·临床病理报告·

鼻窦腺泡状软组织肉瘤

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【摘要】 **目的**　探讨腺泡状软组织肉瘤之临床病理学和免疫表型特征，以及诊断与鉴别诊断要点。**方法与结果**　女性患者，28岁，前额部隆起2个月。头部MRI显示左侧额窦和筛窦占位性病变，累及前颅底伴左侧额窦黏液囊肿。分次行鼻内镜下左侧筛窦、双侧额窦开放和肿瘤部分切除术，以及前颅底-筛窦-额窦肿瘤全切除术和前颅底重建术。组织学特征表现为肿瘤细胞排列成大小不等的腺泡样或器官样结构，被富含血窦样腔隙的纤维结缔组织分隔；细胞体积较大，呈圆形、卵圆形或多角形，胞质丰富呈嗜伊红颗粒状或半透明空泡状，胞核呈圆形或卵圆形，核仁清晰、居中；部分肿瘤组织内可见较多的单核和多核瘤巨细胞，染色质深染，核分裂象罕见；网织纤维包绕肿瘤细胞巢；肿瘤细胞胞质内可见高碘酸-雪夫染色阳性的结晶物质；肿瘤细胞表达TFE3，不表达胶质纤维酸性蛋白、黑色素细胞标志物（HMB45、Melan-A、S-100蛋白）和上皮细胞标志物（细胞角蛋白、上皮膜抗原），Ki-67抗原标记指数约为2%。**结论**　腺泡状软组织肉瘤好发于青少年，以大腿和臀部等深部软组织受累为主，发生于鼻窦或颅内者少见。明确诊断需结合组织病理学和免疫表型特征，应注意与其他组织结构相似的原发性或转移性肿瘤相鉴别。TFE3是腺泡状软组织肉瘤的特异性生物学标志物，*ASPL-TFE3*基因融合是其细胞遗传学特征。

【关键词】 肉瘤，软组织腺泡状；　鼻窦；　免疫组织化学；　病理学

Alveolar soft-part sarcoma in paranasal sinuses

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【**Abstract**】 **Objective**　To investigate clinicopathological features, immune phenotype, diagnosis and differential diagnosis of alveolar soft-part sarcoma (ASPS) in paranasal sinuses. **Methods**　Retrospective study of clinical manifestations, histopathological features and immunohistochemical features was conducted in one case of ASPS in paranasal sinuses. **Results**　A 28-year-old female presented with bulging forehead for 2 months. MRI revealed a well-circumscribed lesion in left frontal and ethmoid sinuses extending to anterior skull base that showed slightly hyperintense signal on T_1WI and hypointense signal on T_2WI without obvious enhancement after contrast administration. The patient subsequently underwent endoscopic open surgery on left ethmoid and bilateral frontal sinuses and performed partial resection of the lesion. Three months after the initial surgery, the patient received reoperation for total removal of residual lesion and reconstructive surgery of anterior skull base. Adjuvant chemotherapy and radiotherapy were not administered. Histologically, the tumor was composed of epithelioid cells arranged in organoid nests and/or alveolar structures varying in size and shape, which were separated by connective tissue richly containing sinusoidal vascular channels. The tumor cells were generally large-sized, round, oval or polygonal with abundant eosinophilic granular or translucent vacuolated cytoplasm. The nuclei showed round or oval shape containing centrally placed and obvious nucleoli. The presence a lot of mono- or multi-nuclear giant cells served as another striking feature. Mitotic activities were rare. Reticular fiber staining indicated that reticular fibers surrounded the nest of tumor cells, and diastase-resistant periodic acid-Schiff (PAS)-positive crystalline inclusions were identified within the cytoplasm of tumor cells. Immunohistochemically, the tumor cells were reactive for TFE3, while were negative for glial fibrillary acidic protein (GFAP), melanophore markers [HMB45, Melan-A and S-100 protein (S-100)], and epithelial markers [cytokeratin (CK) and epithelial membrane antigen (EMA)]. Ki-67 labeling index was low (2%). The patient remained

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well without recurrence 15 months after the second surgery. **Conclusions** ASPS is a rare malignant tumor that tends to occur in adolescents. The tumor is predominantly located in deep soft tissues, such as legs and buttocks. ASPS of paranasal sinus and/or extending to skull base is extremely rare. The accurate diagnosis of ASPS mainly depends on histological and immunohistochemical features, and should be considered in differential diagnosis including the similar morphological pattern of primary or metastatic neoplasms. ASPS is characterized by *ASPL-TFE3* gene fusions, and TFE3 protein is a specific marker for ASPS which displays nuclear labeling with TFE3 by immunohistochemistry.

