·专题讲座·

Sydenham舞蹈病

赵博　王佳伟

【摘要】 Sydenham舞蹈病是风湿热在神经系统的特征性表现，是临床最为常见的儿童获得性舞蹈病。本文通过对近年来与该病相关国内外文献的系统回顾，对其病因、发病机制、临床表现、辅助检查、诊断与治疗，以及最新研究进展等进行归纳总结，以期临床医师在诊断与治疗过程中能够综合患者临床症状、体征及辅助检查结果，做到早诊断、早治疗，从而有效控制临床症状、缩短病程，达到改善患者预后之目的。

【关键词】 舞蹈症；　链球菌感染；　综述

Sydenham´s chorea

ZHAO Bo, WANG Jia-wei

Department of Neurology, Beijing Tongren Hospital, Capital Medical University, Beijing 100730, China

Corresponding author: WANG Jia-wei (Email: wangjwcq@163.com)

【**Abstract**】 Sydenham´s chorea (SC), as one of the most common children acquired chorea, is a characteristic clinical manifestation of rheumatic fever in nervous system. This article analyzed literatures with the disease at home and abroad in recent years, and summarized related knowledge of its etiology, pathogenesis, clinical manifestation, auxiliary examination, diagnosis and treatment. Furthermore, it presented the latest research progress in this field. Clinicians should be comprehensive in the analysis of patients´ symptoms, signs and results of auxiliary examination, so as to fulfill early diagnosis and treatment. Consequently, effective control of the symptoms, shortening of the disease course and improvement of the prognosis can be achieved.

【**Key words**】 Chorea;　Streptococcal infections;　Review

Sydenham舞蹈病（SC）为临床常见的儿童获得性舞蹈病，由Sydenham于1684年首先描述，是风湿热在神经系统的特征性表现，在风湿热患者中的发病率为10%～30%[1]，故亦称风湿性舞蹈病，其临床特征为舞蹈病和神经精神症状。该病以5～15岁的女性儿童或青少年好发[1]，又称小舞蹈病。其病理学机制可能与A组β-溶血性链球菌（GABHS）感染诱发的抗体与大脑抗原发生免疫交叉反应有关[2]。随着社会经济的发展、公共卫生条件的改善和青霉素的广泛应用，Sydenham舞蹈病和风湿热在发达国家的发病率明显下降，但仍有流行性和散发病例[1]；而在一些发展中国家仍是严峻的健康问题。

一、临床表现

首发症状可以出现在GABHS感染后的数小时或数天，也可能发生于感染后数月[3]；呈亚急性隐匿性发病，也有因情绪因素而骤然发病病例。患者在发病早期常伴有情绪不稳、易激动、注意力不集中、学习成绩下降、字迹歪斜、持物不稳等表现，随着不自主运动日趋明显和其他部位逐渐受累方引起注意[4]。既往有Sydenham舞蹈病病史的患者可能于妊娠期或口服避孕药期间复发，称舞蹈病子痫，孕妇流产风险相应增加[5]。

1. 神经系统症状　（1）舞蹈病症状：表现为无法控制、不自主、无规律、幅度不等的急促舞蹈样动作，睡眠期症状可消失；可累及除眼肌外的任何骨骼肌，以面肌和四肢肌常见[6]。通常呈全身性异动，但有20%～35%的患者可表现为偏身舞蹈病[3,7]；可出现言语含糊不清、面具脸、抽搐[8]；也常见运动维持障碍如无法维持闭目或伸舌。其他相关症状还有扮鬼脸、动作笨拙、构音障碍，书写、穿衣、进食困难，以及肌无力或肌张力下降；约有不足2%的患者完全卧床，称为麻痹性舞蹈病[9]。（2）神经精神症状：

doi：10.3969/j.issn.1672-6731.2014.07.004

作者单位：100730 首都医科大学附属北京同仁医院神经内科

通讯作者：王佳伟（Email：wangjwcq@163.com）

表现为情绪不稳和行为异常，大多早于舞蹈病症状，程度不一[1]。常伴有抑郁症（14%）、广泛性焦虑症（16%）、社交恐惧症（24%）和强迫症（24%）[10]，Kuzulugil等[11]于2013年报告1例女性患儿在病程中出现幻觉。

