·神经免疫性疾病·

伴其他自身免疫相关抗体的视神经脊髓炎谱系疾病临床特点分析

李妙嫦 李蕊 杨渝 卢婷婷 邱伟 王玉鸽

【摘要】 **目的** 对比分析伴与不伴其他自身免疫相关抗体阳性[排除水通道蛋白4(AQP4)-IgG]视神经脊髓炎谱系疾病(NMOSDs)的临床特点。**方法** 共90例2014年9月至2017年6月确诊的NMOSDs患者符合入组条件,记录首发症状、首次诊断、单相或多相病程、共病情况、首次发病时峰值和入组时扩展残疾状态量表(EDSS)评分、治疗方案、年复发率(ARR);实验室测定脑脊液白细胞计数和蛋白定量,以及多种血清自身免疫相关抗体;头部和全脊椎MRI观察病灶部位、分布范围和脊髓病灶长度。**结果** 90例患者中34例(37.78%)伴血清自身免疫相关抗体阳性(阳性组),并且以抗核抗体(19例占55.88%)、干燥综合征A型抗体(13例占38.24%)、甲状腺过氧化物酶抗体(12例占35.29%)和甲状腺球蛋白抗体(10例占29.41%)阳性为主;其余56例(62.22%)不伴自身免疫相关抗体阳性(阴性组)。两组均以视神经炎[52.94%(18/34)对58.93%(33/56)]、脑部症状[26.47%(9/34)对17.86%(10/56)]和脊髓炎[14.71%(5/34)对21.43%(12/56)]为主要首发症状(Fisher确切概率法:$P=0.504$),首次诊断($\chi^2=1.634$,$P=0.201$)、单相或多相病程(Fisher确切概率法:$P=1.000$)、共病情况($\chi^2=1.275$,$P=0.302$)、首次发病时峰值($Z=-0.747$,$P=0.455$)和入组时($Z=-0.379$,$P=0.705$)EDSS评分,以及治疗方案($\chi^2=0.662$,$P=0.416$)和年复发率($Z=-0.370$,$P=0.711$)差异均无统计学意义;脑脊液白细胞计数($Z=-1.163$,$P=0.245$)和蛋白定量($Z=-0.340$,$P=0.734$)差异亦无统计学意义。MRI显示68例(75.56%)有颅内病灶[阳性组28例(82.35%)、阴性组40例(71.43%)],主要位于顶叶、额叶和侧脑室;62例(68.89%)存在脊髓病灶[阳性组21例(61.76%)、阴性组41例(73.21%)],均以颈髓和胸髓病灶以及中节段病灶为主;两组颅内病灶分布范围($\chi^2=1.367$,$P=0.242$),以及脊髓病灶分布范围($\chi^2=1.294$,$P=0.255$)和病变长度($Z=-0.647$,$P=0.517$)差异均无统计学意义。**结论** 伴与不伴其他自身免疫相关抗体阳性的NMOSDs患者在首发症状、脑脊液白细胞计数和蛋白定量、MRI病灶分布特征等方面无明显差异,自身免疫相关抗体在NMOSDs患者临床特征方面的价值尚待进一步探讨。

【关键词】 视神经脊髓炎谱系疾病(非*MeSH*词); 自身抗体; 血清学; 脑脊髓液; 磁共振成像

Clinical characteristics of patients with neuromyelitis optica spectrum disorders with other autoantibodies

LI Miao-chang, LI Rui, YANG Yu, LU Ting-ting, QIU Wei, WANG Yu-ge

Department of Neurology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou 510630, Guangdong, China

Corresponding author: WANG Yu-ge (Email: wangyuge1228@163.com)

【**Abstract**】 **Objective** To analyze the clinical characteristics of patients with neuromyelitis optica spectrum disorders (NMOSDs) with or without autoantibodies other than aquaporin 4 (AQP4)-IgG. **Methods** A total of 90 NMOSDs patients were included from September 2014 to June 2017. First symptoms, first diagnosis, monophasic or polyphasic course of disease, comorbidities, Expanded Disability Status Scale (EDSS) score, treatment regimen and annualized relapse rate (ARR) were recorded. Laboratory tests for cerebrospinal fluid (CSF) white blood cell count and protein quantification, as well as serum

doi:10.3969/j.issn.1672-6731.2020.09.007

作者单位:510630 广州,中山大学附属第三医院神经内科[李妙嫦(现在广东省肇庆市第一人民医院神经内科,邮政编码:526011)]

