.个案报道.

椎管内转移性神经内分泌癌1例

李　东　刘洪军　漆　建　侯晓峰

【摘要】神经内分泌肿瘤(NET)是一种罕见的异质性上皮肿瘤,以消化系统和肺部最常见,最常转移至肝、肺、淋巴结,椎管内转移罕见。本文报道1例椎管内转移性神经内分泌癌,为69岁男性,因剑突下疼痛3个月伴突发双下肢活动障碍20 h入院。胸椎MRI显示胸8椎体信号异常,伴椎管内硬脊膜外占位;腰椎CT示腰4椎体及双侧髂骨内斑片状稍高密度影。血清神经特异性烯醇化酶水平明显增高。在全麻下行T7~8椎管内硬脊膜外病变切除术。术中发现病变位于T7~8椎管内硬脊膜外,无明显包膜,实性,鱼肉状,位于硬脊膜囊腹侧,占据大部分椎管,并将硬脊膜囊推向后方。术后病理诊断转移性神经内分泌癌3级。术后症状无改善,家属要求自动出院,2个月死亡。因此,对椎管内转移性肿瘤,原发病灶诊断困难时,建议PET-CT扫描。椎管内转移性NET预后非常差,手术能否改善病人预后有待进一步研究。

【关键词】椎管内转移性肿瘤;神经内分泌肿瘤;神经内分泌癌;显微手术

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Intraspinal metastatic neuroendocrine carcinoma: a case report

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【**Abstract**】Neuroendocrine tumors (NETs) are a kind of rare and highly heterogeneous epithelial tumors, mainly manifested in the digestive system and lungs. The most common metastatic sites are the liver, lungs and lymph nodes, while intraspinal metastasis is relatively rare. This paper presents a case of intraspinal metastatic neuroendocrine carcinoma in a 69-year-old male. The patient was admitted to the hospital due to substernal pain lasting for 3 months and sudden motor dysfunction of both lower extremities for 20 hours. Imaging examinations indicated abnormal signals in the T8 vertebra on thoracic spine MRI, accompanied by an extramedullary epidural space-occupying lesion in the spinal canal; and patchy slightly high-density shadows in the L4 vertebra and bilateral iliac bones on lumbar spine CT. Laboratory tests disclosed a significantly elevated level of serum neuron-specific enolase. Subsequently, an extramedullary epidural lesion resection within T7~T8 was conducted under general anesthesia. Intraoperative observations revealed that the lesion was located in the extramedullary epidural space of the T7~T8 spinal canal, without a distinct capsule, being solid and fish-like in shape, situated on the ventral side of the dural sac, occupying the majority of the spinal canal space and pushing the dural sac posteriorly. The postoperative pathological diagnosis was grade III metastatic neuroendocrine tumor. Despite the surgical treatment, the patient's symptoms did not improve. The family requested an automatic discharge and the patient died two months after the operation. In view of the difficulty in diagnosing the primary lesion of intraspinal metastatic tumors, it is suggested to consider using PET-CT scans in clinical practice for assistance in diagnosis. The prognosis of intraspinal metastatic NET is typically poor, and whether surgery can enhance the prognosis of patients remains to be further investigated.

【**Key words**】Intraspinal metastatic tumors; Neuroendocrine tumors; Neuroendocrine carcinomas; Microsurgery

1 病例资料

69岁男性,因剑突下疼痛3个月伴突发双下肢活动障碍20 h于2022年8月入院。3个月前,开始出现剑突下疼痛,呈持续性针刺样痛,疼痛无明显加重及缓解。20 h前,无明显诱因突发双下肢活动障碍,伴剑突平面下感觉消失。既往史:近3年因反复咯血诊断为"间质性肺炎";近6个月体重减轻15 kg,胃肠镜检查无明显异常。入院体格检查:神志清楚,体型消瘦,被动体位;双下肢肌力Ⅰ级,肌张力降低;剑突平面以下感觉和运动功能丧失,双侧膝、腱反射消失,双侧Babinski征(+)。胸椎MRI显示胸8椎体信号异常,伴椎管内硬脊膜外占位(图1A、1B)。腰椎CT示腰4椎体及双侧髂骨内斑片状稍高密度影。上腹部CT未见异常。腹部超声示前列腺包膜欠光滑,实质内可见强回声斑。血清神经特异性烯醇化酶水平明显增高。因病人出现截瘫,有急诊手术指征,遂在全麻下行T7~8椎管内硬脊膜外病变切除术。术中见病变位于T7~8椎管内硬脊膜外,无明显包膜,实性,鱼肉状,位于硬脊膜囊腹侧,占据大部分椎管,并将硬脊膜囊推向后方。术后病理查见肿瘤细胞巢状分布、筛孔状排列(图1D);免疫组化(图1E):CK(+)、S-100(-)、Syn(+)、CgA(-)、CD56(-)、SSTR2(-)、EMA(-)、PR(-)、Ki-67(+,约30%)、CK7(-)、CK20(-)、CDX2(+,部分),诊断为"椎管内占位"转移性神经内分泌瘤3级(NET G3)。术后予以留置尿管、抗感染、激素冲击、营养神经等综合治疗。术后1周复查胸椎CT并三维重建显示胸8椎体密度不均匀(图1C),病人双下肢肌力无改善、剑突平面下感觉无好转,家属要求自动出院,2个月后随访,病人死亡。

