·病例报告·

发作性睡病与精神分裂症共病一例

丁岩 尹娜 詹淑琴 黄朝阳 李宁 侯月 王黎

【关键词】 发作性睡病； 精神分裂症； 病例报告
【Key words】 Narcolepsy; Schizophrenia; Case reports

Comorbidity of narcolepsy and schizophrenia: one case report

DING Yan, YIN Na, ZHAN Shu-qin, HUANG Zhao-yang, LI Ning, HOU Yue, WANG Li
Department of Neurology, Xuanwu Hospital, Capital Medical University; Beijing Key Laboratory of Neuromodulation, Beijing 100053, China
Corresponding author: ZHAN Shu-qin (Email: shqzhan@hotmail.com)

患儿 女性，15岁，主因日间睡眠增多3年，精神行为异常10个月，于2014年8月5日入院。患儿3年前开始出现日间发作性不可抑制瞌睡，上课时瞌睡，可被他人唤醒或自行觉醒，大笑时自觉双下肢发软，但无跌倒，无睡眠麻痹，无入睡前恐惧和幻觉，日常生活懒散，少动，贪吃，体重增加（具体不详），能继续上学，但学习成绩下降；10个月前出现精神行为异常，住校期间打电话要求回家，曾于凌晨4时未穿衣服“梦游”至老师房间，有时哭闹，被母亲接回家后出现发呆，称自己谈恋爱了（后经证实无此事），时哭时笑，脾气暴躁，自言自语，睡眠质量较差，可见独自躺在某处自言自语“走开”、“不要脸”，询问时不解释，发脾气，多呈坐位或卧位，嗜睡，贪吃，有时看手机。外院行3次多次睡眠潜伏期试验（MSLT），2次平均睡眠潜伏期（SL）缩短，2次出现睡眠始发的快速眼动睡眠（SOREMP）；根据临床症状和多导睡眠图（PSG）监测结果，先后诊断为睡眠障碍，精神分裂症；间断服用中枢兴奋药和抗精神病药（具体方案不详），但患儿依从性差，治疗效果欠佳。为求进一步诊断与治疗，至我院就诊。患儿自发病以来，睡眠质量较差，饮食尚可，大小便正常，体重由76 kg增至91 kg。既往曾因体重指数（BMI）为37.80 kg/m^2（18.50～23.90 kg/m^2，>28 kg/m^{2}定义为肥胖）诊断为肥胖症，予节食、运动和二甲双胍治疗，个人史及家族史无特殊。入院后神经系统检查：神志清楚，语言清晰，表情淡漠，脑神经检查未见明显异常，四肢肌力5级、肌张力正常，腱反射对称存在，双侧指鼻试验稳准，双侧病理征阴性。实验室检查：血常规、血糖、甲状腺功能试验、性激素均于正常值范围。影像学检查：头部MRI显示垂体饱满，余未见明显异常。盆腔超声未见异常。多次行多导睡眠图监测，未见特异性改变。行阳性和阴性症状量表（PANSS）评价，阴性症状量表未见明显阴性症状；阳性症状量表提示常出现幻觉，主要为幻听，多为议论或谈恋爱内容，思维内容常有猜疑或疑被人偷窥，情绪不稳，易激惹，钟情妄想明显。根据临床表现和MSLT试验结果，参照睡眠障碍国际分类第3版（ICSD-3）[1]发作性睡病和中国精神障碍分类与诊断标准第3版（CCMD-3）[2]精神分裂症诊断标准，临床诊断发作性睡病与精神分裂症共病。遂予盐酸哌甲酯控释片（专注达）18 mg/d口服治疗发作性睡病；盐酸氟西汀（百忧解）10 mg/d，后增加剂量至20 mg/d口服抗焦虑和抑郁；奥氮平2.50 mg/晚，后增加剂量至5 mg/晚口服抗精神病。因考虑体重增加停用奥氮平，改为齐拉西酮20 mg/d和托吡酯（妥泰）25 mg/d口服治疗。患儿住院10 d，出院后继续上述药物治疗3个月后随访，发作性睡病症状和精神行为异常明显改善，可以正常上学，学习成绩有所提高，人际关系改善。

讨 论

发作性睡病临床少见，主要表现为白天过度嗜

doi：10.3969/j.issn.1672-6731.2017.09.009

作者单位：100053 北京，首都医科大学宣武医院神经内科 北京市神经调控重点实验室
通讯作者：詹淑琴（Email：shqzhan@hotmail.com）

睡(EDS)、猝倒、睡眠麻痹和入睡前幻觉[3],诊断主要依靠临床表现、MSLT试验和人类白细胞抗原(*HLA*)基因分型[3]。发作性睡病患者常伴精神症状,甚至以精神症状为突出表现,通常于青少年期发病,部分患者与精神分裂症相似[4-5],临床诊断困难。有文献报道,部分患者的发作性睡病与精神疾病如精神分裂症可先后出现[6-7],最终诊断为发作性睡病与精神分裂症共病,与本文患儿相一致。