2. 全身症状　较轻微或不出现全身症状，部分患者可在发病前或病程中出现发热、咽痛、扁桃体炎、关节疼痛等风湿热样表现，心脏受累时可伴心率加快、心脏扩大和杂音；亦可见急性风湿热的其他表现，以及嗜酸性粒细胞比例增加、血清黏蛋白水平升高等[4]。

二、病因与发病机制

Sydenham舞蹈病发病机制与GABHS感染引起的扁桃体炎和咽喉炎密切相关。以抗GABHS抗体与基底神经节组织发生免疫交叉反应为主要病理学特征，故该抗体又称抗基底神经节抗体，可在约83%的患者脑脊液中检出抗基底神经节抗体[12]。目前已发现两种GABHS抗原：一是M蛋白，位于GABHS菌毛外表面，针对M蛋白的免疫球蛋白与大脑抗原发生免疫交叉反应[13]；二是N-乙酰-β-D-氨基葡萄糖，其特异性抗体可与哺乳动物之神经节苷脂发生免疫交叉反应[14]。抗基底神经节抗体通过改变皮质-纹状体环路致基底神经节功能失调，累及壳核出现运动障碍、累及尾状核和皮质出现行为异常。对IgG被动转移动物模型的研究已证实上述抗体的致病性，以及行为和动作的重复性[15]。病理检查显示，Sydenham舞蹈病患者存在基底神经节损伤、动脉炎、内皮肿胀、血管周围细胞圆形渗透、神经核团斑点样出血[16]。

三、辅助检查

1. 细胞学检查　血清学检测外周血白细胞计数增加、红细胞沉降率（ESR）增快、C-反应蛋白（CRP）升高[1]。咽拭子培养可以明确GABHS感染，仅少数患者细菌培养呈阳性[17]。

2. 免疫功能检查　血清IgG、IgM、IgA水平均升高，脑脊液免疫印迹法检测抗基底神经节抗体阳性，诊断灵敏度达92.50%、特异度达94.70%[2]。此外，血清抗DNA酶B抗体和抗溶血性链球菌素O（ASO）水平升高，一般于GABHS引起扁桃体炎或咽喉炎后3～5周达峰值水平，此后数周内逐渐降低，而血清抗DNA酶B抗体在感染后8～12周方达峰值水平，并可在数周至数月内维持较高水平[1]。

3. 影像学检查　有研究显示，大多数Sydenham舞蹈病患者无特征性影像学改变，故影像学是排除其他原因所致舞蹈病的重要方法[1]。头部CT可显示基底节区低密度病灶和水肿，MRI显示基底节体积扩大、神经元损害，特别是尾状核和壳核呈长T_2信号[18]。此外，还可见一些特殊的影像学表现，例如单侧尾状核和壳核囊性变[19]。有研究表明，上述影像学异常可于发病后6～14周内恢复正常[1]。部分患者SPECT扫描可见可逆性纹状体代谢活跃和过度灌注[20]。

4. 脑电图检查　有55%～75%的患者脑电图异常，表现为非特异性轻度弥漫性慢波[1]，α节律减少，局限性痫样放电或偶尔出现的14或6 Hz正相棘波放电[4]。

四、诊断与鉴别诊断

目前，Sydenham舞蹈病的诊断仍采用美国心脏协会（AHA）于1992年修订的Jones标准（表1）[21]。由于Sydenham舞蹈病和链球菌感染相关性儿童自身免疫性神经精神障碍（PANDAS）均有链球菌前驱感染史，临床表现重叠，因此对不典型病例应注意鉴别诊断（表2）[22]。引起舞蹈病的原因有脑血管病、脑炎、遗传代谢性疾病、中毒、链球菌感染后舞蹈病等，还应与其他病因引起的舞蹈病相鉴别，如系统性红斑狼疮、中毒、肝豆状核变性、家族性舞蹈病（包括亨廷顿病），以及甲状腺功能亢进等激素代谢障碍导致的运动异常[1]。除临床表现外，铜蓝蛋白、甲状腺功能试验、抗溶血性链球菌素O、脑脊液、MRI、遗传代谢性疾病筛查等实验室指标均是鉴别诊断的重要方法（图1）[1]。

