·临床病理报告·

脑室内孤立性纤维性肿瘤

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【摘要】 **研究背景** 孤立性纤维性肿瘤是纤维母细胞起源的间叶性梭形细胞肿瘤，多发生于胸膜、纵隔、头颈部、四肢和躯干的皮下和深部软组织。发生于中枢神经系统者少见，多附着于脑(脊)膜，完全位于脑室内而与硬膜无关联者罕见。本文报告1例脑室内原发性孤立性纤维性肿瘤患者，分析其影像学和临床病理学特征，并复习相关文献，探讨其诊断与鉴别诊断要点。**方法与结果** 男性患者，50岁。临床表现为进行性加重的持续性头痛2月余。头部CT显示右侧侧脑室三角区内分界清楚的略高密度孤立性结节。MRI显示右侧侧脑室内占位性病变，T_1WI呈等信号、T_2WI呈高低混杂信号，伴周围脑组织轻度水肿，肿瘤组织内可见黑白相间的“阴阳征”，增强扫描呈明显不均匀强化。MRA显示肿瘤富血管，表现为持续性强化。手术全切除肿瘤。术中可见肿瘤完全位于侧脑室内，灰红色，团状块，质地中等，无包膜，与脉络丛相连，血供丰富。组织学形态显示，肿瘤组织由梭形细胞、胶原基质和丰富的血管构成，部分区域呈细胞丰富区和稀疏区交替分布构象，伴灶性间质黏液变性。部分区域肿瘤细胞排列密集、围绕不同管径的“树枝”状或“鹿角”样血管呈血管周细胞瘤样生长，细胞异型性不明显，核分裂象少见，肿瘤组织内未见出血坏死灶。免疫组织化学染色，肿瘤细胞弥漫性表达波形蛋白、CD34和Bcl-2，灶性表达CD99，不表达细胞角蛋白、上皮膜抗原、胶质纤维酸性蛋白、S-100蛋白、平滑肌肌动蛋白和结蛋白。网织纤维染色显示肿瘤组织内网状纤维丰富，部分区域网状纤维包绕肿瘤细胞。荧光原位杂交检测显示*SYT*基因断裂呈阴性，不存在t(X;18)(p11;q11)易位。病理诊断为(右侧侧脑室内)原发性孤立性纤维性肿瘤。**结论** 脑室内孤立性纤维性肿瘤临床罕见，由于缺乏特征性影像学表现和组织学形态复杂多样，给术前明确诊断带来一定困难。由于孤立性纤维性肿瘤与血管周细胞瘤在组织学形态和免疫表型存在延续和重叠，故考虑二者属同一肿瘤谱系，建议联合应用“孤立性纤维性肿瘤/血管周细胞瘤”的诊断术语。由于该肿瘤发病部位少见，临床应提高警惕，注意与其他具有相似组织病理学构象的疾病相鉴别。

【关键词】 孤立性纤维瘤； 脑室； 免疫组织化学； 原位杂交,荧光； 病理学

Intraventricular solitary fibrous tumor

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【**Abstract**】 **Background** Solitary fibrous tumor (SFT) is a mesenchymal neoplasm of specialized fibroblastic lineage, which frequently occurs in the subcutaneous and deep soft tissue of pleura, mediastinum, head and neck, extremities and trunk. Although most SFTs of the central nervous system (CNS) are dural based, a small subset presents as intraventricular without dural connection. It is a diagnostic challenge for radiologists and histopathologists to differentiate intraventricular SFT from other lesions, such as intraventricular meningioma, synovial sarcoma and Schwannoma, because of the similarities in radiological and histological findings. Herein we describe one case of unusual intraventricular primary SFT in right lateral ventricle. The radiology and clinicopathology of this lesion, as well as its differential diagnosis are discussed. **Methods** The clinical data of one patient with intraventricular SFT occurring in right lateral ventricle was presented retrospectively. Gross totally resected mass was routinely paraffin embedded and stained with hematoxylin and eosin. Dako EnVision immunohistochemical staining system

doi:10.3969/j.issn.1672-6731.2015.10.010

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was used to detect antigen expressions, including vimentin (Vim), cytokeratin(CK), CD34, CD99, Bcl-2, epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), S-100 protein (S-100), smooth muscle actin (SMA) and desmin (Des). **Results** A 50-year-old man presented with progressively aggravated headache for over 2 months. CT revealed a slightly high-density mass in trigone of right lateral ventricle. MRI showed an intraventricular mass with isointense signal on T_1WI, and mixed hyperintensity and hypointensity signal with "black and white pattern" on T_2WI. The mass revealed heterogeneous enhancement after gadolinium administration. Preoperative magnetic resonance angiography (MRA) displayed a highly vascularized lesion with late and persistent enhancement. During surgery, the mass was grey-red, had no capsule and connected with choroid plexus, with moderate texture and rich blood supply. It was located in lateral ventricle entirely. The tumor was removed totally. Microscopic examination showed that the mass was composed of spindle cells, dense collagenous matrix, and prominent blood vessels. In some areas, the hypocellular and alternating hypercellular arrangement, and perivascular hyalinization were found. The tumor was lack of any specific arrangement, resulting in a "patternless pattern". The myxoid matrix was observed in some areas of tumor. However, in other areas, the tumor was composed of markedly spindle cells with branching or "staghorn" vessels, resembling hemangiopericytoma. The spindle tumor cells showed mild atypia without active mitoses and necrosis. Immunohistochemically, the tumor cells were diffusely positive for Vim, CD34 and Bcl-2, focally positive for CD99, and were negative for CK, EMA, GFAP and S-100, SMA and Des. Reticular fiber staining revealed rich reticular fibers within the tumor tissue, and a pericellular pattern was also seen. Fluorescence in situ hybridization (FISH) assay for *SYT* rearrangement showed there was absence of t (X; 18) (p11; q11) in the tumor cells. Based on clinical presentation and histological findings, a final diagnosis of intraventricular primary SFT in right lateral ventricle was made according to the criteria of WHO classification. The patient did not received radiotherapy and was followed-up for one year, without any neurological deficit or signs of recurrence. **Conclusions** Intraventricular SFT is extremely rare and a definite diagnosis should be made under microscopic examination because the preoperatively radiological appearance does not differ from other tumors occurring in ventricle. Since a spectrum between SFT and hemangiopericytoma has been suggested because of overlapped morphological and immunohistochemical features, a diagnostic term of "SFT/hemangiopericytoma" is suggested for those lesions occurring in CNS. Due to the rarity of its site, strictly differential diagnosis should be made when an isolated SFT is encountered in ventricles.

