·临床病理报告·

髓内黑色素性神经鞘瘤

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【摘要】 **目的** 报告1例髓内黑色素性神经鞘瘤患者，结合文献探讨其临床和组织病理学特征、诊断与鉴别诊断、治疗原则。**方法与结果** 男性患者，47岁，胸椎椎管内占位性病变切除术后6年、背部疼痛1年。脊椎MRI显示T_{4-5}平面髓内占位性病变。手术全切除肿瘤。组织学形态观察，肿瘤细胞呈梭形或上皮样，排列成片状、巢团状或交织状，胞质内含数量不等的黑色素颗粒，胞核呈圆形或卵圆形，可见小核仁，未见核分裂象。免疫组织化学染色，肿瘤细胞S-100蛋白、黑色素瘤相关抗原HMB45、黑色素-A和Ⅳ型胶原蛋白呈阳性，上皮膜抗原、胶质纤维酸性蛋白、CD57、孕激素受体、结蛋白和肌浆蛋白呈阴性，Ki-67抗原标记指数约为10%。超微结构观察，肿瘤细胞可见连续基膜，胞质内含不同成熟程度的黑色素小体。最终病理诊断为髓内黑色素性神经鞘瘤。随访18个月，肿瘤无复发。**结论** 髓内黑色素性神经鞘瘤临床罕见，其诊断依靠组织学形态、免疫表型和超微结构特征，应注意与黑色素瘤、黑色素细胞瘤和色素性神经纤维瘤相鉴别。髓内黑色素性神经鞘瘤生物学行为较难预测，可局部复发，应对患者进行长期密切随访。

【关键词】 神经鞘瘤； 黑色素小体； 脊髓； 免疫组织化学； 病理学

Intramedullary melanotic schwannoma

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【**Abstract**】 **Objective** To study the clinicopathologic features, diagnosis, differential diagnosis, treatment and prognosis of intramedullary melanotic schwannoma (IMS). **Methods and Results** A 47-year-old male underwent an excision of thoracic intraspinal space-occupying lesion 6 years ago and was admitted to the hospital with a history of low back pain for one year. Spinal MRI revealed an intramedullary mass at the level of T_{4-5}. Gross total resection of the tumor was done. Histological findings revealed that spindle or epithelioid cells were arranged in sheets, nests or intersecting bundles. The cytoplasms contained varying amounts of melanin pigments. The nuclei were round to oval with small nucleoli but no mitotic figures. Immunohistochemically, the tumor cells were positive for S-100 protein (S-100), HMB45, Melan-A, and Collagen Ⅳ. They were negative for epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), CD57, progestrone receptor (PR), desmin (Des) and myogen. Ki-67 labeling index was about 10%. Ultrastructural findings revealed that the tumor cells were surrounded by continuous basal lamina, and melanin granules in different stages of maturity were present in the cytoplasms. Final pathological diagnosis was IMS. No recurrence of tumor was found after follow-up for 18 months. **Conclusions** Intramedullary melanotic schwannom is a rare neoplasm. The diagnosis relies on its morphological characteristics, immunophenotype and ultra microstructure, and should be differentiated from melanoma, melanocytoma and pigmentary neurofibroma. The biologic behavior of the tumor is difficult to predict. It may occur local recurrence. Therefore, long-term follow-up is required.

【**Key words**】 Neurilemmoma; Melanosomes; Spinal cord; Immunohistochemistry; Pathology

黑色素性神经鞘瘤（MS）是一种临床少见的富含黑色素的神经系统肿瘤，好发于脊髓或靠近中线的自主神经，亦见于消化道、支气管、皮肤、骨骼和软组织等部位。目前文献报道不足200例，发生于髓内的黑色素性神经鞘瘤临床更为罕见。在本研究中，我们报告1例髓内黑色素性神经鞘瘤患者，通

doi:10.3969/j.issn.1672-6731.2016.09.013

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过复习相关文献，对其临床表现、影像学、组织病理学、治疗及预后进行分析，并探讨该病的诊断与鉴别诊断要点。

病历摘要

患者　男性，47岁，因胸椎椎管内占位性病变切除术后6年、背部疼痛1年，于2014年10月29日入院。患者6年前无明显诱因出现左下肢无力，抬腿困难、行走拖拽，但无感觉异常，症状进行性加重，右下肢运动和感觉均正常，于2008年11月19日首次收入我院。入院后体格检查：双下肢肌张力增高，尤以左侧显著，腱反射亢进，右侧脐以下平面痛觉减退。实验室检查各项指标均于正常值范围。脊椎MRI显示，$T_{4\sim5}$平面髓内占位性病变（图1）。临床诊断为$T_{4\sim5}$髓内占位性病变，性质待查。遂行$T_{4\sim5}$髓内占位性病变切除术和椎管内减压术，术中可见病变位于$T_{4\sim5}$平面髓内，呈黑色，实性，质地中等，大小约2.00 cm×1.80 cm×1.00 cm，无明显包膜，血供较丰富。术后病理学检查诊断为黑色素性神经鞘瘤。术后未行放射治疗和药物化疗，临床症状无明显缓解。1年前无明显诱因出现背部持续性疼痛，平躺时缓解、受压时加重，乳头平面有束带感。外院脊椎MRI检查显示，$T_{4\sim5}$平面髓内偏背侧不均匀团块状短T_1、短T_2信号，增强扫描病灶呈明显不均匀强化，考虑髓内肿瘤复发。为求进一步诊断与治疗，再次至我院就诊。患者自发病以来，精神、睡眠、饮食尚可，小便正常、略有便秘，体重未见明显变化。

