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神经梅毒 29 例的回顾性临床分析

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摘要 目的:观察总结神经梅毒的临床特点,以提高神经梅毒的诊断和治疗水平。**方法:**回顾性分析哈尔滨医科大学附属第一医院 2005 年 1 月至 2012 年 12 月神经内科病房收治的 29 例神经梅毒患者的临床资料。**结果:**29 例神经梅毒患者中临床分型:其中,无症状型神经梅毒 2 例,主要表现为患者无症状,仅脑脊液呈轻度炎性反应,梅毒血清反应阳性;梅毒性脑膜炎 6 例,主要表现为头痛、呕吐及脑膜刺激征,偶可见意识障碍、谵妄及抽搐。血管型梅毒 3 例,主要表现为偏瘫、偏身感觉障碍、偏盲、失语等。脊髓痨 11 例,主要表现为感觉异常如束带感和蚁走感,共济失调、内脏危象及阿罗瞳孔等。麻痹性痴呆 7 例,临床表现为进行性痴呆合并神经损害为主。**结论:**神经梅毒的起病隐袭,临床表现复杂多样,神经系统各部位都可受累,容易误诊,。但青霉素治疗有效。对于疑似病例应及时行血清及脑脊液检查,可获得早期诊断,对指导治疗及预后均有重要意义。

关键词:神经梅毒;诊断;治疗

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Retrospective Analysis of 29 Cases with Neurosyphilis

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ABSTRACT Objective: To summarize the object is to observe summarize the clinical features of neurosyphilis, then improve the level of diagnosis and treatment of neurosyphilis. **Methods:** a A retrospective analysis was made on the clinical data of 29 patients with neurosyphilis admitted of from January 2005 January to December 2012 December in the neurological department of internal medicine 29 cases clinical data of patients with neurosyphilis of First Affiliated Hospital of Harbin Medical University. **Results:** Of the 29 cases of with neurosyphilis patients clinical were classified: 2 cases of asymptomatic neurosyphilis were without any symptome, only a mild inflammatory reaction in the cerebrospinal fluid, and syphilis serum reaction. 6 cases were with Syphilitic meningitis, mained with headache, vomiting and meningeal irritation, occasionally visible consciousness disorders, delirium and convulsions. The; 3 case number of meningovascular neurosyphilisvascular type of syphilis were 3, mainly forcharacteristic of hemiplegia, hemidysesthesia, hemianopia, aphasia and otherso on. 11 cases of Spinal spinal tuberculosis waswere found and 11 cases, mainly characteristic offor the sensory abnormalities such as band and formication, ataxia, visceral crisis and Arlo pupil. Paralytic dementia: a report of 7 cases, clinical manifestations of dementia associated with nerve damage mainly. **Conclusion:** neurosyphilis Neurosyphilis had insidious onset, and clinical manifestations are were complex. The nervous system may be involved in different parts, and easy be misdiagnosisd. But penicillin treatment was effective. For suspected cases, it should be prompt in serum and cerebrospinal fluid examination, in order to obtain early diagnosis. It is was significant for the treatment and prognosis of guidance.

Key words: Neurosyphilis; Diagnosis; Therapeutics

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前言

梅毒是由梅毒苍白螺旋体引起的一种慢性、系统性传播疾病,神经系统的梅毒螺旋体感染是一个慢性、隐匿性过程。梅毒在我国是从 20 世纪 80 年代复燃,且发病率呈逐年上升趋势^[1],近年来关于神经梅毒的报道也越来越多,其发病隐袭,临床表现多种多样,容易误诊。为进一步认识和掌握神经梅毒的临床

特征,现对我院神经内科于 2005 年 1 月至 2012 年 12 月收治的 29 例神经梅毒患者的临床资料分析如下:

1 材料与方法

1.1 一般资料

2005 年 1 月至 2012 年 12 月我院神经内科共收治神经梅毒 29 例,均符合神经梅毒的诊断标准。年龄 35-74 岁,平均年龄 47.41 岁,男性 17 例,女性 12 例,均否认冶游史,有 HIV 病史 1 例,均否认吸毒史、输血病史。

1.2 方法

本组 29 例患者均行血常规、血生化、血清梅毒螺旋体滴度

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实验(TRUST)血清快速血浆反应素实验(RPR)、血清梅毒螺旋体血凝实验(TPHA)。脑脊液常规、生化、细胞学、脱落细胞学、脑脊液血清快速血浆反应素实验(RPR)及脑脊液梅毒螺旋体血凝实验(TPHA)。其中行头部CT检查6例,头部MRI检查14例,脊髓MRI检查3例,头部MRA6例,头部MRV检查1例,脊髓传导速度2例,诱发电位2例,9例患者行脑电图检查。

