Alive, 45 mo
8	67/M	30 × 10 × 10	Left CPA	Hearing loss, unstable walk	6 mo	Yes	GTR	No, 44 mo	—	Alive, 44 mo
9	50/F	30 × 30 × 20	Right cerebellar tentorium	Found incidently	3 wk	Yes	GTR	Lost to follow-up	—	Lost to follow-up
10	36/F	40 × 40 × 20	Parasagittal	Headache, dizziness	1 wk	Yes	GTR	No, 43 mo	—	Alive, 43 mo
11a	51/F	70 × 60 × 40	Right cerebellar tentorium	Headache, memory decreasing	2 mo	Yes	GTR	Yes, 31 mo	RS	Alive, 42 mo
11b	—	20 × 10 × 10	Local recurrence	—	—	Yes	RS	Yes, 6 mo	Follow-up	—
12	58/F	40 × 30 × 20	Left CPA	Tinnitus, hearing loss	6 mo	Yes	GTR	No, 36 mo	—	Alive, 36 mo
13	38/M	25 × 20 × 20	Right cranio-orbital	Painless proptosis	3 mo	Yes	GTR	No, 35 mo	—	Alive, 35 mo
14	63/M	12 × 10 × 8	Spinal (L4)	Lower extremity weakness	6 mo	Yes	GTR	No, 33 mo	—	Alive, 33 mo
15a	49/M	40 × 30 × 20	Anterior basalis	Headache	2 wk	Yes	STR	Yes, 15 mo	Craniotomy	18 mo
15b	—	30 × 20 × 20	Local recurrence	—	—	Yes	STR	Yes, 3 mo	Follow-up	Deceased, 3 mo
16	65/M	35 × 25 × 20	Left CPA	Hearing loss	4 mo	Yes	GTR	Yes, 25 mo	Follow-up	Alive, 27 mo
17	11/M	60 × 50 × 40	Parafalcine	Blurred vision	2 wk	Yes	STR+RS	No, 23 mo	—	Alive, 23 mo
18	44/M	15 × 10 × 10	Right cerebellar tentorium	Headache	3 mo	Yes	GTR	No, 19 mo	—	Alive, 19 mo
19a	39/F	30 × 20 × 20	Corpus pineale	Headache, dizziness, diplopia	6 mo	No	STR	Yes, 11 mo	RS	Alive, 17 mo
19b	—	15 × 10 × 10	Local recurrence	—	—	No	RS	No, 6 mo	—	—
20	40/F	30 × 30 × 20	Anterior basalis	Found incidently	1 wk	Yes	GTR	No, 16 mo	—	Alive, 16 mo
21	43/M	40 × 30 × 30	Right cerebellar tentorium	Headache, dizziness, unstable walk	3 mo	Yes	GTR	No, 15 mo	—	Alive, 15 mo
22	60/M	60 × 50 × 40	Anterior basalis	Headache, intelligence decreasing	24 mo	Yes	GTR	No, 11 mo	—	Alive, 11 mo
23	53/F	25 × 25 × 10	Right occipital	Found incidently	1 wk	Yes	GTR	No, 7 mo	—	Alive, 7 mo
24	34/M	45 × 30 × 30	Foramen magnum	Upper extremities weakness	11 mo	Yes	GTR	No, 5 mo	—	Alive, 5 mo

yr years, *mo* months, *wk* weeks, *F* female, *M* male, *CPA* cerebellopontine angle, *GTR* gross total removal, *STR* subtotal removal, *RS* radiosurgery; *a* first surgery, *b* second surgery, *c* third surgery

11 women with a median age of 49.0 years (range 11–67 years; one at <18) at first surgery. The cerebellopontine angle (CPA) was the most affected area (n=6), followed by the cerebellar tentorium (n=5), anterior basalis (n=3), spine (n=2), and cranio-orbit (n=2); other areas included cavernous sinus, parasagittal, parafalcine, corpus pineale, convex and foramen magnum (n=1 for each). The tumors ranged from 12 to 70 mm in diameter, and the median diameter was 35.0 mm. The initial symptoms were coherent with the tumor location and the most frequently encountered symptoms were headache, dizziness, unstable walk and hearing loss. The tumor presented with a dural origin in 20 cases (83%). Gross total resection (GTR) was achieved in 18 cases (75%); subtotal resection (STR) was achieved in six cases (25%) at first surgery. None of the patients received chemotherapy. There was no operative mortality (death within 1 month of surgery).

Radiological findings

Computed tomography (CT) data were available in ten cases. On CT scans, the attenuation of the lesions showed predominantly hyperattenuation (n=9) or isoattenuation (n=1) compared with the adjacent brain parenchyma. Two lesions showed bone infiltrations, and no bone thickening was seen. No lesion also contained calcification on CT images. Magnetic resonance imaging (MRI) data were available in 18 cases. MRI showed homogeneous hypointensive (n=5) or isointensive (n=7) signal intensity and heterogeneous mixed isointense and hypointense signal intensity (n=6) on T1-weighted images; whereas most of the tumors were predominantly isointense (n=13) and hypointense (n=4) to the cortex on T2-weighted images. On postcontrast MR images, all lesions showed marked enhancement (n=18). Fourteen tumors had the dural tail sign (Fig. 1).