五、治疗与预防

临床治疗主要采用三步法治疗方案：治疗潜在感染、预防复发和对症治疗[1]。

1. 治疗潜在感染　即使发病过程中无急性风湿热征象的患者亦应卧床休息，镇静、预防性应用抗生素等[4]。Cilliers[23]建议：青霉素500 mg（2次/d）口服，10天为1个疗程。而国内则通常采用青霉素（400～800）×10^3 U肌肉注射（1～2次/d），10～14天为1个疗程[4]。

2. 预防复发　儿童期预防性应用青霉素可以有效减少风湿热和Sydenham舞蹈病的复发，同时可以降低咽部GABHS的潜在致病性并阻止毒株的传播（表3）[24]。Berrios等[25]建议：每28天肌肉注射青霉素或口服青霉素V钾250 mg（2次/d）。然而，部分患者尽管长期规律应用青霉素，仍复发[26]。

表1 Jones标准(1992年版)[21]

Table 1. Jones criteria (1992)[21]

Diagnostic criteria
Two major or one major and two minor manifestations must be present, plus evidence of antecedent group A Streptococcus infection
Chorea and myocarditis do not require evidence of antecedent group A Streptococcus infection
Recurrent episode requires only one major or several minor manifestations, plus evidence of antecedent group A Streptococcus infection
Major manifestations
Carditis
Polyarthritis
Chorea
Erythema marginatum
Subcutaneous nodules
Minor manifestations
Arthralgia
Fever
Elevated erythrocyte sedimentation rate or C-reactive protein concentration
Prolonged PR interval on ECG
Evidence of antecedent group A Streptococcus infection
Positive throat culture or rapid antigen test for group A Streptococcus
Elevated or rising streptococcal antibody titer

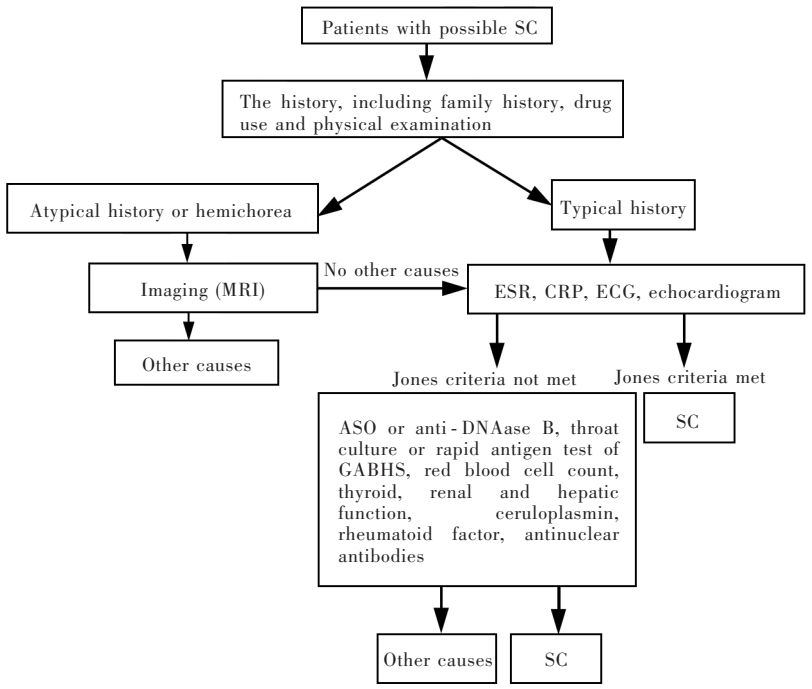
表2 Sydenham舞蹈病与链球菌感染相关性儿童自身免疫性神经精神障碍的鉴别诊断[22]

Table 2. Differential diagnosis between Sydenham´s chorea and PANDAS[22]