【Key words】 Solitary fibrous tumors; Cerebral ventricles; Immunohistochemistry; In situ hybridization, fluorescence; Pathology

孤立性纤维性肿瘤(SFT)是纤维母细胞起源的间叶性梭形细胞肿瘤,好发于胸膜、纵隔、头颈部、四肢和躯干的皮下和深部软组织[1-2],发生于中枢神经系统者少见。自1996年Carneiro等[3]首次报告发生于脑膜的孤立性纤维性肿瘤以来,陆续有原发性中枢神经系统孤立性纤维性肿瘤的报道。2007年世界卫生组织(WHO)中枢神经系统肿瘤分类将其作为一种独立疾病实体归类为间叶性非脑膜上皮肿瘤[4]。尽管大多数颅内和椎管内孤立性纤维性肿瘤均附着于脑(脊)膜,但仍有少数位于脑实质或脑室内,与硬脑膜无关。根据Bisceglia等[5]对中枢神经系统原发性孤立性纤维性肿瘤的统计,1996–2011年共有220例颅内和椎管内孤立性纤维性肿瘤患者,其中仅13例发生于脑室内,约占5.91%;国内也仅见脑室内孤立性纤维性肿瘤的个案报道[6]。由于孤立性纤维性肿瘤缺乏特征性影像学表现,术前明确诊断困难,常误诊为脑膜瘤。该肿瘤组织学形态多样,既可表现为单一的梭形细胞实体性病变,又可表现为间质胶原变性、黏液变性和脂肪细胞化生等组织学变异型,常误诊为包括滑膜肉瘤和黏液性神经纤维瘤等在内的其他梭形细胞肿瘤,是临床诊断与治疗的难点。我们报告1例发生于侧脑室的少见脑室内原发性孤立性纤维性肿瘤患者,通过复习文献对其影像学和组织学形态特征、免疫表型,以及治疗和预后进行分析,以期提高对该病的诊断与鉴别诊断能力。

病历摘要

患者 男性,50岁。主因头痛2月余并进行性加重,于2014年1月10日入院。患者近2个月来无明显诱因出现持续性头痛,初期仅为颞枕部轻微胀痛,休息后自行缓解,未予特殊处理,仅行数次头颈部按摩以缓解疼痛,但自觉症状无好转。约1周前头痛症状加重,整个头部持续性胀痛,伴头晕,休息

后不能缓解，影响正常工作和生活。患者自发病以来，精神、睡眠可，食欲减退，无发热、耳鸣、眩晕等症状与体征，大小便正常。

既往史、个人史及家族史　患者平素身体健康，工作和生活正常。自述30年前曾患肺结核，已治愈，具体治疗过程和方案不详。否认肝炎及其他传染病病史，否认手术、外伤和输血史，否认食物和药物过敏史，预防接种史不详。无疫区疫水、特殊化学物质或放射性物质接触史。已婚，育有一女，妻子、女儿均身体健康。家族中无遗传性疾病病史，无类似疾病病史。

体格检查　患者体温36.5 ℃，心率85 次/min，呼吸18 次/min，血压148/95 mm Hg（1 mm Hg = 0.133 kPa）。神志清楚，语言流利。全身皮肤和黏膜无紫绀、黄染。全身浅表淋巴结未触及、无肿大。双侧颞顶部轻度压痛。四肢外观无畸形，无明显肌萎缩，肌力和肌张力正常，无感觉障碍。双眼视力、视野正常。神经系统检查第Ⅰ～Ⅲ、Ⅴ、Ⅶ～Ⅸ、Ⅺ～Ⅻ对脑神经未见异常。脑膜刺激征阴性，双侧腱反射阳性，病理征未引出，无颈项强直。

辅助检查　实验室检查：血常规正常，凝血功能四项、乙型肝炎五项和传染病四项均呈阴性，肿瘤标志物筛查甲胎蛋白（AFP）和癌胚抗原（CEA）阴性。影像学检查：胸部X线显示，双肺陈旧性结核灶。盆腹腔B超未见肝脏、脾和淋巴结肿大。头部CT检查可见右侧侧脑室三角区内分界清楚的占位性病变（图1a）。MRI显示，病变位于右侧侧脑室三角区内，大小约28 mm × 22 mm × 20 mm，与周围脑组织分界清楚，与脑膜无粘连，T_1WI呈等或稍低信号、T_2WI呈高低混杂信号，伴周围脑组织轻度水肿，中线向左侧轻度偏移，病灶内可见黑白相间的“阴阳征”；增强扫描呈不均匀明显强化（图1b～1e）。MRA显示，肿瘤主要由右侧脉络丛后外侧动脉的小分支供血，并可见持续性强化（图1f）。

