

· 临床病理报告 ·

【编者按】首都医科大学宣武医院报告 1 例临床罕见的存在脊髓压迫症状的脊柱痛风石患者。在病理学方面,通过对病例术中冰冻病理学和手术切除组织病理学检查,表明痛风石在不同状态下具有不同形态学特点,其中,术中送检的新鲜标本在光学显微镜下可见痛风石呈棕色线样结晶,偏振光显微镜下呈双折光性;而经甲醛溶液固定的石蜡切片,由于单钠尿酸盐结晶的溶解,在光学显微镜下痛风石转变为白色不定形物质,偏振光显微镜下呈单折光性。提示在病理学诊断过程中应考虑到组织的理化特性和组织处理过程对组织形态的改变。在临床表现方面,提示在存在脊髓压迫症状的椎管内硬膜外病变的鉴别诊断中,除外结核病、中枢神经系统淋巴瘤、转移瘤和脂肪瘤等,还应结合患者病史和血清尿酸等相关实验室检查,排除脊柱痛风石形成的可能。因此,该病例具有一定的临床和病理学价值,值得病理科和神经内外科医师借鉴。

存在脊髓压迫症状的脊柱痛风石

李卓 王玮 付永娟 卢德宏

【摘要】目的 报告 1 例发生于胸椎的椎管内痛风石患者的临床特点、病理学特征、诊断与治疗要点,以期提高对该病的认识。方法与结果 男性患者,36 岁,临床表现为双下肢无力伴麻木 2 个月、加重 2 周,胸椎 MRI 显示 T₉₋₁₀ 平面椎管内外沟通性占位性病变。手术分块全切除病变。冰冻病理学检查,纤维结缔组织内可见棕色线样结晶,局部累及骨组织,周围异物肉芽肿形成;棕色线样结晶于偏振光显微镜下呈双折光性。手术切除标本病理学检查可见白色不定形物质,其间散在少量残留的棕色线样晶体;白色不定形物质于偏振光显微镜下呈单折光性。最终病理诊断为痛风石形成。随访 6 个月,可辅助拐杖行走。结论 脊柱痛风石为尿酸盐结晶沉积于脊柱关节内所致,应与结核病、中枢神经系统淋巴瘤、转移瘤、脂肪瘤等椎管内硬脊膜外占位性病变相鉴别,穿刺活检术或手术发现尿酸盐结晶可明确诊断。

【关键词】 痛风; 胸椎; 病理学

Tophaceous gout of spine causing neural compression

LI Zhuo, WANG Wei, FU Yong-juan, LU De-hong

Department of Pathology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

Corresponding author: LU De-hong (Email: ludehong05@sina.com.cn)

【Abstract】 Objective To investigate the imaging and clinicopathological features of spinal tophaceous gout in thoracic vertebra and the key points of its diagnosis and treatment, in order to improve the recognition of this disease. Methods and Results A 36-year-old male was admitted because of weakness and numbness of both lower extremities for 2 months with progressive aggravation for 2 weeks. MRI revealed an extradural mass compressing the spinal cord at T₉₋₁₀. The tumor was totally removed by piecemeal resection. Histopathological examination of the fresh specimen by light microscope demonstrated brown linear crystals, which showed strong birefringence in polarized light microscope, located in fibrous connective tissue, with local bone invasion and foreign body granuloma. However, histopathological examination of the removed specimen demonstrated white amorphous materials, with scatteredly distributed remaining brown linear crystals, which showed single refraction in polarized light microscope. The final pathological diagnosis was tophaceous gout. The patient was followed-up for 6 months. He stopped taking

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作者单位:100053 北京,首都医科大学宣武医院病理科

通讯作者:卢德宏 (Email:ludehong05@sina.com.cn)

anti-uric acid drugs by himself and could walk with crutch. **Conclusions** Tophaceous gout of spine is caused by uratic deposition in spinal joints, which needs to be differentiated from other intraspinal extradural space-occupying lesions like tuberculosis, central nervous system lymphoma, metastatic tumors and lipomyoma. A definite diagnosis of tophaceous gout of spine requires histopathological examination detecting uratic crystals.