Item	Sydenham´s chorea	PANDAS
Age of onset	5–15 years	3 years–puberty
Sex	Female predominance	The ratio of male to female is 2.60 to 1
Pathogen	GABHS	Streptococcus, subtypes undetermined
Physical symptom	Choreatic movements causing functional impairment	Choreiform movements with no functional impairment
Psychiatric symptom	Obsessive-compulsive disorder, excessive movement, anxiety, ADHD, paranoia and sleep disturbance	Emotional lability, separation anxiety, ADHD, oppositional behavior
Duration	In most cases 1–6 months, or may persisting up to 2 years	Remitting-relapsing course
MRI	Volumetric increase in caudate, putamen and globus pallidus	Volumetric increase in caudate, putamen and globus pallidus
Use of antibiotics	Prevent recurrence	Unclear

PANDAS, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection, 链球菌感染相关性儿童自身免疫性神经精神障碍; GABHS, Group A β-hemolytic Streptococcus, A组β-溶血性链球菌; ADHD, attention deficit hyperactivity disorder, 注意缺陷多动障碍

3. 舞蹈病和神经精神症状的治疗　舞蹈病通常呈良性自限性病程,无需特殊治疗。对于部分机体功能障碍且病程迁延的患者,需长期治疗。基于两项原则:(1)药物纠正基底神经节神经生化的不平衡。异常运动可能与过量的多巴胺能神经递质传递增加,胆碱能、γ-氨基丁酸能递质在基底神经节传递减少有关。丙戊酸钠通过刺激γ-氨基丁酸分泌而能有效抑制患者之运动症状[27],而氟哌啶醇、匹莫齐特、苯巴比妥、卡马西平通过阻断多巴胺能受体而发挥药效,减少舞蹈病症状[28]。然而,目前尚无特定的首选药物。由于多巴胺能受体阻断剂药物不良反应明显,因此仅适用于对丙戊酸钠治疗无效或罕见麻痹性舞蹈病患者。(2)减轻脑组织炎症反应。抗炎药物如水杨酸盐和糖皮质激素可以通过抑制自身免疫反应而有效减少运动异常[29],由于不良反应明显,糖皮质激素仅适用于麻痹性舞蹈病,或传统药物治疗无效或产生不可耐受的不良反应的患者[30]。静脉注射免疫球蛋白(IVIg)或血浆置换疗法可以清除体内异常自身抗体,可能具有一定疗效[31]。上述药物亦可减轻神经精神症状,即使不予



SC, Sydenham´s chorea, Sydenham舞蹈病 ESR, erythrocyte sedimentation rate, 红细胞沉降率
CRP, C-reactive protein, C-反应蛋白 ASO, antistreptolysin O, 抗溶血性链球菌素O
GABHS, Group A β-hemolytic Streptococcus, A组β-溶血性链球菌

图1 Sydenham舞蹈病诊断流程图[1]

Figure 1 Diagnostic flowchart of possible Sydenham´s chorea[1].

表3 青霉素预防性抗感染治疗的时间标准[24]

Table 3. Duration of penicillin prophylaxis on anti-infective therapy[24]

Category of patients	Duration of prophylaxis
Patients without proven carditis	For 5 years after most recent attack, or until 18-year-old (whichever is longer)
Patients with carditis	
Mild mitral regurgitation	For 10 years after most recent attack, or at least until 25-year-old or healed carditis (whichever is longer)
More severe valvular disease	Lifelong
After valve surgery	Lifelong

治疗，神经精神症状通常持续时间较短且大多数患者可以耐受。对于症状严重者，苯二氮䓬类或苯巴比妥类镇静催眠药可能有效，如选择性5-羟色胺再摄取抑制剂(SSRI)可有效缓解伴强迫症患者的临床症状，抗抑郁药对部分患者临床症状的改善也有帮助[3]。

六、预后

大多数Sydenham舞蹈病患者均呈良性自限性病程，数月至2年不等[32]，约有25%的患者病程迁延，可持续2年或更长时间，称为持续性Sydenham舞蹈病[33]。痊愈后一般不遗留严重后遗症，仅少数病例遗留一些轻微的神经体征如突发性随意动作、动作不协调等；有10%～30%的患者可复发[34]。Sydenham舞蹈病患者的预后主要取决于其心脏并发症的转归[26]。

参 考 文 献

[1] Oosterveer DM, Overweg-Plandsoen WC, Roos RA. Sydenham´s chorea: a practical overview of the current literature. Pediatr Neurol, 2010, 43:1-6.