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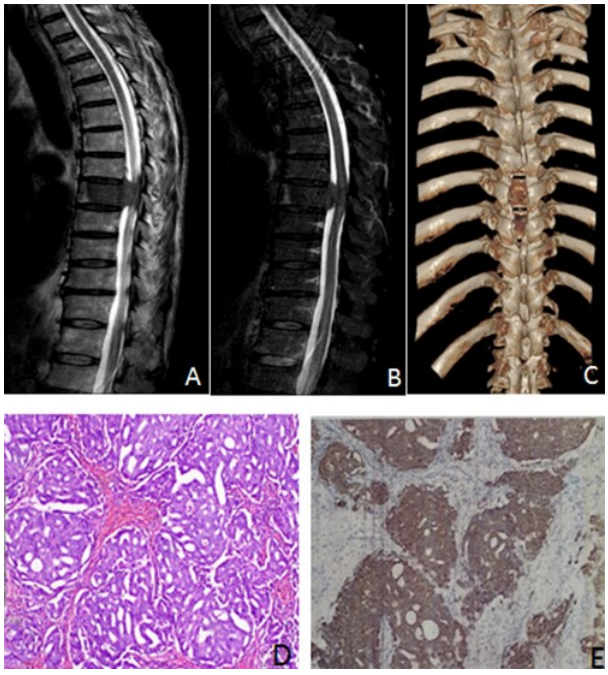

图1 T7~8椎管内转移性神经内分泌癌手术前后影像及术后病理表现

A、B. 术前胸椎MRI平扫显示胸8椎体T_1WI、T_2WI及压脂序列呈低信号，椎管内硬膜外见梭形异常信号影，大小约1.5 cm×0.6 cm×2.6 cm，以宽基底与椎管相连，邻近脊髓及蛛网膜下腔受压；C. 术后1周复查胸椎CT并三维重建显示胸8椎体密度不均匀；D、E. 术后组织HE染色(×100；D)及免疫组化染色(×100；E)见巢状分布、筛孔状排列肿瘤细胞，免疫组化支持转移性神经内分泌癌3级(NET G3)

Figure 1 Pre- and post-operative images and postoperative pathological manifestations of a patient with intraspinal metastatic neuroendocrine carcinoma within the T7~T8 spinal canal

A-B: Preoperative MR images of the thoracic spine reveal that the T8 vertebra exhibites a low signal intensity on T_1WI, T_2WI, and fat-suppressed sequences; a fusiform abnormal signal shadow is discernible in the epidural space of the spinal canal, approximately 1.5 cm×0.6 cm×2.6 cm in size, connected to the spinal canal with a broad base, and the adjacent spinal cord and subarachnoid space are compressed. C: Thoracic spine CT and three-dimensional reconstruction one week postoperatively demonstrate heterogeneous density of the T8 vertebra. D-E: Postoperative tissue HE staining (×100; D) and immunohistochemical staining (×100; E) indicate that the tumor cells are distributed in nests and arranged in a cribriform pattern, and the immunohistochemical results support the diagnosis of grade 3 metastatic neuroendocrine tumor (NET G3).

2 讨 论

神经内分泌肿瘤(neuroendocrine tumor，NET)是一类起源于肽能神经元和神经内分泌细胞、能够产生生物活性胺和(或)多肽激素的异质性肿瘤，可发生于全身多种器官和组织。NET主要分布在胃肠道和支气管，转移至椎管是非常罕见的，通常是转移性疾病的继发性结果[1]。2010年，WHO根据Ki-67值选择将NET分为G1(≤2%)、G2(3%~20%)、G3(>20%)三类，其中G1和G2分级为NET，G3为神经内分泌癌[2]。根据WHO分级系统，高级别NET(NET-G3)预后不良[3]。NET通常在神经或器官受压的情况下才被发现，症状主要与肿瘤的位置和是否有分泌功能有关。在椎管内病变的情况下，肿块效应包括神经根痛和脊髓病。本文病人剑突以下疼痛符合T8神经根痛，双下肢截瘫符合脊髓病表现。NET可以分泌血管活性肽和胺，导致类癌综合征[4]。本文病例曾因肺泡毛细血管扩张致反复咯血。文献报道，在初步诊断为NET时，近一半病人已经有远处转移[5]。本文病例符合神经内分泌癌远处转移伴类癌综合征表现。

