Diagnosis and treatment of solitary fibrous tumor/hemangiopericytoma of central nervous system. Retrospective report of 17 patients and literature review

Long MA, Lu Wang, Xiaoxuan Fang, Cong-hai Zhao, Libo Sun

Department of Neurosurgery, China-Japan Union Hospital, Jilin University, China.

Correspondence to: Libo Sun, NO.126, XianTai Street, China-Japan Union Hospital, Jilin University, ChangChun, Jilin, 130033, China
E-mail: sunlibo@jlu.edu.cn

Submitted: 2017-09-04 Accepted: 2018-02-05 Published online: 2018-07-12

Key words: central nervous system neoplasms; solitary fibrous tumor; hemangiopericytoma; diagnosis; therapy; prognosis

Abstract
To investigate the diagnosis, treatment and prognosis of solitary fibrous tumor (SFT)/hemangiopericytoma (HPC) of central nervous system (CNS), we retrospectively reviewed records of 17 patients who were treated for CNS SFT/HPC at the Department of Neurosurgery, China-Japan Union Hospital of Jilin University from December 2010 to June 2016, and reevaluated their pathological diagnoses according to the 2016 WHO classification of CNS tumors. We then analyzed their clinical symptoms, imaging characteristics, treatments and outcomes. Clinical manifestations of CNS SFT/HPC were diverse, but mainly included headache, increased intracranial pressure, seizures, and focal neurological deficits. In MRI, CNS SFT/HPC usually shows heterogeneous signals, and unusual enhancements; we saw lobulated shapes in 13 patients and necrotic or cystic changes in 12 patients. Tumors of all 17 patients were resected surgically; 9 patients also received postoperative adjuvant radiotherapy. Mean follow-up time was 21 months (range: 2–67 months). The 17 surgeries included 11 total resections, 4 subtotal resection, and 2 partial resections. We followed up 12 patients; 9 of the patients who received total resections had no disease progression; among the 6 patients who did not receive total resections, 2 died of tumor recurrence, 1 has not shown any disease progression. Thus, extent of resection has an apparently crucial influence on prognosis. Postoperative radiotherapy should be chosen carefully, based on resection extent and pathologic grade.

INTRODUCTION
Solitary fibrous tumor (SFT)/hemangiopericytoma (HPC) of the central nervous system (CNS) is a new diagnosis proposed by WHO in 2016 (Louis et al. 2016a). Here, we analyzed retrospectively clinical data of 17 patients with CNS SFT/HPC who were admitted to Department of Neurosurgery, China-Japan Union Hospital, Jilin University, from December 2010 to June 2016, and reclassified their diagnoses according to the new classification system. We have summarized their clinical characteristics, diagnoses, treatments and outcomes, in the light of previous literature.
MATERIALS AND METHODS

Clinical data
We enrolled 17 patients with SFT/HPC, including 9 men and 8 women, whose average age was 48.8 years (range: 33–78 years). Clinical manifestations included headache and dizziness in 11 patients, nausea and vomiting in 4 patients, weakness in lower limbs and gait instability in 2 patients, and ataxia, facial numbness, and hearing loss in 1 patient each. Average duration of primary SFT/HPC symptoms in 13 patients was 8.5 months (range: 2 weeks to 60 months); 4 patients of recurrent SFC/HPC were the first recurrence, the recurrence time was 8 years and 14 years after operation (Table 1).

Imaging data
All patients underwent preoperative CTs, and plain and enhanced MRI scans. Magnetic resonance venography (MRV) was performed in 4 patients whose foci were involved in their intracranial venous sinuses, and 3 patients underwent diffusion tensor imaging (DTI). Magnetic resonance angiography (MRA) and proton magnetic resonance spectroscopy (1H resonance spectroscopy, 1H-MRS) were performed in 2 patients. We found 19 clear-boundary foci, 3 of which were found in 1 patient.

