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以中枢神经系统受累为首发表现的干燥综合征1例并文献复习*

李 婉[1] 高婷婷[1] 张鲁宁[1] 吴艺虹[1] 郑志超[2] 赵 岩[2△]

(1 沈阳医学院奉天医院风湿免疫科 辽宁 沈阳 110024;
2 辽宁省肿瘤医院大连医科大学附属临床肿瘤学院 胃外科 辽宁 沈阳 110042)

摘要 目的:提高对干燥综合征中枢神经系统损害的认识,了解其特点及治疗。**方法:**报告1例以中枢神经系统受累为首发表现的干燥综合征病例,并对相关文献进行复习。**结果:**此例患者以脊髓病变为首发症状,长期口干、眼干,查体及实验室等相关检查诊断干燥综合征明确。**结论:**干燥综合征可存在中枢神经系统损害,其中脊髓病变较常见,应注意完善影像学及脑脊液检查,并与系统性红斑狼疮等结缔组织病相鉴别。

关键词:干燥综合征;中枢神经系统

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Primary Sjögren Syndrome with Central Nervous System Disorder: a Case Report and Review of Literature*

LI Wan[1], GAO Ting-ting[1], ZHANG Lu-ning[1], WU Yi-hong[1], ZHENG Zhi-chao[2], ZHAO Yan[2△]

*(1 Department of Rheumatology, Shenyang Medical College affiliated Fengtian Hospital, Shenyang, Liaoning, 110024, China;
2 Department of Stomach Surgery, Liaoning Cancer Hospital and Institute, Clinical Oncology College of Dalian Medical University, Shenyang, Liaoning, 110042, China)*

ABSTRACT Objective: To better understand the clinical features and treatment of primary Sjögren Syndrome with central nervous system disorder. **Methods:** Report a case of central nervous system involvement as the first manifestation of primary Sjögren Syndrome and reviewed the related literature. **Results:** This patient with spinal cord lesions as the first symptoms, with long-term dry mouth, dry eyes and the examination and laboratory diagnosis of primary Sjögren Syndrome clear. **Conclusion:** The primary Sjögren Syndrome can exist in damage to the central nervous system, especially the spinal cord lesions. We should pay attention to the imaging and cerebrospinal fluid examination and identify with the connective tissue disease such as systemic lupus eythematosus.

Key words: Primary Sjögren syndrome; Central nervous system

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原发性干燥综合征(primary Sjogren's Syndrome, pSS)是一种主要累及外分泌腺体的慢性炎症性自身免疫疾病。临床除有唾液腺和泪腺受损,功能下降而出现口干、眼干外,尚有其他外分泌腺体及腺体外其他器官的受累而出现多系统损害的症状[1]。我科收治1例以中枢神经系统受累为首发表现的干燥综合征,现报告如下:

1 病例摘要

27岁女性患者,以"下肢酸痛1周,乏力3天,加重1天"为主诉入院。入院前1周,患者劳累后出现双下肢酸痛,自觉为骨及关节疼痛,无肌肉疼痛,2-3天后酸痛感消失,逐渐出现双下肢乏力,以左腿为主,自觉右侧肢体"发木"且对温度的感知减退,并出现排尿困难。1天前上述症状加重,于我院门诊检查类风湿因子升高,补体偏低,SSA、SSB阳性,收入院。既往长期自觉口干、眼干。病来乏力,睡眠差。

查体:颜面皮肤发红,舌质干,猖獗龋。双下肢轻度浮肿。颅神经查体无阳性体征。颈软;双上肢肌张力正常;右下肢肌力5级,左下肢肌力4级;双上肢腱反射正常,双下肢腱影像学检查:颈部磁共振(平扫+增强):C5-6椎间盘T2WI信号减低,C4-5间盘纤维环后缘轻度局限性突出,相应硬膜囊前缘略受压,脊髓形态及信号未见异常改变,增强扫描未见异常强化。胸部磁共振(平扫+增强):T2-8水平脊髓内可见条状长T2信号,增强扫描未见异常强化(如图1)。

肺HRCT:右肺上叶胸膜下淡片影,双肺局限性肺气肿。唾液腺ECT:双侧腮腺摄取功能、酸刺激后排泌功能未见异常,双侧颌下腺显影不良,摄取功能重度受损,唾液腺自主排泌功能未见异常。肌电图:未见异常。

Schirmer试验:左眼3 mm,右眼2 mm。泪膜破裂时间测定:左眼4 s,右眼2 s。

化验检查:血常规:血红蛋白105 g/L;尿常规:尿蛋白1+,潜血2+,pH 7.0,比重1.007;血沉35 mmH_2O;C反应蛋白1.26 mg/L;类风湿因子131 IU/ml;补体C3 0.45 g/L,C4 0.14 g/L;免

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作者简介:李婉(1985-),女,医学学士,从事风湿免疫病方面的研究
△通讯作者:赵岩,E-mail: zhaoyan@medmail.com.cn,传真:024-84316246
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疫球蛋白 IgG 22.6 g/L;CTD II III:ANA 1:80+,SSA +,SSB +,Ro- 52+;肝功能:白蛋白 32.6 g/L;血钙 1.92 mmol/L;ANCA(-);尿微量蛋白测定见肾损害以肾小球为主;血清蛋白电泳 γ 球蛋白 29.6 %;24 小时尿蛋白定量 0.248 g/24H。

于我科及神经内科协同诊治情况下,诊断:干燥综合征,脊髓病变。应用甲泼尼龙 250 毫克日一次静点 3 天,续 120 毫克日一次静点 3 天,续 80 毫克日一次静点 3 天,续醋酸泼尼松 30 毫克日一次及硫酸羟氯喹 0.2 日两次口服,并营养神经等药物治疗,患者症状明显好转,排尿困难缓解,可下地行走,右侧肢体痛温觉明显恢复。病情好转后出院。