既往史、个人史及家族史均无特殊。

体格检查　患者体温36.6 ℃，脉搏84次/min，呼吸20次/min，血压128/80 mm Hg（1 mm Hg = 0.133 kPa）。营养、发育良好。皮肤、巩膜无黄染，皮肤无长毛黑痣和色斑。全身浅表淋巴结未触及。头部外观无明显异常，颈部对称、柔软，鼻咽部未见异常。心、肺、腹部检查无明显异常。双下肢无水肿。背部皮肤见一术后瘢痕、右下肢见一烫伤愈合瘢痕。神经科专科检查：神志清楚，语言清晰，对答切题，双侧瞳孔等大、等圆，直径均为3 mm，对光反射灵敏；鼻唇沟对称，伸舌居中，口角无歪斜；左下肢肌力4级、右下肢5级，肌张力均正常；左下肢感觉敏感，右下肢感觉正常；双侧腱反射亢进，踝阵挛和Babinski征阳性，剑突下至脐平面感觉减退，无“袖套-袜套”样感觉平面；共济运动检查未见明显异常。

辅助检查　实验室检查各项指标均于正常值范围。脊椎MRI显示，$T_{4\sim5}$平面髓内偏背侧极不均匀团块影，T_1WI呈高信号、T_2WI呈低信号，横断面最大径约1.80 cm×2.10 cm、矢状位最大径约4.40 cm，增强扫描病灶呈明显不均匀强化，考虑髓内肿瘤复发；亦可见肿瘤头部和尾部脊髓空洞形成，累及延髓至T_9平面（图2）。

诊断与治疗经过　临床诊断为$T_{4\sim5}$髓内占位性病变。遂于2014年10月31日在全身麻醉下行$T_{4\sim5}$髓内占位性病变切除术。术中可见肿瘤位于$T_{4\sim5}$平面髓内，呈黑色，质地较韧，约为2.30 cm×1.50 cm×1.00 cm大小，无明显包膜、与周围组织界限清晰，血供较丰富，脊髓受压变薄、部分受累，可见色素沉着。手术全切除肿瘤，行组织病理学检查。（1）大体标本观察：手术切除标本为不规则破碎组织块，呈黑褐色，实性，质地中等，大小约2.50 cm×2.20 cm×1.20 cm，无明显包膜，血供较丰富。经4%中性甲醛溶液固定，常规脱水、透明、石蜡包埋，制备4 μm切片，分别行HE染色和免疫组织化学染色。（2）HE染色：光学显微镜观察，肿瘤细胞呈梭形或上皮样，梭形细胞呈束状或交织状排列，上皮样细胞呈疏松片状或巢团状排列，胞质内含数量不等黑色素颗粒，胞核呈圆形或卵圆形，染色质较细腻，核仁小且明显，未见核分裂象；肿瘤组织呈局部浸润性生长（图3）。（3）免疫组织化学染色：采用EnVision二步法进行检测，检测用Ⅰ抗、Ⅱ抗和检测系统参见表1。结果显示，肿瘤细胞胞核和胞质弥漫性表达S-100蛋白（S-100，图4a），胞质表达黑色素瘤相关抗原HMB45（图4b）、胞质表达黑色素-A（Melan-A，图4c），基底膜表达Ⅳ型胶原蛋白（图4d），不表达上皮膜抗原（EMA）、胶质纤维酸性蛋白（GFAP）、CD57、孕激素受体（PR）、结蛋白（Des）和肌浆蛋白（myogen），Ki-67抗原标记指数约10%（图4e）。（4）超微结构观察：石蜡包埋的肿瘤组织经二甲苯脱蜡、二甲苯和树脂1∶1比例浸透、树脂聚合包埋，H7650型透射电子显微镜（日本Hitachi公司）观察显示，肿瘤细胞可见连续基膜，胞质内含有不同成熟程度的黑色素小体（图5）。结合临床病史和组织病理学检查，最终病理诊断为黑色素性神经鞘瘤。患者术后恢复良好，未予放射治疗和药物化疗。患者共住院13 d，出院时一般状况良好。随访18个月，肿瘤无复发。