Therapeutic method
All 17 patients underwent tumor surgical resections, a total of 17 surgeries. Two patients also underwent

Tab. 1. Clinic data of 17 patients with HPC/SFT

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age</th>
<th>Position</th>
<th>The mass diameter</th>
<th>Clinical symptoms</th>
<th>Classification in WHO</th>
<th>Therapies</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>56</td>
<td>Frontal lobe parenchyma</td>
<td>4.0*2.4cm</td>
<td>Dizziness, headache</td>
<td>II</td>
<td>TR</td>
<td>Clinical cure</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>38</td>
<td>Anterior skull base</td>
<td>4.4<em>2.7</em>2.9cm</td>
<td>Dizziness, headache, upper limb numbness</td>
<td>II</td>
<td>TR,PPR</td>
<td>Clinical cure</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>47</td>
<td>Anterior skull base</td>
<td>2.4*2.4cm</td>
<td>Interrupted occipital headache</td>
<td>II</td>
<td>TR</td>
<td>Delayed bleeding in 4 days after surgery, conservative treatment</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>44</td>
<td>Near frontal sinus falx</td>
<td>4*5cm</td>
<td>Interrupted occipital headache</td>
<td>II</td>
<td>TR,PPR</td>
<td>Postoperative right</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>63</td>
<td>in vertebral canal</td>
<td>2.6*1.4cm</td>
<td>Occipital and neck pain for two months</td>
<td>II</td>
<td>TR,PPR</td>
<td>Clinical cure</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>40</td>
<td>Anterior skull base, communicated with the extracranial</td>
<td>12<em>5</em>2cm</td>
<td>Second operation, headache</td>
<td>II</td>
<td>SR,PPR</td>
<td>Dead after 8 months</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>43</td>
<td>Middle cranial base</td>
<td>3.0<em>2.0</em>3.4cm</td>
<td>Nausea, vomiting, headache, stroke onset</td>
<td>II</td>
<td>PR</td>
<td>Coma, death after 2 months</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>33</td>
<td>Lateral occipital sinus</td>
<td>3*3cm</td>
<td>Unclear vision</td>
<td>II</td>
<td>TR,PPR</td>
<td>Clinical cure</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>39</td>
<td>Cerebellum tentorial</td>
<td>3.9<em>2.7</em>3.1cm</td>
<td>Progressive headache, stiff neck</td>
<td>II</td>
<td>TR</td>
<td>Loss to follow-up</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>57</td>
<td>Frontal lobe parenchyma</td>
<td>4.4<em>3.5</em>5.1cm</td>
<td>Meningiomas, headache</td>
<td>III</td>
<td>TR,PPR</td>
<td>Clinical cure</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>55</td>
<td>Multiple intracranial tumor</td>
<td></td>
<td>Headache, dizziness and memory loss</td>
<td>II</td>
<td>PR</td>
<td>2 months after surgery, tumor stroke, the family abandoned</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>49</td>
<td>Anterior skull base</td>
<td>4.1<em>3.9</em>4.3cm</td>
<td>Nausea and vomiting</td>
<td>II</td>
<td>TR</td>
<td>Loss to follow-up</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>50</td>
<td>Middle cranial base</td>
<td>5.2cm*4.2cm</td>
<td>Ataxia and headache</td>
<td>Atypical SFT</td>
<td>TR</td>
<td>Loss to follow-up</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>78</td>
<td>Left CPA</td>
<td>3*3</td>
<td>Nausea and vomiting</td>
<td>SFT</td>
<td>SR,PPR</td>
<td>Died of lung infection</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>40</td>
<td>Middle cranial base</td>
<td>3.7<em>5.8</em>4.6cm</td>
<td>Nausea and vomiting</td>
<td>II</td>
<td>SR,PPR</td>
<td>Remote postoperative bleeding, drilling</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>47</td>
<td>Frontal lobe parenchyma</td>
<td>3.4*4.0.3.5</td>
<td>Headache, scalp numbness</td>
<td>II</td>
<td>TR</td>
<td>Loss to follow-up</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>53</td>
<td>Near frontal sinus falx</td>
<td>3<em>4</em>6</td>
<td>Headache</td>
<td>II</td>
<td>SR,PPR</td>
<td>Loss to follow-up</td>
</tr>
</tbody>
</table>
drilling and drainage for postoperative intracranial hemorrhage. During surgery, all tumors appeared as red or gray-red nodules with hard-tough texture. In 11 patients, tumor envelope structures were clear. In 10 patients, the tumor bases were attached to the meninges, with abundant blood supplies.

