

多系统萎缩的早期综合诊断

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摘要 目的 探讨多系统萎缩(multiple system atrophy, MSA)患者的临床表现及神经影像学新特征(脑桥“十字征”和“壳核裂隙征”)在 MSA 早期诊断中的临床意义。**方法** 回顾性分析 21 例临床诊断为多系统萎缩(MSA)患者的临床表现和头部 MRI 资料。**结果** 21 例 MSA 患者中, Shy-Drager 综合征(MSA-A) 9 例, 早期临床表现为体位性低血压, 泌尿生殖功能障碍, 头部 MRI 检查脑桥“壳核裂隙征”和“十字征”为 I 期; 橄榄体脑桥小脑萎缩(MSA-C) 5 例, 3 例发病后 1 年头部 MRI 脑桥“十字征”达 II 期; “壳核裂隙征”为 I 期, 2 例发病后 3 年头部 MRI 脑桥“十字征”达 IV 期。黑质纹状体变性(MSA-P) 7 例: 早期临床均有运动迟缓、震颤等表现, 3 例发病后 1 年脑桥“十字征” I 期, “壳核裂隙征” III 期; 3 例发病后 2 年脑桥“十字征” I 期, “壳核裂隙征” I 期; 另 1 例发病后 9 月脑桥“十字征” I 期, “壳核裂隙征” II 期。**结论** 认为临床表现与头部 MRI 检查显示的新的影像学特征结合有助于 MSA 早期诊断。

关键词 多系统萎缩; 磁共振成像; Shy-Drager 综合征; 橄榄体脑桥小脑萎缩; 黑质纹状体变性

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Early Comprehensive Diagnosis in Multiple System Atrophy

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ABSTRACT Objective: To analyze the clinical manifestations as well as correlation between clinical manifestations and the new neuroimage characteristics (pontine "cross sign" and "putaminal slit") for early diagnosis of MSA. **Methods:** 21 patients with diagnostic as multiple system atrophy (MSA) were retrospectively analyzed for clinical manifestations and brain MRI findings. **Results:** In 21 patients with MSA, 9 patients were MSA-A, early clinical manifestations of orthostatic hypotension, urogenital dysfunction, MRI showed stage I "Cross sign" and "putaminal slit". 5 patients were MSA-C, early clinical appear unstable walking, ataxia and other performance, MRI showed stage II "Cross sign" and stage I "putaminal slit" after onset. 7 patients were MSA-P, early clinical are bradykinesia, tremor and other performance, 3 patients reached stage I "Cross sign" and stage IV "putaminal slit" one years after onset, 3 patient reached stage I "Cross sign" and stage I "putaminal slit" two years after onset, another patient reached stage I "Cross sign" and stage II "putaminal slit" nine months after onset. **Conclusions:** Clinical manifestations and the new neuroimage characteristics were very important for early diagnosis of MSA.

Key words: MSA; MRI; Shy-Drager syndrome; Olivopontocerebellar atrophy; Striatonigral degeneration

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多系统萎缩(multiple system atrophy, MSA)是一组病因不明的神经系统疾病, 临床主要表现为植物神经功能障碍、帕金森综合征、共济失调和锥体外系功能损害等。本病早期缺乏典型的特征, 相关症状出现较慢, 易与体位性低血压、晕厥、帕金森病、进行性核上性麻痹等混淆, 误诊率高。“十字征”和“壳核裂隙征”是近年随着影像学技术发展在 MSA 患者中发现的新的神经影像学表现^[1]。2002 年 Horimoto 等^[2]评价了这些改变出现的时期与临床及分型的关系, 本研究回顾性分析了本科收治的 21 例临床诊断 MSA 患者的临床表现和影像学特点, 探讨其在 MSA 早期诊断中的临床意义。