【Key words】 Gout; Thoracic vertebrae; Pathology

脊柱痛风石是一类因尿酸盐结晶沉积于脊柱关节内形成痛风石的晶体相关性关节病,临床较为罕见,可发生于颈椎、胸椎、腰椎各节段,可同时或不伴周围关节痛风。由于该病临床表现多样,影像学检查阳性检出率较低且无特异性,早期诊断和治疗较为困难,易与其他椎管内硬脊膜外占位性病变相混淆。本文报告 1 例发生于胸椎的椎管内痛风石患者,概述其临床特点、病理学特征、诊断与治疗要点,以期提高对该病的认识。

病历摘要

患者 男性,36 岁,因双下肢无力伴麻木 2 个月,加重 2 周,于 2015 年 12 月 9 日入院。患者 2 个月前无明显诱因出现双下肢无力,尚可行走,日间与夜间行走状况无差异,休息后未见明显缓解,伴双下肢麻木、痛温觉减退,大小便无异常,当地医院予对症支持治疗(具体方案不详),效果欠佳。症状呈进行性加重,2 周前明显加重,不能行走,尤以右下肢显著且伴疼痛,有时感觉疼痛自臀部向右下肢发散,大小便无障碍。为求进一步诊断与治疗,至我院就诊,门诊行胸椎 MRI 检查显示, T₉₋₁₀ 平面椎管内外沟通性占位性病变,考虑神经源性肿瘤可能性大,以“胸椎占位性病变”收入院。患者自发病以来睡眠、饮食欠佳,大小便正常,体重无明显变化。

既往史、个人史及家族史 既往有血清尿酸增高史 2 年,未予药物控制。否认关节疼痛史,否认手术史、外伤史和输血史。个人史及家族史无特殊。

体格检查 患者体温 36.8 °C,呼吸 18 次/min,脉搏 76 次/min,血压 120/80 mm Hg (1 mm Hg = 0.133 kPa);神志清楚,语言流利,一般状况良好,双耳耳廓多发白色结节,胸椎曲度可, T₉₋₁₁ 棘突压痛,双上肢肌力 5 级、左下肢 3 级、右下肢 3 级,肌张力正常,共济运动无异常, T₁₂ 平面以下痛温觉减退、深感觉稍减退,双侧 Hoffman 征阴性、Laseque 征可疑阳性、Babinski 征阳性,双侧膝腱反射亢进、踝阵挛阳性。

辅助检查 实验室检查:血尿便常规、肝肾功能试验、甲状腺功能试验、血清红细胞沉降率(ESR)、C-反应蛋白(CRP)、肿瘤标志物筛查均于正常值范围;血清甘油三酯(TG) 2.50 mmol/L (0.45 ~ 2.25 mmol/L),尿酸 667 μmol/L (155 ~ 428 μmol/L)。影像学检查:胸椎 CT 显示, T₉₋₁₀ 平面椎管内占位性病变(图 1);MRI 显示, T₉₋₁₀ 平面椎管内外沟通性占位性病变,考虑神经源性肿瘤可能性大,椎管受压狭窄,脊髓缺血变性(图 2)。头部 CT 无明显异常。