[2] Gordon N. Sydenham´s chorea, and its complications affecting the nervous system. Brain Dev, 2009, 31:11-14.

[3] Zomorrodi A, Wald ER. Sydenham´s chorea in Western Pennsylvania. Pediatrics, 2006, 17:E675-679

[4] Kou CY. Clinical treatment of Sydenham´s chorea. Zhong Wai Jian Kang Wen Jian, 2011, 44:404-405.[寇传玉. 小舞蹈病临床治疗. 中外健康文摘, 2011, 44:404-405.]

[5] Maia DP, Fonseca PG, Camargos ST, Pfannes C, Cunningham MC, Cardoso F. Pregnancy in patients with Sydenham´s chorea. Parkinsonism Relat Disord, 2012, 18:458-461.

[6] Rodopman-Arman A, Yazgan Y, Berkem M, Eraksoy M. Are sensory phenomena present in Sydenham´s chorea: evaluation of

13 cases? Neuropediatrics, 2004, 35:242-245.
[7] Sudhindra BK. Rheumatic chorea. Indian Pediatr, 1996, 33:47-49.
[8] Panzer J, Dalmau J. Movement disorders in paraneoplastic and autoimmune disease. Curr Opin Neurol, 2011, 24:346-353.
[9] Cardoso F, Seppi K, Mair KJ, Wenning GK, Poewe W. Seminar on choreas. Lancet Neurol, 2006, 5:589-602.
[10] Moreira J, Kummer A, Harsányi E, Cardoso F, Teixeira AL. Psychiatric disorders in persistent and remitted Sydenham's chorea. Parkinsonism Relat Disord, 2014, 20:233-236.
[11] Kuzulugil D, Sheldrick K, Wood A, Whitehall J. Hallucinations in severe, repeated Sydenham's chorea in an indigenous girl in North-West Queensland. J Paediatr Child Health, 2013, 49:72-74.
[12] Church AJ, Dale RC, Cardoso F, Candler PM, Chapman MD, Allen ML, Klein NJ, Lees AJ, Giovannoni G. CSF and serum immune parameters in Sydenham's chorea: evidence of an autoimmune syndrome? J Neuroimmunol, 2003, 136(1/2):149-153.
[13] Kirvan CA, Swedo SE, Kurahara D, Cunningham MW. Streptococcal mimicry and antibody-mediated cell signaling in the pathogenesis of Sydenham's chorea. Autoimmunity, 2006, 39:21-29.
[14] Kirvan CA, Swedo SE, Heuser JS, Cunningham MW. Mimicry and autoantibody-mediated neuronal cell signaling in Sydenham chorea. Nat Med, 2003, 9:914-920.
[15] Hallett J, Kiessling L. Genetics of childhood disorders: XXXV. Autoimmune disorders, part 8: animal models for noninflammatory autoimmune disorders of the brain. J Am Acad Child Adolesc Psychiatry, 2002, 41:223-225.
[16] Bonthius DJ, Karacay B. Sydenham's chorea: not gone and not forgotten. Semin Pediatr Neurol, 2003, 10:11-19.
[17] Ozer S, Hallioglu O, Ozkutlu S, Celiker A, Alehan D, Karagöz T. Childhood acute rheumatic fever in Ankara, Turkey. Turk J Pediatr, 2005, 47:120-124.
[18] Faustino PC, Terreri MT, da Rocha AJ, Zappitelli MC, Lederman HM, Hilário MO. Clinical, laboratory, psychiatric and magnetic resonance findings in patients with Sydenham's chorea. Neuroradiology, 2003, 45:456-462.
[19] Hagiwara K, Tominaga K, Okada Y, Kido M, Yamasaki R, Shida N, Yamashita Y. Post-streptococcal chorea in an adult with bilateral striatal encephalitis. J Clin Neurosci, 2011, 18:708-709.
