

副肿瘤性小脑共济失调1例病例报道及文献复习

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摘 要

副肿瘤性小脑变性(paraneoplastic cerebellar degeneration, PCD)也称为副肿瘤性小脑共济失调, 是最常见的副肿瘤性神经综合征之一。本文报告了1例主因头晕1月, 双下肢无力10天, 加重伴构音障碍6天的患者, 经相关辅助检查及治疗后, 确诊为PCD。根据该病例, 我们进行了相关文献的回顾。

关键词

肿瘤, 运动失调, 头晕, 病例报道

Paraneoplastic Cerebellar Ataxia: A Case Report and Literature Review

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Abstract

Paraneoplastic cerebellar degeneration (PCD), also known as paraneoplastic cerebellar ataxia, is one of the most common paraneoplastic neurological syndromes. This article reports a patient who suffered from dizziness for one month, weakness in both lower limbs for 10 days, and worsening accompanied by articulation disorders for 6 days. After auxiliary examination and treatment, the patient was diagnosed with paraneoplastic cerebellar ataxia. Based on this case, we

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conducted a review of relevant literature.

Keywords

Tumor, Motor Disorders, Dizziness, Case Report

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1. 病例回顾

患者, 72岁, 女性, 主因头晕1月, 双下肢无力10天, 加重伴构音障碍6天入院。既往体健。1个月前患者出现持续性头晕, 呈昏沉感, 与体位改变无关, 行走不稳, 伴恶心, 未呕吐; 10天前出现双下肢无力, 搀扶尚可行走, 伴吞咽困难, 无饮水呛咳; 6天前自觉上述症状较前加重, 伴构音障碍, 尚能与人正常交流。查体: T: 36.5°C, P: 79次/分, R: 18次/分, BP: 128/74 mmHg。神志清楚, 双眼左侧注视时可见水平震颤, 构音障碍, 吟诗样言语, 咽反射减弱。四肢肌力IV级, 肌张力正常, 躯干及四肢肌肉无萎缩, 双侧指鼻试验及跟膝胫试验欠稳准, 醉酒步态, 无自主运动。双侧感觉未见异常。两侧肱二头肌反射(+), 肱三头肌反射(+), 膝腱反射(+), 踝反射(+).

颅脑CT及MRI未见异常, 胸CT平扫及增强示右肺上叶不规则片状实变, 考虑肿瘤性病变可能性大, 建议穿刺活检。化验血自身抗体谱检测: ANA抗核抗体阳性。抗神经节苷脂谱抗体: 血清中抗GM4抗体IgG呈现弱阳性, 血清中抗GM3、GM4抗体IgM呈现弱阳性。脑脊液墨汁染色、抗酸染色及自身免疫脑炎抗体6项、小脑15项未见明显异常。肿瘤全项无异常。期间患者症状逐渐加重, 一般状态差, 考虑为: PCD, 给予激素治疗效果欠佳, 加用丙种球蛋白治疗, 症状明显好转。后转入胸外科行CT引导下经皮肺穿刺活检, 病理回报: (右肺上叶)中分化腺癌, 进一步验证为PCD。

2. 讨论

PCD是一种罕见疾病, 是第二常见的免疫介导的小脑共济失调, 表现为快速进展的小脑综合征[1][2]。如本病例所示, PCD的患者症状可能会迅速进展并且非常虚弱, 这些症状常在患者的恶性肿瘤被发现之前表现出来。因此, 早期诊断是至关重要的, 因为它可能会导致隐性癌症的发现[3]。

2.1. 发病机制

大量文献表明, PCD的发病机制可归因于自身免疫反应[4][5]。当潜在的恶性肿瘤接触到免疫特异性神经元的蛋白质时, 特别是当表面受体是抗原时, 就会引发自身免疫反应[6], 从而引发细胞毒性T细胞反应或抗体的直接致病作用。PCD的主要特征之一是浦肯野神经元的破坏, 临床表现通常是亚急性小脑综合征, 即类似于后循环卒中或前庭神经元炎[7][8][9]。

2.2. 相关抗体

PCD是在没有肿瘤或转移灶直接侵袭的情况下, 而由癌症的远程影响引起的[10], 它神经功能的缺陷可能发生在确诊癌症之前的数月或数年, 约80%的PCD患者中, 可以检测到神经元抗体[11]。研究表明: 自身抗体是多种多样的, 这些抗体主要针对细胞内的抗原(细胞核及细胞质)和质膜抗原[12]。其中与

细胞内抗原结合的抗体包括与小脑蛋白 cdr2 结合的抗 Yo (PCA1)抗体(可抑制 c-Myc)、影响 RNA 转录后调节的抗 Hu (ANNA1)抗体和与 RNA 结合蛋白 NOVA 家族结合的抗 Ri (ANNA2)抗体[13] [14]。另一部分与质膜抗原结合的抗体包括作用于 Delta/notch 样表皮生长因子相关受体的 PCA-Tr 抗体、mGLUR1-IgG 和 VGCC-IgG [15] [16]。可以推测, 虽然并不是所有 PCD 均会有特异性的抗体出现, 但是如果这些抗体被检测出来后, 我们应持续观察患者的病情变化, 因为其高度可提示为 PCD。

2.3. 影像学检查

磁共振成像(MRI)为 PCD 的患者提供了又一个重要的诊断依据, 其结果取决于疾病的阶段。例如: 急性 PCD 在 MRI 中通常是正常的, 但在慢性疾病中可以显示小脑萎缩, 尤其在 T1 序列中最为明显[17]。目前也已发现了与特定抗体相关的影像学病例。其中, 在患有 Hu 或 Yo 抗体的患者的报告中, MRI 就能显示弥漫性脑白质病变[18]和两个小脑半球的弥漫性软脑膜增强。

2.4. 治疗

小脑综合征在发病时症状可能很轻微, 但会在几天或几周内恶化[19]。治疗包括立即根除潜在的癌症、类固醇、免疫球蛋白、血浆置换和维持性免疫疗法。有效的早期肿瘤治疗可以通过减少抗原呈递来降低自身免疫驱动力, 从而治疗副肿瘤综合征。但这些效应不能立即显现, 因此在大多数情况下, 皮质类固醇被选择作为急性免疫治疗的一线治疗方法。从病理生理学的角度来说, 一方面它可以减轻脑部的炎症、水肿和血脑屏障的破坏, 另一方面它又可以导致产生抗体的浆细胞凋亡[20]。如果患者对皮质类固醇缺乏治疗效果、症状严重或者快速恶化时, 应同时考虑静脉注射免疫球蛋白(IVIG) [21]或血浆置换(PLEX) [22]来使循环自身抗体减少, 以缓解患者的症状。

总之, 随着辅助检查技术的进步与发展, 副肿瘤性疾病在如今临床工作中越来越常见, 尤其是 PCD。本研究通过报道 PCD 的病例 1 例, 对其发病机制、相关抗体、影像学检查及治疗的相关文献进行了复习。随着对 PCD 研究的深入, 期望更多的预防及治疗措施应用于临床。

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