诊断与治疗经过 临床诊断为 T₉₋₁₀ 平面椎管内外沟通性占位性病变,性质待查。于 2015 年 12 月 15 日在全身麻醉下行胸椎管内外沟通性占位性病变切除术。术中可见 T₁₀ 椎旁占位性病变,呈乳白色石膏样, T₉₋₁₀ 椎体横突、椎弓根部分骨质破坏,硬脊膜完整。手术切除 T₉₋₁₀ 椎体棘突和双侧椎板,分块全切除病变,行组织病理学检查。(1)大体标本观察:术中冰冻病理学标本和手术切除标本均为灰白、灰红色破碎组织一堆,局部呈粉末状,其内有少许骨组织,分别为 2 cm × 1 cm × 1 cm 和 3.00 cm × 3.00 cm × 0.80 cm 大小(图 3)。冰冻病理学标本经乙醇固定,制备 5 μm 层厚组织切片,行 HE 染色;手术切除标本经体积分数为 4% 中性甲醛溶液固定,常规脱水、石蜡包埋,制备 3 μm 层厚组织切片,行 HE 染色。(2)术中冰冻病理学检查:光学显微镜观察显示,纤维结缔组织内可见棕色线样结晶,局部累及骨组织,周围散在淋巴细胞和少量多核巨细胞浸润,并可见异物肉芽肿形成(图 4a, 4b);偏振光显微镜观察显示,棕色线样结晶呈双折光性,晶体呈细线样,双侧尖锐,局部呈放射状或车辐状排列(图 4c)。(3)手术切除标本病理学检查:光学显微镜观察显示,棕色线样结晶溶解,形成白色不定形物质,其间散在少量残留的棕色线样晶体(图 5);偏振光显微镜观察显示,白色不定形物质呈单折光性。最终病理诊断为痛风石形成。患者术后一般状况和背部切口愈合良好,共住院 10 d。出院后随访 6 个月,可辅助拐杖行走。