Microscopic findings

Microscopic examination showed spindle to oval cells were disposed in wavy fascicles between prominent, eosinophilic bands of collagen. Dense bands of collagen appeared in cross section as minute nodules that separated individual tumor cells. The majority of tumors exhibited a biphasic pattern with focal areas of hyalinization. On initial operation

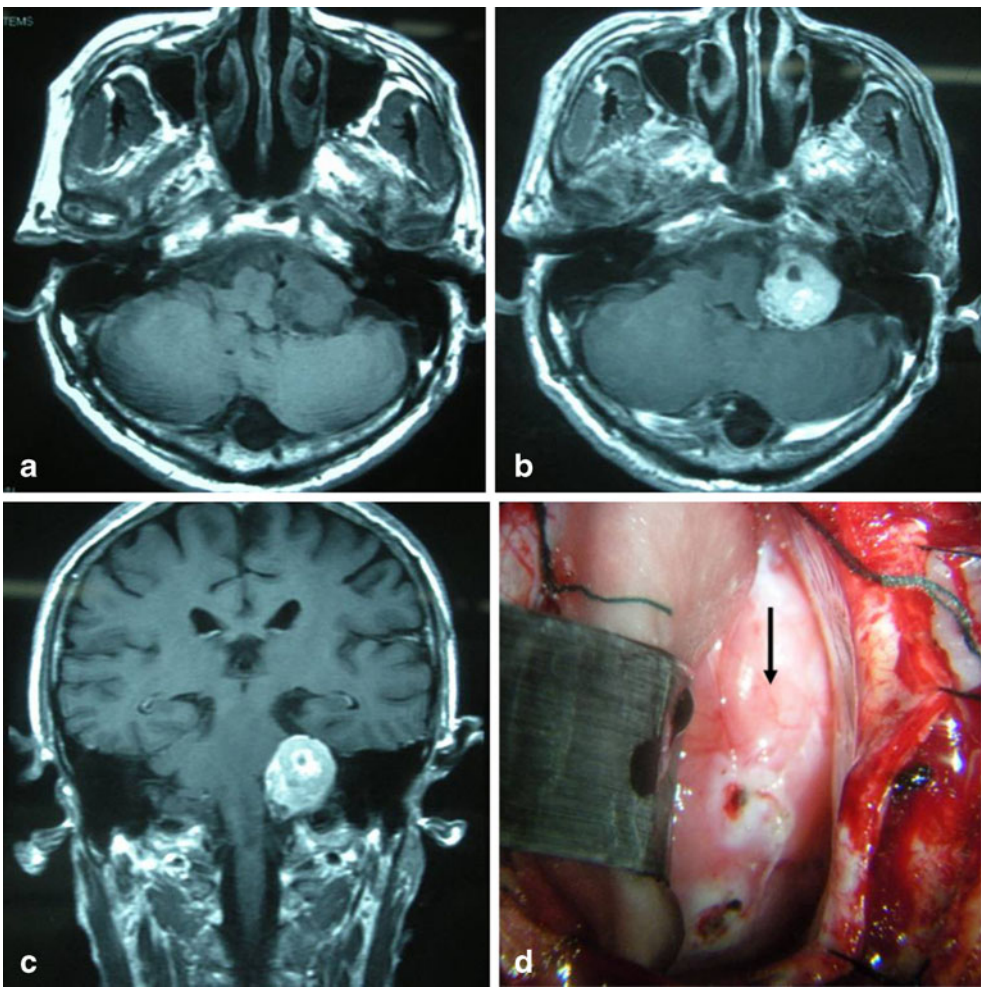

Fig. 1 (Case 16.) A 65-year-old man with hearing loss for 4 months. **a** Non-enhanced axial T1-weighted MR image shows heterogeneous mixed isointensive and hypointensive lesion at CPA zone. **b, c** Axial and coronal T1-weighted MR images show the mass enhances strongly after the administration of Gd-based contrast agent. **d** Intraoperative photograph shows the intracranial lesion (*arrow*) has clear boundary

of 22 cases, cellular areas with partial hemangiopericytoma (HPC) pattern were noted in six cases; mitotic features were absent in ten cases, scarce in eight cases, and more than four per ten HPFs in four cases; focal necrosis was noted in five cases; cerebral parenchyma was infiltrated in five cases. Two patients (cases 3, 15) who recurred showed more conspicuous atypia on second specimen. Twenty-three of the 27 specimens were positive for RF (85%). (Figs. 2, 3, 4)

Immunohistochemical findings

In our series, 24 cases had 27 specimens which had immunohistochemical staining. Table 2 showed that diffuse positive immunoreactivity with CD34 (100%), CD99 (100%) and vimentin (100%). Twenty-four lesions were positive for Bcl-2 (89%) and ranged from+to +++; seven lesions were positive for S-100 (26%). However, all the 27 lesions showed diffuse negative immunoreactivity with EMA, CK, MBP, HBM-45 and GFAP. The MIB-1 LI varied from 1% to 12% (mean 4.2%) on initial operation. The MIB-1 LI in recurrence was higher than in no recurrence (6.0% versus 3.4%, p=0.029). Two patients (cases 3, 15) who recurred showed higher MIB-1 LI on second specimen. (Figs. 2, 3, 4)