诊断与治疗经过　临床拟诊为脑室内脑膜瘤。入院后1周于气管插管全身麻醉下行右侧顶枕叶肿瘤切除术。术中可见肿瘤完全位于右侧侧脑室内，直径约2.50 cm，呈灰红色，团块状，质地中等，无包膜，与脉络丛相连，血供丰富。手术全切除肿瘤，术中瘤体出血明显。切除标本行组织病理学检查。（1）大体标本观察：手术切除组织为不规则破碎组织数块，直径0.50～1.50 cm，呈灰红或灰黄色、质地中等、无完整包膜（图2）。经体积分数为10%中性甲醛溶液固定、石蜡包埋制备组织切片，行HE染色和免疫组织化学染色。（2）HE染色：肿瘤组织由密集排列的短梭形和卵圆形细胞构成，呈现细胞丰富区和稀疏区交替分布特征。大部分区域肿瘤细胞呈无结构性生长（patternless pattern），胞质较少，分界不清，胞核染色质均匀；部分区域肿瘤细胞呈血管周细胞瘤（HPC）样生长，血供丰富，血管管径大小不一，扩张呈血窦样、“树枝”状或“鹿角（staghorn）”样，管壁周围包绕一层稍厚的胶原纤维套。肿瘤细胞短梭形，呈片状弥漫分布于血管周围和血管间，胞核轻度异型性，仅见个别核分裂象（1/10个高倍视野），无多核瘤巨细胞和怪异核细胞。肿瘤间质可见局灶性黏液变性区域，无明显增生，呈瘢痕样胶原纤维和脂肪细胞化生表现。肿瘤组织全埋制片，其内未见出血坏死灶（图3）。（3）免疫组织化学染色：EnVision二步法检测试剂盒购自丹麦Dako公司。检测用波形蛋白（Vim，1∶100）、细胞角蛋白（CK，1∶200）、上皮膜抗原（EMA，1∶100）、胶质纤维酸性蛋白（GFAP，1∶100）、CD34（1∶100）、CD99（1∶100）、S-100蛋白（S-100，1∶100）、平滑肌肌动蛋白（SMA，1∶100）、Bcl-2（1∶100）、结蛋白（Des，1∶100）和Ki-67抗原分别购自美国Santa Cruz公司和丹麦Dako公司。结果显示，短梭形肿瘤细胞Vim、CD34和Bcl-2均呈弥漫性强阳性、CD99呈灶性阳性，CK、EMA、GFAP、S-100、SMA和Des均呈阴性，Ki-67抗原标记指数约为3%（图4）。（4）特殊染色：网织纤维染色，肿瘤组织含丰富网状纤维，在血管周细胞瘤样区域中肿瘤细胞周围均包绕网状纤维（图5）。（5）荧光原位杂交（FISH）检测：采用*SYT*基因断裂探针（美国Vysis公司）检测t（X；18）（p11；q11）易位情况。结果显示，*SYT*基因断裂呈阴性，提示肿瘤不存在t（X；18）（p11；q11）易位，不支持滑膜肉瘤的诊断（图6）。最终病理诊断为（右侧侧脑室内）原发性孤立性纤维性肿瘤。患者术后恢复良好，无明显神经系统异常，头痛症状消失。术后15 d出院，未接受放射治疗和药物化疗，规律随访1年，术后3和6个月时分别复查头部MRI，未见肿瘤复发，目前仍在随访中。

讨　论

孤立性纤维性肿瘤是纤维母细胞起源的梭形细胞肿瘤，最初由Klemperer和Rabin[7]于1931年描述，并命名为“局限性纤维性间皮肿瘤（localized

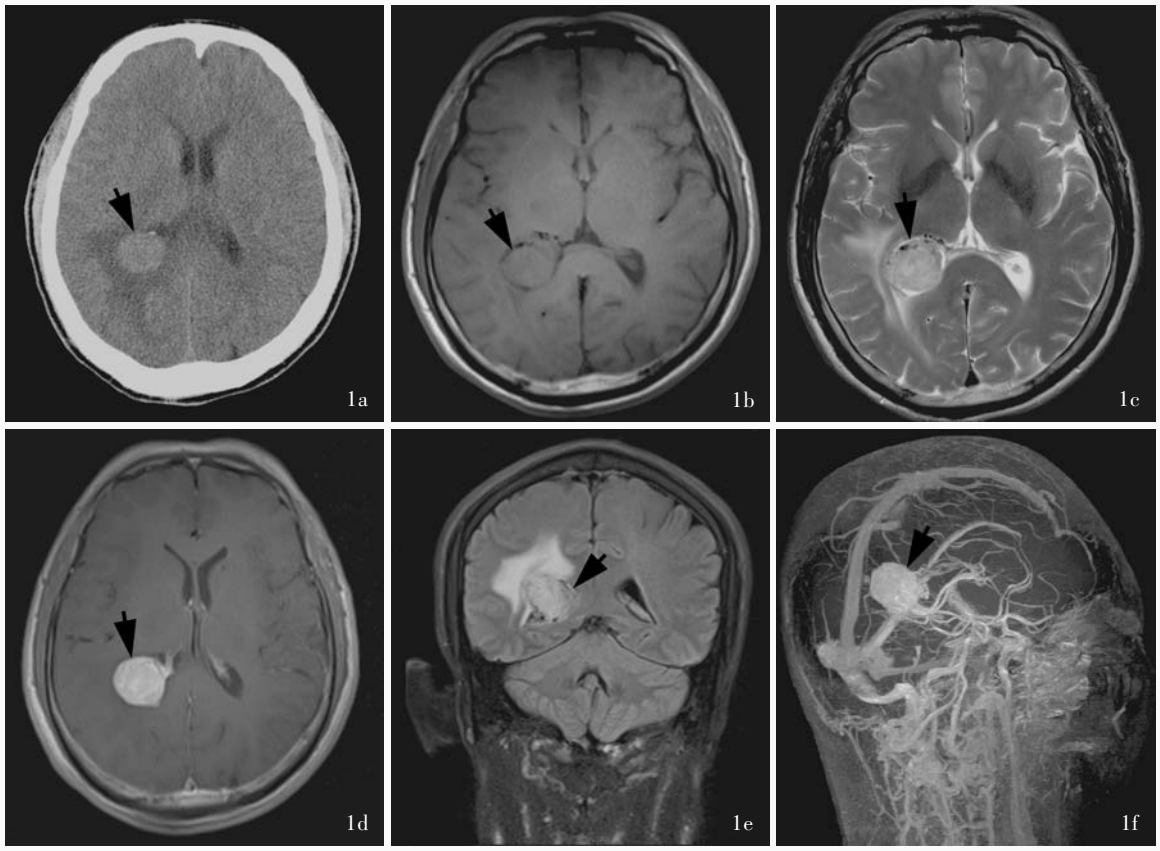
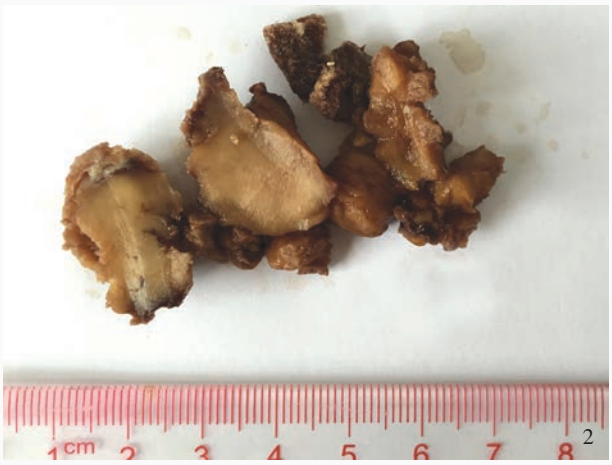
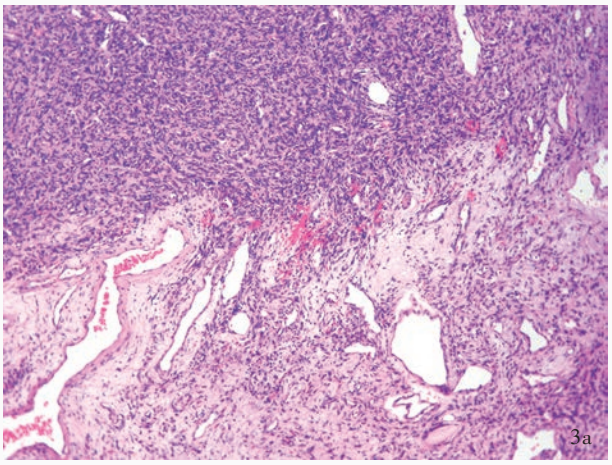