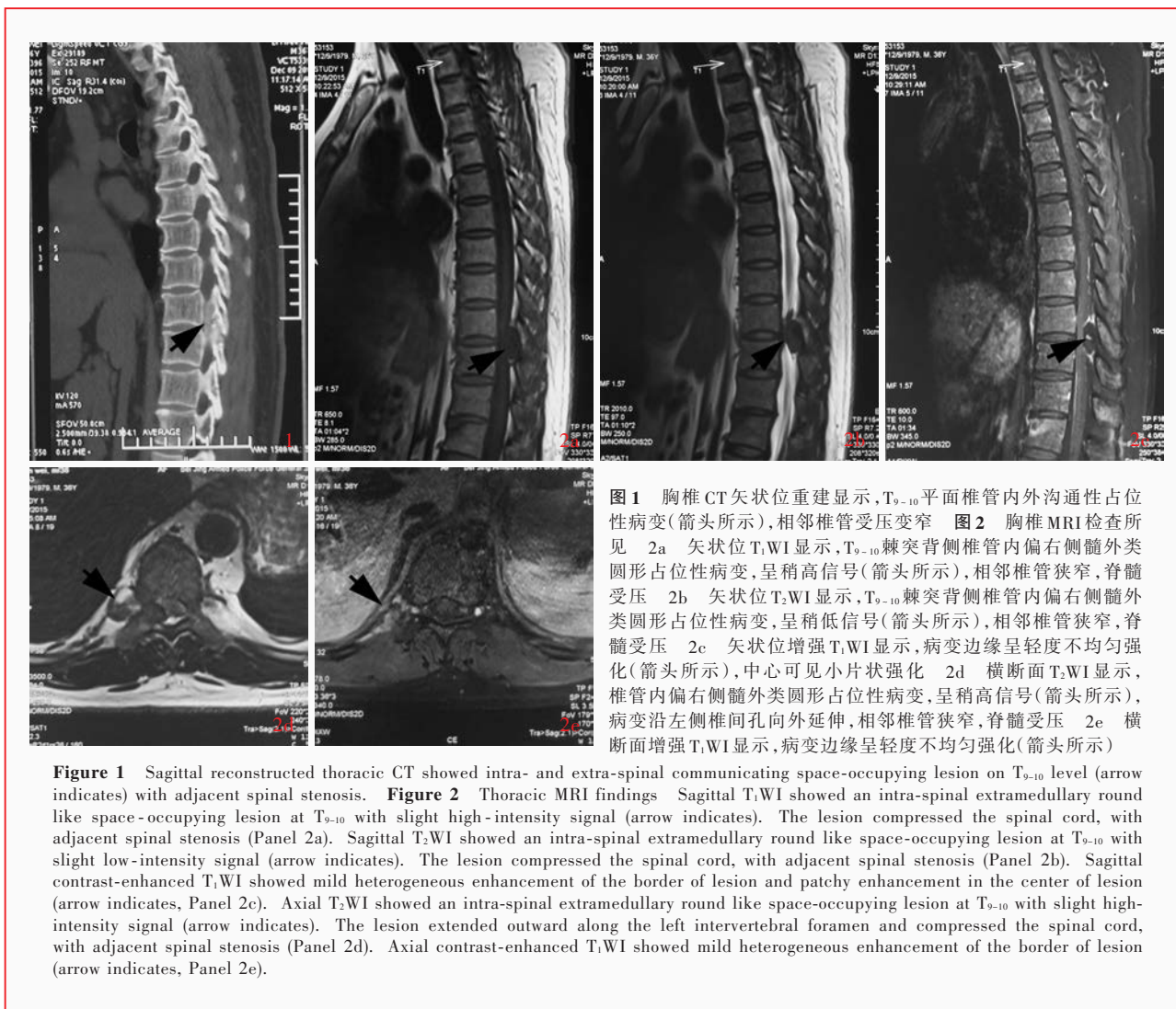


Figure 1 Sagittal reconstructed thoracic CT showed intra- and extra-spinal communicating space-occupying lesion on T₉₋₁₀ level (arrow indicates) with adjacent spinal stenosis. **Figure 2** Thoracic MRI findings. Sagittal T₁WI showed an intra-spinal extramedullary round like space-occupying lesion at T₉₋₁₀ with slight high-intensity signal (arrow indicates). The lesion compressed the spinal cord, with adjacent spinal stenosis (Panel 2a). Sagittal T₂WI showed an intra-spinal extramedullary round like space-occupying lesion at T₉₋₁₀ with slight low-intensity signal (arrow indicates). The lesion compressed the spinal cord, with adjacent spinal stenosis (Panel 2b). Sagittal contrast-enhanced T₁WI showed mild heterogeneous enhancement of the border of lesion and patchy enhancement in the center of lesion (arrow indicates, Panel 2c). Axial T₂WI showed an intra-spinal extramedullary round like space-occupying lesion at T₉₋₁₀ with slight high-intensity signal (arrow indicates). The lesion extended outward along the left intervertebral foramen and compressed the spinal cord, with adjacent spinal stenosis (Panel 2d). Axial contrast-enhanced T₁WI showed mild heterogeneous enhancement of the border of lesion (arrow indicates, Panel 2e).

讨 论

痛风是单钠尿酸盐(MSU)沉积导致的晶体相关性关节病。痛风石是由于嘌呤代谢障碍,尿酸产生增多和(或)排泄减少,导致大量单钠尿酸盐晶体沉积的结果。皮下痛风石的典型部位是耳廓,表现为皮下隆起大小不一的黄白色赘生物,破溃后排出白色粉状或糊状物。关节内痛风石多发生于跖趾关节、膝关节、踝关节、腕关节等部位,引起关节骨质破坏、关节周围组织纤维化、继发退行性变等,表现为持续性关节肿痛、压痛、畸形和功能障碍等^[1]。

当单钠尿酸盐晶体大量沉积时,通过激活炎症体产生白细胞介素-1(IL-1),引起中性粒细胞浸润,中性粒细胞通过与骨母细胞粘附,引起骨基质表面的骨母细胞皱缩,IL-1同时促进痛风石周围生成大量破骨细胞,并将其激活;单钠尿酸盐晶体可同时