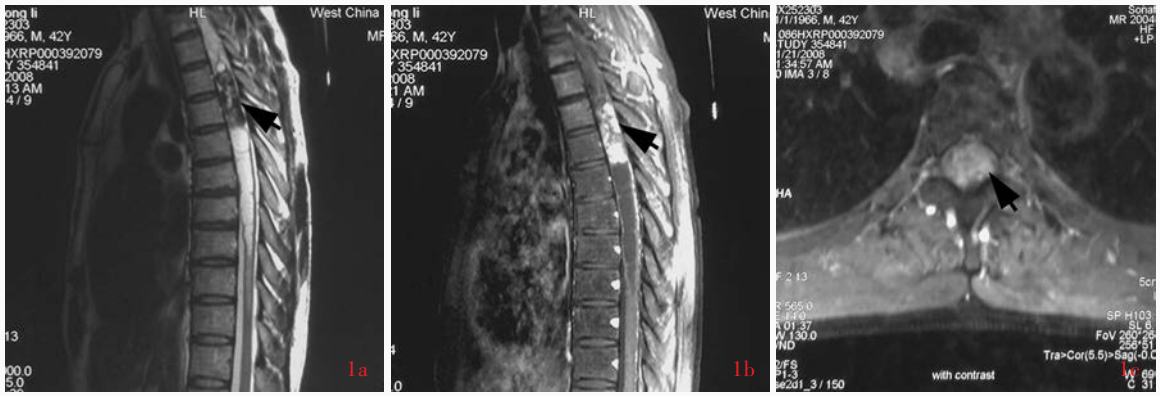

图1 首次入院时脊椎MRI检查所见 1a 矢状位T_2WI显示，T_{4-5}平面髓内实性占位性病变，呈高低混杂信号，信号强度不均匀（箭头所示）；其上下髓内可见囊性低信号影，其内可见线样分隔 1b 矢状位增强T_1WI显示，T_{4-5}平面髓内实性占位性病变，呈明显异常对比强化（箭头所示），其上下髓内囊性低信号区未见强化 1c 横断面增强T_1WI显示，髓内病灶呈不均匀强化（箭头所示）

Figure 1 Spinal MRI findings on the first admission Sagittal T_2WI showed a space-occupying mass with mixed heterogeneous intensity at the level of T_{4-5} (arrow indicates). Intramedullary cystic hypointense shadow with linear division could be seen (Panel 1a). Sagittal T_1WI with contrast demonstrated a mass with obvious enhancement at the level of T_{4-5} (arrow indicates). The intramedullary cystic hypointense shadow did not show enhancement (Panel 1b). Axial T_1WI with contrast demonstrated heterogeneous enhancement within the spinal cord (arrow indicates, Panel 1c).

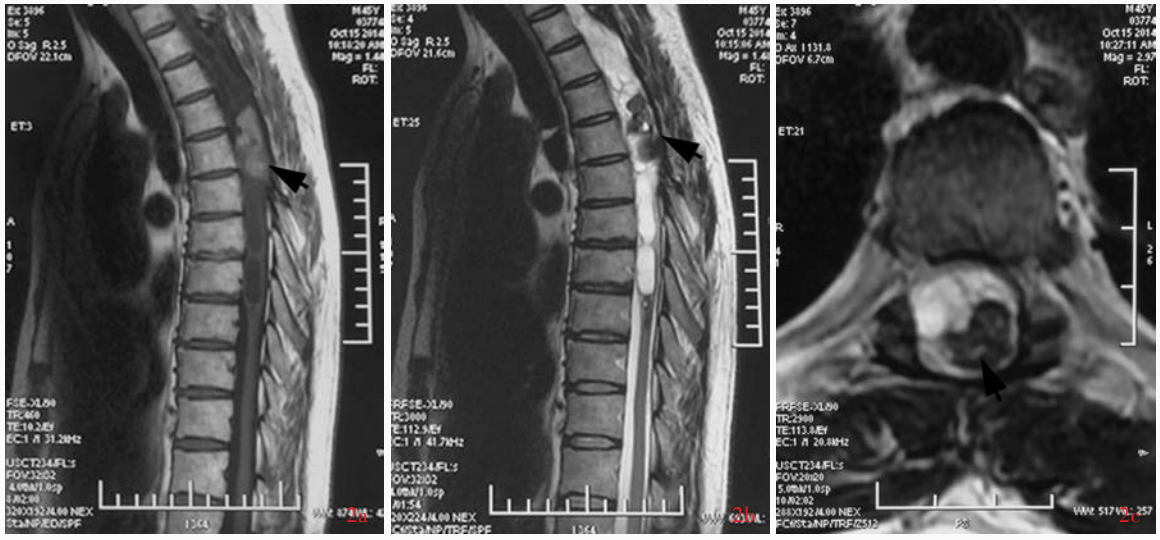

图2 再次入院时脊椎MRI检查所见 2a 矢状位T_1WI显示，T_{4-5}平面髓内不均匀高信号影（箭头所示） 2b 矢状位T_2WI显示，T_{4-5}平面髓内不均匀低信号影，其内可见小片状高信号影（箭头所示） 2c 横断面T_2WI显示，髓内不均匀低信号影（箭头所示）

Figure 2 Spinal MRI findings on the second admission Sagittal T_1WI showed a heterogeneous hyperintense mass at the level of T_{4-5} (arrow indicates, Panel 2a). Sagittal T_2WI showed a heterogeneous hypointense mass and patchy hyperintense shadow within the mass at the level of T_{4-5} (arrow indicates, Panel 2b). Axial T_2WI showed a heterogeneous hypointense mass within the spinal cord (arrow indicates, Panel 2c).