【Key words】 Sarcoma, alveolar soft part; Paranasal sinuses; Immunohistochemistry; Pathology

腺泡状软组织肉瘤(ASPS)为临床少见恶性肿瘤,世界卫生组织(WHO)2013年公布的软组织与骨肿瘤分类将其定义为上皮样肿瘤,组织病理学表现以相对一致、较大且富于嗜酸性和颗粒性胞质的上皮细胞样肿瘤组织呈实性巢状和(或)腺泡状结构为特征[1]。其发病率占软组织肉瘤的0.50%~1.00%[2],任何年龄均可发病,高峰发病年龄为15~35岁,女性多见[3],30岁以下患者中男女发病比例约为1∶2,30岁以上患者中男性略高于女性[4-5];成年患者以大腿或臀部等深部软组织好发[6-7],儿童和婴幼儿则以头颈部多见,特别是舌和眼眶为最常见原发部位[1],其他少见部位包括肺[8]、胃[9]、肝脏[10]、乳腺[11]、心脏[12]、膀胱[13]、肾脏[14],以及女性生殖系统[15]。原发于鼻窦和颅底的腺泡状软组织肉瘤临床少见,本文报告1例发生于鼻窦并累及颅底的腺泡状软组织肉瘤患者,对其临床病理学特点和免疫表型进行分析,并结合文献探讨与组织形态学相似肿瘤的鉴别诊断。

病历摘要

患者 女性,28岁。主因前额部隆起2个月,于2013年9月20日入院。患者2个月前无意中发现前额部隆起,无视力下降、复视。当地医院头部MRI检查显示额窦和筛窦占位性病变,可疑嗅神经母细胞瘤侵犯鼻窦,伴左侧上额窦黏液囊肿。为求进一步诊断与治疗遂入我院。患者自发病以来,无头痛、头晕,无恶心、呕吐,无视力、意识和精神障碍,睡眠、饮食尚可,大小便正常,发病以来体重无明显变化。

既往史、个人史及家族史 患者既往体格健康,曾于5个月前行剖宫产术。个人史和家族史均无特殊。

体格检查 患者体温36.5 ℃,脉搏83次/min,呼吸18次/min,血压116/63 mm Hg(1 mm Hg = 0.133 kPa)。神志清楚,一般状况良好。神经系统检查未发现明显异常。头颈部检查鼻外观无畸形,双侧鼻腔黏膜慢性充血,鼻中隔无偏曲,左侧中鼻甲外侧可见淡红色肿物,鼻道无脓性分泌物;额窦隆起,质地较硬,各鼻窦区无压痛。耳、咽、喉检查未见明显异常。

诊断与治疗经过 入院后头部MRI显示,左侧筛窦、额窦和前颅底占位性病变(图1)。临床诊断:左侧筛窦、额窦和前颅底占位性病变,考虑嗅神经母细胞瘤。于2013年9月10日转入耳鼻咽喉头颈外科,5 d后全身麻醉下经鼻内镜行左侧筛窦、双侧额窦开放和占位性病变部分切除术。术中见肿瘤淡红色,质地较软,有部分包膜,局部侵犯额窦后壁骨质,与硬脑膜粘连,血供丰富。术中冰冻病理检查考虑脑膜来源肿瘤。术后病理检查考虑肌周皮细胞瘤,不排除颗粒细胞瘤。于2013年12月18日再次入神经外科,全身麻醉下行前颅底-筛窦-额窦肿瘤全切除术和前颅底重建术。术中可见额窦扩大,其内可见灰白色肿瘤组织,部分有包膜,与额窦粘连、质地中等,血供丰富,肿瘤组织侵蚀筛板。术中将额窦、筛窦内黏膜刮除干净,并磨除肿瘤侵蚀的额窦后壁、筛板等骨质,全切除肿瘤。行组织病理学检查。(1)大体标本观察:两次手术切除标本均为灰黄、灰白色破碎组织块,大小分别为2.80 cm×2.00 cm×1.80 cm和4 cm×4 cm×4 cm,质地柔软。经体积分数为10%中性甲醛溶液固定、常规脱水、石蜡包埋、4 μm连续切片,分别行HE染色和免疫组织化学染色。(2)HE染色:肿瘤细胞排列成大小不等的腺泡样或器官样结构,被富含血窦样腔隙的纤维结缔组织分隔;肿瘤细胞体积较大,呈圆形、卵圆形或多角形,胞质丰富呈嗜伊红颗粒状或半透明空泡状,胞核呈圆形或卵圆形,核仁清晰、居中。部分区域可见较多单核和多核瘤巨细胞,染色质深染,核分裂象罕见(图2)。(3)免疫组织化学染色:采用