抑制骨母细胞活性、功能和分化,单钠尿酸盐晶体与骨母细胞膜直接接触使膜裂解并导致细胞坏死^[2],引起关节骨质破坏。

1950年,Kersley等^[3]首次报告脊柱痛风病例,随后的文献多以个案报道为主,与发生于其他部位的痛风相似,脊柱痛风好发于男性,多发生于中老年人群^[4-5]。脊柱痛风可发生于脊柱各节段,尤以腰椎常见^[6],部分脊柱痛风的患者可以出现长期背痛、牵涉痛、神经功能障碍,并可为首发症状。部分脊柱痛风患者也可由于局限性或全身性炎症反应而出现脊柱疼痛、发热等症状,易与脊柱炎、硬脊膜外脓肿相混淆^[7-9]。脊柱痛风的影像学检查并无特异性且阳性检出率较低^[10],X线多表现为骨质破坏和继发性骨质增生^[11]。由于存在单钠尿酸盐晶体沉积,CT多表现为关节旁和(或)椎管内硬脊膜外低密度团块影^[12],对显示骨质破坏、痛风石内钙化形成

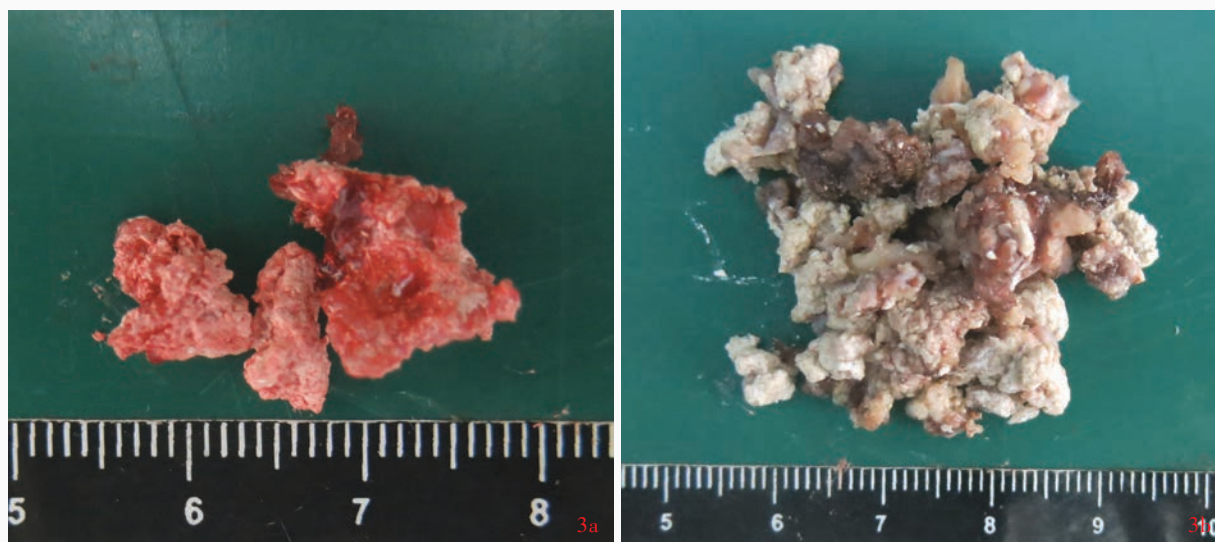


图3 大体标本观察可见灰白色破碎组织一堆,局部呈粉末状,其内可见骨组织 3a 术中切除新鲜标本 3b 术后经甲醛溶液固定标本

Figure 3 Gross findings revealed piles of grey-white broken tissue, with powder and bone tissue. Fresh specimen during the operation (Panel 3a). Specimen fixed in formalin after operation (Panel 3b).