Prognosis and survival analysis

Prognosis was assessed by clinic service and telephone interview. Among all 24 patients, one was lost to connection, and follow-up information was available for 23 patients. The follow-up was from 5 months to 176 months (median: 36.0 months). Among these patients, nine patients (cases 1, 3, 5, 6, 7, 11, 15, 16 and 19; 37.5%) experienced tumor recurrence or progression with the median initial recurrence time of 25 months, and one patient (case 15) died from the progression three months after the second operation. All the other patients were alive at the latest follow-up evaluation. The 23 patients who had follow-up underwent 29 surgeries, including 20 GTRs and nine STRs. Among these 20 GTRs (including the first, second and third operation: 1a, 1b, 2, 3a, 3b, 4, 6c, 8, 10, 11a, 12–14, 16, 18, 20–24), four cases (cases 1a, 3a, 11a, 16; 20%) recurred with the median recurrence time of 33.5 months. Among these nine STRs (including the first and second operation: 5a, 5b, 6a, 6b, 7, 15a, 15b, 17, 19a), seven cases (cases 5a, 6a, 6b, 7, 15a, 15b, 19a; 77.8%) progressed with the median recurrence time of 15.0 months. Incomplete surgical resection was significantly associated with recurrence (p=0.010). And Log-rank test showed obvious survival benefit for the patients undergoing GTR than STR (p<0.001). (Fig. 5) Six patients (cases 5, 6, 7, 15, 17, 19) had nine STRs overall (first or second operation: cases 5a, 5b, 6a, 6b, 7, 15a, 15b, 17, 19a), and postoperative adjuvant radiosurgery following STR was performed on two patients (cases 5b, 17). All those treated solely with STR (cases 5a, 6a, 6b, 7, 15a, 15b, 19a) experienced tumor recurrence or progression; however, the two patients (cases 5b, 17) who were administered adjuvant

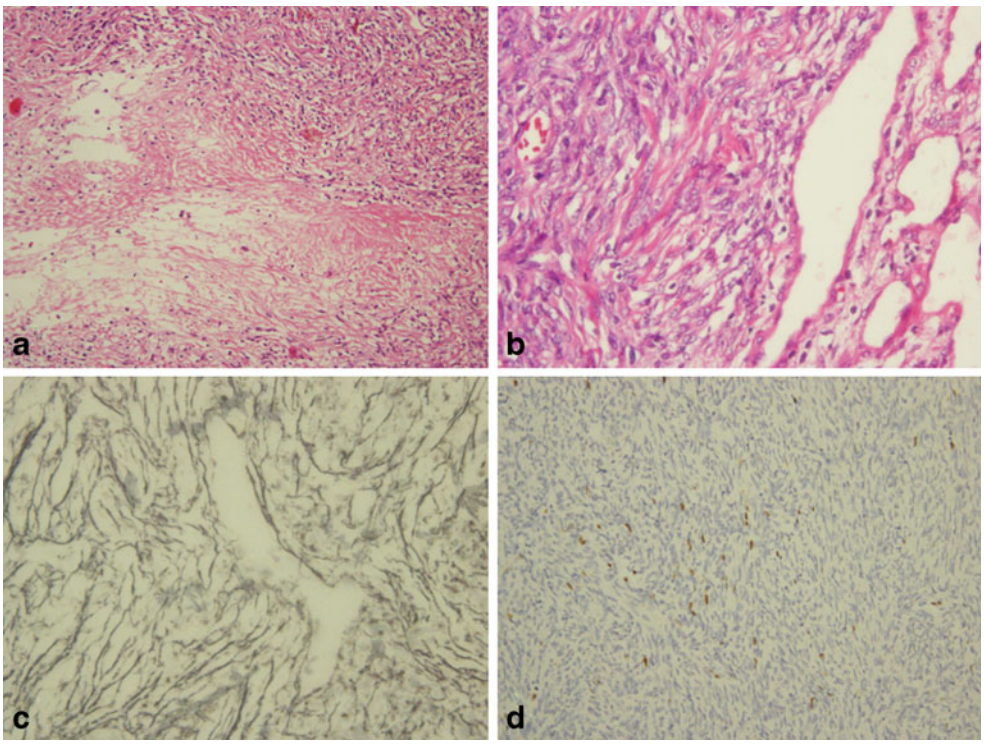

Fig. 2 (Case 3, the first operation.) **a** Hematoxylin and eosin staining shows the focal necrosis. **b** The tumor cells are composed of dense collagenous bands and dilated vessels. **c** Silver staining shows focal reticular fibers. **d** The tumor cells have a moderate MIB-1 labeling index (5%)