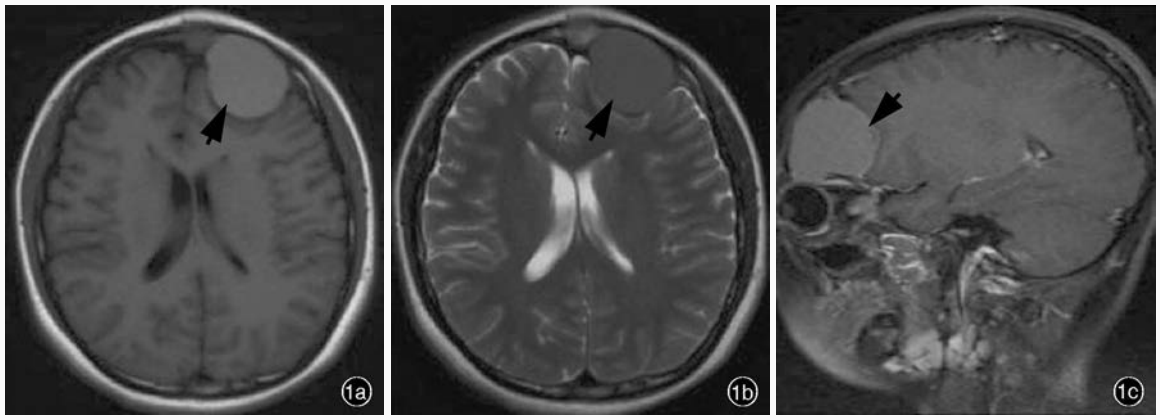

图1　头部MRI检查所见　1a　横断面T_1WI显示，左侧额窦和前颅底类圆形稍高信号影（箭头所示），与脑组织界限清晰　1b　横断面T_2WI显示，左侧额窦和前颅底类圆形稍低信号影，强度均匀（箭头所示）　1c　矢状位增强T_1WI显示，病灶无明显强化（箭头所示）

Figure 1　Cranial MRI findings. Axial T_1WI demonstrated a solid and round-shaped well-demarcated lesion showing slightly hyperintense signal (arrow indicates) in the left frontal sinus and anterior skull base. The adjacent normal brain tissue was compressed by the lesion (Panel 1a). Axial T_2WI showed hypointense signal of the lesion (arrow indicates, Panel 1b). Sagittal contrast-enhanced T_1WI showed no obvious enhancement of the lesion (arrow indicates, Panel 1c).

SP-9000通用型免疫组织化学检测试剂盒（北京中杉金桥生物技术有限公司），检测用抗体TFE3（1∶250）、CD56（1∶100）、波形蛋白（Vim，1∶400）、突触素（Syn，1∶100）、神经元特异性烯醇化酶（NSE，1∶75）、平滑肌肌动蛋白（SMA，1∶400）、结蛋白（Des，1∶200）、肌调蛋白（MyoD1，1∶150）、P53（1∶75），胶质纤维酸性蛋白（GFAP，1∶400）、异柠檬酸脱氢酶1（IDH1，1∶200）、人绒毛膜促性腺激素（hCG，工作液滴度）、淋巴管内皮细胞标志物D2-40（1∶100）、HMB45（1∶50）、Melan-A（1∶150）、S-100蛋白（S-100，1∶2000）、CD68（1∶100）、α1-抗胰蛋白酶（α1-AT，工作液滴度）、CD31（1∶40）、CD34（1∶100）、细胞角蛋白（CK，1∶200）、上皮膜抗原（EMA，1∶200），以及Ki-67抗原均购自北京中杉金桥生物技术有限公司。结果显示：肿瘤细胞胞核表达TFE3，阳性率约50%（图3a），胞质表达CD56，少数肿瘤细胞表达Vim、Syn、NSE和SMA（图3b），肿瘤组织富血窦，内皮细胞表达CD34（图3c），P53阳性率约3%，Ki-67抗原标记指数约为2%（图3d）；肿瘤细胞不表达神经胶质细胞标志物（GFAP、IDH1），肌源性标志物（Des、MyoD1），生殖细胞标志物（hCG），淋巴管内皮细胞标志物（D2-40），黑色素细胞标志物（HMB45、Melan-A、S-100），组织细胞标志物（CD68、α1-AT），以及上皮细胞标志物（CK、EMA）。（4）特殊染色：网织纤维染色显示，网织纤维包绕肿瘤细胞巢（图4a）。消化后高碘酸-雪夫（PAS）染色肿瘤细胞胞质内可见阳性的结晶状物质（图4b）。最终病理诊断：（左侧筛窦、额窦和前颅底）腺泡状软组织肉瘤。术后患者病情稳定，未辅助放射治疗和药物化疗。随访15个月肿瘤无复发。

讨　论

1952年，Christopherson等[16]首次报告12例组织来源不明、呈腺泡状或器官样排列的软组织恶性肿瘤，称为腺泡状软组织肉瘤。2013年世界卫生组织软组织和骨肿瘤分类将其归为未能确定分化的肿瘤[1]。

典型腺泡状软组织肉瘤的组织学形态呈器官样、巢状或腺泡状结构排列，被富含血窦样腔隙的纤维结缔组织分隔，大小和形态各异，但相对一致。常规组织学诊断主要依据上述腺泡状结构[2]，但是若组织标本取材不当，缺乏上述典型腺泡状结构，或细胞形态发生变异，出现胞质内空泡、多核瘤巨细胞、横纹肌样细胞和间变特征[7]，或肿瘤发生于头颈部和四肢以外的少见部位，均可能导致诊断困难甚至误诊。据文献报道，约有22%的患者肿瘤细胞胞质内可见特征性菱形或棒状结晶体，数量不等，消化后PAS染色较HE染色更易于观察且有助于诊断[3]。