Surgical approaches were selected according to the site of each tumor. For a patient whose tumor was located in the skull base, because of its low basal position, we chose the improved and extended middle cranial fossa approach and resected the tumor after transection of the zygomatic arch. For a patient with a tumor in the cerebellopontine, we chose a posterior sigmoid sinus approach. For a patient with a tumor in the vertebral canal, we chose a posterior median approach. We considered relationships between the foci and important nerves and vascular tissue, with electrophysiological monitoring used in all surgeries. Nine patients also underwent adjuvant radiotherapy (RT).

Follow-up
Follow-up time averaged 21 months (range: 2–67 months), and included both imaging and telephone follow-up.

RESULTS

Imaging
Most of the CT images showed mixed- and high-density shadows; a few only showed high-density shadow and cystic degeneration but no calcification. MRI showed equal T1 signal, and high or mixed T2 signal. We saw 13 lobulated cases, 12 cases with necrosis, cystic degeneration and/or uneven enhancement, and 7 cases with void vessels or blood flow shadows. Two patients had skull invasion and in-extracranial communication.

Enhanced MRI scan showed obvious tumor enhancement, with obvious “dural tail signs” in 5 patients. MRV showed invaded and occluded intracranial venous sinuses, and MRA showed abundant tumor blood supplies (Figure 1).

DTI examination showed fiber bundles around tumor were interrupted or compressed. 1H MRS showed that the aspartic acid peak decreased obviously and disappeared in part of the region, the creatine peak decreased, and the choline peak increased significantly (Figure 2).

Fig. 1. MRV shows invasion and occlusion of the intracranial venous sinus.

Fig. 2. DTI examination shows the fiber bundle around the tumor was interrupted or compressed. 1H-MRS shows that the aspartic acid peak decreased obviously and disappeared in a part of the region, the creatine peak decreased, and the choline peak increased significantly. There is no inositol peak at 3.56 ppm.
Four patients had tumors in their anterior skull bases, 3 in their middle cranial bases, 2 near their frontal sinus falces, 2 patients in their parietal parenchyma, 1 patient each with tumors in the frontal lobe parenchyma, lateral occipital sinus, tentorial cerebellum, cerebellopontine angle, or vertebral canal, and 1 patient had multiple intracranial tumors. The smallest tumor was 1.5×2.0×2.4 cm; the largest was 2.5×5.5×12.0 cm, located in the anterior skull base and extending extracranially.

Surgical outcome and complications
Of the 17 patients, total resections were achieved in 11 patients, subtotal resections in 4 patients, and partial resections in 2 patients. Of the 2 patients who underwent partial resections, 1 patient had lesions in the frontal, parietal and temporal lobes. After resection of the parietal lobe lesions, residual lesions were treated with adjuvant RT (Figure 3).

One patient suffered a considerable bleeding during surgery, for which a hematoma cavity was formed. After the hematoma was removed, the tumor was not completely removed, and 3 days after surgery, the residual tumor wound closure showed bleeding.

Patients’ families abandoned treatment for different reasons. An elderly patient had a successful operation, but died of pulmonary infection owing to long-term bed rest. A patient was diagnosed with hematencephalon a day after surgery and underwent drilling drainage. Two patients were diagnosed with delayed cerebral hemorrhage; one had hemorrhaged during surgery but improved through conservative treatment, and the other patient bled in an area far from the lesions, and improved after drilling drainage.

Pathological results
According to the 2007 WHO classification standard for CNS tumors, these 17 patients had been diagnosed (respectively) with 13 cases of differentiated HPC, and one case each of anaplastic HPC, typical SFT, atypical SFT, and SFT-or-HPC. According to the 2016 WHO classification standard, all the patients were diagnosed with SFT/HPC, including 3 Grade I cases, 13 Grade II cases, and 1 Grade III case.

Follow-up results
Of the 17 patients, 12 were followed up, 5 were lost to follow-up, 1 patient died, and 1 was abandoned by his
family. In the 12 followed-up patients, 7 patients who underwent total tumor resections had no disease progression in follow-up period. In the subtotal resection group (n=3), 1 patient underwent postoperative RT and died of disease progression 8 months later, 1 is in smooth condition. One patient who received a partial resection underwent postoperative RT, residual tumor stroked in 2 months postoperatively, the family abandoned treatment on the patient.