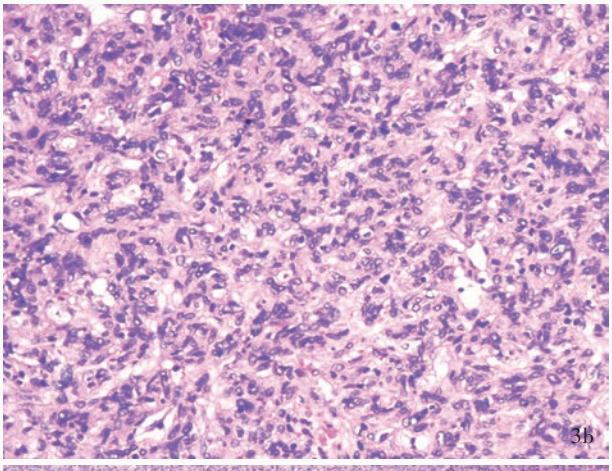
图1 头部影像学检查所见 1a 横断面CT显示，右侧侧脑室三角区内占位性病变（箭头所示），呈略高密度，边界清楚，周围脑组织轻度水肿 1b 横断面T_1WI显示，右侧侧脑室内结节状占位性病变（箭头所示），呈等信号，与周围脑组织分界清楚 1c 横断面T_2WI显示，病灶呈高低混杂信号，其内可见黑白相间的"阴阳征"（箭头所示） 1d 横断面增强T_1WI显示，病灶呈不均匀明显强化（箭头所示） 1e 冠状位增强T_1WI显示，病灶完全位于右侧侧脑室内，呈不均匀强化（箭头所示） 1f MRA显示，肿瘤血供丰富（箭头所示）

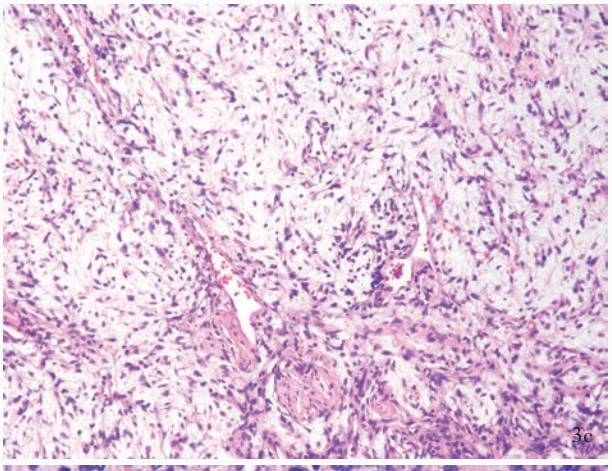
Figure 1 Preoperative cranial imaging findings. Axial CT demonstrated a space-occuping slightly high-density mass in the trigone of right lateral ventricle (arrow indicates) with clear boundary and mild edema surrounding the lesion (Panel 1a). Axial T_1WI demonstrated a well-defined, nodular and space-occupying lesion located in right lateral ventricle with isointense signal (arrow indicates, Panel 1b). Axial T_2WI showed a lesion with mixed hyperintensity and hypointensity signals with "black and white pattern" (arrow indicates, Panel 1c). Axial enhanced T_1WI showed a heterogeneous enhancing lesion (arrow indicates, Panel 1d). Coronal enhanced T_1WI showed the mass was located in right lateral ventricle entirely with heterogeneous enhancement (arrow indicates, Panel 1e). MRA displayed a highly vascularized lesion (arrow indicates, Panel 1f).