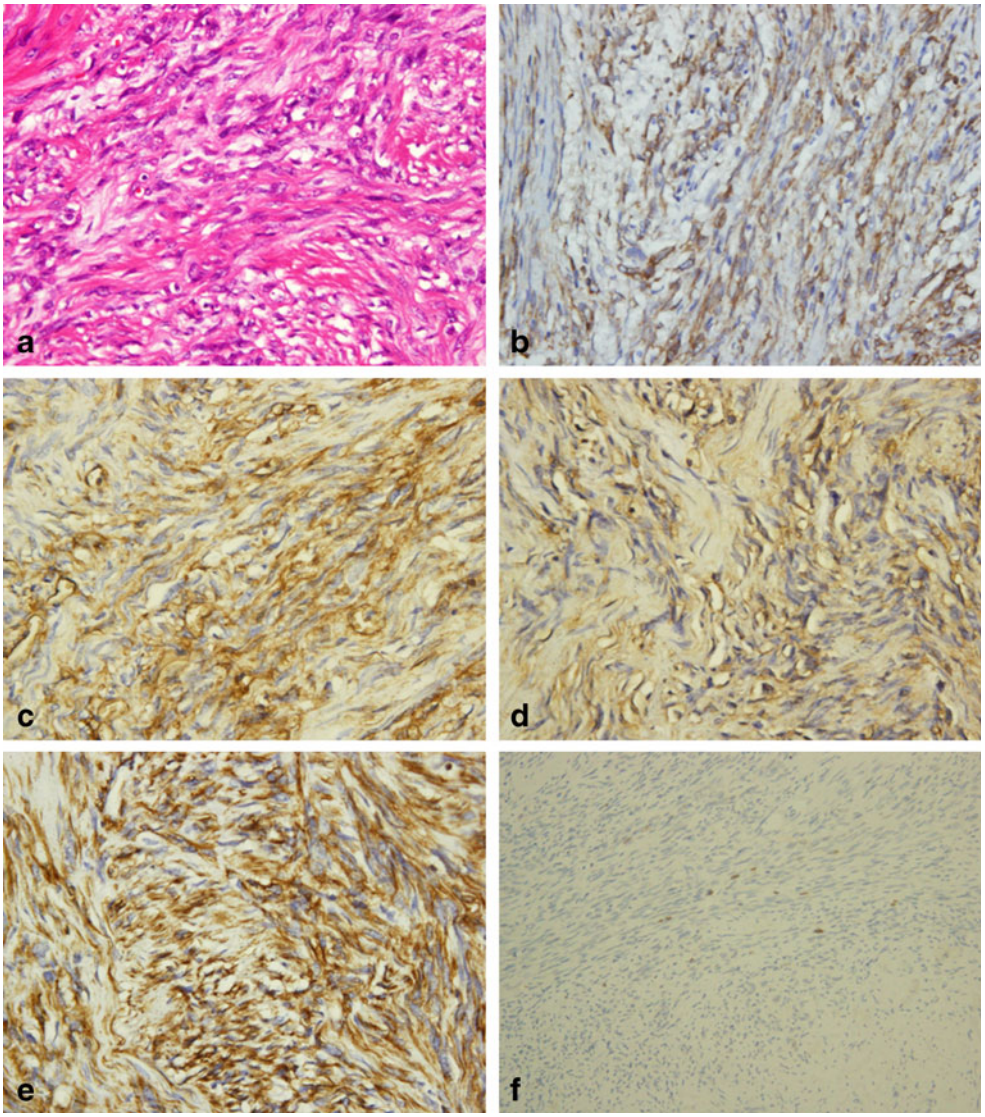

Fig. 3 (Case 5, the first operation.) **a** The tumor cells are composed of spindle shaped cells, with the presence of dense collagenous bands. **b** The tumor cells are positive for Bcl-2. **c** The tumor cells are diffuse and strongly positive for CD34. **d** The tumor cells are positive for CD99. **e** The tumor cells are positive for vimentin. **f** The tumor cells have a relatively low MIB-1 labeling index (2%)

radiosurgery after STR did not recur or progress. Adjuvant radiosurgery seemed to improve the prognosis (p=0.028). One patient (case 11) who had initial GTR recurred 31 months postoperatively and radiosurgery was performed. However, the progression could not be hampered. The pattern of recurrence was local recurrence without CSF seeding or extracranial metastasis in our series.

Discussion

Demography and clinical presentation

Based on the new World Health Organization (WHO) Classification of tumors of the CNS published in 2007, CNS SFT has recently emerged as a distinct clinicopathologic entity among the meningeal tumors [12]. About 100 cases of SFT have been reported directly involving the neuraxis, both in the spinal cord and in the brain in the English literature, largely in the form of isolated case reports, with a few series [2, 6, 8, 15, 21–23]. The biological behavior of CNS SFTs was poorly understood, partly due to limited number of reported cases. The cellular origin of SFT was still undefined. It was initially thought that CNS SFT originated from CD34-positive dural-based fibroblasts or dendritic cells [1, 17]. However, Kim et al. [8] deduced that the possible origin for SFT was the mesenchyma of cerebral vasculature. Four of our cases did not present a dural origin, which conduced to Kim et al.'s hypothesis. In the literature, the median age was 44.5–55.0 years, and the male:female ratio was 4:14–23:20 [2, 15, 21]. The age of onset (49.0 years) and male:female ratio (13:11) in our series were similar to that in the literature. So the data showed that CNS SFTs trended to occur in adults and did not have a marked sex bias, although puerile and elderly populations were also affected.

