UNUSUAL SOLITARY FIBROUS TUMORS IN THE CENTRAL NERVOUS SYSTEM: A REPORT OF TWO CASES

Shih-Wen Hu, Kun-Bow Tsai, Sheau-Fang Yang, Kung-Shing Lee,[1] and Chee-Yin Chai
Departments of Pathology and [1]Neurosurgey, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan.

Solitary fibrous tumors (SFTs) are uncommon, and most are found in the pleura. Extrapleural SFTs are rare and have been found in the lung, pericardium, mediastinum, soft tissue of any site, and upper respiratory tract. SFTs of the central nervous system (CNS) are very rare. The biologic features are unknown and remain poorly understood from a clinical standpoint. Most neurosurgeons do not believe that SFTs can present as primary CNS neoplasms. Most SFTs are clinically benign and indolent, and recurrences after surgical excision are scarce. Because malignant transformation or metastasis has been reported, all SFTs should be treated as having malignant potential. Long-term follow-up is recommended. We report two cases, so that surgeons may recognize that this is an entity different from other spindle-cell CNS tumors.

Key Words: solitary fibrous tumor, extrapleural, central nervous system
(*Kaohsiung J Med Sci* 2005;21:179–84)

First differentiated from mesothelioma by Klemperer and Rabin in 1931 [1], solitary fibrous tumors (SFTs) usually arise in the pleura [2–4]. They have also been found outside the pleura, including in the soft tissues, lung, mediastinum, pericardium, upper respiratory tract, peritoneum [4], tentorium, cerebellopontine angle, spinal dura, parasagittal region, meninges [5], intraventricular region [6], liver [7], external auditory meatus [8], falciform ligament [9], and posterior cranial fossa [10]. SFTs within the central nervous system (CNS), however, are rare. With increasing awareness of primary extrapleural sites, reports of SFTs are increasing. The exact incidence in the CNS is not clear, but is reported to be low [2]. It is said that CNS SFTs account for approximately 0.09% of all meningeal tumors [3]. There has been little published on the clinical behavior of SFTs in the CNS due to their rarity [11]. Most series primarily give pathologic information rather than analyzing clinicopathologic correlates of tumor behavior [11]. The clinical course, histogenesis, cytogenetics, prognosis, and treatment protocol for CNS SFTs are still unknown [12]. We report two peculiar cases of SFTs in the CNS, in a male and a female patient.

Received: November 3, 2004 Accepted: December 14, 2004
Address correspondence and reprint requests to: Dr. Chee-Yin Chai, Department of Pathology, Kaohsiung Medical University Chung-Ho Memorial Hospital, 100 Tzyou 1st Road, Kaohsiung 807, Taiwan.
E-mail: cychai@kmu.edu.tw

CASE PRESENTATIONS

Case 1

A 58-year-old male patient presented with a progressive intermittent unsteady gait, left hemiparesis, tinnitus, dizziness, and tremor in both hands. Grade II astrocytoma in the right frontal lobe had been diagnosed 11 years earlier and he had been followed regularly by the clinic. Magnetic resonance imaging (MRI) disclosed a bulky, relatively well-defined lesion about 8.3 cm in diameter in the right temporo-occipital lobe that seemed to be extra-axial. This tumor exhibited a low T1 weighted signal, a heterogeneous high T2 weighted signal, multiple small intermediate-signal nodules within the mass on the T1 weighted image (WI) and T2WI, and punctuated low T2 weighted signal dots (Figure 1). Mild brain edema in the right parietal lobe was also seen. The impression from radiologic evidence was that the mass was a meningioma. Due to the possibility of recurrent astro-

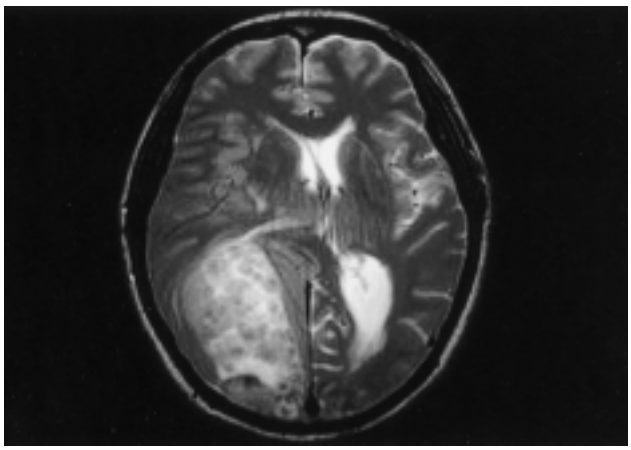

Figure 1. *Magnetic resonance image demonstrates a heterogeneous high T2 weighted signal.*

cytoma and persistent symptoms, the patient underwent surgery about 4 months after presentation. Frozen sections supported the diagnosis of meningioma. The patient has received regular follow-up and has remained disease-free for the 10 months since his surgery.