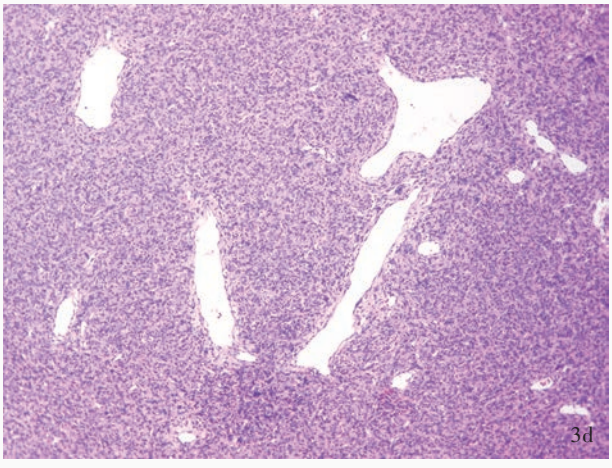
fibrous mesothelioma)"，由于肿瘤与胸膜相连且呈分界清楚的孤立性结节，故最初认为其由间皮细胞向纤维母细胞分化而来。但随后的研究发现，除胸膜外，孤立性纤维性肿瘤还可发生于全身各部位，而且免疫组织化学染色和超微结构观察显示肿瘤细胞既不表达间皮细胞标志物，也不具有间皮细胞的微绒毛特征[8-9]，提示孤立性纤维性肿瘤并非间皮细胞起源肿瘤，而可能起源于表达CD34的树突状间质细胞[10]。2002年WHO软组织肿瘤分类将胸膜外孤立性纤维性肿瘤（extrapleural SFT）确定为一种独立的中间型肿瘤类型而归类于纤维母细胞/肌纤维母细胞起源肿瘤，同时，由于其与血管周细胞瘤在组织学形态和免疫表型上存在延续和重叠，故二者共用同一疾病分类代码[1]。而在2007年WHO中枢神经系统肿瘤分类中，孤立性纤维性肿瘤和血管周细胞瘤则作为两种独立疾病实体，不但各有其独立的疾病分类代码，而且将孤立性纤维性肿瘤归类于中枢神经系统非脑膜上皮起源的间叶性肿瘤（WHO Ⅰ级），仅认为孤立性纤维性肿瘤与血管周细胞瘤之间可能存在过渡[11]。由于血管周细胞瘤并不显示任何血管周细胞的分化，实际上具有纤维母细胞的性质并与孤立性纤维性肿瘤存在组织学形态的延续和过渡[12-13]，因此在最新版的2012年WHO软组织肿瘤分类中，仅保留"胸膜外孤立性纤维性肿瘤"的名称，建议不再使用"血管周细胞瘤"的诊断术语，认为两种病变属同一肿瘤谱系[2]。我们考虑，











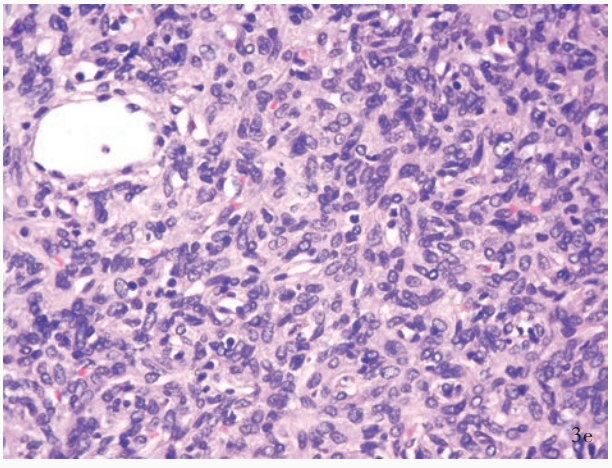


图2 大体标本观察显示，送检组织呈灰黄色、散块状、质地中等、无包膜，直径0.50～1.50 cm **图3** 光学显微镜观察所见 HE染色 3a 肿瘤组织由梭形细胞、胶原基质和丰富的血管构成，部分区域呈现典型的细胞丰富区和稀疏区交替分布构象。肿瘤组织内血管丰富，管壁可见胶原变性 ×200 3b 经典型孤立性纤维性肿瘤区域中梭形细胞弥漫性分布，呈无结构性生长，胞质较少，分界不清，胞核染色质均匀、异型性不明显 ×400 3c 部分区域间质呈明显黏液变性，表现为黏液性孤立性纤维性肿瘤的组织学构象 ×400 3d 部分区域肿瘤细胞密集分布，血管管径大小不等，可见“树枝”状或“鹿角”样分支，呈血管周细胞瘤样生长 ×200 3e 该区域肿瘤细胞仍为梭形，胞核轻度异型性，核分裂象不易见，未见出血坏死灶 ×400

Figure 2 General observation of samples revealed the lesion was small gray-yellow fragments and had no capsule, measuring 0.50–1.50 cm in diameter. **Figure 3** Optical microscopy findings. HE staining The mass was composed of spindle cells, dense collagenous matrix and prominent blood vessels. The alternating hypocellular and hypercellular areas, and perivascular hyalinization were found in the mass (Panel 3a). × 200 Tumor cells were spindle-shaped with limited cytoplasm, even chromatin and indistinct borders. The mass was lack of any specific arrangement resulting in a "patternless pattern" (Panel 3b). × 400 Myxoid matrix was observed in some areas, resembling myxoid variant of SFT (Panel 3c). × 400 In the hypercellular areas, "branching" or "staghorn" vessels could be seen, resembling hemangiopericytoma (Panel 3d). × 200 In hemangiopericytoma-like areas, the nuclei of spindle tumor cells showed mild atypia without active mitoses and necrosis (Panel 3e). × 400