通讯作者:王玉鸽,Email:wangyuge1228@163.com

autoimmune-related antibodies, including anti-nuclear antibody (ANA), A type and B type Sjögren's syndrome antibody (SSA and SSB), thyroid peroxidase (TPO) and thyroglobulin (TG) antibodies, anti-double stranded DNA antibody (dsDNA), perinuclear antineutrophil cytoplasmic antibody (pANCA), anti-endothelial cell antibody (AECA), Ro-52 antibody, Jo-1 antibody, anti-cardiolipin antibody (ACA), anti-mitochondria antibody M2 subtype (AMA-M2), human leukocyte antigen-B27 (HLA-B27), and myelin oligodendrocyte glycoprotein (MOG) antibody were examined. Brain and whole spine MRI were performed to observe the lesion site, distribution and length of spinal cord lesions. **Results** Among the 90 patients, 34 (37.78%) were accompanied by autoimmune-related antibodies (positive group), including 19 (55.88%) ANA positive cases, 13 (38.24%) SSA positive cases, 12 (35.29%) TPO antibody positive cases, and 10 (29.41%) TG antibody positive cases. The remaining 56 patients (62.22%) were not accompanied by autoimmune-related antibodies (negative group). In both groups, optic neuritis [52.94% (18/34) vs. 58.93% (33/56)], brain symptoms [26.47% (9/34) vs. 17.86% (10/56)] and myelitis [14.71% (5/34) vs. 21.43% (12/56)] were the main initial symptoms (Fisher exact probability: $P = 0.504$). There were no significant differences in the first diagnosis ($\chi^2 = 1.634$, $P = 0.201$), monophasic or polyphasic course (Fisher exact probability: $P = 1.000$), comorbidities ($\chi^2 = 1.275$, $P = 0.302$), EDSS score at the peak of the first onset ($Z = -0.747$, $P = 0.455$) and at the inclusion ($Z = -0.379$, $P = 0.705$), treatment plan ($\chi^2 = 0.662$, $P = 0.416$) and ARR ($Z = -0.370$, $P = 0.711$). There was no statistically significant difference in CSF white blood cell count ($Z = -1.163$, $P = 0.245$) and protein quantification ($Z = -0.340$, $P = 0.734$). MRI showed that 68 cases (75.56%) had intracranial lesions [28 cases (82.35%) in the positive group and 40 cases (71.43%) in the negative group], mainly located in the parietal lobe, frontal lobe and lateral ventricle. There were 62 cases (68.89%) with spinal lesions [21 cases (61.76%) in the positive group and 41 cases (73.21%) in the negative group], which were mainly cervical and thoracic myeloid lesions and medium-length segment lesion. There were no statistically significant differences in intracranial lesions ($\chi^2 = 1.367$, $P = 0.242$), spinal cord lesions ($\chi^2 = 1.294$, $P = 0.255$) or lesion length ($Z = -0.647$, $P = 0.517$) between 2 groups. **Conclusions** There were no significant differences between NMOSDs patients with and without other autoimmune-related antibodies in terms of initial symptoms, CSF white blood cell count and protein quantification, MRI lesion distribution characteristics, etc. The value of autoimmune-related antibodies in clinical characteristics of NMOSDs patients remains to be further explored.

【Key words】 Neuromyelities optica spectrum disorders (not in *MeSH*); Autoantibodies; Serology; Cerebrospinal fluid; Magnetic resonance imaging

Conflicts of interest: none declared

视神经脊髓炎谱系疾病(NMOSDs)是一种危及生命、相对罕见的中枢神经系统自身免疫性疾病,临床表现为急性视神经炎、长节段横贯性脊髓炎(LETM)和延髓极后区表现,导致永久性神经功能缺损[1-2]。水通道蛋白4(AQP4)-IgG是其特异性自身抗体,测定血清AQP4-IgG可有助于早期诊断与治疗[3]。在NMOSDs患者体内亦常可检出其他自身免疫相关抗体,包括抗核抗体(ANA)、干燥综合征A型(SSA)或B型(SSB)抗体,易引起系统性自身免疫性疾病[4]。研究显示,伴自身免疫相关抗体的NMOSDs患者临床症状较严重,脊髓受累节段相对较长,急性期激素治疗效果较差,发病后1年复发率较高[5]。这些自身免疫相关抗体是否参与NMOSDs的发病机制尚未明确。本研究对比分析伴或不伴自身免疫相关抗体阳性(排除AQP4-IgG)NMOSDs患者首发症状、脑脊液白细胞计数和蛋白定量、MRI病灶分布特征等的差异,探讨其他自身免疫相关抗体在NMOSDs临床特征方面的价值。