发作性睡病患者常存在入睡前幻觉,这些幻觉经历多数是不愉快的,常伴恐惧和威胁,导致患者出现恐惧、焦虑症状和抑郁症状,甚至表现为异常行为,因此易与精神分裂症相混淆[8]。也有发作性睡病误诊为精神分裂症的个案报道[7]。虽然目前尚无大样本研究,但早在1884年即已有发作性睡病与精神分裂症共病的病例报道[9]。

本文患儿以白天过度嗜睡发病,未接受中枢兴奋药治疗,约2年后出现明显精神症状,结合MSLT试验和精神分裂症相关量表测验,发作性睡病与精神分裂症共病诊断明确,同时予中枢兴奋药和抗精神病药,临床症状明显改善。

发作性睡病与精神分裂症共病,二者之间是否存在某种联系?目前对此有3种假说:(1)二者可能是两种不同疾病,并无明显关联性,仅是偶然发生于某例患者。然而,一项小样本临床研究显示,精神分裂症患者发作性睡病发生率明显高于正常人群[10],故不能用偶然发生解释。(2)某些发作性睡病患者精神症状较为突出,易误诊为合并精神分裂症。此观点的提出基于临床观察到部分发作性睡病患者精神症状可于利他林治疗后完全缓解[8]。但上述现象仅见于部分患者。研究显示,发作性睡病患者精神症状虽然表现为各种幻觉,但多为幻视,而精神分裂症常出现幻听,同时发作性睡病妄想相对少见[8],二者临床症状仍有一定差异,可资鉴别。(3)精神分裂症可能是发作性睡病治疗药物——中枢兴奋药如利他林、安非他命等的不良反应[11],常于停药后症状好转或消失。但部分患者先出现精神分裂症再出现发作性睡病症状[6],故无法解释二者之间的联系。因此我们推测,发作性睡病与精神分裂症共病,二者之间可能存在某种特殊的联系。

目前已经明确在免疫调节方面发挥重要作用的*HLA* DQB1*0602基因与发作性睡病的发生密切相关。*HLA* DQB1*0602基因在正常人群中阳性率为12%~38%,而在1型发作性睡病(伴猝倒)患者中高达85%[12]。但Nimgaonkar等[13]认为,精神分裂症患者*HLA* DQB1*0602基因阳性率低于正常人群,表明*HLA* DQB1*0602基因是精神分裂症的保护因素。约85%的发作性睡病患者携带精神分裂症的保护性基因,因此推测发作性睡病患者精神分裂症发生率极低,但此推测与多项研究结果不符[14-15]。2014年,Huang等[16]的研究纳入发作性睡病与精神分裂症共病患者、精神分裂症患者和正常对照者,结果显示,发作性睡病与精神分裂症共病患者*HLA* DQB1*0301/0602基因阳性率明显高于精神分裂症患者和正常对照者。因此我们认为,发作性睡病与精神分裂症共病,二者之间可能存在某种联系,但这一假设尚待更多研究证实。

目前,发作性睡病与精神分裂症共病的治疗药物主要是中枢兴奋药和抗精神病药,但单纯应用中枢兴奋药可能引起甚至加重精神症状,单纯应用抗精神病药亦疗效欠佳[17-20],本文患儿联合应用两种药物有一定疗效,若能明确发作性睡病与精神分裂症之间的联系和共病的潜在机制,将为此类患者的治疗提供新的方向。结合本文患儿的药物治疗反应,中枢兴奋药和抗精神病药联合应用可能使此类患者获益,尚待更多大样本临床研究证实。

参 考 文 献

[1] American Academy of Sleep Medicine. International classification of sleep disorders. 3rd ed. Darien: American Academy of Sleep Medicine, 2014: 146-161.

[2] Chinese Medical Association Psychiatric Branch. Classification and diagnostic criteria of mental disorders in China. 3rd ed. Ji´nan: Shandong Science and Technology Press, 2001: 75-78. [中华医学会精神科分会. CCMD-3中国精神障碍分类与诊断标准. 3版. 济南: 山东科学技术出版社, 2001: 75-78.]

[3] Berkowski JA, Shelgikar AV. Disorders of excessive daytime sleepiness including narcolepsy and idiopathic hypersomnia. Sleep Med Clin, 2016, 11:365-378.

[4] Tandon R, Keshavan MS, Nasrallah HA. Schizophrenia: "just the facts" what we know in 2008. 2: epidemiology and etiology. Schizophr Res, 2008, 102:1-18.

[5] Nishino S. Clinical and neurobiological aspects of narcolepsy. Sleep Med, 2007, 8:373-399.

[6] Canellas F, Lin L, Juliù MR, Clemente A, Vives-Bauza C, Ollila HM, Hong SC, Arboleya SM, Einen MA, Faraco J, Fernandez-Vina M, Mignot E. Dual cases of type 1 narcolepsy with schizophrenia and other psychotic disorders. J Clin Sleep Med, 2014, 10:1011-1018.

[7] Chen MH, Bai YM, Chen YS, Huang KL, Hsu JW, Su TP. Comorbidity of narcolepsy and schizophrenia in an adolescent patient. J Chin Med Assoc, 2014, 77:598-600.