和周围软组织改变有重要意义^[11]。MRI典型表现为T₁WI低信号、T₂WI高信号的占位性病变,但部分患者T₁WI可见与软组织相等或稍低信号,T₂WI低或高信号^[7,10,13]。双源CT(DECT)是目前对周围关节单钠尿酸盐结晶沉积较为敏感的影像学检查方法,对痛风的阳性检出率较高^[10]。

痛风石由单钠尿酸盐结晶及其外周包绕的多核巨细胞和单核细胞等构成^[14]。HE染色为棕色两端尖的针形晶体,呈放射状排列,在偏振光显微镜下呈强烈双折光性,单钠尿酸盐结晶溶于水,不溶于乙醇,经甲醛溶液固定后的标本,棕色针形晶体溶解,形成白色不定形物质,在偏振光显微镜下呈单折光性^[15]。单钠尿酸盐结晶周围骨组织骨母细胞和衬细胞消失,破骨细胞增多^[16]。单钠尿酸盐结晶沉积可以引起周围组织内肉芽肿性反应,光学显微镜下可见棕色线样结晶周围散在单核细胞和多核巨细胞浸润,应注意与结核等肉芽肿性病变相鉴别^[17]。脊柱痛风石的明确诊断依赖于手术或穿刺活检术,如在痛风石抽吸物或手术切除标本中发现单钠尿酸盐结晶,即可明确诊断。

痛风性关节炎需与缺少全身症状和呼吸系统特异性影像学改变的结核性关节炎相鉴别,二者影像学均可见关节骨质破坏和关节腔狭窄^[18],组织学均表现为肉芽肿形成和坏死灶,但结核性病变抗酸

染色多可见抗酸杆菌,而痛风性关节炎在偏振光显微镜下可见双折光性的单钠尿酸盐结晶^[19]。由于单钠尿酸盐结晶溶于水,故经甲醛溶液固定的标本于光学显微镜下可见棕色线样晶体溶解,形成白色不定形物质,偶可见少量残留的棕色线样晶体,诊断时易忽视,需引起病理科医师的重视。而增加切片厚度、减少标本在甲醛溶液中的固定时间或改用乙醇固定标本对保存单钠尿酸盐结晶有很大帮助,可以提高单钠尿酸盐的阳性检出率。患者临床资料和外科医师的术前诊断对该病的病理学诊断均具有重要意义。

痛风最佳治疗方案包括非药物治疗和药物治疗两方面。药物治疗需根据临床分期进行个体化治疗。治疗药物包括非甾体抗炎药(NSAID)、秋水仙碱、糖皮质激素、降尿酸药物等。通过控制血清尿酸水平,减少或消除体内沉积的单钠尿酸盐晶体。经治疗,痛风导致的关节症状和功能障碍可以获得改善。然而对于存在脊髓压迫症状的患者应尽早实施手术解除压迫症状,改善神经功能,减少对神经的损伤^[20]。该例患者由于未能及时解除脊髓压迫症状,术后神经功能恢复较差。