讨 论

黑色素性神经鞘瘤是一种临床少见的富含黑色素的神经系统肿瘤，同时具有施万细胞和黑色素细胞特征。黑色素性神经鞘瘤最早由Hodson[1]于1961年率先描述，目前文献报道不足200例，发生于髓内者仅8例（表2）。黑色素性神经鞘瘤好发于青年，中位年龄37岁，发病高峰年龄较普通神经鞘瘤早10岁，无明显性别差异，主要发生于脊髓或靠近中线的自主神经，亦见于消化道、支气管、皮肤、骨骼和软组织等[2-3]。临床表现取决于肿瘤部位和生长速度，主要为局部肿物、受累部位疼痛及相应神经系统症状[2]。黑色素性神经鞘瘤可以分为沙粒体型和非沙粒体型，约50%的沙粒体型黑色素性神经

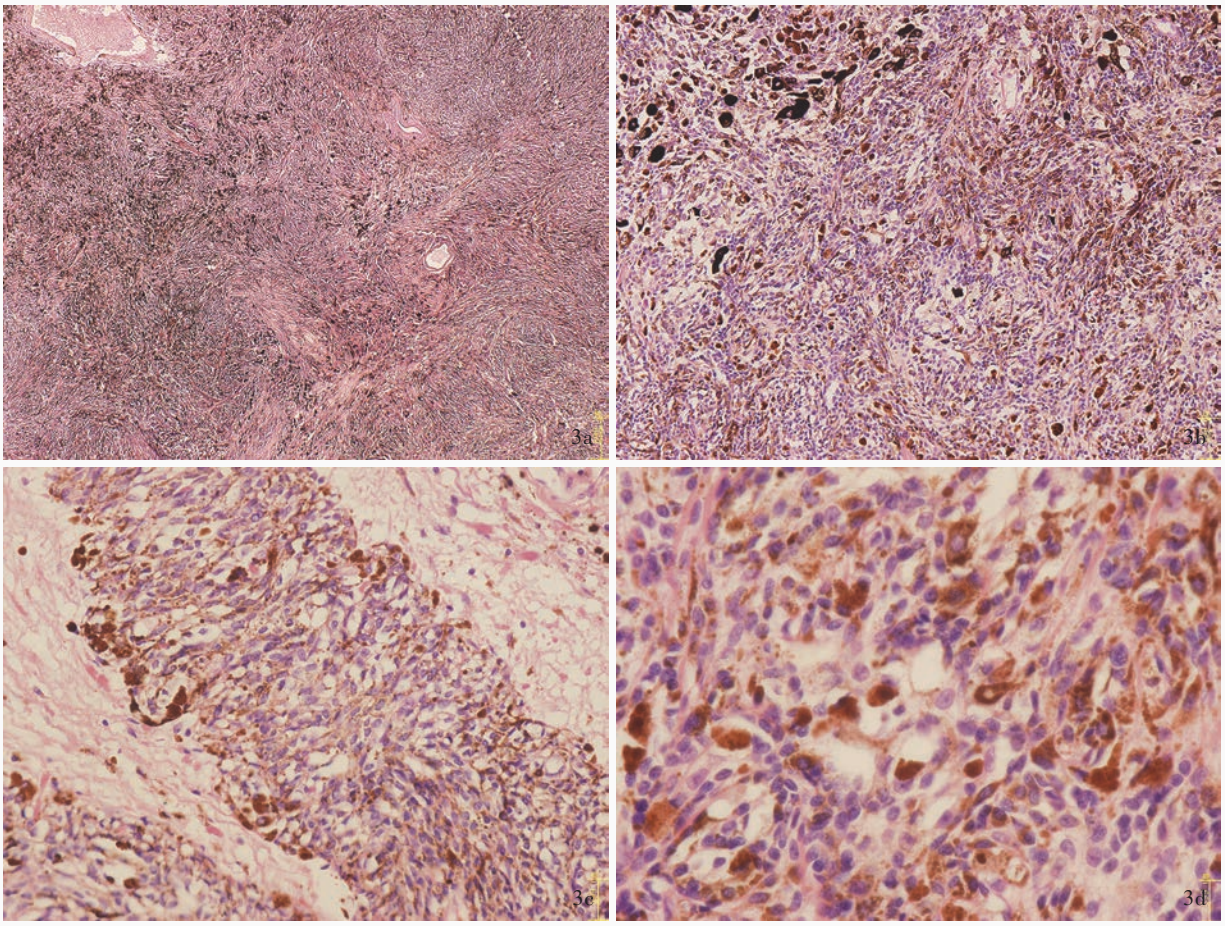

图3 光学显微镜观察所见 HE染色 3a 富含黑色素的梭形肿瘤细胞呈束状或旋涡状排列，其间可见血管组织 ×10 3b 富含黑色素的上皮样肿瘤细胞呈疏松片状排列 ×50 3c 富含黑色素的上皮样肿瘤细胞呈巢团状排列，肿瘤组织呈浸润性生长 ×100 3d 肿瘤细胞胞质内富含黑色素，胞核呈圆形或卵圆形、可见小核仁 ×200

Figure 3 Optical microscopy findings HE staining Pigmented spindle cells were arranged in fascicular or swirling pattern, with notable vascular tissue (Panel 3a). ×10 Pigmented epithelioid cells were arranged in a sheet pattern (Panel 3b). ×50 Pigmented epithelioid cells were arranged in a nest-like pattern with invasive growth (Panel 3c). ×100 Melanin pigments were presented in the cytoplasms, and the nuclei were round or oval with small nucleoli (Panel 3d). ×200

表1 免疫组织化学检测项目表

Table 1. Antibodies used for immunohistochemical examination