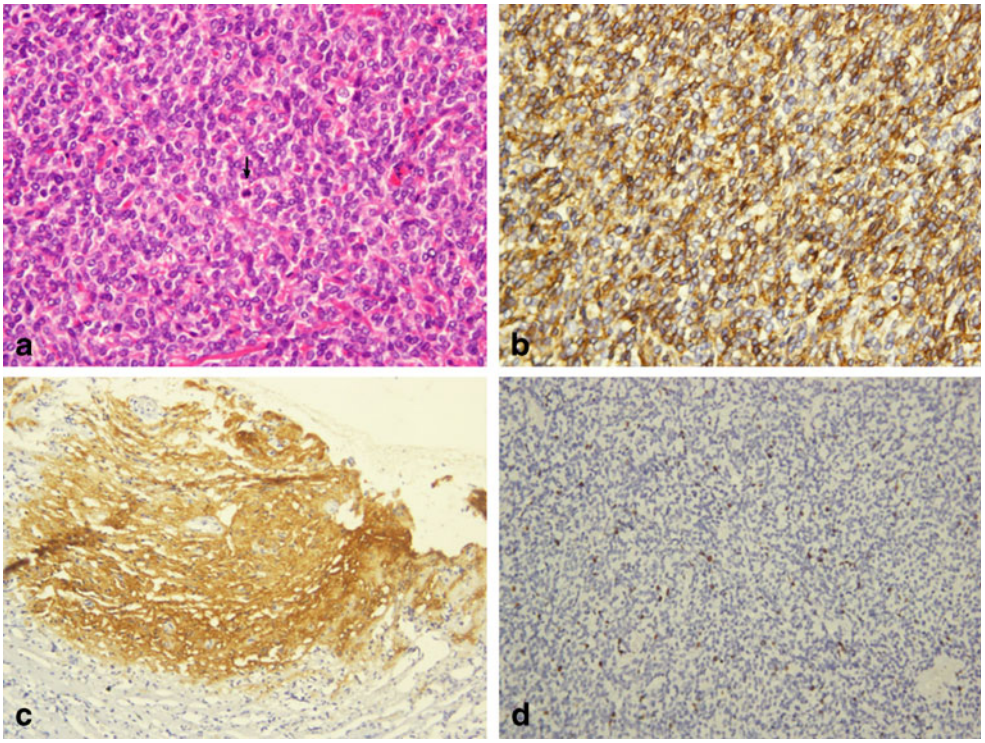

Fig. 4 (Case 15, the second operation.) **a** The tumor cells are composed of moderately hypercellular proliferation of spindle shaped cells with dense collagenous bands and the mitosis can be seen (*arrow*). **b** The tumor cells are diffuse and strongly positive for CD34. **c** GFAP shows infiltrated brain tissues. **d** The tumor cells have a high MIB-1 labeling index (12%)

It was generally believed that SFT was predominantly located in the posterior fossa and spine [2, 21]. In our series, the CPA zone was the most frequently affected area (n=6); however, only two cases were located in the spine. Consistent with the anatomical localization, the most common presenting symptoms were headache, dizziness, unstable walk and hearing loss. We found that the CNS SFTs mostly occurred in the CPA, but were rarely located at the convexity compared with meningioma.

Histopathological findings

The CNS SFT was usually well-circumscribed encapsulated lesion resembling neurilemmoma, meningioma or HPC because of its radiological and histological similarity, although their clinical courses were different [6, 23, 24]. Although neurilemmoma was usually easily distinguished by its microscopic features, such as nuclear pseudopalisading and wavy nuclei, sometimes it might be confused with SFT, especially when located at the CPA and when the more cellular Antoni A pattern was dominant. Though positive staining for CD34 was a characteristic of SFT, which was 100% positive in our series, it was also positive in 89% of neurilemmomas [25]. Therefore, strong immunoreactivity for S100 was most useful to discriminate from SFT, which had a negative S-100 staining [20, 24]. However, S-100 was 26% positive in our series, which was due to the partial HPC pattern in the focal zone. SFT might look similar to fibrous meningioma (FM) because of the morphology, disposition of the cells and collagen bundles. However, FM had whorls and psammoma bodies, and it lacked brightly eosinophilc bands of collagen. FM cells tended to be slimmer than those of SFTs. They are positive for EMA, whereas SFTs were not. And CD34 might be focally positive rather than diffuse in FM. Excluding HPC was more critical because HPC had a high rate of both local recurrence and systemic metastases to aggressive management. However, the overlap of morphologic and clinical features between them led to misdiagnosis for each other. The distinction was not difficult in the typical SFT that did not contain highly cellular areas, but could be problematic in ones that did. SFT cells were disposed in wavy fascicles; however, the cells were jumbled in HPCs. Fascicles of elongated undulating cells of SFT were associated with collagenous bands, which were different from closely packed, randomly oriented HPC cells with little intervening fibrosis. HPC had “staghorn” sinusoidal vessels and fine reticulin patterns, and lacked the universal cellular elongation and brightly eosinophilc bands of collagen [26]. CD34 was not as helpful in this differential diagnosis of HPC as it was when distinguishing SFT and meningioma, because about 40% of HPCs were CD34-positive. However, CD34 was more often strong and diffuse in SFTs, whereas it was usually focal and weak in HPCs. In our series, CD34 was 100% positive. Likewise, strong Bcl-2 positivity might be useful in distinguishing SFT and HPC from meningioma, but not SFT from HPC. Even though staining with Bcl-2 was strong in most SFTs, which was 89% positive in our series, mainly strongly positive, a significant percentage (50%) of HPCs were positive as well [21]. Delicate,