对象与方法

一、观察对象

1. 纳入与排除标准 (1)均符合2006年视神经脊髓炎(NMO)诊断标准[2]或2015年NMOSDs诊断标准[6]。(2)血清AQP4-IgG呈阳性反应(细胞转染法)。(3)近2年发作≥2次或者近1年发作≥1次。(4)年龄≥18岁。(5)排除肝肾功能和血常规异常,合并严重全身性疾病、先天性疾病、遗传性疾病、恶性肿瘤、免疫缺陷、全身或局部感染等,以及妊娠期或哺乳期女性。

2. 一般资料 选择2014年9月至2017年6月在中山大学附属第三医院神经内科门诊和住院治疗的NMOSDs患者共90例,男性6例,女性84例;发病年龄10~65岁,平均(35.99±13.36)岁;病程0.04~22.20年,中位病程2.42(0.75,5.34)年。

二、研究方法

1.临床资料采集 记录患者首发症状(包括视神经炎、脑部症状、脊髓炎、视神经合并脊髓炎、脑部症状合并脊髓炎),首次诊断(视神经脊髓炎或NMOSDs),单相或多相病程、共病情况(包括系统性红斑狼疮、干燥综合征、乙型或丙型肝炎、直肠腺癌)、首次发病时峰值和入组时神经功能及残疾状态[扩展残疾状态量表(EDSS)]、治疗方案(激素或激素+硫唑嘌呤)、复发次数[年复发率(ARR)]等。

2.其他自身免疫相关抗体检测 (1)血清:患者于入组时抽取外周静脉血8 ml,间接免疫荧光法(IFA)测定抗核抗体(ANA)、抗内皮细胞抗体(AECA)、核周抗中性粒细胞胞质抗体(pANCA),化学发光免疫分析法(CIA)检测甲状腺过氧化物酶(TPO)和甲状腺球蛋白(TG)抗体,酶联免疫吸附试验(ELISA)测定SSA和SSB、抗双链DNA抗体(dsDNA)、Ro-52抗体、Jo-1抗体、抗心磷脂抗体(ACA)、抗线粒体抗体M2亚型(AMA-M2)、人类白细胞抗原B27(HLA-B27)、髓鞘少突胶质细胞糖蛋白(MOG)抗体。(2)脑脊液:本组有43例患者入组时腰椎穿刺抽取脑脊液共8 ml,测定白细胞计数[正常参考值:(0~4)×10^6/L]和蛋白定量(正常参考值:100~400 mg/L)。

3.MRI检查 所有患者均于入组时行头部和全脊椎MRI检查,观察病灶部位、分布和脊髓病灶长度,根据脊髓受累节段分为短节段病灶(≤3个脊髓节段)、中节段病灶(4~9个脊髓节段)和长节段病灶(≥10个脊髓节段)。

4.统计分析方法 采用SPSS 17.0统计软件进行数据处理与分析。计数资料以相对数构成比(%)或率(%)表示,采用χ^2检验或Fisher确切概率法。呈正态分布的计量资料以均数±标准差($\bar{x}\pm s$)表示,采用两独立样本的t检验;呈非正态分布的计量资料以中位数和四分位数间距[$M(P_{25},P_{75})$]表示,采用Mann-Whitney U检验。以$P\leq 0.05$为差异具有统计学意义。

结 果

本组90例患者中34例(37.78%)实验室检查伴其他自身免疫相关抗体阳性(阳性组),13例(38.24%)1种抗体阳性、12例(35.29%)2种抗体阳性、5例(14.71%)3种抗体阳性以及4例(11.76%)≥4种抗体阳性,其中,ANA阳性者55.88%(19/34)、SSA阳性38.24%(13/34)、SSB阳性11.76%(4/34)、TPO抗体阳性35.29%(12/34)、TG抗体阳性29.41%(10/34)、dsDNA阳性8.82%(3/34)、ACA和HLA-B27阳性各占5.88%(2/34),pANCA、AECA、Ro-52抗体、Jo-1抗体、AMA-M2和MOG抗体阳性各占2.94%(1/34),表明NMOSDs患者以ANA、SSA和SSB、TPO和TG抗体阳性最为常见;余56例(62.22%)患者不伴其他自身免疫相关抗体阳性(阴性组)。两组患者性别、发病年龄、病程、首发症状、首次诊断、单相或多相病程、共病情况、首次发病时峰值和入组时EDSS评分,以及治疗方案和年复发率差异均无统计学意义($P>0.05$,表1)。