Antibody Ⅰ	Clone ID	Company	Restorative procedure	Dilution ratio	Antibody Ⅱ company	Dyeing system
S-100	16/f5	Maixin (China)	Citric acid	1∶100	Dako (America)	EnVision
Melanosome	HMB45	Dako (Denmark)	EDTA	1∶50	Dako (America)	EnVision
Melan-A	A103	Zhongshan (China)	Citric acid	1∶100	Dako (America)	EnVision
Collagen Ⅳ	PHM-12	Maixin (China)	Pepsin	Ready-to-use	Dako (America)	EnVision
EMA	E29	Dako (Denmark)	Citric acid	1∶100	Dako (America)	EnVision
GFAP	6F2	Dako (Denmark)	Citric acid	1∶10 000	Dako (America)	EnVision
PR	1E2	Roche (Switzerland)	EDTA	Ready-to-use	Roche (Switzerland)	EnVision
CD57	NK-1	Zhongshan (China)	Citric acid	1∶100	Dako (America)	EnVision
Desmin	D33	Dako (Denmark)	Citric acid	1∶100	Dako (America)	EnVision
Myogen	EP162	Zhongshan (China)	Citric acid	1∶50	Dako (America)	EnVision
Ki-67	MIB-1	Dako (Denmark)	EDTA	1∶100	Dako (America)	EnVision

S-100，S-100 protein，S-100蛋白；EMA，epithelial membrane antigen，上皮膜抗原；GFAP，glial fibrillary acidic protein，胶质纤维酸性蛋白；PR，progesterone receptor，孕激素受体；EDTA，ethylenediaminetetraacetic acid，乙二胺四乙酸