1 对象和方法

1.1 研究对象

选择我院神经内科 2003 年 1 月 -2008 年 10 月期间出院诊断为 MSA 患者 21 例, 其中男性 13 例, 女性 8 例, 发病年龄 40-63 岁, 平均(51±10.5)岁, 从起病到临床诊断病程 0.6-4 年, 平均 2.3 年。根据 1999 年 Gilman^[1]等提出的 MSA 的临床特征和诊断标准, 均无家族史, 无酒精中毒及服用苯妥英钠史, 无高血压病史, 无明确的全身性疾病或其他原因导致的上述本病特征。头部 MRI 检查除外后颅窝病变及先天性畸形。

1.2 诊断标准

根据 Gilman^[1]关于 MSA 的诊断分为: (1)可疑 植物神经 / 排尿功能障碍、帕金森综合征、小脑症状和皮质脊髓束受损征四大类中, 有一项功能障碍加其它项中的 2 个特征。(2)拟诊 植物神经 / 排尿功能障碍加对左旋多巴反应差的帕金森综合征或小脑功能障碍。(3)确诊 病理学存在高密度的少突胶质细胞胞质包涵体并伴有黑质纹状体和橄榄桥脑小脑通路的改变。

1.3 头部 MRI 脑桥“十字征”和“壳核裂隙征”分期

依据 Horimoto^[2]等提出的分期方法: (1)脑桥 T2 像的“十字征”改变分为 6 期: 0 期, 无改变; 1 期, T2WI 垂直高信号开始出

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现,Ⅱ期,清晰的 T2WI 垂直高信号出现;Ⅲ期,T2WI 水平高信号,继垂直信号开始出现;Ⅳ期,水平和垂直高信号均清晰可见;Ⅴ期,脑桥腹侧水平高信号线的前方高信号或脑桥基底部萎缩。(2)“壳核裂隙征”分成 4 期 Ⅰ期,无改变;Ⅱ期,裂隙状高信号位于一侧壳核;Ⅲ期,裂隙状高信号位于双侧壳核,但一侧比另一侧信号弱;Ⅳ期,裂隙状高信号位于双侧壳核,信号强度相同。

2 结果

2.1 临床表现

本组 21 例患者中 Shy-Drager 综合征 (MSA-A) 9 例,橄榄体脑桥小脑萎缩 (MSA-C) 型 5 例,黑质纹状体变性 (MSA-P) 型 7 例。首发症状以自主神经功能障碍起病者 9 例,表现为排尿困难、体位性低血压等症状;以小脑症状起病者 5 例,表现为行走不稳、言语不清;以帕金森综合征症状起病者 7 例,表现为运动迟缓。(见表 1) ①自主神经功能障碍:以尿便障碍为最常

见,其中尿失禁 5 例,不完全性膀胱排空 3 例,便秘 1 例,直立性低血压 6 例。在 6 例直立性低血压男性患者中,有 5 例表现为性功能障碍。②小脑性共济失调:5 例患者均有小脑症状,以共济失调为主,其中 3 例患者出现眼球震颤和意向性震颤。③帕金森综合征:7 例患者均有帕金森综合征的表现,均存在强直,其中 5 例表现运动迟缓,2 例表现震颤。

2.2 头部 MRI 检查结果

21 例 MSA 患者中,“十字征”Ⅰ期 16 例,Ⅱ期 3 例,Ⅳ期 2 例;“壳核裂隙征”Ⅰ期 15 例,Ⅱ期 1 例,Ⅲ期 3 例。Shy-Drager 综合征 9 例,头部 MRI 检查脑桥“壳核裂隙征”和“十字征”为Ⅰ期;橄榄体脑桥小脑萎缩 5 例,3 例发病后 1 年头部 MRI 脑桥“十字征”达Ⅱ期;“壳核裂隙征”为Ⅰ期,2 例发病后 3 年头部 MRI 脑桥“十字征”达Ⅳ期。黑质纹状体变性 7 例 3 例发病后 4 年脑桥“十字征”Ⅰ期,“壳核裂隙征”Ⅲ期;3 例发病后 2 年脑桥“十字征”Ⅰ期,“壳核裂隙征”Ⅰ期;另 1 例发病后 3 年脑桥“十字征”Ⅰ期,“壳核裂隙征”Ⅱ期。(见图 1)。