Case 2

A 35-year-old female sought treatment after 1 month of intermittent headaches with associated bilateral blurred vision and a decreased field of vision. She had no contributory medical history. Bilateral mydriasis and vessel engorgement were seen in bilateral retinas. Computed tomography (CT) revealed an amorphous and well-margined low-attenuation lesion in the left cerebellopontine angle (Figure 2). Meningioma with compression of the brain stem and fourth ventricle, and obstructive hydrocephalus were suspected. The patient underwent surgery approximately 1 month later. Frozen section confirmed the diagnosis of meningioma. The postoperative course was uneventful.

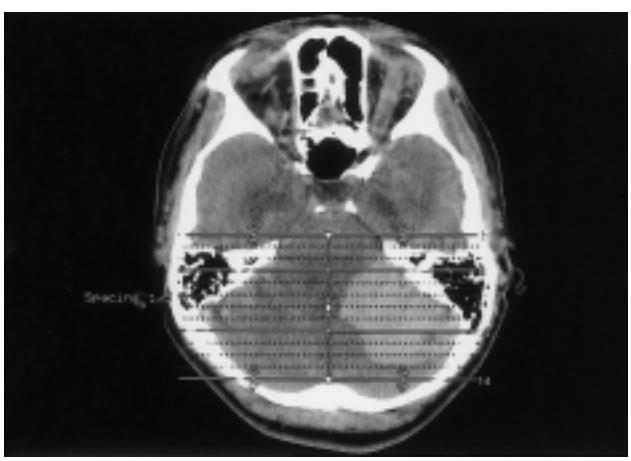

Figure 2. *Computed tomography reveals an amorphous and well-margined low-attenuation lesion located in the left cerebellopontine angle.*

Characteristics

Microscopically, both cases showed similar features of randomly alternating hyper- and hypocellular areas, interspersed with a thick collagen background. Tumor cells were vesicular and bland-appearing ovoid to spindle-shaped. Their nuclei had fine chromatin but there was no atypia, nucleoli, necrosis, or mitotic figures (Figure 3). Scattered thin-walled small vessels were also seen. Case 2 had a focal hemorrhage. Repeated immunohistochemical studies in both cases were strongly and diffusely positive for CD34 and Bcl-2 and diffusely but weakly positive with vimentin. There was no immunoreactivity with epithelial membrane antigen (EMA), S-100 protein, cytokeratin (CK), CD117, factor VIII, estrogen receptor, progesterone receptor, synaptophysin, glial fibrillary acidic protein, HMB-45, calretinin, desmin, smooth muscle actin (SMA), periodic acid Schiff (PAS), and CD31. The collagen bundles stained green with Masson's trichrome stain. Interlacing reticulin fibers were well demonstrated by reticulin stain (Figure 4). The MIB-1 labeling index was approximately 2% in Case 1 and less than 1% in Case 2.

DISCUSSION

SFT is an uncommon and benign tumor [2]. Differential diagnosis includes fibrous meningioma (FM) [2,3], fibrosarcoma [3], meningeal sarcoma [5], meningeal myofibroblastoma (MM) [5], schwannoma, neurofibroma [3,6], hemangiopericytoma (HPC) [2,3,6], and gastrointestinal stromal tumor (GIST) [13]. FM is strongly positive for EMA and negative for CD34 [5]. Lack of expression of S-100 allows us to discriminate SFT from schwannoma and neurofibroma, while no staining with SMA and desmin helps to separate SFT from smooth muscle tumors and MM [3,5]. Sarcoma was unlikely because there was no anaplasia, including nuclear pleomorphism, increased mitotic figures, and necrosis [5]. CD34, a 100-kDa sialyated transmembrane glycoprotein, is expressed in hematopoietic stem cells, myeloid progenitor cells, the endothelium, endothelial progenitor cells, and certain mesenchymal cells in the dermis [2,3,14]. It is invariably and strongly expressed in SFT and is considered a definitive marker of this entity [2,8,10,14–18]. Intracranial SFTs are typically dura-based, CD34-positive, mesenchymal neoplasms, and their histogenesis