NET的影像学特征缺乏特异性。本文病例既往因反复咳嗽、咯血多次就诊呼吸内科，行胸腹部CT检查误诊为肺间质性疾病，导致疾病进展。此次入院后胸腹部CT、腹部彩色超声多普勒、胃肠镜检查均未发现明显可疑占位。因病人表现为双下肢截瘫伴剑突以下平面感觉消失，遂将病变定位至胸髓，行胸椎MRI检查后明确了腹痛和截瘫原因，但急诊手术后病情较重，未行全身PET-CT检查和前列腺穿刺活检，故肿瘤原发病灶诊断不清。结合反复咯血史且神经特异性烯醇化酶明显升高，从疾病一元论考虑原发病灶为肺神经内分泌癌可能性大。从诊治流程分析，该病早期诊断存在巨大困难，因此，在面对伴有感觉异常的腹痛且常规实验室和影像学检查无明显异常的，应考虑椎管内病变可能，对转移性肿瘤原发病灶诊断困难时，应行PET-CT扫描。

病因不明的NET约占所有NET的10%。转移性NET病人预后非常差，5年生存率在19%~38%[6]。近年来，胰岛素瘤相关-1已成为神经内分泌肿瘤的高级、敏感、特异的生物标志物[7]，与诊断放射性核素结合，可用于神经内分泌肿瘤的诊断，也可通过将成像同位素替换为治疗同位素用于治疗，这一领域被称为肽受体放射性核素治疗。因此，转移性NET的全身治疗选择已大幅扩大，但目前手术仍然是局部肿瘤治疗的基石。

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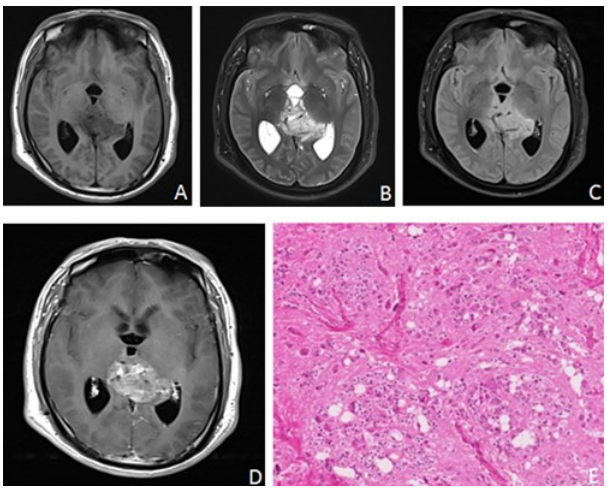

图1 中分化松果体实质瘤术前影像表现及术后病理表现

A-D. 术前头颅MRI显示第三脑室后部、松果体区不规则肿块影，边界欠清，部分突入侧脑室内，双侧脑室扩大，T_1WI呈低信号，T_2WI呈高信号，FLAIR呈稍高信号，增强扫描病灶呈明显不均匀强化，内可见流空血管影；E. 术后病理检查(HE，×100)，显微镜下可见肿瘤细胞呈小圆形，弥漫分布或假菊形团样排列

Figure 1 Preoperative imaging features and postoperative pathological features of a patient with pineal parenchymal tumor of intermediate differentiation

A-D: Preoperative head MRI reveals an irregular mass shadow in the posterior part of the third ventricle and the pineal region, with indistinct boundaries, partially protruding into the lateral ventricles, and bilateral ventricular dilation; the mass shows a low signal on T_1WI, a high signal on T_2WI, a slightly high signal on FLAIR, and significantly heterogeneous enhancement on enhanced scan, with visible flow-void vascular shadows. E: Postoperative pathological examination (HE, ×100), the tumor cells are small and round, diffusely distributed or arranged in pseudorosette-like patterns under the microscope.

较低，术前明确诊断仍然比较困难，最终确诊需要结合病理学检查。其镜下特点表现为瘤细胞呈弥漫或分叶状分布，可见假菊形团，其免疫组化标记Syn、NF、CgA可呈阳性，增殖指数在3%~10%[5]。手术切除是目前PPTID的首选治疗方法，可减轻肿块占位效应并获取肿瘤标本，术后再辅以放、化疗，可改善病人预后。

【利益冲突声明】：本文不存在任何利益冲突。

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