阳性组有21例患者行脑脊液检查,白细胞计数(0~210)×10^6/L、中位值4(0,8)×10^6/L,其中14例正常、7例升高(1例>20×10^6/L);蛋白定量130~700 mg/L、中位值为270(165,504) mg/L,13例正常、8例升高。阴性组22例行脑脊液检查,白细胞计数(0~100)×10^6/L、中位值4.50(2.00,15.00)×10^6/L,11例正常、11例升高(3例>20×10^6/L);蛋白定量100~930 mg/L、中位值305(233,453) mg/L,14例正常、8例升高。两组脑脊液白细胞计数和蛋白定量差异无统计学意义(均$P>0.05$,表2)。

头部MRI检查,90例患者中计68例存在颅内病灶,阳性组占82.35%(28/34)、阴性组71.43%(40/56),分别位于丘脑、额叶、颞叶、顶叶、枕叶、延髓极后区、脑干、大脑脚、视神经、半卵圆中心、侧脑室等,两组病灶分布范围差异无统计学意义(均$P>0.05$,表3)。全脊椎MRI检查共有62例患者呈现脊髓受累征象,阳性组占61.76%(21/34)、阴性组73.21%(41/56),均以颈髓和胸髓病灶以及中节段病灶为主,两组患者脊髓病灶分布和病变长度比较,差异无统计学意义(均$P>0.05$,表4)。

讨 论

本研究NMOSDs患者男女比例为1∶14,平均发病年龄为(35.99±13.36)岁,与既往文献报道相一致[7];首发症状以视神经、脊髓炎、脑部症状为主,亦与文献报道相符[8],且伴与不伴其他自身免疫相关抗体阳性的NMOSDs患者性别、年龄、病程和首发症状均无明显差异,提示除AQP4-IgG外,NMOSDs患者无论是否伴其他自身免疫相关抗体阳性,均好发于育龄期女性,且以视神经炎、脊髓炎、脑部症状为主要首发症状。

表1 阳性组与阴性组患者临床资料的比较

Table 1. Comparison of clinical data between positive group and negative group

观察指标	阳性组（n=34）	阴性组（n=56）	统计量值	*P*值
性别[例(%)]			0.041	0.839
男性	3(8.82)	3(5.36)		
女性	31(91.18)	53(94.64)		
发病年龄($\bar{x}\pm s$,岁)	34.06±14.77	37.16±12.54	1.063	0.291
病程[$M(P_{25},P_{75})$,年]	2.37 (0.75,5.00)	2.52 (0.75,5.97)	-0.258	0.796
首发症状[例(%)]			—	0.504
视神经炎	18(52.94)	33(58.93)		
脑部症状	9(26.47)	10(17.86)		
脊髓炎	5(14.71)	12(21.43)		
视神经合并脊髓炎	1(2.94)	1(1.79)		
脑部症状合并脊髓炎	1(2.94)	0(0.00)		
首次诊断[例(%)]			1.634	0.201
NMO	24(70.59)	46(82.14)		
NMOSDs	10(29.41)	10(17.86)		
病程[例(%)]			—	1.000
单相	0(0.00)	1(1.79)		
多相	34(100.00)	55(98.21)		
共病情况[例(%)]	29(85.29)	53(94.64)	1.275	0.259
系统性红斑狼疮	2(5.88)	0(0.00)		
干燥综合征	2(5.88)	0(0.00)		
乙型肝炎	1(2.94)	2(3.57)		
丙型肝炎	0(0.00)	1(1.79)		
直肠腺癌	0(0.00)	1(1.79)		
首次发病时峰值EDSS评分[$M(P_{25},P_{75})$]	3.00 (2.00,3.25)	3.00 (2.00,3.88)	-0.747	0.455
入组时EDSS评分[$M(P_{25},P_{75})$]	4.00 (3.00,5.00)	4.00 (3.00,5.00)	-0.379	0.705
治疗方案[例(%)]			0.662	0.416
激素	28(82.35)	42(75.00)		
激素+硫唑嘌呤	6(17.65)	14(25.00)		
ARR[$M(P_{25},P_{75})$]	1.19 (0.44,2.65)	0.98 (0.40,2.00)	-0.370	0.711