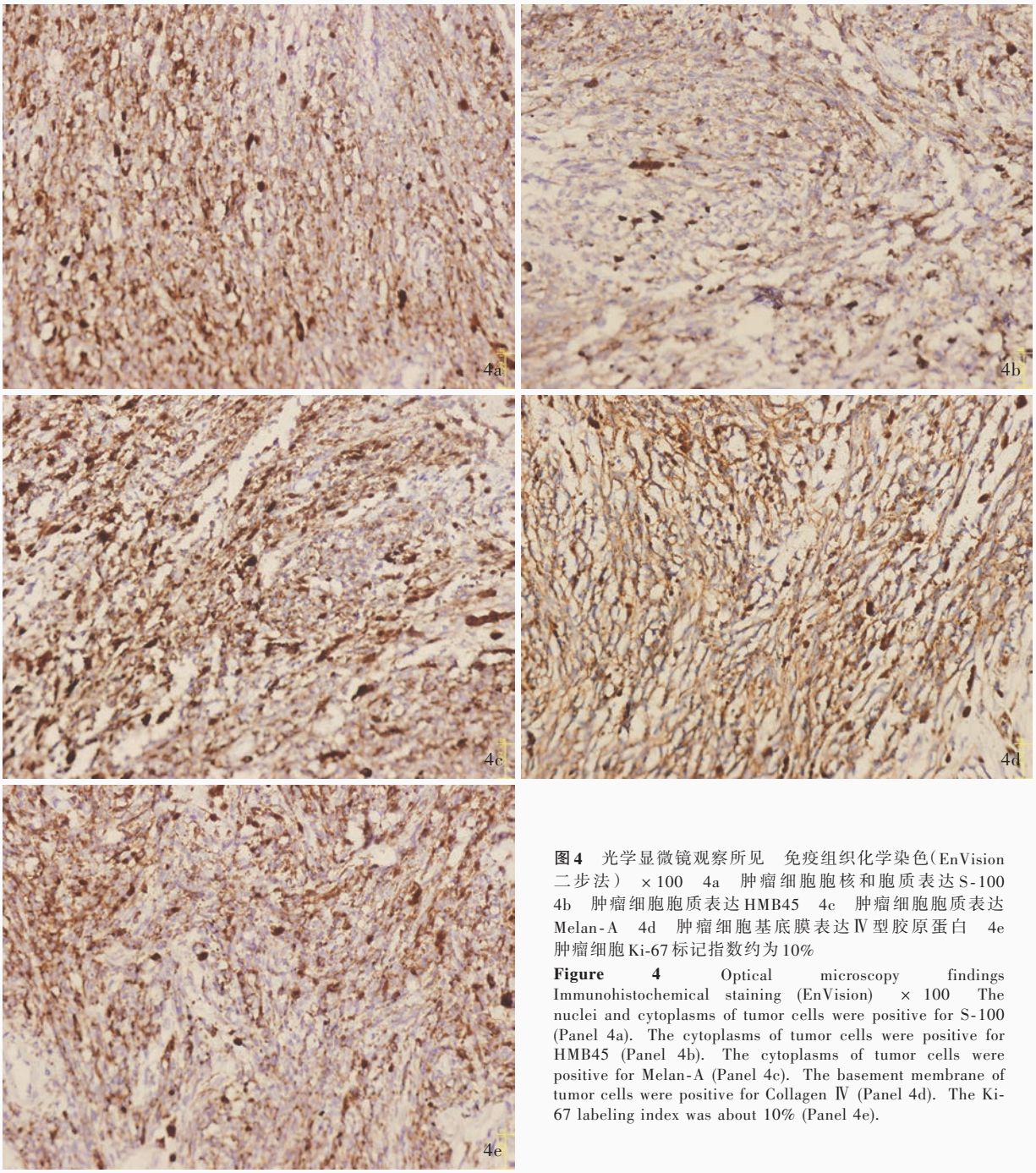

图4 光学显微镜观察所见 免疫组织化学染色(EnVision二步法) ×100 4a 肿瘤细胞胞核和胞质表达S-100 4b 肿瘤细胞胞质表达HMB45 4c 肿瘤细胞胞质表达Melan-A 4d 肿瘤细胞基底膜表达Ⅳ型胶原蛋白 4e 肿瘤细胞Ki-67标记指数约为10%

Figure 4 Optical microscopy findings Immunohistochemical staining (EnVision) × 100 The nuclei and cytoplasms of tumor cells were positive for S-100 (Panel 4a). The cytoplasms of tumor cells were positive for HMB45 (Panel 4b). The cytoplasms of tumor cells were positive for Melan-A (Panel 4c). The basement membrane of tumor cells were positive for Collagen Ⅳ (Panel 4d). The Ki-67 labeling index was about 10% (Panel 4e).

鞘瘤患者伴Carney综合征,该综合征是一种常染色体显性遗传性疾病,表现为心脏、乳腺和皮肤黏液瘤,皮肤色素沉着及内分泌功能亢进[3-4]。通常伴Carney综合征的患者发病年龄早于不伴Carney综合征者[3]。

大体标本观察,肿瘤组织与周围组织分界清楚,呈圆形或卵圆形,有的可见黑棕色或灰蓝色包膜,切面因黑色素含量不等,呈黑色、棕褐色或灰蓝色,可伴出血、囊性变等[2-3]。组织学形态观察,肿瘤细胞可呈片状、束状、巢团状或交织状排列,细胞形态差异较大,可呈梭形、多边形或上皮样,细胞界限不清,常呈合体细胞样外观,类似普通神经鞘瘤[3]。肿瘤细胞胞质内含有数量不等的Masson-Fontana染色阳性的黑色素颗粒,可呈细颗粒状或粗团块状;