DISCUSSION

SFT and HPC are both solid tumors that arise from mesenchymal tissue and are found mostly in soft tissue, rarely in the CNS. Since 1996, when Carneiro et al. (1996) first reported CNS SFT, about 200 patients have been reported, including 28 Chinese patients described in one report (Yin Weininger et al. 2009).

HPC is less rare, and accounts for about 1% of intracranial tumors, and 2%–3% of meningeal tumors. Stout and Murray described HPC for the first time in 1942, and noted that this tumor with a rich blood supply was made up of perivascular cells (Louis et al. 2016a). Until WHO divided meningioma into two subtypes in 1993, HPC existed as an independent diagnosis; and was further divided into differentiated HPC and variant HPC by WHO in 2007.

The development of molecular pathology showed SFT and HPC both to have reversed 12q13 and the NAB2–STAT6 fusion gene, leading to nuclear STAT6 expression, which can be detected immunohistochemically. This expression inevitably causes their diagnoses to overlap (Carneiro et al. 1996).

On patient in our cohort was diagnosed as “HPC-or-SFT” Zhang Jie and coworkers (Zhang Jie & Du Guhong 2010) retrospectively analyzed 106 patients with CNS HPC, but they also could not exclude the possibility of SFT in their cohort. Bouvier et al. (2012) noted that HPC and SFT have similar clinical and morphological features, including their component vascular pericytes (Yin Weininger et al. 2009); they also found a patient with primary HPC that recurred as SFT postoperatively, whereas 4 patients with primary SFT recurred with HPC.

Because of these findings, in 2016, WHO combined CNS SFT and HPC into SFT/HPC and proposed the following classifications: Grade I SFT/HPC showed more collagen and relatively low cell density; Grade II showed more cells and less collagen, mast cells and “staghorn” vessels; Grade III showed more features of the HPC variants—specifically, >5 nuclear fission images every 10 high magnification fields (Fountas et al. 2006).

Because the SFT/HPC was only recently identified as a diagnosis and the number of patients is small, epidemiological studies of SFT/HPC are rare. After Fargen et al. (2011) evaluated 189 cases of SFT, they noted that incidence peaks at 51 to 60 years of age. Bisceglia et al (2011) analyzed 217 SFT cases (103 males and 114 females) and found that 89.58% of patients were >30 years old, whereas those <18 years old accounted for only 3.64% (Louis et al. 2007b). Rutkowski’s study (Rutkowski et al. 2010) included 563 HPC cases, whose average age of morbidity was 41 years old, and who were 55% men and 45% women; they found incidence did not significantly differ by sex (Zhang Jie & Du Guhong 2010), which was similar to our results. A group of 15 patients included one patient whose tumor was located in the atlas spinal canal. According to the literature, the probability of SFT/HPC occurring in the spinal canal is 5%–6% – mostly in the cervical or thoracic segments (Bouvier et al. 2012; Fargen et al. 2011).

In our group, one patient had a rare case of primary intracranial multiple tumors. Although multiple intercranial and spinal SFT/HPC have been reported previously (Fargen et al. 2011; Bisceglia et al. 2011), to our knowledge, this is the first report of a patient with multiple intracranial tumors. We consider that the intracranial multiple lesions was caused by intracranial tumor spread over the patient's 2-year disease course.

In addition to the 2 patients who relapsed, the possibility of SFT/ HPC was excluded preoperatively. All 17 patients in our cohort were misdiagnosed, 16 as having meningioma, and 1 as having hemangioblastoma. Considering that images for some patients featured typical “dural tail signs,” the possibility of SPF/HPC should not be ignored, especially for putative “meningiomas” with lobulated shapes or necrotic signals in diagnostic images. These patients underwent 1H-MRS and MRA to confirm diagnoses, and MRV and DTI to help guide their surgeries. Barba et al. (2001) thought that SFT/HPC would increase inositol peaks to about 3.56 ppm in 1H-MRS (Rutkowski et al. 2010). However, no patients in this group had inositol peaks. SFT/HPC could be differentiated from meningioma on this basis. Reportedly, MRAs in 2 patients showed tumors to have rich blood supplies but no stain (Shirzadi et al. 2013). As MRA failed to show whether the external carotid artery could supply blood flow to the tumor, its diagnostic value was lower than that of digital subtraction angiography (DSA).