表 1 21 例多系统萎缩 (MSA) 患者临床表现和分型
Table 1 Manifestations and classification of 21 MSA cases

Clinical classification	Number of case	Age of onset(y)	Course of disease(y)	First symptom	Symptom	Signs
MSA-C	5	40-62	0.5-4	Unsteady gait	Unsteady gait, pitch change, drinking cough	Dysarthria, horizontal nystagmus, bilateral refers to nose with knee-skin test instability, can not walk a straight line
MSA-P	7	8-60	0.5-3.5	Bradykinesia	Bradykinesia, talk reduce, reduce facial expressions	Slow motion, speak slowly, dull expression, increased lead-pipe
MSA-A	9	48-63	0.5-3.2	Orthostatic dizziness	Orthostatic dizziness, urinary dysfunction	Orthostatic hypotension, decreased blood pressure after standing for more than 30 mmHg, voiding dysfunction, constipation

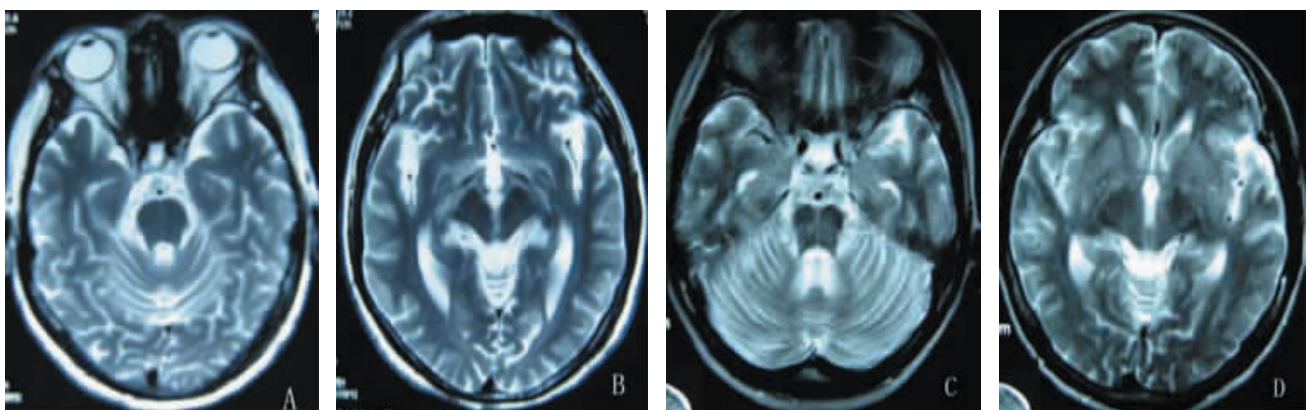


图 1 多系统萎缩患者头颅 MRI

Fig.1 Cranial MRI in patients with multiple system atrophy

A: Pontine "cross sign" Ⅰ, T2WI vertical high signal began to appear 脑桥 "十字征" Ⅰ期, T2WI 垂直高信号开始出现; B: Pontine "cross sign" Ⅱ, T2WI clear vertical signal appear 脑桥 "十字征" Ⅱ期, 清晰的 T2WI 垂直高信号出现; C: Pontine "cross sign" Ⅳ, T2WI high signal in both the horizontal and vertical visible 脑桥 "十字征" Ⅳ期, T2WI 水平和垂直高信号均清晰可见; D: "Putamenal slit" Ⅲ, Slit-like high signal intensity in the bilateral putamen "壳核裂隙征" Ⅲ期, 裂隙状高信号位于双侧壳核。