腺泡状软组织肉瘤起源不明，肿瘤细胞表达肌源性标志物，曾认为起源于肌肉组织，但仅有50%的患者表达Des且常为局限性[1]。部分病例肿瘤细

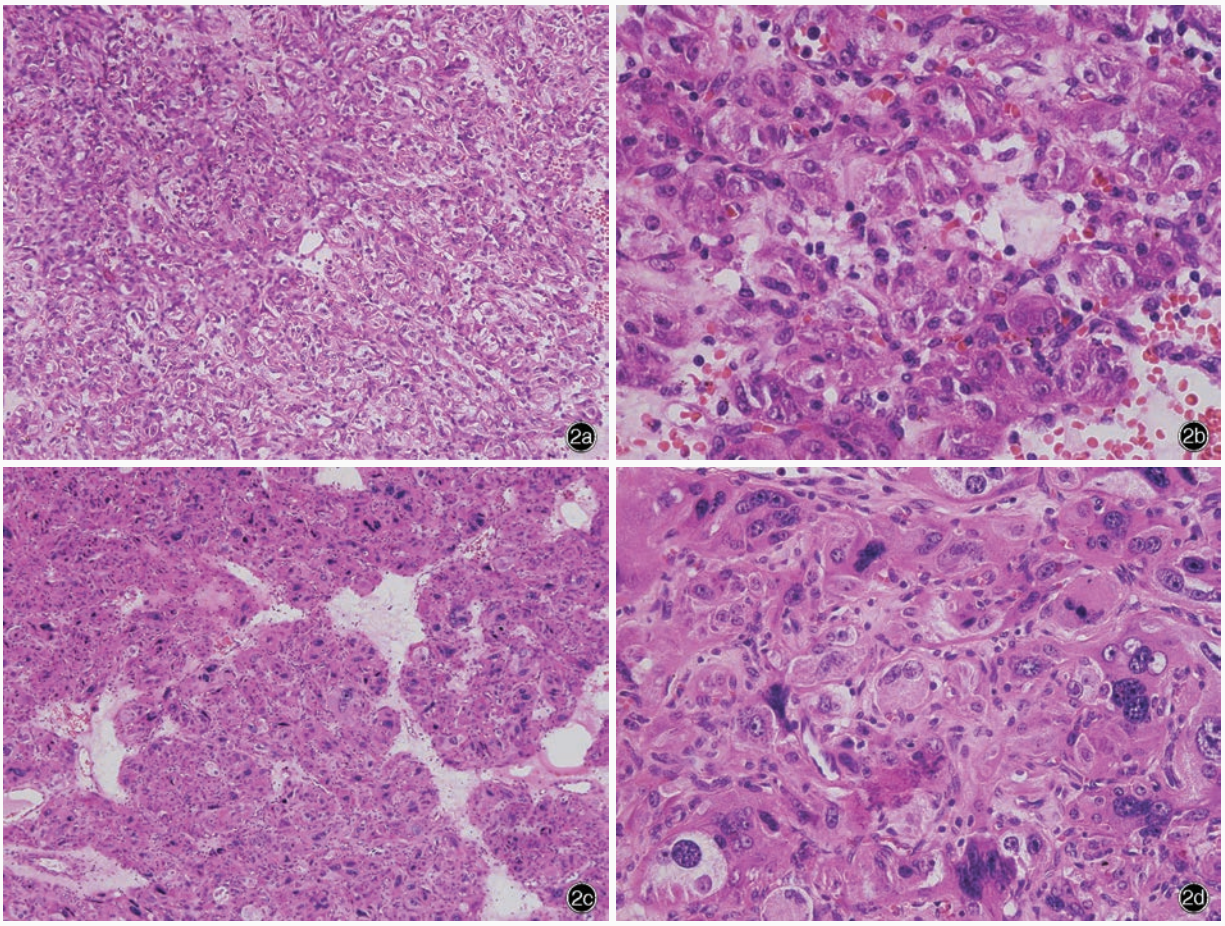

图2 光学显微镜观察所见 HE染色 2a 肿瘤细胞排列成腺泡样或器官样结构，被富含血窦样腔隙的纤维结缔组织分隔 ×100 2b 肿瘤细胞呈圆形或卵圆形，胞质丰富呈嗜伊红颗粒状或透明空泡状，胞核呈圆形或卵圆形，可见居中的小核仁 ×400 2c 肿瘤细胞体积较大，胞质呈嗜酸性或泡沫状。肿瘤细胞为多形性，可见较多的单核和多核瘤巨细胞，染色质深染 ×200 2d 多核瘤巨细胞胞核为圆形，核仁嗜酸性，核分裂象罕见 ×400

Figure 2 Optical microscopy findings. HE staining The tumor was composed of alveolar or organic patterns separated by fibrous connective tissue richly in sinusoidal vascular channels (Panel 2a). ×100 The tumor cells were round or oval and had abundant eosinophilic granular or clearly vacuolated cytoplasm. Nuclei were round or oval with small centrally-located nucleoli (Panel 2b). ×400 The tumor cells were large-sized with abundant eosinophilic or foamy cytoplasm, and showed pleomorphism with mono- or multi-nuclear giant cells and hyperchromatic nuclei (Panel 2c). ×200 Multi-nuclear giant cells displayed round nuclei with small eosinophilic nucleoli. No mitoses was seen (Panel 2d). ×400