Table 2 Summary of the histological features of CNS SFT in the present series

Case no.	Age/sex	Partial HPC	Mitosis/10HPF	Necrosis	Brain invasion	MIB-1 LI	CD34	CD99	Bcl-2	S-100	Vimentin	EMA	MBP	RF	CK	HMB−45	GFAP
1a	43/M	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
1b		+	4	Focus	+	4	+	+	++	+	+	-	-	+	-	-	-
2	47/F	-	-	-	-	1	+	+	+++	-	+	-	-	-	-	-	-
3a	55/M	+	4	Focus	+	5	+	+	+	+	+	-	-	+	-	-	-
3b		+	7	Focus	+	9	+	+	++	+	+	-	-	+	-	-	-
4	24/F	-	-	-	-	3	+	+	-	-	+	-	-	-	-	-	-
5a	55/M	-	1	-	-	2	+	+	+++	-	+	-	-	+	-	-	-
5b		-	-	-	-	2	+	+	++	-	+	-	-	+	-	-	-
6a	60/F	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
6b		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
6c		+	3	Focus	+	4	+	+	+	-	+	-	-	+	-	-	-
7	49/F	-	-	-	-	2	+	+	++	-	+	-	-	+	-	-	-
8	67/M	-	-	-	-	2	+	+	-	-	+	-	-	+	-	-	-
9	50/F	-	-	-	-	1	+	+	+	-	+	-	-	-	-	-	-
10	36/F	+	2	-	-	4	+	+	+++	-	+	-	-	+	-	-	-
11	51/F	+	5	Focus	-	6	+	+	+++	+	+	-	-	+	-	-	-
12	58/F	+	-	Focus	-	4	+	+	+++	+	+	-	-	+	-	-	-
13	38/M	-	-	-	-	2	+	+	-	-	+	-	-	+	-	-	-
14	63/F	-	2	-	-	2	+	+	+	-	+	-	-	+	-	-	-
15a	49/M	-	3	Focus	+	10	+	+	+++	-	+	-	-	+	-	-	-
15b		+	5	Focus	+	12	+	+	+++	-	+	-	-	+	-	-	-
16	65/M	-	4	-	+	8	+	+	++	-	+	-	-	+	-	-	-
17	11/M	+	3	-	-	5	+	+	+	+	+	-	-	+	-	-	-
18	44/M	-	2	-	-	3	+	+	+++	-	+	-	-	+	-	-	-
19	39/F	-	-	-	+	3	+	+	+++	+	+	-	-	-	-	-	-
20	40/F	-	-	-	-	2	+	+	+++	-	+	-	-	+	-	-	-
21	43/M	-	1	-	-	4	+	+	+++	-	+	-	-	+	-	-	-
22	60/M	-	2	-	-	5	+	+	+++	-	+	-	-	+	-	-	-
23	53/F	+	4	Focus	+	5	+	+	+	-	+	-	-	+	-	-	-
24	34/M	-	-	-	-	2	+	+	+++	-	+	-	-	+	-	-	-

HPC hemangiopericytoma, MIB-1 LI*p* MIB-1 labeling index, *HPF* high-power fields, Bcl-2*p* B-cell lymphoma 2 [negative (−: <5%), weakly positive (+: 5-25%), moderate positive (++: 26-50%), strong positive (+++: >50%)], *EMA* epithelial membrane antigen, *RF* reticulin fibers, *GFAP* glial fibrillary acidic protein

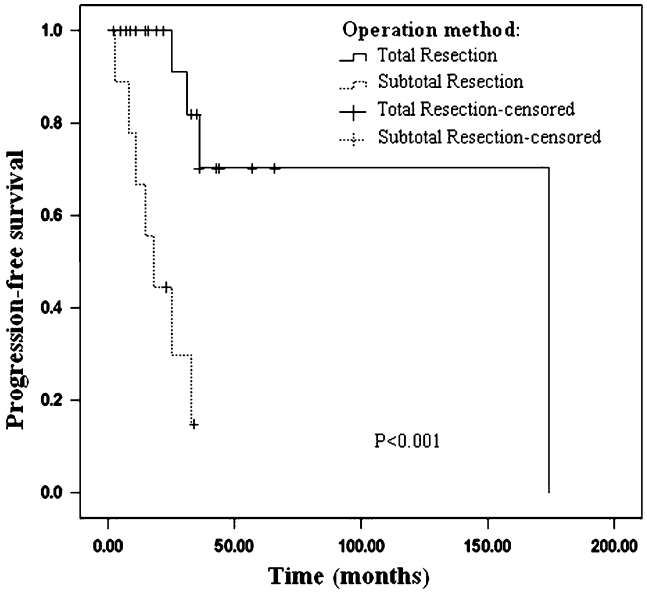

Fig. 5 Kaplan–Meier curve showing the progression-free survival relating to operation method in solitary fibrous tumor of CNS. Twenty-nine patients are involved in the curve with 20 undergoing GTR and nine undergoing STR. Log-rank test shows obvious survival benefit for the patients undergoing GTR than STR ($p<0.001$)