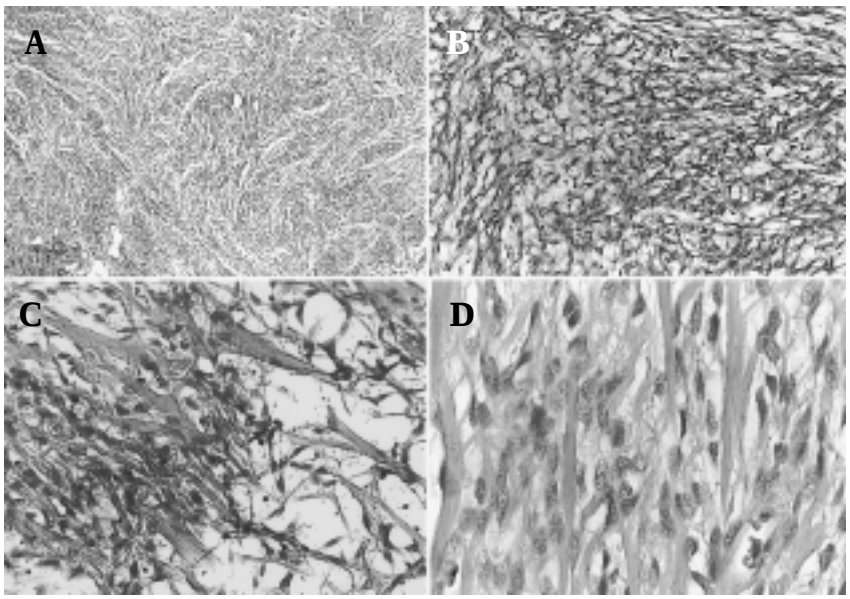

Figure 3. *Microscopic appearance. (A) The hypercellular area exhibits a vague fascicular growth pattern (hematoxylin & eosin, original magnification × 40). (B) Some areas show hypocellularity (hematoxylin & eosin, original magnification ×100). (C) Interspersed collagen background (hematoxylin & eosin, original magnification × 200). (D) No malignant cytologic features (hematoxylin & eosin, original magnification ×400).*

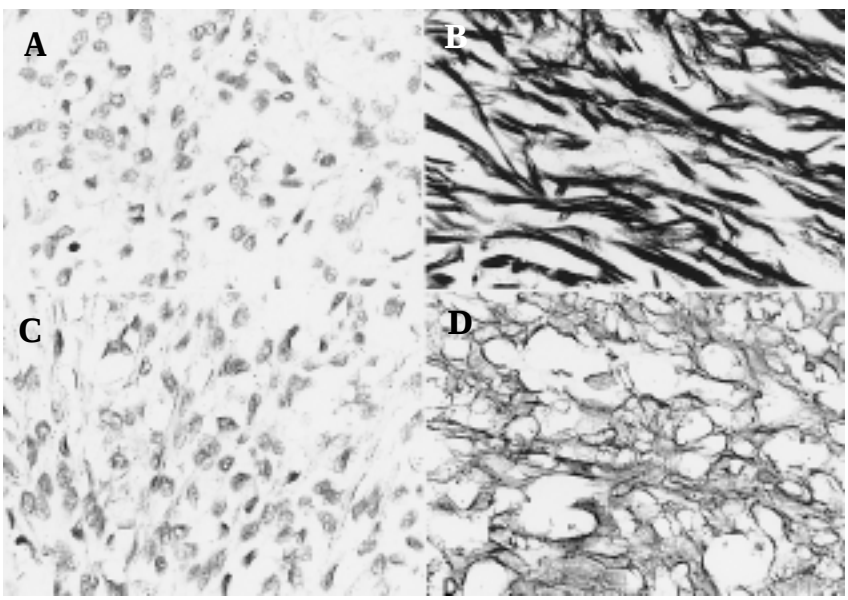

Figure 4. *Immunohistochemical features. (A) Epithelial membrane antigen staining is negative. (B) Reticulin stain highlights interspersed reticulin background. (C) S-100 staining is diffusely negative. (D) Diffuse and strong CD34 immunopositivity. (Original magnification ×400.)*

remains elusive [6,19]. However, CD34 can be lost in high-grade foci [20]. In both of our cases, the tumor was strongly and diffusely positive for CD34, and SFT was the diagnosis.