胞表达MyoD1，20%～30%的病例表达SMA，30%～50%的病例表达NSE和Vim。腺泡状软组织肉瘤不表达上皮细胞标志物（CK和EMA）、神经内分泌标志物（Syn和CgA），以及黑色素细胞标志物（HMB45和Melan-A）[17]。研究显示，*TFE3*融合基因产生的融合蛋白可被抗TFE3多克隆抗体标记，用于腺泡状软组织肉瘤的诊断。抗TFE3多克隆抗体诊断腺泡状软组织肉瘤灵敏度为97.50%、特异度为99.60%[18]。对于发生于少见部位且组织病理学表现不典型的病例，肿瘤细胞胞核TFE3呈弥漫性强阳性，提示腺泡状软组织肉瘤[7,19]。

腺泡状软组织肉瘤发病原因与不平衡染色体易位t(X;17)(p11;q25)有关[20]，导致位于Xp11的*TFE3*基因与位于17q25的*ASPL*基因融合，形成ASPL-TFE3融合蛋白，定位于细胞核，具有异常转录因子功能，从而导致腺泡状软组织肉瘤[21]。

据文献报道，首发于鼻腔或鼻窦区的腺泡状软组织肉瘤临床少见[5,22-23]。该例患者诊断困难是由于肿瘤发生在少见部位，肿瘤细胞多形性明显，可见多核瘤巨细胞，HE染色未见明确的胞质内棒状结晶体。根据腺泡状软组织肉瘤的临床表现和组织病理学特征，应注意与下列疾病进行鉴别。(1)副神经节瘤：可发生于任何年龄阶段，肿瘤主要沿交感神经纤维分布，好发于颅底至盆腔底的任何部

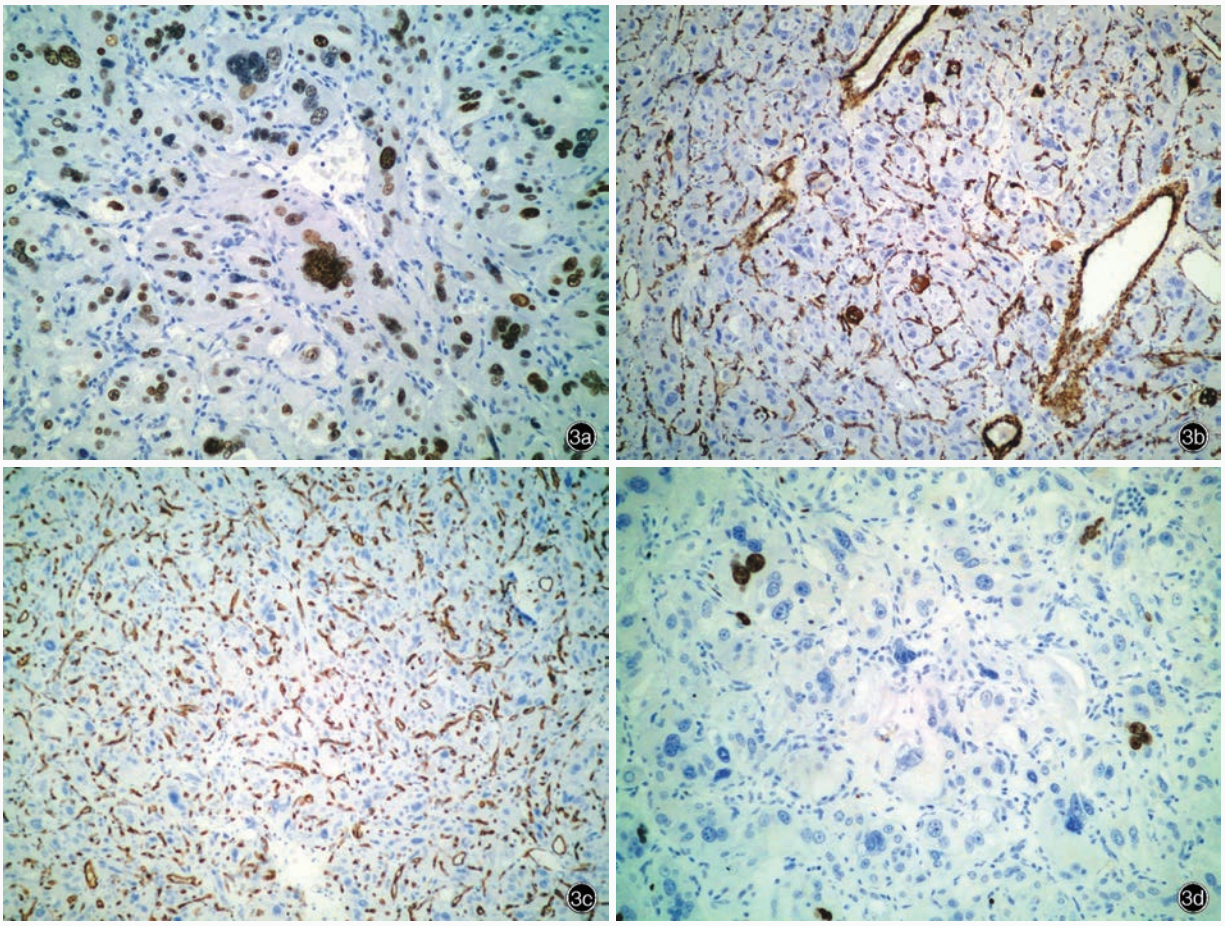

图3　光学显微镜观察所见　免疫组织化学染色(SP二步法)　3a　肿瘤细胞胞核表达TFE3,阳性率约为50%　×400　3b　少数肿瘤细胞表达SMA　×100　3c　肿瘤组织富于血窦,内皮细胞表达CD34　×100　3d　Ki-67抗原标记指数约为2%　×400