prominent, pericellular reticulin fibers were more typical of HPC, whereas reticulin staining in SFT, even in the HPC-like cellular areas, generally revealed only coarse collagenous septa. Hayashi et al. [6] deduced that although differential diagnosis would undoubtedly prove difficult in some cases, meticulous pathological examinations with CD34, Bcl-2, and reticulin staining would help to distinguish SFT from HPC. However, it was still unknown to what extent of these biological differences presented a predictive factor for postoperative outcome [8, 9].

Treatment, outcome and prognosis

Clinically, 13–23% of pleural SFTs manifested with local invasion, recurrence, intrathoracic spread or distant metastasis [4]. However, the clinical behavior and prognosis of CNS SFTs were still obscure to us. It was generally accepted that CNS SFT pursued a slow, indolent and non-aggressive course [2]. However, Pizem et al. [19] reported a malignant intracranial SFT with four recurrences over a 30-year period and he found six cases of recurrence or metastasis in the literature. In two large series of CNS SFTs, the recurrence rate was 50% and 16.7%, respectively. The median recurrence time was 32 months and 35 months, respectively [15, 21]. In our series, the recurrence rate was 37.5%. So we observed a lower recurrence rate in our series than that in Metellus et al.'s series [15], which had a 50% recurrence rate. But we found the study had a longer follow-up period of 45 months, and four of his patients even had a length of the follow-up period between 10 and 20 years. However, the median follow-up period in our series was 36.0 months, which was shorter than Metellus et al.'s [15] (Table 3). Maybe it was the main reason for the different prognosis.

As for predictive factors for recurrence, it was indefinite up to date. The majority of SFTs appeared to be benign on histology, but an analysis of 223 pleural SFTs identified 82 cases with atypical features [5]. To date, no study had defined the criteria for malignant CNS SFT. The malignant histological features described for pleural SFT—hypercellularity, moderate-to-marked cytological atypia, necrosis, and more than four mitoses per ten HPFs and/or an infiltrative margin—could be applied for meningeal SFT [15]. Several histologically malignant CNS SFTs have been reported; some SFTs even metastasized outside of the CNS [11, 18, 19, 26]. Lawlor et al. [11] also thought more aggressive variants had been associated with higher rates of recurrence and metastasis. They also showed a case of malignant SFT of the dura that was characterized by numerous amianthoid fibers. Tihan et al. [21] reported one case with anaplastic features recurred 11 months after the initial surgery, even GTR and adjuvant radiotherapy. However, it was reported that SFTs with hypercellular foci, without other signs of malignancy, did not behave more aggressively than those without such hypercellular foci [19]. According to the above criteria [15], three cases (cases 3, 11, 23) accorded with the atypia and both recurred. And one patient (case 15), who approached the criteria on the first operation, recurred and accorded with criteria on the second operation. It seemed that atypical patients were inclined to recur. We also found cellular areas with a partial HPC pattern was noted in six cases, four of which had focal necrosis, five of which showed mitosis, two of which showed brain invasion. It seemed that the patients who had an HPC pattern were correlated with atypia. Maybe HPC patterns could be considered as an additional criterion for malignant change in CNS SFT. Certainly the cases were limited and atypical indexes were numerous so that it was very difficult for us to have a statistical analysis to demonstrate the correlation between recurrence and sole index and to predicate the prognosis. Previous reports suggested that MIB-1 LI could be used to predict the prognosis in patients with meningiomas. For conventional meningioma, mean MIB-1 LI is 4% for grade I, 7% for grade II, and 15% for grade III tumors [27]. In our series, the MIB-1 LI varied from 1% to 12% (mean 4.2%) and the MIB-1 LI in recurrence was higher than in no recurrence (6.0% versus 3.4%, $p=0.029$). Thus, MIB-1 LI might be a vital factor to predict prognosis.

In Tihan et al.'s study [21], SFT seemed to be successfully managed by surgery alone, and the 5-year survival probability was 100%. Two out of three subtotally