Prior to establishment of SFT/HPC diagnosis, characteristics of HPC imaging included: (a) lobulated appearance; (b) abundant blood supply, mainly supported by the internal and external carotid arteries; and (c) multiple cystic or necrotic signals, rare calcifications, and obviously uneven enhancements on enhanced MRI scans. As SFT had a lower incidence, its imaging characteristics were less defined. MRI signals for SFT were considered by some to be changeable, with more mixed signals based on T1 isosignals and low T2 signals, and rare calcifications (Shirzadi et al. 2013; Radley & McDonald 2001). With enhanced MRI scanning, T2-low signal areas were clearly strengthened. In addition, areas rich or lacking in tumor cell that appear alternately, as the “Yin and Yang” or “black and white” pattern, support the diagnosis of SFT. In DSA, both SFT...
and HPC were found to be rich in blood supply; SFT could also be seen the presence of double blood supply. Thus, as HPC and SFT have similar imaging features, their combined diagnosis can reduce the incidence of presurgical misdiagnosis (Yang Jun et al. 2001).

Although intracranial SFTs and HPCs showed similar clinical distributions by patient sex, age, tumor site and tumor size (Yang Jun et al. 2001; Barba et al. 2001), Bouvier et al. (2012) showed (using univariate analysis) that SFT/HPC prognosis was closely related to the degree of surgical resection. A retrospective study of 189 patients with SFT by Fargen et al. (2011) showed that, compared with a 14% recurrence rate from total resection, the relapse rate from subtotal resection could be as high as 54%. The study of 15 patients with HPC by Kumar et al. (2012) also showed that patients with total resection had longer median survival.

Radiotherapy for SFT is not widely researched. Five SFT patients who did not receive total resections underwent postsurgical RT, but the results were not satisfactory (Zhai Bo Zhi et al. 2010). Although RT after HPC surgery is widely used as an auxiliary modality, a consensus on optimal RT treatment is not available for these patients. Rutkowski et al. (2010) thought that postoperative RT could not effectively prolong survival of HPC patients (Clarenqon et al. 2011); those who received RT doses >50 Gy in his study had even worse outcomes than patients who received lower doses. The current study showed that the prognosis of patients who underwent total tumor resections was better; although patients who did not receive total resections underwent adjuvant RT, their prognosis is not ideal. Possibly patients in whom complete tumor resections were not feasible had a longer or more severe disease for which prognosis was not improved by RT. Because the SFT/HPC diagnosis is so recently established, selection of RT for patients with HPC/SFT should be carefully considered with regard to the extent of resection and tumor pathological grading.

As the benefits of postoperative RT or chemotherapy on SFT/HPC are unclear, well-executed surgical treatment is required. At the same time, the tumor’s rich blood supply brings great challenges to the surgeon. Death from intraoperative bleeding has been reported, as has intraoperative bleeding that led to only partial or subtotal resections (Kumar et al. 2012). In our group, 1 patient was unable to receive a total resection because of intraoperative bleeding, and 4 patients suffered postoperative hemorrhages.

Suspected SFT/HPC patients need complete examinations. DSA can assist in diagnosis and preoperative embolization of feeding arteries (Zeng et al. 2016). DTI examinations are needed for lesions in functional areas, and MRVs for lesions located near sinuses. The SFT/HPC lesions were hard, which made use of ultrasonic aspirators less effective; although capsule-like structure may be visible, the coating is not complete. Most of the patients were treated with tumor resections; their tumors were resected completely or partially. For tumors seated near important nerve or vascular tissue, intraoperative electrophysiological monitoring can improve surgical guidance. The key to successful resection is properly addressing the tumor wound and hemostasis. Three of our patients suffered postoperative delayed bleeding. Even if intraoperative hemostasis is effective, postoperative bleeding is possible, and thus more attention should be paid to related risk factors (Ambrosini-Spaltro & Eusebi 2010).

REFERENCES


Long Ma, Lu Wang, Xiaoxuan Fang, Cong-hai Zhao, Libo Sun