Figure 3　Optical microscopy findings.　Immunohistochemical staining (SP)　The positive rate of TFE3 in the nuclei of tumor cells was about 50% (Panel 3a).　×400　A few tumor cells were positive for SMA (Panel 3b).　×100　The tumor tissue contained various vascular sinuses, and endothelial cells were positive for CD34 (Panel 3c).　×100　Ki-67 labeling index was about 2% (Panel 3d).　×400

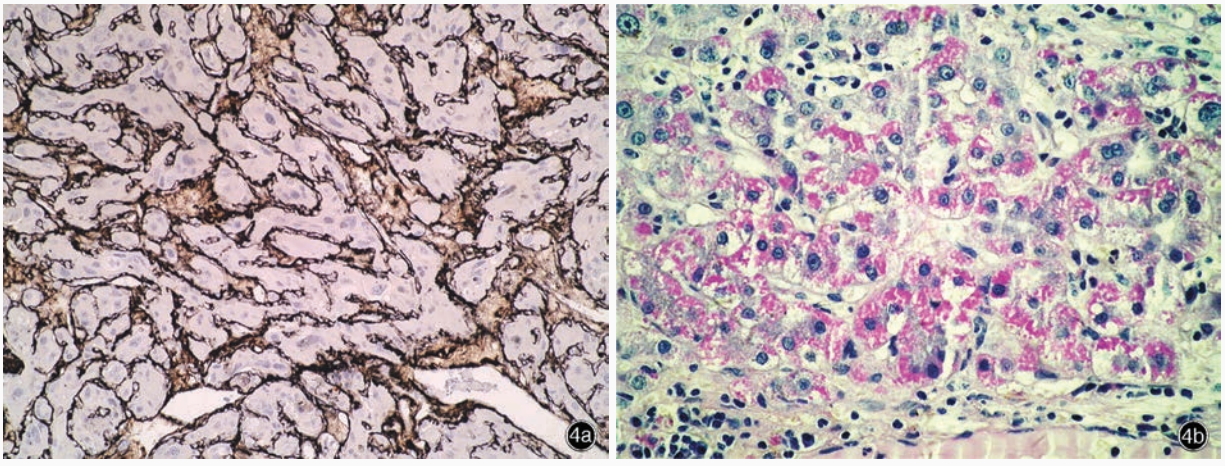

图4　光学显微镜观察所见　4a　网织纤维包绕肿瘤细胞巢　网织纤维染色　×100　4b　肿瘤细胞胞质内可见PAS阳性结晶物质　PAS染色　×400

Figure 4　Optical microscopy findings.　Reticular fibers enveloped the nests of tumor cells (Panel 4a).　Reticular fiber staining　×100　Diastase-resistant PAS-positive crystalline inclusions were identified within the cytoplasm of tumor cells (Panel 4b).　PAS staining　×400