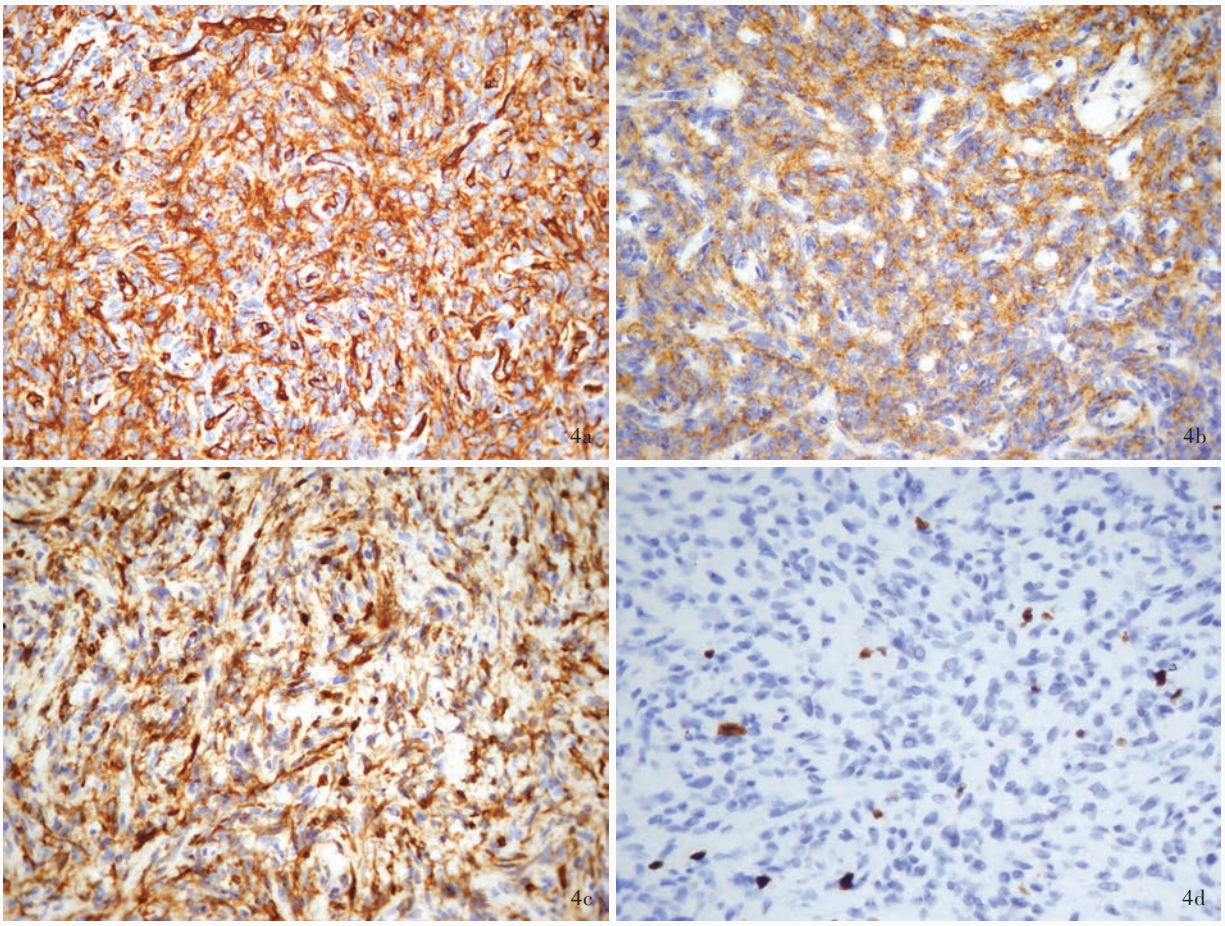


图4 光学显微镜观察所见 免疫组织化学染色(EnVision二步法) ×400 4a 肿瘤细胞弥漫性表达CD34 4b 肿瘤细胞弥漫性表达Bcl-2 4c 肿瘤细胞灶性表达CD99 4d 肿瘤细胞Ki-67抗原标记指数约为3%

Figure 4 Optical microscopy findings. Immunohistochemical staining (EnVision) ×400 The tumor cells were diffusely positive for CD34 (Panel 4a) and Bcl-2 (Panel 4b), and focally positive for CD99 (Panel 4c). Ki-67 labeling index was about 3% (Panel 4d).

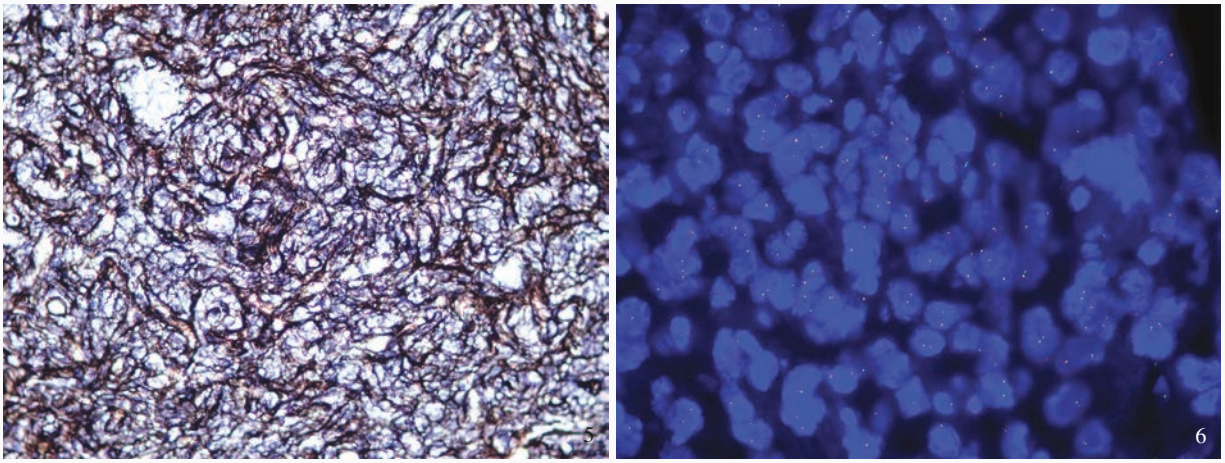


图5 光学显微镜观察显示,肿瘤组织内网状纤维丰富,肿瘤细胞周围均包绕网状纤维 网织纤维染色 ×400 **图6** 荧光显微镜观察显示,肿瘤细胞*SYT*基因断裂呈阴性,提示无t(X;18)(p11;q11)易位 荧光原位杂交染色 ×400

Figure 5 Optical microscopy findings. Rich reticular fibers within the tumor tissue could be seen, and tumor cells were surrounded by reticular fibers. Reticular fiber staining ×400 **Figure 6** Fluorescence microscopy showed negative result for *SYT* breaking, suggesting absence of t (X; 18) (p11; q11) in the tumor cells. FISH staining ×400