Calretinin immunohistochemistry, when reported in SFT-related literature, is negative [19]. SFTs are immunoreactive for Bcl-2 at 80–100% [17,21–23], and both our cases were Bcl-2 positive. A high percentage of SFTs (75–100%) also express CD99 [21,22]. CD117 staining is positive in GIST and negative in SFTs [13,17]. Both of our cases were CD117 negative and GIST was excluded. There is controversy over the immunohistochemical expression of factor VIII, with one positive report [21] and two negative reports in the literature [24,25]. HMB-45, CD31, and PAS are rarely discussed and are negative in literature reports [26–28], which is in line with our cases. CK is negative in SFTs [24, 29]. Unlike SFT, meningeal HPC can metastasize and has high rates of recurrence. HPC must, therefore, be differentiated from benign spindle-cell tumors of the CNS, including SFTs [29]. HPC is CD34 positive but with a patchy and weak staining pattern, unlike the diffuse and strong CD34 positivity of SFTs [29]. A common histologic pattern of SFT is alternate hyper- and hypocellular areas with bland-looking ovoid to spindle-shaped cells, packed by reticulin fibers [2,5,6]. An HPC-like vascular pattern can be found in SFTs [3], but was not seen in either of our cases. From the histopathologic and immunohistochemical

features (Table), our cases are both rare SFTs of the CNS.

Ultrastructurally, SFTs reveal fibroblastic or myofibroblastic differentiation supporting a mesenchymal, rather than meningothelial, origin [5,30,31]. They lack the pinocytic vesicles and dense laminae characteristic of HPC [10]. Hence, SFTs are different from HPCs.

CT shows an isodense irregular mass [10]. MRI is superior to CT because it gives better resolution of heterogeneous internal composition [32]. MRI does not reveal uniform or specific features, but shows diversity, such as two components on T2WI [15], T1 weighted hypointensity homogeneously enhanced with gadolinium [15], T1 isointensity with T2 hypointensity [32], and T1 weighted isointensity with T2 weighted slightly high intensity and mixed intensity [33]. In Case 1, MRI gave a low T1 weighted signal and a heterogeneous high T2 weighted signal. In Case 2, only CT was performed and revealed an amorphous and well-margined low-attenuation lesion, unlike in previous reports [10]. Therefore, imaging might not be able to provide a definite diagnosis.

SFTs are rare and generally benign [8,9]. Local invasion or malignant transformation is uncommon and malignant cases in the CNS are even more scarce [2,9]. Death due to an SFT has only been reported once [31]. The criteria for malignancy include hypercellularity, more than four mitoses per 10 high-power fields, and pleomorphism [23]. In our cases, no anaplastic features were noted. The MIB-1 labeling index seems to play a role in differentiation of benign and malignant lesions, with a higher MIB-1 labeling index in malignancies [34].

Hypoglycemia is rarely associated with SFTs, and it was not seen in our cases [7]. In Case 1, the patient had a medical history of astrocytoma in a different location. There is no contributory medical history associated with SFTs in the literature, except for one associated with schizophrenia for 20 years [18]. The biologic behavior is uncertain and the cytogenetic background is poorly understood [35]. DNA ploidy analysis in one report illustrated diploid content [36]. Comparative genomic hybridization reveals some loss in chromosomes 13 and 20q and some gains in 5q, 7, 8, 12, and 18 [35]. In spite of the lack of anaplasia, comparative genomic hybridization shows a loss in 20q, complex genomic imbalances, and primitive features [35]. HPC does not have these changes [37].

Use of chemotherapy or radiotherapy is not promising [16]. The histogenesis and unpredictable behavior of SFTs are a mystery [19,22]. Regardless of the benign appearance, every case of SFT needs careful and long-term follow-up [4, 22,35].

Table. Immunohistochemical comparison of tumors

	EMA	CD34	S-100	SMA	Desmin	CD117
SFT	–ve	+ve	–ve	–ve	–ve	–ve
Meningioma	+ve	–ve				
Myofibroblastoma				+ve	+ve	
Schwannoma			+ve			
Neurofibroma			+ve			
HPC		+ve*				
GIST						+ve

*Patchy and weak staining. EMA = epithelial membrane antigen; SMA = smooth muscle actin; SFT = solitary fibrous tumor; HPC = hemangiopericytoma; GIST = gastrointestinal stromal tumor; –ve = negative; +ve = positive.