由于脊柱痛风石临床罕见,可以背部疼痛、神经压迫症状为首发症状,影像学检查无特异性,临床常与其他椎管内硬脊膜外占位性病变如脊柱结

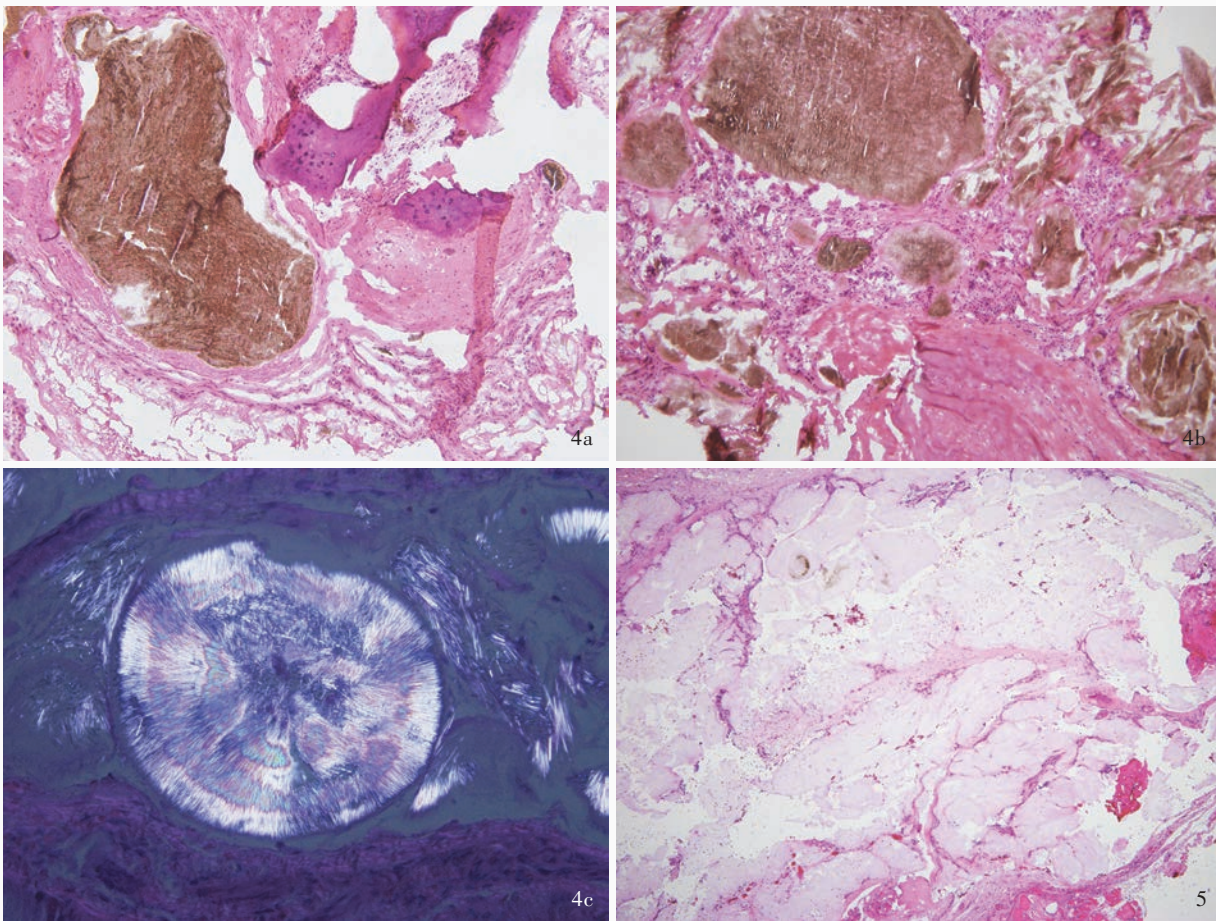


图 4 术中冰冻病理学检查所见 HE 染色 4a 光学显微镜观察显示,纤维结缔组织内可见棕色线样晶体,局部累及骨组织 ×100 4b 光学显微镜观察显示,晶体周围散在淋巴细胞和少量多核巨细胞浸润,可见异物肉芽肿形成 ×100 4c 偏振光显微镜观察显示,棕色线样结晶呈双折光性,晶体呈细线样,双侧尖锐,局部呈放射状或车轮状排列 ×400 **图 5** 手术切除标本光学显微镜观察显示,棕色线样结晶溶解,形成白色不定形物质,其间散在少量残留棕色线样晶体 HE 染色 ×40

Figure 4 Histopathological examination of the fresh specimen HE staining Optical microscope showed brown linear crystals in fibrous connective tissue, with bone invasion (Panel 4a). ×100 Optical microscope showed scattered lymphocytes and multinuclear giant cells infiltration surround the crystals, and foreign body granuloma could be observed (Panel 4b). ×100 Polarized light microscope showed birefringence of brown linear crystals, which were sharp on both sides and radially or spoke-like arranged (Panel 4c). ×400 **Figure 5** Histopathological examination of the removed specimen showed brown linear crystals were dissolved and formed white amorphous materials, with scatteredly distributed remaining brown linear crystals. HE staining ×40