3 讨论

多系统萎缩(MSA)是一组在中老年人群中散发的中枢神经系统变性疾病,以神经系统不同部位受累的临床表现为首发症状,经常以某一系统损害为突出表现,临床进展缓慢,使早期诊断比较困难。MSA-A以植物神经功能障碍为主,泌尿生殖系统症状、直立性低血压可能预示着MSA的开始^[3-4]。MSA-P早期主要表现为运动不能、僵硬、颤抖,姿势稳定性损害及头颈肌张力障碍^[3,5-6],在早期诊断中此类病人往往误诊帕金森病^[7],MSA-C早期表现主要以进行性步态和肢体共济失调、构音障碍、小脑性眼球功能损害^[8]。最近一项对MRI与18F-脱氧葡萄糖PET相比较研究表明,后者对区分MSA-P与PD的敏感性高^[9]。最近发现,一些警示性症状如颈项前屈、吸气喘鸣和眼球运动异常已建议指向早期MSA诊断^[10-11]。随着MRI的发展,常规磁共振可支持MSA的诊断^[12-13],它可显示壳核、小脑中脚和脑桥的萎缩^[14]。曾经认为磁共振T2像的单独异常信号(十字征)是MSA-C的典型表现,但是自从MSA-P病人也出现了十字征后,十字征已被认为是诊断MSA病人的典型特征^[15-16]。“十字征”的机制是脑桥核及桥横纤维变性,上述解剖位置含水量增加,而齿状核发出的小脑上脚和锥体束并未受损之故,从而形成MRI上T2加权像上脑桥的十字形高信号影。“壳核裂隙征”反映了铁沉积或组织密度的降低。Konagaya等^[17]认为这是由于壳核萎缩及壳核与外囊增大的间隙内胶质细胞活化增生的结果。虽然壳核后外侧低信号在PD和MSA患者中都可出现,但是壳核外侧缘缝隙样T2高信号和壳核萎缩同时出现却对诊断MSA有着很高的特异性^[18-19]。

本组病人中,MSA-A组早期临床表现均以体位性低血压,泌尿生殖功能障碍为主,有1例病人因反复尿频、尿急就诊于泌尿外科,2例病人因晕厥就诊于心内科,病程在平均1.7年左右头颅MRI开始出现“十字征”。MSA-P早期临床均有运动迟缓、震颤等表现,早期易误诊为“帕金森病”但服用“左旋多巴”效果差,本组有2例病人在外院诊断为帕金森病,服用左旋多巴1年左右未见效果,病程在9个月左右头颅MRI出现“壳核裂隙征”,1年左右有“十字征”出现。MSA-C早期临床出现行走不稳、共济失调等表现,但需排除小脑症状,头颅MRI出现“十字征”较早,本组中最早在1年左右出现。本组所有患者均存在“十字征”和“壳核裂隙征”。因此,在本研究组中我们结合MSA早期可能出现的临床症状及MRI表现,使得本组病人的平均早期临床诊断率在10个月左右,大大提高了MSA的早期诊断,从而尽可能改善患者的生存质量。

综上所述,MSA的确诊需要神经病理学证实,由于临床病理取材困难,MSA的临床诊断主要依靠临床表现和影像学资料,我们认为结合本组病人,详细的临床表现及体征,结合头颅MRI上影像学特征,有助于MSA早期诊断,近期研究发现随着影像学技术的发展,PET技术的应用对MSA早期诊断也有帮助,通过统计学参数表明18F-脱氧葡萄糖PET的技术有助于鉴别PD和帕金森病的诊断和确认MSA-C病人皮层区低代谢改变^[20],同时它揭示了在MSA病人进展变化过程中皮层及皮层下的改变^[21],但PET昂贵的费用限制了它的临床普及应用。

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总之,我们认为,对于复位后骨折情况稳定的患者,可以运用石膏夹板固定可获得满意效果;对于桡骨远端骨折不稳定者,采用切开复位后 T 形钢板内固定,不但可以维持桡骨的长度,而且可以提早进行功能锻炼,使得关节功能得以恢复,其恢复时间明显缩短,获得较好的疗效。

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