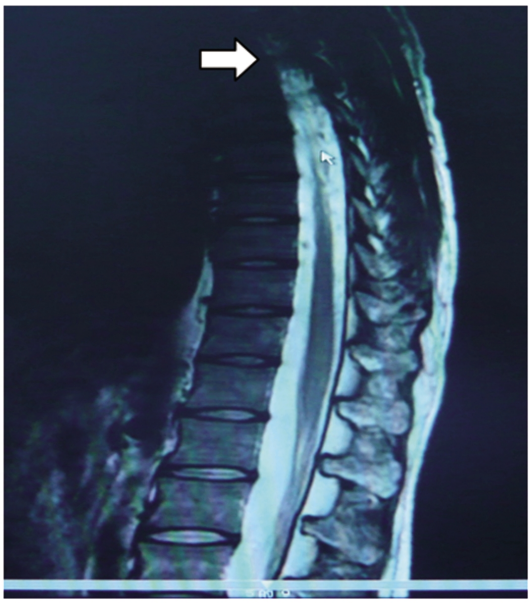

图 1 胸部磁共振:T2-8 水平脊髓内可见条状长 T2 信号

Fig.1 Chest magnetic resonance: Strip T2 intra spinal cord signal was observed at the level between T2 and T8

2 讨论及文献复习

原发性干燥综合征(primary Sjogren's syndrome,pSS)是一种自身免疫病,它主要累及外分泌腺体,呈慢性炎症性改变。其起病隐匿,病情轻重差异较大。pSS 多见于中年女性,除口干、眼干、浅表部位粘膜腺体受累所致的局部症状外,还可出现全身乏力、低热等症状。约有 2/3 患者出现系统损害。如皮肤,骨骼肌肉,肾,肺,消化系统,血液系统都可出现非特异性改变。pSS 累计神经系统的发生率为 5%足有,且以周围神经损害为多见。

pSS 中枢神经系统损害(CNS-SS)发生率较低,具体发病率在数值上仍无确切报道。Alexander 等报道 [2,3] 其发病率约为 20-25 %;北京协和医院的费允云及张奉春对 1990 年 1 月至 2006 年 6 月住院的 pSS 患者进行回顾性分析,发现诊断 CNS-SS 共 21 例,占 pSS 同期住院患者总数的 4.1 %[4]。尚有研究认为其发病率极低,趋近于 0%[5]。我院至今仅诊断此 1 例以中枢神经系统受累为首发症状的 pSS 的病例。

少数 CNS-SS 患者呈急性或亚急性起病,但多起病隐匿。Delalande 等报道的 82 例中枢神经受累的 pSS 病例中,也有少数患者以中枢神经系统为首发表现[6]。有统计提示,肺脏受累可能作为干燥 CNS-SS 的独立危险因素之一[7]。CNS-SS 的临床表现多样,病变累及脑、脊髓和视神经。其中,CNS-SS 较常累及脊髓[6],多表现为反复发作的急性横断性脊髓炎、慢性进行性脊髓病和神经源性膀胱等[2,3,8,9]。本病例即表现为脊髓受累。既往文献表明,在 CNS-SS 早期,病情通常可自行缓解,但多趋于反复、多灶和慢性进展,发作间期病情可以长期稳定[2,3]。

本病例存在长期口干及眼干病史,SSA、SSB 阳性,Schirmer 试验阳性,唾液腺 ECT 见唾液腺损害,符合 pSS 国际诊断标准[10]。有报道指出,CNS-SS 中抗 SSA 抗体阳性患者较阴性患者中枢神经病变更加严重和广泛[11],且其他自身抗体亦可能参与致中枢神经系统病变[12-14]。而除血清学及影像学检查外,脑脊液对判断 CNS-SS 病情活动有一定的意义[4]。此外,尚有 CNS-SS 为无菌性脑膜炎及非霍奇金淋巴瘤等报道 [15,16],可见完善影像学及脑脊液检查对于 CNS-SS 的诊断及判断病情程度是非常重要的。比较遗憾的是,本病例并未进行脑脊液检查因此并不能完全明确脑脊液改变情况。

由于系统性红斑狼疮中枢神经系统受累 -- 神经精神性狼疮(NPSLE)较常见。因此诊断 CNS-SS 需明确与 NPSLE 相鉴别[17]。本病例以脊髓受累而非脑实质受累为主,尿蛋白低于 0.5 g/24 小时,Ds-DNA 阴性,均不支持系统性红斑狼疮诊断。但需注意,一部分以干燥综合征起病的患者,随着病情进展,可能合并或发展至系统性红斑狼疮等其他结缔组织病。

对于 CNS-SS 治疗方案的选择,可针对不同的临床特征决定不同的治疗方法[18]:对于病情稳定自限的患者,可以暂观察;病情活动和进展时,可以给予激素治疗,对于激素不敏感的患者可加用免疫抑制剂,免疫抑制剂中,首选环磷酰胺。对于难治性、复发性的 CNS-SS 患者,有报道[19]指出大剂量丙种球蛋白和血浆置换有效。亦有报道,生物制剂似疗效不理想[20],故对于其治疗方案的选择,尚需进一步探讨。

此病例增进了我们对于干燥综合征中枢神经系统受累的认识,提醒我们,在临床工作中,对于存在中枢神经系统损害表现,并疑诊结缔组织病的病例,除注重排查系统性红斑狼疮外,尚需与干燥综合征相鉴别。

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