核、中枢神经系统淋巴瘤、转移瘤、脂肪瘤和血管瘤等相混淆。对于临床上出现存在脊髓压迫症状的患者,若存在痛风病史或高尿酸血症,特别是存在皮下或其他部位痛风石时,应考虑脊柱痛风石的可能,必要时通过穿刺活检术或手术加以明确诊断。

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· 临床医学图像 ·

非典型脑膜瘤

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Atypical meningioma

YAN Xiao-ling

Department of Pathology, Tianjin Huanhu Hospital, Tianjin 300350, China (Email: ll934065@126.com)

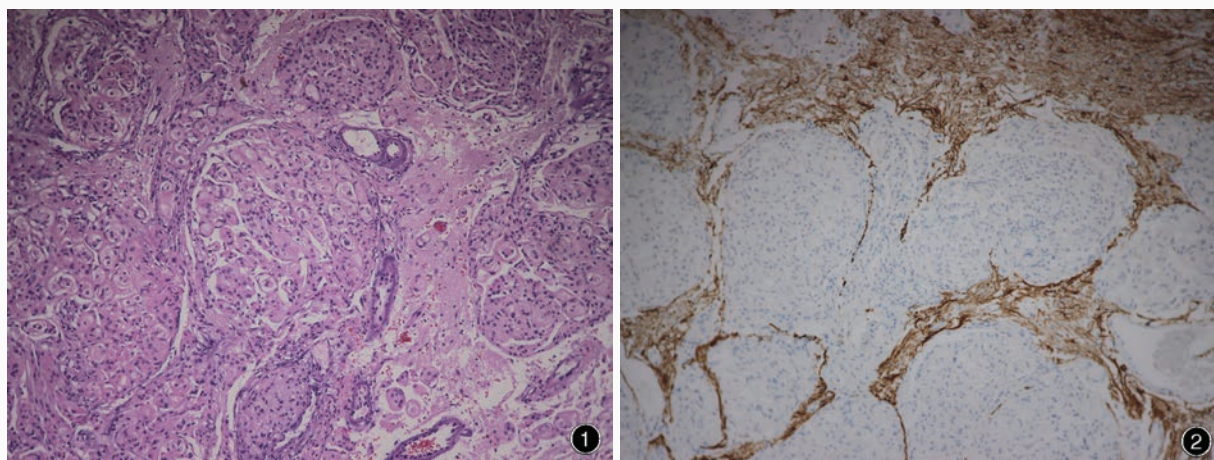


图1 光学显微镜观察显示,脑膜瘤细胞呈舌状浸润周围脑组织 HE染色 ×100 图2 光学显微镜观察显示,肿瘤周围脑组织胞质GFAP呈阳性 免疫组织化学染色(EnVision二步法) ×100

Figure 1 Optical microscopy showed tongue-like protrusions infiltrated into adjacent brain parenchyma. HE staining ×100

Figure 2 Optical microscopy showed cytoplasm of brain tissue around the tumor was positive for GFAP. Immunohistochemical staining (EnVision) ×100

2016年世界卫生组织(WHO)中枢神经系统肿瘤分类将非典型脑膜瘤定义为良性和恶性脑膜瘤中间类型,属WHO II级。组织学形态观察,胞核分裂活性增强,肿瘤侵犯周围脑组织,或具备肿瘤细胞密度高、小细胞伴核质比高、核仁明显、不规则或片状生长、局灶自发性坏死中的3个及以上特点,其中,脑组织浸润为2016年最新定义,以肿瘤细胞呈不规则舌状浸润周围脑组织为特点(图1),肿瘤组织与脑组织之间无软脑膜,脑组织浸润常引起星形胶质细胞增生。免疫组织化学染色可见肿瘤组织周围胶质纤维酸性蛋白(GFAP)呈阳性的脑组织(图2)。

(天津市环湖医院病理科阎晓玲供稿)