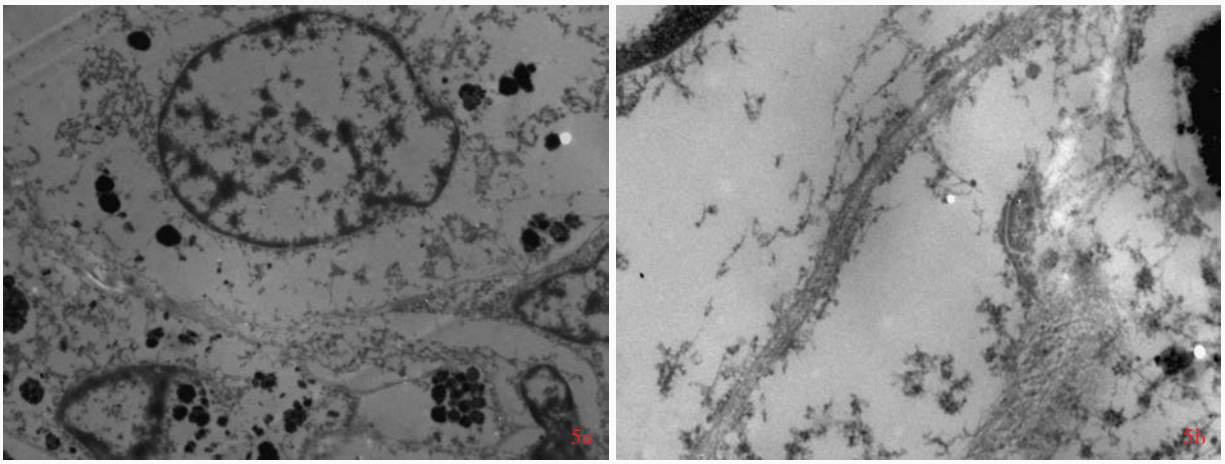

图5 透射电子显微镜观察所见 5a 肿瘤细胞胞质内富含黑色素小体 ×1200 5b 肿瘤细胞可见连续基膜 ×5000

Figure 5 Transmission electron microscopy findings The melanosomes existed in the cytoplasm of tumor cells (Panel 5a). ×1200 Continuous basal lamina could be seen in tumor cells (Panel 5b). ×5000

表2 9例髓内黑色素性神经鞘瘤患者的临床资料

Table 2. Clinical data of 9 patients with intramedullary melanotic schwannoma

No.	Literature resource	Age (year)	Sex	Symptom	Duration	Location	Tumor size (cm)	Treatment	Follow-up/outcome
1	Santaguida, et al [5]	35	Male	Right neck pain and right hemiparesis	10 months	C_{4-5}	—	Gross total resection, chemotherapy and radiotherapy	4 years/partial neurological recovery
2	Hoover, et al [6]	62	Female	Thighs pain	Several years	T_{11}	1.20	Gross total resection	10 months/ neurological recovery
3	Solomon, et al [13]	69	Male	Right Brown-Sequard's syndrome	4 years	Caudal medulla-C_3	—	Gross total resection	—
4	Marchese and McDonald [14]	72	Female	Quadriparesis	2 years	C_{4-6}	2.00	Partial resection	Partial functional recovery
5	Sola-Pérez, et al [15]	63	Female	Right cervical dorsal radicular pain	—	C_7-T_1	4.00	Fine needle aspiration for diagnosis	—
6	Acciarri, et al [16]	44	Female	Spastic quadriparesis	10 years	T_{2-3}	3.00	Gross total resection	4 months/partial neurological recovery
7	Mouchaty, et al [17]	56	Female	Lower limbs were not improved correspondingly to arms	6 months	Conus medullaris	4.00	Gross total resection	One year/partial neurological recovery
8	Mohamed, et al [18]	43	Male	Left leg weakness	2 years	T_{9-10}	2.60	Gross total resection	6 months/ neurological recovery
9	Current case	47	Male	Lower back pain	One year	T_{4-5}	2.50	Gross total resection	18 months/ neurological recovery

—, not reported, 未报道

胞核呈圆形或卵圆形，染色质较细腻、可见小核仁，核分裂象未见或罕见。部分可见胞核呈模糊“栅栏”状或“旋涡”状排列，类似普通神经鞘瘤或神经纤维瘤[3]。沙粒体型黑色素性神经鞘瘤可见分层同心圆状钙化，常为局灶性，数量不等[2]。若肿瘤细胞异型性明显、核仁呈嗜酸性、核分裂象增多、浸润周围组织、坏死等，应考虑为恶性黑色素性神经鞘瘤。免疫组织化学染色显示，肿瘤细胞S-100、HMB45、Melan-A、Ⅳ型胶原蛋白、层黏连蛋白(laminin)、波形蛋白(Vim)等呈阳性，GFAP通常呈阴性，Ki-67抗原标记指数<5%[2-3]。超微结构观察显示，肿瘤细胞有一连续基膜，胞质内含有不同成熟程度的黑色素小体[5-6]。

黑色素性神经鞘瘤在MRI上通常呈边界清楚的占位性病变。由于肿瘤细胞胞质内黑色素含顺磁性物质而使T_1WI呈高信号、T_2WI呈低信号，肿瘤内黑色素含量越多、T_1和T_2弛豫时间越短[7-8]；增强扫描病灶呈轻中度强化。若伴肿瘤内出血，信号强度更为复杂[7]。