[8] Fortuyn HA, Lappenschaar GA, Nienhuis FJ, Furer JW, Hodiamont PP, Rijnders CA, Lammers GJ, Renier WO, Buitelaar JK, Overeem S. Psychotic symptoms in narcolepsy: phenomenology and a comparison with schizophrenia. Gen Hosp

Psychiatry, 2009, 31:146-154.
[9] Morton WJ. A case of morbid somnolence. J Nerv Ment Dis, 1884, 11:615-619.
[10] Ullman KC. Narcolepsy and schizophrenia. Am J Psychiatry, 1977, 134:822.
[11] Pawluk LK, Hurwitz TD, Schluter JL, Ullevig C, Mahowald MW. Psychiatric morbidity in narcoleptics on chronic high dose methylphenidate therapy. J Nerv Ment Dis, 1995, 183:45-48.
[12] Mignot E. Genetic and familial aspects of narcolepsy. Neurology, 1998, 50(2 Suppl 1):16-22.
[13] Nimgaonkar VL, Rudert WA, Zhang X, Trucco M, Ganguli R. Negative association of schizophrenia with HLA DQB1*0602: evidence from a second African-American cohort. Schizophr Res, 1997, 23:81-86.
[14] Wilcox J. Psychopathology and narcolepsy. Neuropsychobiology, 1985, 14:170-172.
[15] Davison K, Bagley CR. Schizophrenia-like psychoses associated with organic disorders of the central nervous system: a review of the literature//Herrington RN. Current problems in neuropsychiatry. Ashdord: Br J Psychiatry Special Publication, 1969: 113-185.
[16] Huang YS, Guilleminault C, Chen CH, Lai PC, Hwang FM. Narcolepsy-cataplexy and schizophrenia in adolescents. Sleep Med, 2014, 15:15-22.
[17] Auger RR, Goodman SH, Silber MH, Krahn LE, Pankratz VS, Slocumb NL. Risks of high-dose stimulants in the treatment of disorders of excessive somnolence: a case-control study. Sleep, 2005, 28:667-672.
[18] Kondziella D, Arlien-Soborg P. Diagnostic and therapeutic challenges in narcolepsy-related psychosis. J Clin Psychiatry, 2006, 67:1817-1819.
[19] Undurraga J, Garrido J, Santamaría J, Parellada E. Treatment of narcolepsy complicated by psychotic symptoms. Psychosomatics, 2009, 50:427-428.
[20] Fernandez V, Davies S, Walters N. Treatment dilemmas in a young man presenting with narcolepsy and psychotic symptoms. Case Rep Psychiatry, 2011:ID804357.

（收稿日期：2017-08-07）

Epigenetic Methods in Neuroscience Research published

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

This volume presents state-of-the-art methods for reliable detection of epigenetic changes in the nervous system. *Epigenetic Methods in Neuroscience Research* guides readers through methods for the analyses of chromatin remodeling, transposable elements, non-coding RNAs, such as micro RNAs (miRNAs), and circadian oscillations, including: analysis of DNA methylation in neuronal and glial cells or small tissue samples; sensitive method for quantification of alternative methylated forms of cytosines by liquid chromatography/mass spectrometry; affinity-based detection of modified cytosines by immunohistochemistry or methylated DNA immunoprecipitation; chromatin immunoprecipitation (ChIP); miRNA high-throughput profiling and the in situ detection of miRNA subtle expression in the brain; analysis of genes with alternative 3′ untranslated regions (3′UTRs); and the cite-specific delivery of chromatin-modifying drugs. Written in the popular Neuromethods series style, chapters include the kind of detail and key advice from the specialists needed to get successful results in your own laboratory.

Concise and easy-to-use, *Epigenetic Methods in Neuroscience Research* provides multidisciplinary epigenetic approach to study genome, and neural, plasticity that will help the reader to successfully address the challenges associated with neurodevelopmental, psychiatric, and neurodegenerative disorders.

The price of eBook is 79.72€, and hardcover is 94.99€. Visit link.springer.com for more information.

Epilepsy Towards the Next Decade published

Epilepsy Towards the Next Decade (ISBN: 978-3-319-12282-3, eBook ISBN: 978-3-319-12283-0) was published by Springer International Publishing in 2015. The editor of this book is Pasquale Striano, Pediatric Neurology and Muscular Diseases Unit, University of Genoa.

This volume is a comprehensive collection of the most recent knowledge on the biological bases of various kinds of epilepsies and modern clinical approaches to their treatment. Epilepsy affects about 0.5%-1.0% of the world′s population and the main goal of its treatment is to eliminate seizures without creating side effects. Despite numerous advances in the treatment of epilepsy and the approval of several new antiepileptic drugs, about 30% of patients continue to experience recurrent seizures which are medically, physically, and/or socially disabling. The editor of this volume hopes that by bridging the gap between the fundamental biology of epilepsy and its clinical implications he might spur further research and treatment options.

The price of eBook is 118.99€, and hardcover is 139.99€. Visit link.springer.com for more information.