—，Fisher exact probability，Fisher确切概率法。Two-independent-sample *t* test for comparison of onset age, Mann-Whitney *U* test for comparison of duration, EDSS at the peak of the first onset and at the inclusion and ARR, and χ^2 test for comparison of others，发病年龄的比较行两独立样本的*t*检验，病程、首次发病时峰值EDSS、入组时EDSS和ARR的比较行Mann-Whitney *U*检验，其余各项的比较行χ^2检验。NMO，neuromyelitis optica，视神经脊髓炎；NMOSDs，neuromyelitis optica spectrum disorders，视神经脊髓炎谱系疾病；EDSS，Expanded Disability Status Scale，扩展残疾状态量表；ARR，annualized relapse rate，年复发率

NMOSDs患者大多合并有多种系统性免疫性疾病[9-10]。一项纳入88例儿童NMOSDs患者的临床研究显示，在57例(64.77%)伴其他自身免疫相关抗体阳性(不包括AQP4-IgG)的患者中，18例(20.45%)合并系统性自身免疫性疾病如系统性红斑狼疮、干燥综合征、幼年类风湿关节炎等[11]。据文献报道，约50%的NMOSDs患者合并其他自身免疫相关抗体阳性，而自身免疫相关抗体阳性更支持NMOSDs之诊断[12]。Wu等[13]发现，NMOSDs患者血清ANA阳性检出率显著高于多发性硬化患者，该作者认为ANA有助于这两种疾病的鉴别诊断。Chen等[14]的研究显示，NMOSDs常与其他自身免疫相关抗体阳性如ANA和SSA阳性并存，且ANA阳性更多见于AQP4-IgG阳性的NMOSDs患者，但NMOSDs较少合并系统性免疫性疾病。尽管其他自身免疫相关抗体阳性如ANA或SSA阳性同样常见于NMOSDs患者，但仍以AQP4-IgG特异性最高，AQP4-IgG不表达于其他疾病导致的视神经病变或脊髓病变[15]。Asgari等[16]对208例系统性红斑狼疮患者进行为期20年的随访，其中仅30例(14.42%)出现中枢神经系统脱髓鞘改变，2例进展为NMOSDs，且临床主要表现为脊髓炎，血清AQP4-IgG阳性。Qiao等[17]对1985–2013年收治的616例干燥综合征患者的临床资料进行回顾分析，仅43例(6.98%)进展为NMOSDs。由此可见，AQP4-IgG阳性的NMOSDs患者合并系统性红斑狼疮和(或)干燥综合征为共病表现，而非系统性红斑狼疮和(或)干燥综合征的并发症[18]。本研究有34例(37.78%)患者伴其他自身免疫相关抗体阳性，以ANA[19例(55.88%)]、SSA[13例(38.24%)]、TPO抗体[12例(35.29%)]和TG抗体[10例(29.41%)]阳性为主；其中4例(4.44%)合并系统性自身免疫性疾病(包括系统性红斑狼疮2例、干燥综合征2例)，4例(4.44%)合并肝炎(包括乙型肝炎3例、丙型肝炎1例)，1例(1.11%)合并直肠腺癌。最近研究显示，血清游离甲状腺素(FT_4)有可能成为首次发病的NMOSDs患者的预后预测指标，高FT_4水平是神经功能障碍和高复发率的预测因素($HR=1.18$，95% CI：1.05～1.32；$P=0.05$)[19]。在本研究中，阳性组患者总复发次数为93次，中位年复发率为1.19(0.44,2.65)，阴性组总复发次数为156次，中位年复发率为0.98(0.40,2.00)，组间差异无统计学意义。

研究显示，有60%～88%的NMOSDs患者MRI可检出颅内病灶[20-23]。Cacciaguerra等[24]的影像学回顾分析显示，116例NMOSDs患者中59例(50.86%)存在典型的颅内病变，约32.76%(38/116)的患者病变沿侧脑室分布，本研究NMOSDs患者也

表2 阳性组与阴性组患者脑脊液白细胞计数和蛋白定量的比较[$M(P_{25},P_{75})$]

Table 2. Comparison of CSF indexes between positive group and negative group [$M\ (P_{25},\ P_{75})$]

组别	例数	白细胞计数(×10⁶/L)	蛋白定量(mg/L)
阳性组	21	4.00(0.00, 8.00)	270.00(165.00,504.00)
阴性组	22	4.50(2.00,15.00)	305.00(233.00,453.00)
Z值		-1.163	-0.340
P值		0.245	0.734

表3 阳性组与阴性组患者颅内病灶分布范围的比较[例(%)]