位；肿瘤实质由器官样或小梁状结构的卵圆形或多边形主细胞与位于周围的梭形支持细胞组成；网织纤维染色可见清晰的器官样结构，其间为纤维血管性间质；肿瘤细胞胞质嗜酸性、略呈颗粒状，胞质内可见玻璃样小体；部分肿瘤细胞呈空泡状或透明状，可见胞核异形、核仁居中，染色质较均匀或呈点彩状，偶见核内假包涵体；肿瘤细胞表达CgA、NSE、Syn等神经内分泌标志物，支持细胞表达S-100。腺泡状软组织肉瘤好发于四肢和头颈部，位于肌肉深部组织，肿瘤细胞巢大小不一，胞质内可见PAS染色阳性的棒状结晶体，肿瘤细胞表达MyoD1和SMA，特别是胞核呈TFE3强阳性，不表达CgA、NSE和Syn。(2)肾上腺皮质癌：临床罕见，发病年龄40～50岁，常伴腹部包块或远隔转移；大部分肿瘤细胞分泌激素并伴功能性皮质醇分泌，导致男性化；肿瘤以较宽的纤维条带分隔为特征，可见实性或腺泡样结构，肿瘤细胞与正常皮脂腺细胞相似，胞核异型性明显，非典型核分裂象多见；肿瘤细胞内可见嗜酸性透明球状小体，PAS染色阳性；表达Vim、抑制素-α(inhibin-α)和Melan-A。腺泡状软组织肉瘤呈现巢状或器官样结构，被纤细的血窦样腔隙分隔；肿瘤巢中心黏附性较差，可形成腺泡样结构；肿瘤细胞胞质内可见棒状结晶体，PAS消化后呈阳性，肿瘤细胞不同程度表达Des，胞质表达MyoD1，不表达inhibin-α和Melan-A。(3)颗粒细胞瘤：以中老年患者多见，发病部位与腺泡状软组织肉瘤相似，好发于头颈部、四肢、躯干皮肤和皮下组织，尤以舌部好发；肿瘤直径一般小于3 cm，呈片状、巢状或梁索状排列，间质缺乏血窦，器官样排列不明显；肿瘤细胞体积较大，呈多角形、圆形或卵圆形，胞质丰富，呈嗜酸性、颗粒状，可见空泡状胞核，核仁不明显；肿瘤细胞S-100呈强阳性，同时表达CD68、NSE和TEF3[18]，胞质PAS染色阳性，电子显微镜观察可见胞质内有丰富的溶酶体。腺泡状软组织肉瘤为器官样结构，间质富于血窦样毛细血管网，肿瘤细胞胞质可见棒状结晶体，PAS染色消化后呈阳性；棒状结晶体由单层膜包绕，呈纤维状网格结构，直径4.50～5.00 nm[2,17]。(4)腺泡状横纹肌肉瘤：好发于10～25岁青少年，多位于四肢深部软组织、其次为头颈部；肿瘤细胞排列成腺泡状或巢状，巢中央肿瘤细胞因退行性变和坏死而失去黏附性致脱落，形成特征性腺泡状结构；腺泡间为纤维血管间隔，而器官样结构不明显，缺乏窦状血管网；肿瘤由原始小圆形细胞和幼稚横纹肌母细胞组成，前者形似原始神经外胚层肿瘤细胞，部分患者可见散在胞质嗜酸性的横纹肌母细胞，以及由横纹肌母细胞融合的多核巨细胞；肿瘤细胞表达Des、肌浆蛋白、SMA和MyoD1，其中MyoD1为胞核表达。腺泡状软组织肉瘤含丰富血窦样毛细血管网，形成特殊的器官样结构，肿瘤细胞胞质丰富，PAS染色可见棒状或菱形结晶体；部分患者胞质MyoD1表达阳性，胞核TFE3呈强阳性，可资鉴别。(5)肾透明细胞癌：原发性肾透明细胞癌因肾区或腹部包块形成，经影像学检查不难作出诊断。腺泡状软组织肉瘤主要应与发生远隔转移的肾透明细胞癌相鉴别。后者好发于成人，血尿为其临床常见症状；肿瘤细胞可呈巢状、片状或腺泡状排列，由纤细的分枝状小血管网分隔，胞质透亮，无PAS染色阳性的结晶体；肿瘤细胞表达EMA、PCK、CD10和肾细胞癌标志物(RCC、Vim)。此外，还应与Xp11.2易位/*TFE3*融合基因相关性肾癌相鉴别。后者好发于儿童和青少年，呈乳头状或巢状结构，肿瘤细胞呈透明状或嗜酸性，伴沙粒体或透明小体。免疫组织化学染色EMA阴性或呈局灶性阳性，CAM5.2、Vim和CD10、RCC阳性，TFE3亦阳性[18,21,24]。腺泡状软组织肉瘤为器官样和腺泡状结构，被血窦样腔隙的纤维结缔组织分隔，肿瘤细胞胞质可见特征性PAS染色阳性的菱形或棒状结晶体，MyoD1、SMA表达阳性，CD10、RCC和EMA阴性。(6)血管周上皮样细胞肿瘤(PEComa)[25]：以女性多见，好发于子宫和镰状韧带，其他软组织和内脏少见；肿瘤富于薄壁血管，管壁与卵圆形上皮样或梭形肿瘤细胞相融合，上皮样肿瘤细胞胞质透明、梭形肿瘤细胞胞质呈嗜酸性颗粒状，组织学形态与腺泡状软组织肉瘤相似；胞核小且居中，可见核仁；肿瘤细胞表达黑色素细胞标志物，95%以上的病例HMB45阳性，并不同程度表达Melan-A、小眼相关转录因子(MITF)和S-100，以及肌源性标志物Des和SMA，约有10%的病例表达TFE3[26]。腺泡状软组织肉瘤黑色素细胞标志物表达阴性，可资鉴别。

腺泡状软组织肉瘤为相对惰性的恶性肿瘤，生长缓慢，至晚期可发生远隔部位转移，转移率为20%～40%[6]；以血行转移为主，常见的转移部位分别为肺(100%)、淋巴结(74%)、骨骼(57%)和脑(43%)，临床常以肺、骨骼或脑转移为首发症状[8]，约有1/3的患者于明确诊断时即已经发生肺或脑转移[17,27]。2、5、10和20年生存率分别为77%、60%、

38%和15%[3]。腺泡状软组织肉瘤的治疗主要采取病灶根治性切除手术，术后是否辅助放射治疗和药物化疗，尚未肯定。晚近文献报道，多靶点酪氨酸激酶抑制剂舒尼替尼对腺泡状软组织肉瘤具有一定疗效[28-29]。本文患者术后未接受放射治疗、药物化疗或靶向治疗，随访15个月，肿瘤无复发，一般状况良好。

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·临床医学图像·

生长激素腺瘤

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Growth hormone producing adenoma