黑色素性神经鞘瘤应注意与原发性或转移性黑色素瘤、黑色素细胞瘤等相鉴别。(1)黑色素瘤：肿瘤组织呈浸润性生长，边界不清；肿瘤细胞形态

多样，可呈上皮样、梭形或极其怪异，细胞异型性明显，黑色素可以丰富、稀少或缺如，胞核大、核仁大且呈嗜酸性，核分裂象多见，常伴坏死；免疫组织化学染色，S-100、HMB45、Melan-A均呈阳性，但Ⅳ型胶原蛋白和层黏连蛋白呈阴性[9]。(2)黑色素细胞瘤：常发生于脑膜和脊膜，为孤立性低级别肿瘤，一般不侵犯周围组织；肿瘤细胞梭形或卵圆形，呈巢状排列，与脑膜瘤“旋涡”状结构相似，胞质内含有数量不等黑色素，胞核呈卵圆形或逗点状，可见嗜酸性小核仁，细胞无明显异型性和核分裂象；肿瘤细胞巢边缘可见明显黑色素沉积的肿瘤细胞和巨噬细胞；免疫组织化学染色，多数肿瘤细胞S-100、HMB45、Melan-A和小眼畸形转录因子(MITF)呈阳性，Ki-67抗原标记指数通常＜2%；超微结构观察，肿瘤细胞间连接少，肿瘤细胞周围无广泛基膜样物质围绕[10]。(3)色素性神经纤维瘤：临床少见，约50%患者伴Ⅰ型神经纤维瘤病；通常发生于头颈部、臀部或小腿，多见于弥漫性神经纤维瘤中，部分患者同时具有弥漫性和丛状神经纤维瘤特征；大体标本观察通常无黑色素沉积，需行组织病理学检查方可见黑色素沉积；黑色素细胞呈树突状或上皮样分散于肿瘤组织中，通常聚集于肿瘤表面[2-3]。

黑色素性神经鞘瘤的治疗首选手术完整切除病灶，对于不能完整切除或复发患者，术后可辅助放射治疗和药物化疗，并密切随访。Santaguida等[5]报告1例$C_{4\sim5}$髓内黑色素性神经鞘瘤患者，术后予卡铂化疗6个疗程，2年后复发，行放射治疗，总剂量54 Gy。既往认为，黑色素性神经鞘瘤属良性惰性病变[2-3]。目前，多项研究显示其生物学行为难以预测，在没有明显恶性组织病理学特征的情况下也可发生转移[3]。有文献报道，仅53%的患者无症状生存期＞5年[11]。Torres-Mora等[12]的研究显示，黑色素性神经鞘瘤复发率为35%、转移率为44%，且核分裂象＞2/10个高倍视野(HPF)与肿瘤转移相关，因此认为黑色素性神经鞘瘤是一种恶性肿瘤。

结合文献资料报道的8例髓内黑色素性神经鞘瘤患者，共9例患者(含本文患者)的临床资料详见表2[5-6,13-18]：男性4例，女性5例；年龄35～72岁，中位年龄56岁；病程6个月至10年，中位病程35个月；肿瘤最大径通常＜4 cm；临床主要表现为疼痛和相应神经系统症状，均不伴Carney综合征；影像学表现与发生于其他部位的黑色素性神经鞘瘤相似。此外，本文患者两次手术前脊椎MRI均显示病变相邻上下节段脊髓空洞样改变，类似室管膜瘤伴发的脊髓空洞症，这也是髓内黑色素性神经鞘瘤的证据之一。大体标本、组织学形态和免疫表型等亦与发生于其他部位的黑色素性神经鞘瘤相似。9例患者均为非沙粒体型髓内黑色素性神经鞘瘤，本文患者光学显微镜观察可见肿瘤局部浸润性生长。其中8例行胸椎椎管内占位性病变切除术，7例病灶完整切除，1例肿瘤复发后行放射治疗和药物化疗。7例患者有随访资料，随访时间4～48个月。本文患者6年前行$T_{4\sim5}$平面髓内占位性病变切除术，术中可见病灶位于$T_{4\sim5}$平面髓内，呈黑色，与周围组织分界清晰。复习患者6年前的临床资料，其影像学表现、组织学形态学和免疫表型与本次结果相符，提示肿瘤复发，且组织学形态发现肿瘤局部浸润性生长，故认为是肿瘤复发的原因。

综上所述，髓内黑色素性神经鞘瘤是一种临床少见的富含黑色素的神经系统肿瘤，其临床诊断依靠组织形态学、免疫表型和超微结构特征，应注意与黑色素瘤、黑色素细胞瘤、色素性神经纤维瘤等相鉴别。其生物学行为较难预测，总体预后良好，可局部复发，应对患者进行长期密切随访。

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颅内恶性黑色素瘤的显微外科治疗:二例报告及文献复习. 中国现代神经疾病杂志, 2013, 13:447-452.]
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（收稿日期:2016-07-26）

Epigenetic Methods in Neuroscience Research published

Epigenetic Methods in Neuroscience Research (ISBN: 978-1-4939-2753-1, eBook ISBN: 978-1-4939-2754-8) will be published by Springer in 2016. The editor of this book is Nina N. Karpova, Neuroscience Center, University of Helsinki.

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