Table 3. Comparison of intracranial lesion distribution between positive group and negative group [case (%)]

病灶	阳性组(n=34)	阴性组(n=56)	χ^2值	P值
颅内病灶	28(82.35)	40(71.43)	1.367	0.242
丘脑	2(5.88)	0(0.00)	—	0.140
额叶	9(26.47)	14(25.00)	0.024	0.877
颞叶	2(5.88)	5(8.93)	0.014	0.907
顶叶	9(26.47)	10(17.86)	0.942	0.332
枕叶	1(2.94)	4(7.14)	0.136	0.712
延髓极后区	6(17.65)	5(8.93)	0.796	0.372
脑干	3(8.82)	5(8.93)	0.000	1.000
大脑脚	3(8.82)	4(7.14)	0.000	1.000
视神经	3(8.82)	13(23.21)	2.997	0.083
半卵圆中心	4(11.76)	7(12.50)	0.000	1.000
侧脑室	5(14.71)	8(14.29)	0.000	1.000

—,Fisher exact probability,Fisher确切概率法

表4 阳性组与阴性组患者脊髓病灶分布范围和病变长度的比较[例(%)]

Table 4. Comparison of spinal cord lesion distribution and length between positive group and negative group [case (%)]

病灶	阳性组(n=34)	阴性组(n=56)	χ^2值	P值
脊髓病灶	21(61.76)	41(73.21)	1.294	0.255
颈髓病灶	18(52.94)	37(66.07)	1.535	0.215
胸髓病灶	14(41.18)	29(51.79)	0.552	0.457
病变长度			-0.647	0.517
短节段	6(17.65)	9(16.07)		
中节段	11(32.35)	22(39.29)		
长节段	4(11.76)	10(17.86)		

可见特征性的颅内病变,病灶主要位于顶叶、额叶和侧脑室。方玮[25]发现,合并系统性免疫性疾病的NMOSDs患者脊髓病灶节段长于不合并系统性免疫性疾病者。唐友莲[5]认为,伴其他自身免疫相关抗体阳性的NMOSDs患者较不伴自身免疫相关抗体阳性患者的脊髓病灶节段更长。本研究有62例(68.89%)患者累及脊髓[阳性组21例(61.76%)、阴性组41例(73.21%)],均以颈髓和胸髓病灶多见、中节段病灶为主,两组患者脊髓病灶分布和病变长度均无明显差异,与国内研究相似[26]。

本研究有43例行腰椎穿刺脑脊液检查,18例(41.86%)白细胞计数升高[阳性组7例(33.33%)、阴性组11例(50%)],16例(37.21%)蛋白定量升高[阳性组8例(38.10%)、阴性组8例(36.36%)],与既往国内同类研究结论相近[27],而白细胞计数升高比例低于国外文献报道(79%)[28]。Wingerchuk等[4]认为,与多发性硬化相比,NMOSDs患者更易出现脑脊液白细胞计数升高。孙昊等[4]的研究显示,与不伴非特异性自身免疫相关抗体阳性的患者相比,伴非特异性自身抗体阳性的NMOSDs患者中枢神经系统鞘内炎症反应更明显。但本研究伴与不伴其他自身抗体阳性的NMOSDs患者脑脊液白细胞计数和蛋白定量差异无统计学意义。

综上所述,除AQP4-IgG外,伴与不伴其他自身免疫相关抗体阳性的NMOSDs患者在首发症状、脑脊液白细胞计数和蛋白定量、MRI病灶分布特征等方面均无明显差异,自身免疫相关抗体在NMOSDs患者临床特征方面的价值尚待进一步研究。

利益冲突 无

参 考 文 献

[1] Oh J, Levy M. Neuromyelitisoptica: an antibody - mediated disorder of the central nervous system[J]. Neurol Res Int, 2012: ID460825.

[2] Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised diagnostic criteria for neuromyelitisoptica[J]. Neurology, 2006, 66:1485-1489.

[3] Marignier R, Giraudon P, Vukusic S, Confavreux C, Honnorat J. Anti - aquaporin - 4 antibodies in Devic´s neuromyelitisoptica: therapeutic implications[J]. Ther Adv Neurol Disord, 2010, 3: 311-321.