[20] Beato R, Siqueira CF, Marroni BJ, Boanova LG, de Lima CF, Maia DP, Nattan M, Cardoso F. Brain SPECT in Sydenham's chorea in remission. Mov Disord, 2014, 29:256-258.
[21] Special Writing Group of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association. Guidelines for the diagnosis of rheumatic fever: Jones Criteria, 1992 update. JAMA, 1992, 268:2069-2073.
[22] van Toorn R, Weyers HH, Schoeman JF. Distinguishing PANDAS from Sydenham's chorea: case report and review of the literature. Eur J Paediatr Neurol, 2004, 8:211-216.
[23] Cilliers AM. Rheumatic fever and its management. BMJ, 2006, 333:1153-1156.
[24] Rheumatic fever and rheumatic heart disease. World Health Organ Tech Rep Ser, 2004, 923:1-122.
[25] Berrios X, Quesney F, Morales A, Blazquez J, Bisno AL. Are all recurrences of "pure" Sydenham chorea true recurrences of acute rheumatic fever? J Paediatr, 107:867-872.
[26] Ekici F, Cetin II, Cevik BS, Senkon OG, Alpan N, Degerliyurt A, Güven A, Ateş C, Cakar N. What is the outcome of rheumatic carditis in children with Sydenham's chorea? Turk J Pediatr, 2012, 54:159-167.
[27] Sabui TK, Pant P. Sodium valproate in the treatment of Sydenham's chorea. Indian J Paedr, 2010, 77:703.
[28] Demiroren K, Yavuz H, Cam L, Oran B, Karaaslan S, Demiroren S. Sydenham's chorea: a clinical follow-up of 65 patients. J Child Neurol, 2007, 22:550-554.
[29] Walker AR, Tani LY, Thompson JA, Firth SD, Veasy LG, Bale JF Jr. Rheumatic chorea: relationship to systemic manifestations and response to corticosteroids. J Pediatr, 2007, 151:679-683.
[30] Teixeira AL Jr, Cardoso F. Corticosteroids in the treatment of acute Sydenham's chorea. Pediatr Neurol, 2006, 34:168-169.
[31] Garvey MA, Snider LA, Leitman SF, Werden R, Swedo SE. Treatment of Sydenham's chorea with intravenous immunoglobulin, plasma exchange, or prednisone. J Child Neurol, 2005, 20:424-429.
[32] Gimeno H, Barry S, Lin JP, Gordon A. Functional impact of Sydenham's chorea: a case report. Tremor Other Hyperkinet Mov (NY), 2013, 3:1-4.
[33] Cardoso F. Sydenham's chorea. Handb Clin Neurol, 2011, 100:221-229.
[34] Cao Y, Guan XZ. A case repot: basal ganglia hemorrhage in elderly sufferring from Sydenham's chorea. Jian Kang Bi Du, 2012, 11:570.[曹阳, 管兴志. 伴基底节区出血的老年小舞蹈病1例报道. 健康必读, 2012, 11:570.]

(收稿日期:2014-06-11)

·小词典·

中英文对照名词词汇(三)

梅毒螺旋体 treponema pallidum(TP)
酶联免疫斑点试验 enzyme-linked immunospot assay(ELISPOT)
美国精神障碍诊断与统计手册第4版 Diagnostic and Statistical Manual of Mental Disorders Fourth Edition(DSM-Ⅳ)
美国心脏协会 American Heart Association(AHA)
蒙特利尔认知评价量表 Montreal Cognitive Assessment(MoCA)
脑内出血 intracerebral hemorrhage(ICH)
脑室内出血 intraventricular hemorrhage(IVH)
脑室外神经细胞瘤 extraventricular neurocytoma(EVN)
内嗅皮质 entorhinal cortex(EC)
牛海绵状脑病 bovine spongiform encephalopathy(BSE)
帕金森病 Parkinson's disease(PD)
培养分泌蛋白-10 culture filtrate protein-10(CFP-10)
前颗粒蛋白 progranulin(PGRN)