这一概念也应适用并贯穿于中枢神经系统孤立性纤维性肿瘤和血管周细胞瘤的诊断体系：(1)中枢神经系统孤立性纤维性肿瘤应属中间型肿瘤，并非单纯良性病变。(2)血管周细胞瘤与富细胞性孤立性纤维性肿瘤在组织学形态和免疫表型上存在延续和重叠。(3)建议对发生在中枢神经系统的疾病联合使用“孤立性纤维性肿瘤/血管周细胞瘤(WHO Ⅱ级)”或“恶性孤立性纤维性肿瘤/间变性血管周细胞瘤(WHOⅢ级)”的诊断术语。

中枢神经系统孤立性纤维性肿瘤临床较为罕见，Carneiro等[3]回顾既往65年(1930–1995年)的6348例中枢神经系统肿瘤患者，仅16例(0.25%)为孤立性纤维性肿瘤。Fargen等[14]和Bisceglia等[5]于2011年分别回顾近15年(1996–2011年)中枢神经系统孤立性纤维性肿瘤的发病情况，其结果显示：(1)多发生于30岁以上成人；儿童和青少年少见，不足10%。(2)无性别差异。(3)临床症状取决于肿瘤部位和大小，最为常见的症状为头痛(颅内病变)和颈背部疼痛(椎管内病变)，其他如视力障碍、感觉异常、运动障碍等均可发生，少数患者以颅内出血为首发症状。(4)大多数病变发生于颅内(幕上多见)，发生于椎管内者不足1/3(胸椎多见)；大部分肿瘤起源于硬脑膜，或与颅底、鞍底相连，少数发生于脑室内(5.90%)和脑实质内(1.40%)，与硬脑膜无关，个别发生于脑室内者与脉络丛相连，推测可能起源于脉络丛间质细胞[15-17]。(5)病灶均为孤立性结节，直径1～13 cm，约50%以上病灶直径＞5 cm，与周围脑组织分界清楚，部分有包膜，恶性孤立性纤维性肿瘤可侵犯颅骨和周围脑组织。(6)具有恶性生物学行为的孤立性纤维性肿瘤除在中枢神经系统内复发、播散外，少数还可发生远隔转移[18-19]。

孤立性纤维性肿瘤组织学形态多样，影像学表现也呈现多样化而缺乏特征性，因此，术前影像学检查虽可明确肿瘤大小及其与周围组织的关系，但难以定性诊断。附着于脑(脊)膜者易误诊为脑(脊)膜瘤，位于脑桥小脑角(CPA)者易误诊为神经鞘瘤，位于鞍区者易误诊为垂体腺瘤，发生于脑室内者少见，易误诊为脉络丛乳头状瘤、室管膜瘤、室管膜下瘤等。孤立性纤维性肿瘤CT表现为边界清楚的等密度结节，囊性变区域呈低密度，增强扫描呈不均匀强化；MRI表现为T_1WI等或稍低信号，T_2WI低或中低混杂信号，增强扫描呈不均匀强化，一般不出现“脑膜尾征”，可资与脑膜瘤相鉴别。Kim等[15]发现的孤立性纤维性肿瘤T_2WI“阴阳征”以及Weon等[20]发现的“黑白相间征”，即T_2WI显示肿瘤组织内高低信号交替征象，是诊断与鉴别诊断颅内孤立性纤维性肿瘤的重要影像学依据。Clarençon等[21]认为，T_2WI呈黑白相间的“阴阳征”和低信号区域在增强后呈明显强化、缺乏“脑膜尾征”、磁共振波谱(MRS)肌醇峰升高，均是孤立性纤维性肿瘤的特征性影像学表现，可资与脑膜瘤及其他梭形细胞肿瘤相鉴别。由于颅内和椎管内孤立性纤维性肿瘤组织中含有丰富血管，故全脑血管造影和MRA检查可见病变呈高度血管化，由颈内外动脉或椎-基底动脉系统供血，并常可见持续性强化征象[22]，与其他中枢神经系统间叶性梭形细胞肿瘤有所不同。因此，尽管颅内孤立性纤维性肿瘤术前难以明确诊断，具有上述特征时，经验丰富的神经外科医师和影像科医师仍会将该肿瘤作为重点考虑的病变加以鉴别[23]。

由于缺乏特征性影像学表现，中枢神经系统孤立性纤维性肿瘤的组织学诊断即显得尤为重要。孤立性纤维性肿瘤主要由3种成分构成，即梭形细胞、胶原基质和丰富的血管。这些成分在不同病例中的比例各不相同，导致不同病例之间、同一病例不同区域之间组织学构象截然不同。经典型孤立性纤维性肿瘤呈现细胞丰富区和稀疏区交替分布特征，肿瘤组织内血管丰富，管壁常见胶原变性；硬化性孤立性纤维性肿瘤则表现为肿瘤细胞间含粗细不等、形状不一的胶原纤维，甚至呈瘢痕样[24]；富细胞性孤立性纤维性肿瘤呈现形态单一的梭形细胞弥漫性分布构象，含管径大小不一的血管，呈“树枝”状或“鹿角”样，网织纤维染色可见网状纤维包绕肿瘤细胞，即血管周细胞瘤样组织学构象；黏液性孤立性纤维性肿瘤可见间质黏液变性；部分孤立性纤维性肿瘤可见含多核瘤巨细胞和假血管性裂隙，即巨细胞血管纤维瘤(GCA)，目前此类肿瘤也归于孤立性纤维性肿瘤的少见组织学形态；还有成脂性孤立性纤维性肿瘤(fat-forming SFT)，即在经典型或富细胞性孤立性纤维性肿瘤背景中出现脂肪细胞，这些脂肪细胞可散在或片状分布形成肿瘤主体，甚至掩盖其他肿瘤成分，即脂肪瘤样血管周细胞瘤(LHPC)[1-2]。由于组织学形态复杂多样，中枢神经系统孤立性纤维性肿瘤不同组织学形态所需鉴别的疾病有所不同：经典型孤立性纤维性肿瘤应注意与纤维性脑膜瘤相鉴别；硬化性孤立性纤维性