[4] Sun H, Wang CJ, Wang G, Wang BJ, Guo SG. Neuromyelitisoptica spectrum disorders with common non-organ-specific autoantibodies[J]. Shandong Da Xue Xue Bao (Yi Xue Ban), 2016, 54:50-54.[孙昊, 汪春娟, 王戈, 王宝洁, 郭守刚. 视神经脊髓炎谱系疾病伴常见非器官特异性自身抗体的特点[J]. 山东大学学报(医学版), 2016, 54:50-54.]

[5] Tang YL. The analysis on clinical and imageological features of neuromyelitisoptica with positive autoantibodies[D]. Nanning: Guangxi Yi Ke Da Xue, 2016.[唐友莲. 伴自身抗体阳性的视神经脊髓炎临床和影像学特点分析[D]. 南宁: 广西医科大学, 2016.]

[6] Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, de Seze J, Fujihara K, Greenberg B, Jacob A, Jarius S, Lana - Peixoto M, Levy M, Simon JH, Tenembaum S, Traboulsee AL, Waters P, Wellik KE, Weinshenker BG;

International Panel for NMO Diagnosis. International consensus diagnostic criteria for neuromyelitisoptica spectrum disorders [J]. Neurology, 2015, 85:177-189.

[7] Flanagan EP, Cabre P, Weinshenker BG, Sauver JS, Jacobson DJ, Majed M, Lennon VA, Lucchinetti CF, McKeon A, Matiello M, Kale N, Wingerchuk DM, Mandrekar J, Sagen JA, Fryer JP, Robinson AB, Pittock SJ. Epidemiology of aquaporin - 4 autoimmunity and neuromyelitisoptica spectrum [J]. Ann Neurol, 2016, 79:775-783.

[8] Cabre P, Heinzlef O, Merle H, Buisson GG, Bera O, Bellance R, Vernant JC, Smadja D. MS and neuromyelitisoptica in Martinique (French West Indies)[J]. Neurology, 2001, 56:507-514.

[9] Iyer A, Elsone L, Appleton R, Jacob A. A review of the current literature and a guide to the early diagnosis of autoimmune disorders associated with neuromyelitisoptica[J]. Autoimmunity, 2014, 47:154-161.

[10] Zhang B, Zhong Y, Wang Y, Dai Y, Qiu W, Zhang L, Li H, Lu Z. Neuromyelitisoptica spectrum disorders without and with autoimmune diseases[J]. BMC Neurol, 2014, 14:162.

[11] McKeon A, Lennon VA, Lotze T, Tenenbaum S, Ness JM, Rensel M, Kuntz NL, Fryer JP, Homburger H, Hunter J, Weinshenker BG, Krecke K, Lucchinetti CF, Pittock SJ. CNS aquaporin-4 autoimmunity in children[J]. Neurology, 2008, 71: 93-100.

[12] Neuroimmunology Branch, Chinese Society of Immunology; Neuroimmunology Group, Neurology Branch, Chinese Medical Association; Professional Committee on Neuroimmunization, Neurology Branch, Chinese Medical Doctor Association. Guidelines for diagnosis and treatment of optic neuromyelitis spectrum disease in China[J]. Zhongguo Shen Jing Mian Yi Xue He Shen Jing Bing Xue Za Zhi, 2016, 23:155-166.[中国免疫学会神经免疫学分会,中华医学会神经病学分会神经免疫学组, 中国医师协会神经内科医师分会神经免疫专业委员会. 中国视神经脊髓炎谱系疾病诊断与治疗指南[J]. 中国神经免疫学和神经病学杂志, 2016, 23:155-166.]

[13] Wu L, Huang D, Yang Y, Wu W. Combined screening for serum anti-nuclear and anti-aquaporin-4 antibodies improves diagnostic accuracy for distinguishing neuromyelitisoptica from multiple sclerosis[J]. Eur Neurol, 2014, 72:103-108.

[14] Chen C, Sun XB, Wang YG, Shu YQ, Ling F, Peng LS, Lu ZQ, Qiu W. Multiple autoantibodies and neuromyelitisoptica spectrum disorders[J]. Neuroimmunomodulation, 2016, 23:151-156.

[15] Lennon VA, Wingerchuk DM, Kryzer TJ, Pittock SJ, Lucchinetti CF, Fujihara K, Nakashima I, Weinshenker BG. A serum autoantibody marker of neuromyelitisoptica: distinction from multiple sclerosis[J]. Lancet, 2004, 364:2106-2112.

[16] Asgari N, Jarius S, Laustrup H, Skejoe HP, Lillevang ST, Weinshenker BG, Voss A. Aquaporin - 4 - autoimmunity in patients with systemic lupus erythematosus: a predominantly population-based study[J]. Mult Scler, 2018, 24:331-339.