Table 3 Comparison of clinicopathologic features observed in different series

	Tihan et al.	Metellus et al.	Mekni et al.	Present study
Total no of cases	18	18	8	24
Age range (yr)	7-81	33-75	39-59	11-67
Median age (yr)	54.0	55.0	44.5	49.0
Children	ND	0	0	1
Sex ratio (male:female)	4:14	9:9	4:4	13:11
Location				
cranio-orbital	0	2	0	2
supratentorial	11	4	7	8
posterior fossa	3	6	1	12
spine	4	6	0	2
Surgical treatment				
total removal	15	10	6	18
subtotal removal	3	7	2	6
partial removal	0	1	0	0
Adjuvant treatment				
radiotherapy	3	2	0	0
radiosurgery	0	1	2	4
chemotherapy	0	1	0	0
MIB-1 LI	1-10% (3%, 9 cases)	1-25% (5%)	2-25%	1-12% (4.2%)
Necrosis	ND	2	2	5
Mitotic features	ND	7 absent, 8 scare, 3≥4/HPF	1 absent, 5 scare, 2≥4/HPF	10 absent, 8 scare, 4≥4/HPF
Brain infiltrated	ND	1	1	5
Bone infiltrated	ND	2	1	0
Number of follow-up	15	18	8	23
Follow-up period	5-97 (median 45.5 mo)	18-262 (median 45.0 mo)	36-120 (median 54.0 mo)	5-176 (median 36.0 mo)
Recurrences	3	9	1	9
Recurrence rate	16.7%	50%	12.5%	37.5%
Recurrence time	35.0 mo	32.0 mo	6.0 mo	25.0 mo
Metabasis	0	1	0	0

yr years, *mo* months, *ND* no display, *HPF* high-power fields, *MIB-1 LI* MIB-1 labeling index

resected tumors recurred 32 and 62 months respectively after initial resection. No recurrence was encountered among the gross totally resected tumors. Metellus et al.'s study [15] showed that tumor recurrence or progression occurred in nine patients (50%) during a mean 45-month follow-up. Among these nine patients, only two (22.2%) had initial GTR. In contrast, in the other nine patients without recurrent or progressive disease, GTR was initially achieved in eight cases (88.9%). Incomplete surgical resection was significantly associated with recurrence. Mekni et al.'s study [14] showed that no recurrence was encountered among the gross totally resected tumors; however, one of the two patients who had STR recurred 6 months after initial surgery, even applied adjuvant radiotherapy. In our 29 surgeries, the recurrence rate after GTR was 20% (4/20) and the median recurrence time was 33.5 months; in contrast, the recurrence rate after STR was 77.8% (7/9) and the median recurrence time was 15.0 months. The results also showed that the recurrence rate of GTR was obviously lower than STR, and the recurrence time of GTR was longer than STR (p=0.010). So the prognosis of CNS SFT might be highly related to the situation of its initial treatment. GTR was favored to prevent leaving microscopic nests of cells of SFT behind as a nidus for recurrence. The extent of resection might be predictive fo7r recurrence in SFT. The goal of the treatment in SFT was to achieve radical surgical removal as much as possible.

SFT mostly had a stiff consistency, and frequently grew at the CPA; they were inclined to be invasive regarding vascular and nerve structures. Sometimes total resection was hard to be attained in order to avoid vascular and cranial nerve injuries. Nevertheless, when the lesion could not be totally resected, radiotherapy or radiosurgery should

be considered [, 25]. Nakahara et al. [16] reported a shrinkage of occipital residual SFT at a 4-year follow-up after radiosurgery. Yin et al. [25] reported also STR of sella SFT plus an adjuvant radiosurgery could control the residual tumor at a 44-month follow-up and deduced that postoperative radiosurgery might be helpful to control the residual tumor. Macfarlane et al. [13] reported the treatment of a highly vascular intracranial SFT by combination of surgery, radiotherapy, and toremifene and the tumor showed a dramatic reduction in size with no recurrence at an 18-month follow-up. In our series, all cases of treatment by STR only (cases 5a, 6a, 6b, 7, 15a, 15b, 19a) experienced tumor recurrence or progression; however, the two patients (cases 5b, 17) who were administered adjuvant radiosurgery after STR did not recur or progress. Adjuvant radiosurgery seemed to improve the prognosis (p=0.028). When the total removal could not be achieved, postoperative radiosurgery might be an option.

Conclusions

CNS SFT is a rare mesenchymal tumor with a propensity to recur and a tendency to present in adults. The most commonly affected area is the CPA. Some SFTs do not present a definite dural origin. Immunohistochemistry should be used to differentiate SFT from other tumors. The extent of resection, MIB-1 LI and some anaplastic features, such as hypercellularity, mitosis, necrosis, and brain invasion, might be predictive for recurrence in SFT. Partial HPC pattern might also be a vital index for atypia. Postoperative radiosurgery might be an option in incompletely resected SFT. Postoperative regular and long-term follow-up remains mandatory to monitor recurrence.

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Conflicts of interest None.

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Comment

Neurosurgery at Huashan Hospital, Shanghai, is at its own level of magnitude [1]. In 9 years (2002–10), they operated on 6,700 meningiomas, 183 hemangiopericytomas (rare) and 28 solitary fibrous tumors (very rare) of the CNS. Their 28 solitary fibrous tumours make obviously the largest published series to date - but that is only secondary here. The most important point is the change of times. China and its megacities allow the creation of huge neurosurgical units compared with our European ones, and such units (1) may produce series of patients five- to ten-times larger than published from Europe, (2) may allow subspecialization with tens of neurosurgeons and dedicated instrumentation into a much deeper level that in standard European units, and (3) may at best represent the frontline of neurosurgical decidation and innovation.

Young neurosurgeons, look East!

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