肿瘤应与侵袭性纤维瘤(纤维瘤病)相鉴别;富细胞性孤立性纤维性肿瘤应与单相性滑膜肉瘤、纤维肉瘤、纤维组织细胞瘤、低度恶性肌纤维母细胞肉瘤等相鉴别;黏液性孤立性纤维性肿瘤应与脊索瘤、脊索样脑膜瘤、黏液性神经纤维瘤、神经鞘瘤、恶性外周神经鞘膜瘤等相鉴别;成脂性孤立性纤维性肿瘤应与脂肪化生性脑膜瘤、梭形细胞脂肪瘤、脂肪肉瘤等相鉴别。尽管需要鉴别的疾病较多,但由于孤立性纤维性肿瘤较为特异的免疫表型,使得大部分疾病的鉴别诊断并不十分困难。有90%~95%的孤立性纤维性肿瘤弥漫性表达CD34,同时表达CD99和Bcl-2,约30%病例不同程度表达EMA和SMA,少数灶性表达Des、S-100和广谱细胞角蛋白(PCK)[2]。这些免疫学标志物的联合应用可以区别脑膜瘤、神经纤维瘤、神经鞘瘤、脊索瘤、脂肪肉瘤、纤维肉瘤等组织学形态相似的肿瘤。单相性滑膜肉瘤也可发生于硬脑膜,有血管周细胞瘤样外观且同时表达CD99和Bcl-2,与富细胞性孤立性纤维性肿瘤难以鉴别,但滑膜肉瘤一般不表达CD34,且90%以上者可见t(X;18)(p11;q11)易位,而孤立性纤维性肿瘤虽也可见2p21、6p11、9q22~23、9q22、12q15等基因异常[2],但从未见t(X;18)(p11;q11)易位,故荧光原位杂交检测*SYT*基因断裂有助于二者的鉴别诊断。本文患者肿瘤组织局部区域即为富细胞性孤立性纤维性肿瘤,与滑膜肉瘤相似,但肿瘤细胞弥漫性表达CD34,且*SYT*基因断裂阴性,故排除滑膜肉瘤的诊断。晚近研究显示,神经生长因子诱导基因A结合蛋白2(NAB2)-信号传导与转录激活因子6(STAT6)融合基因*NAB2-STAT6*可以作为孤立性纤维性肿瘤的特异性分子标志物,参与其发生与发展过程[25]。肿瘤细胞胞核表达STAT6蛋白可资与其他梭形细胞肿瘤相鉴别[26]。令人遗憾的是,由于缺少融合基因探针和抗体,本文患者未能检测*NAB2-STAT6*基因和STAT6蛋白表达水平,尚待进一步研究。

中枢神经系统孤立性纤维性肿瘤的诊断还应注意非典型组织学形态和恶性表现。Bisceglia等[5]于2011年回顾分析220例中枢神经系统孤立性纤维性肿瘤患者,其中有29例(13.18%)原发性孤立性纤维性肿瘤和5例(2.27%)复发性孤立性纤维性肿瘤患者出现一种以上不典型组织学形态,如细胞多形性、细胞密度增加、胞核异型性、核分裂象增多、坏死等。软组织非经典性和恶性孤立性纤维性肿瘤的组织学诊断标准已经明确,即在经典型孤立性纤维性肿瘤区域外,还可见细胞密度增加、核异型性明显、核分裂象增多(≥4/10个高倍视野),以及出血坏死灶,组织学形态类似纤维肉瘤或多形性未分化肉瘤(恶性纤维组织细胞瘤)成分,即可诊断为非经典性和恶性孤立性纤维性肿瘤[2],这一标准与2007年WHO中枢神经系统肿瘤分类中间变性血管周细胞瘤的诊断标准相一致[11],因此在诊断时可联合使用"恶性孤立性纤维性肿瘤/间变性血管周细胞瘤(WHOⅢ级)"的诊断术语。尽管非经典性和恶性孤立性纤维性肿瘤或肿瘤次全切除者常发生局部复发,一些良性孤立性纤维性肿瘤也可见复发和周围组织浸润破坏[27-28],侵犯脑实质和颅骨者一般预后不良,也进一步说明孤立性纤维性肿瘤是可复发的中间型肿瘤,而非单纯良性病变。因此,应区分孤立性纤维性肿瘤是自发性坏死还是放射治疗导致的坏死,前者是肿瘤呈恶性和高复发率的指标。此外,Ki-67抗原标记指数也有助于肿瘤预后的判断,即使没有明显的组织学变异型,如果Ki-67抗原标记指数>5%,仍高度提示预后不良,如脑实质浸润、脑脊液播散、颅内多发性转移等[5]。尽管目前普遍认为手术全切除的颅内和椎管内孤立性纤维性肿瘤无需术后辅助治疗,但如果肿瘤切除不完全、复发,特别是肿瘤具有较高的增殖指数时,提示除全切除肿瘤外还应予以更积极的辅助治疗,如放射治疗或伽玛刀治疗等[22,29-30]。本文患者组织学形态既无非经典性,Ki-67抗原标记指数亦未超过5%,故手术全切除后未予以放射治疗,需长期随访观察病情进展。

中枢神经系统,特别是脑室内原发性孤立性纤维性肿瘤临床罕见,由于缺乏特征性影像学表现和组织学形态复杂多样,术前诊断与鉴别诊断具有一定困难。因此,在诊断颅内和椎管内孤立性纤维性肿瘤时应提高警惕性,并注意与其他具有相似组织学形态的肿瘤相鉴别。由于组织学形态和免疫表型的延续和重叠,我们认为,中枢神经系统孤立性纤维性肿瘤与血管周细胞瘤属同一肿瘤谱系,但考虑到目前采用的WHO中枢神经系统肿瘤分类未明确将两种病变合并,故建议联合使用"孤立性纤维性肿瘤/血管周细胞瘤"的诊断术语。只有充分了解脑室内孤立性纤维性肿瘤的临床表现、影像学和组织病理学特征,才能避免可能出现的诊断陷阱而得出正确结论。

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（收稿日期：2015-07-31）