[17] Qiao L, Wang Q, Fei Y, Zhang W, Xu Y, Zhang Y, Zhao Y, Zeng X, Zhang F. The clinical characteristics of primary Sjogren's syndrome with neuromyelitisoptica spectrum disorder in China: a STROBE - compliant article [J]. Medicine (Baltimore), 2015, 94:e1145.

[18] Pittock SJ, Lennon VA, de Seze J, Vermersch P, Homburger HA, Wingerchuk DM, Lucchinetti CF, Zéphir H, Moder K, Weinshenker BG. Neuromyelitisoptica and non-organ-specific autoimmunity[J]. Arch Neurol, 2008, 65:78-83.

[19] He Q, Li L, Li Y, Lu Y, Wu K, Zhang R, Teng J, Zhao J, Jia Y. Free thyroxine level is associated with both relapse rate and poor neurofunction in first-attack neuromyelitisoptica spectrum disorder (NMOSD) patients[J]. BMC Neurol, 2019, 19:329.

[20] Pittock SJ, Lennon VA, Krecke K, Wingerchuk DM, Lucchinetti CF, Weinshenker BG. Brain abnormalities in neuromyelitisoptica [J]. Arch Neurol, 2006, 63:390-396.

[21] Kim W, Park MS, Lee SH, Kim SH, Jung IJ, Takahashi T, Misu T, Fujihara K, Kim HJ. Characteristic brain magnetic resonance imaging abnormalities in central nervous system aquaporin-4 autoimmunity[J]. Mult Scler, 2010, 16:1229-1236.

[22] Ito S, Mori M, Makino T, Hayakawa S, Kuwabara S. "Cloud-like enhancement" is a magnetic resonance imaging abnormality specific to neuromyelitisoptica[J]. Ann Neurol, 2009, 66:425-428.

[23] Kim JE, Kim SM, Ahn SW, Lim BC, Chae JH, Hong YH, Park KS, Sung JJ, Lee KW. Brain abnormalities in neuromyelitisoptica[J]. J Neurol Sci, 2011, 302:43-48.

[24] Cacciaguerra L, Meani A, Mesaros S, Radaelli M, Palace J, Dujmovic-Basuroski I, Pagani E, Martinelli V, Matthews L, Drulovic J, Leite MI, Comi G, Filippi M, Rocca MA. Brain and cord imaging features in neuromyelitisoptica spectrum disorders [J]. Ann Neurol, 2019, 85:371-384.

[25] Fang W. Clinical and imaging characteristics of optic neuromyelitis spectrum disease with systemic autoimmune disease[D]. Hangzhou: Zhejiang University, 2017.[方玮. 伴系统性自身免疫病的视神经脊髓炎谱系疾病的临床和影像特点[D]. 杭州: 浙江大学, 2017.]

[26] Ji MQ, Qin YL, Jiao YJ, Jiao JS, Deng TT, Zi YX, Han MY, Jin M.Clinical characteristics of patients with neuromyelitisoptica spectrum disorders[J]. Yan Ke Xin Jin Zhan, 2020, 40:184-187.[冀美琦, 秦亚丽, 矫毓娟, 焦劲松, 邓婷婷, 訾迎新, 韩梦雨, 金明. 视神经脊髓炎谱系疾病患者临床特点分析[J]. 眼科新进展, 2020, 40:184-187.]

[27] Liu HQ, Ren HT, Xu Y, Gao XY, Li W, Zhang JW, Guan HZ. The characteristics of the cerebrospinal fluid cytology in AQP4-IgG positive neuromyelitisoptica spectrum disorders [J]. Zhongguo Shen Jing Mian Yi Xue He Shen Jing Bing Xue Za Zhi, 2008, 25:6-10.[刘慧勤, 任海涛, 徐雁, 高鑫雅, 李玮, 张杰文, 关鸿志. AQP4-IgG阳性视神经脊髓炎谱系疾病的脑脊液细胞学特点[J]. 中国神经免疫学和神经病学杂志, 2008, 25:6-10.]

[28] Bergamaschi R, Tonietti S, Franciotta D, Candeloro E, Tavazzi E, Piccolo G, Romani A, Cosi V. Oligoclonal bands in Devic´sneuromyelitisoptica and multiple sclerosis: differences in repeated cerebrospinal fluid examinations[J]. Mult Scler, 2004, 10:2-4.

（收稿日期:2020-09-02）
（本文编辑:彭一帆）