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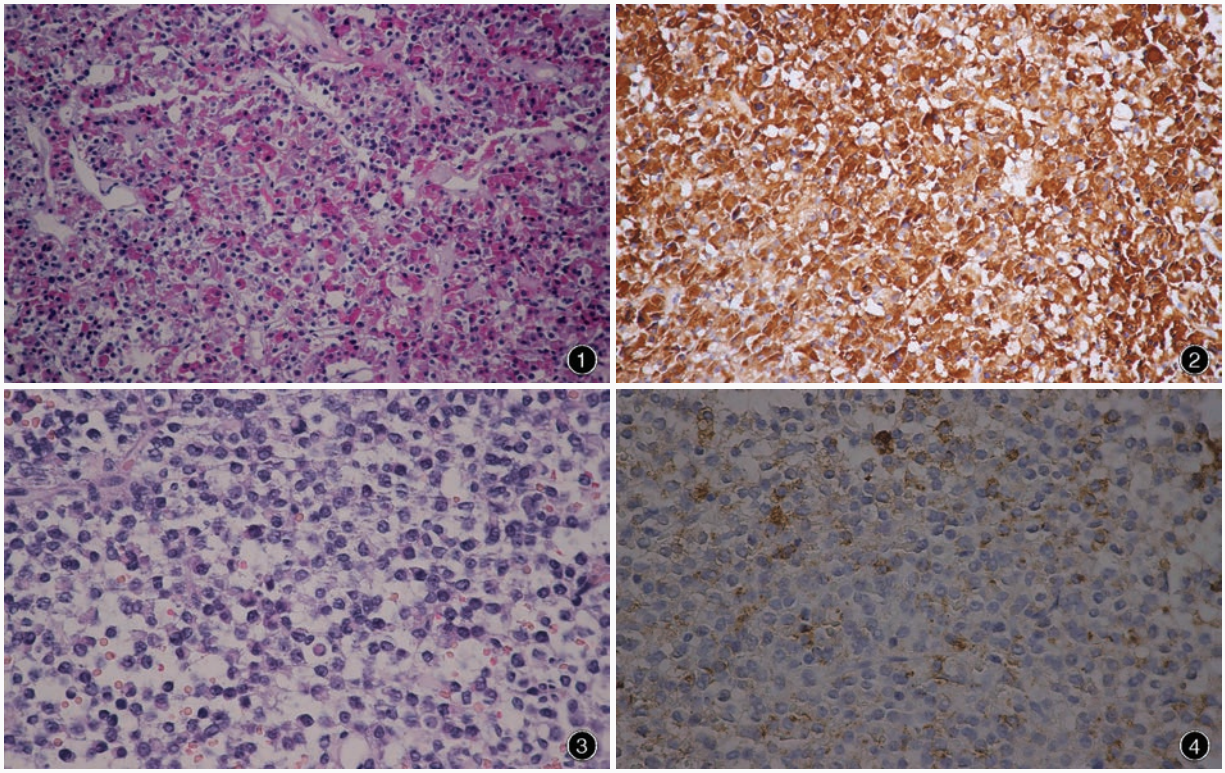

图1 光学显微镜观察显示，密颗粒型生长激素腺瘤细胞呈巢状，胞质呈强嗜酸性 HE染色 中倍放大 **图2** 光学显微镜观察显示，密颗粒型肿瘤细胞GH呈一致性弥漫性强阳性 免疫组织化学染色（SP二步法） 中倍放大 **图3** 光学显微镜观察显示，疏颗粒型生长激素腺瘤细胞中等大小、呈圆形，主要特征为嗜酸性纤维小体造成的核内凹 HE染色 高倍放大 **图4** 光学显微镜观察显示，疏颗粒型生长激素腺瘤细胞少量表达GH 免疫组织化学染色（SP二步法） 高倍放大

Figure 1 Optical microscopy findings. The densely granulated somatotroph adenoma cells formed as nest and had abundant strongly acidophilic cytoplasms. HE staining medium power magnified **Figure 2** Optical microscopy findings. The densely granulated cells showed strong, uniform and diffuse positivity for GH. Immunohistochemical staining (SP) medium power magnified **Figure 3** Optical microscopy findings. The sparsely granulated tumor cells were medium sized and round, mainly characterized by nuclear indentations by acidophilic fibrous bodies. HE staining high power magnified **Figure 4** Optical microscopy findings. The sparsely granulated cells showed scant immunoreactivity for GH. Immunohistochemical staining (SP) high power magnified

分泌生长激素（GH）的垂体腺瘤可随发病年龄出现巨人症或肢端肥大症，无功能病例少见。纯生长激素腺瘤是由单一分泌生长激素的肿瘤细胞组成，分为密颗粒型和疏颗粒型。密颗粒型生长激素腺瘤由中等大小、圆形或多角形嗜酸性肿瘤细胞组成，呈弥漫性生长，胞质呈颗粒状，胞核圆形，染色质纤细、松散，核仁明显（图1）。胞质GH呈一致性弥漫性强阳性（图2）。疏颗粒型生长激素腺瘤是嫌色性腺瘤，肿瘤细胞较小、呈圆形，部分含明显核仁，核周胞质区的淡嗜酸性纤维小体即圆形包涵体是其诊断特征（图3）。纤维小体挤压胞核向外周移动，呈新月形。胞质GH表达不一致，常较稀少（图4）。

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