References

1. Klemperer P, Rabin CB. Primary neoplasia of the pleura: a report of five cases. *Arch Pathol* 1931;11:385-412.
2. Suzuki SO, Fukui M, Nishio S, Iwaki T. Clinicopathological features of solitary fibrous tumor of the meninges: an immunohistochemical reappraisal of cases previously diagnosed to be fibrous meningioma or hemangiopericytoma. *Pathol Int* 2000; 50:808–17.
3. Brunori A, Cerasoli S, Donati R, et al. Solitary fibrous tumor of the meninges: two new cases and review of the literature. *Surg Neurol* 1999;51:636–40.
4. Lee WA, Lee MK, Jeen YM, et al. Solitary fibrous tumor arising in gastric serosa. *Pathol Int* 2004;54:436–9.
5. Prayson RA, McMahon JT, Barnett GH. Solitary fibrous tumor of the meninges. Case report and review of the literature. *J Neurosurg* 1997;86:1049–52.
6. Kocak A, Cayli SR, Sarac K, Aydin NE. Intraventricular solitary fibrous tumor: an unusual tumor with radiological, ultrastructural, and immunohistochemical evaluation: case report. *Neurosurgery* 2004;54:213–6.
7. Chithriki M, Jaibaji M, Vandermolen R. Solitary fibrous tumor of the liver with presenting symptoms of hypoglycemic coma. *Am Surg* 2004;70:291–3.
8. Izumaru S, Yoshida Y, Nakashima T. A solitary fibrous tumor in the external auditory meatus. *Auris Nasus Larynx* 2004;31: 65–7.
9. Gidwani AL, Mullan FJ, Kenny B. Solitary fibrous tumor of the falciform ligament containing multiple foci of malignant transformation. *J Clin Pathol* 2004;57:546–7.
10. Nawashiro H, Nagakawa S, Osada H, et al. Solitary fibrous tumor of the meninges in the posterior cranial fossa: magnetic resonance imaging and histological correlation—case report. *Neurol Med Chir* 2000;40:432–4.
11. Gold JS, Antonescu CR, Hajdu C, et al. Clinicopathologic correlates of solitary fibrous tumors. *Cancer* 2002;94:1057–68.
12. Kim KA, Gonzalez I, McComb JG, Giannotta SL. Unusual

presentations of cerebral solitary fibrous tumors: report of four cases. *Neurosurgery* 2004;54:1004–9.
13. Shidham VB, Chivukula M, Gupta D, et al. Immunohistochemical comparison of gastrointestinal stromal tumor and solitary fibrous tumor. *Arch Pathol Lab Med* 2002;126: 1189–92.
14. Sawada N, Ishiwata T, Naito Z, et al. Immunohistochemical localization of endothelial cell markers in solitary fibrous tumor. *Pathol Int* 2002;52:769–76.
15. Sawauchi S, Arakawa H, Taya K, et al. Solitary fibrous tumor of the fourth ventricle: case report. *No Shinkei Geka* 2003;31: 551–5. [In Japanese]
16. Munks S. Solitary fibrous tumor (SFT) of the nasal mucosa. *Laryngorhinootologie* 2003;82:655–8. [In German]
17. Kumagai M, Suzuki H, Takahashi E, et al. A case of solitary fibrous tumor of the parotid gland: review of the literature. *Tohoku J Exp Med* 2002;198:41–6.
18. Kohmura T, Nakashima T, Hasegawa Y, Matsuura H. Solitary fibrous tumor of the paranasal sinuses. *Eur Arch Otorhinolaryngol* 1999;256:233–6.
19. Morgan MB, Smoller BR. Solitary fibrous tumors are immunophenotypically distinct from mesothelioma(s). *J Cutan Pathol* 2000;27:451–4.
20. Ng HK, Choi PCL, Wong CW, Poon WS. Metastatic solitary fibrous tumor of the meninges. Case report. *J Neurosurg* 2000; 93:490–3.
21. Alawi F, Stratton D, Freedman PD. Solitary fibrous tumor of the oral soft tissues: a clinicopathologic and immunohistochemical study of 16 cases. *Am J Surg Pathol* 2001;25:900–10.
22. Chen HJ, Zhang HY, Li X, et al. Solitary fibrous tumor: the clinicopathologic and immunohistochemical characteristics of 26 cases. *Sichuan Da Xue Xue Bao Yi Xue Ban* 2004;35:675–9.
23. Zhang H, Lucas DR, Pass HI, Che M. Disseminated malignant solitary fibrous tumor of the pleura. *Pathol Int* 2004;54: 111–5.
24. Khalifa MA, Montgomery EA, Azumi N, et al. Solitary fibrous tumors: a series of lesions, some in unusual sites. *South Med J* 1997;90:793–9.
25. Suster S, Nascimento AG, Miettinen M, et al. Solitary fibrous tumors of the soft tissue. A clinicopathologic and immunohistochemical study of 12 cases. *Am J Surg Pathol* 1995;19: 1257–66.
26. Alston SR, Francel PC, Jane JA Jr. Solitary fibrous tumor of the spinal cord. *Am J Surg Pathol* 1997;21:477–83.
27. Hanau CA, Miettinen M. Solitary fibrous tumor: histological and immunohistochemical spectrum of benign and malignant variants presenting at different sites. *Hum Pathol* 1995;26:440–9.
28. Carneiro SS, Scheithauer BW, Nascimento AG, et al. Solitary fibrous tumor of the meninges: a lesion distinct from fibrous meningioma. A clinicopathologic and immunohistochemical study. *Am J Clin Pathol* 1996;106:217–24.
29. Perry A, Scheithauer BW, Nascimento AG. The immunophenotypic spectrum of meningeal hemangiopericytoma: a comparison with fibrous meningioma and solitary fibrous tumor of meninges. *Am J Surg Pathol* 1997;21:1354–60.
30. Nielsen GP, O'Connell JX, Dickersin GR, Rosenberg AE. Solitary fibrous tumor of soft tissue: a report of 15 cases, including 5 malignant examples with light microscopic, immunohistochemical, and ultrastructural data. *Mod Pathol* 1997;10:1028–37.
31. Fukunaga M, Naganuma H, Nikaido T, et al. Extrapleural solitary fibrous tumor: a report of seven cases. *Mod Pathol* 1997;10:443–50.
32. Gigantelli JW, Kincaid MC, Soparkar CN, et al. Orbital solitary fibrous tumor: radiographic and histopathologic correlations. *Ophthal Plast Reconstr Surg* 2001;17:207–14.
33. Hayashi S, Kurihara H, Hirato J, Sasaki T. Solitary fibrous tumor of the orbit with extraorbital extension: case report. *Neurosurgery* 2001;49:1241–5.
34. Sun Y, Naito Z, Ishiwata T, et al. Basic FGF and Ki-67 proteins useful for immunohistological diagnostic evaluations in malignant solitary fibrous tumor. *Pathol Int* 2003;53:284–90.
35. Amo-Takyi BK, Gunther K, Peters I, et al. Benign solitary fibrous pleural tumour. Evidence of primitive features and complex genomic imbalances, including loss of 20q. *APMIS* 2001;109:601–6.
36. Challa VR, Kilpatrick SE, Ricci P, et al. Solitary fibrous tumor of the meninges. *Clin Neuropathol* 1998;17:73–8.
37. Miettinen MM, el-Rifai W, Sarlomo-Rikala M, et al. Tumor size-related DNA copy number changes occur in solitary fibrous tumors but not in hemangiopericytomas. *Mod Pathol* 1997;10:1194–200.

罕見的中樞神經系統單獨纖維瘤 — 兩個病例報告

胡士文[1] 蔡坤寶[1] 楊曉芳[1] 李昆興[2] 蔡志仁[1]

高雄醫學大學 [1]病理科 [2]神經外科

單獨纖維瘤是少見的腫瘤，大部分發生於肋膜。肋膜外的單獨纖維瘤罕見，發生部位包括肺、心包膜、縱膈腔、任何地方的軟組織、上呼吸道，發生於中樞神經系統的單獨纖維瘤更佔肋膜外腫瘤的少數，因此文獻上少見。對許多人而言中樞神經系統的單獨纖維瘤是新的名詞，其生物特質目前未明，從臨床上了解不多，即使現在，大部分的神經外科醫師還是很難接受這種診斷。臨床表現上大部分是良性，追蹤後發生復發的案例極少，但仍有文獻報告過惡性轉變或轉移的病例。故所有的單獨纖維瘤應該視為有惡性轉變的可能，建議要長期追蹤。我們報告兩個罕見的中樞神經系統單獨纖維瘤，讓臨床醫師了解這種不同於其他中樞神經系統的腫瘤。

關鍵詞：單獨纖維瘤，肋膜外，中樞神經系統

（高雄醫誌 **2005;21:179–84**）

收文日期：**93** 年 **11** 月 **3** 日

接受刊載：**93** 年 **12** 月 **14** 日

通訊作者：蔡志仁醫師

高雄醫學大學附設中和紀念醫院病理科

高雄市 **807** 三民區自由一路 **100** 號