2 结果

2.1 临床表现

29例神经梅毒患者中,以急性脑梗死为首发症状3例,主要表现为偏瘫、偏身感觉障碍、失语;精神异常2例,表现为行为异常、胡言乱语;颅内高压2例,表现为头痛、呕吐及脑膜刺激征;脑缺血发作8例,表现为头晕伴有恶心、呕吐及视物旋转;晕厥5例,表现为突发意识障碍;共济失调4例,表现为站立不稳、头晕、行走不稳,查体可见指鼻试验、跟膝胫试验、闭目难立征阳性;脊髓损害6例,表现为双下肢或四肢无力麻木无力,行走不稳、排尿无力、深感觉障碍;痴呆11例,特别是近期记忆力明显下降,计算力、理解力下降,智能减退,反应迟钝;癫痫发作3例,表现为全身强直-阵挛发作,其中一例伴有舌咬伤;周围神经损害2例,表现为四肢麻木无力、四肢末梢型感觉减退;神经根刺激症状2例,表现为针刺样或者闪电样疼痛;胃危象1例,表现为阵发性上腹部剧痛及持续性呕吐,无腹肌强直及压痛;肠危象2例,表现为肠绞痛、腹泻及里急后重;脑神经损害12例,其中表现为展神经麻痹1例;视物旋转3例,视物模糊4例,视物双影3例,复视1例,口唇发绀1例,饮水呛咳3例,构音障碍1例。

2.2 实验室检查

血清梅毒全部阳性,血TRUST阳性19例,血RPR阳性4例,血TPPA阳性4例。脑脊液RPR阳性2例,脑脊液TPPA阳性2例,脑脊液压力升高1例,脑脊液糖及氯化物升高4例,脑脊液梅毒抗体阳性1例,脑脊液蛋白升高9例,脑脊液免疫球蛋白升高12例,脑脊液细胞数升高10例。

2.3 影像学检查

其中行头部CT检查6例,阳性6例:右侧颞枕叶软化灶1例,左额脑梗死1例,脑室扩展,脑裂增宽1例,腔隙性脑梗死3例。头MRI检查14例,其中腔梗8例,双顶部皮髓交界异常信号1例,脑梗死2例,双额软化灶1例、胶质瘤2例。脊髓MRI检查3例,其中T1-T4水平脊髓病变炎症病变1例,T7-T11水平脊髓背侧异常信号1例,其中C3、4、5、6、7、T5、6、7、L1、2、3、4、5椎体退行性变,间盘变性,间盘突出1例。头MRA检查6例,脑动脉硬化性病变4例(大脑后动脉轻度动脉硬化2例,大脑中动脉硬化2例),大脑中动脉狭窄2例,双侧大脑前中后动脉硬化,伴双侧大脑后动脉远端狭窄1例。头MRV检查1例,左侧横窦、乙状窦显影略淡1例。脊髓传导速度2例,其中右侧皮层电位波幅较左侧偏低1例,双侧T4-6脊髓传导速度减慢1例。诱发电位2例,1例右眼P100重复性差,右耳I-III波波幅低,1例双耳I波波幅降低,右侧皮层电位较左侧低。

2.4 其他检查

9例患者行脑电图检查,其中8例表现为广泛中-重度异常脑电图,1例为广泛轻度异常脑电图。

2.5 治疗与转归

临床确诊的29名患者除3例青霉素过敏外,其余均给予青霉素,2400万U/d,每日4次静脉滴注,疗程为10-14天,后改为苄星青霉素240万u肌肉注射,每周一次,连续3周。在青霉素注射前为防止吉海反应,口服泼尼松10mg,2次/d,连续3d。脑血管型梅毒或者麻痹性痴呆患者均加用抗血小板聚集、脑保护、改善脑循环等治疗。对于可以引起颅内压增高的脑血管型梅毒和脑膜型梅毒加用呋塞米或者甘露醇等脱水治疗。其中3例青霉素过敏者给予头孢曲松钠2.0g一日两次静脉滴注,疗程为14天。癫痫发作给予抗癫痫药,精神症状突出给予抗精神病药物。出院后失访6例。获随访23例,随访3个月至1年,患者症状有明显好转,18例复查血TRUST滴度下降,复查脑脊液中细胞数和免疫球蛋白都有不同程度下降,2例病毒性脑膜炎患者基本痊愈,3例无效。

3 讨论

追溯梅毒出现的历史,最早在15世纪欧洲出现,所以有“西班牙”病,“波兰”病等名称,反映了其起源的争论^[2]。梅毒的发病率在1850年后稳定下降,随之在19世纪80、90年代男性同性恋间增加。神经梅毒(neurosyphilis)是密苍白螺旋体(*treponema pallidum*)感染所引起的慢性的中枢神经系统疾病^[3],可以侵犯脑实质、脑膜、脑血管、脊髓等。过去人们认为神经梅毒是梅毒的晚期表现,属于梅毒III期,实际上各期梅毒均可发生中枢神经系统损害而致神经梅毒。早期梅毒主要是侵犯皮肤和黏膜,部分患者早期症状轻,未引起注意或无明显临床症状而未治疗,而致进展为晚期梅毒,侵犯中枢神经系统和心血管系统。神经梅毒分为5种类型,即无症状型神经梅毒、梅毒性脑膜炎、血管型梅毒、脊髓痨和麻痹性痴呆^[4]。针对I期及II期梅毒抗生素的应用,大大减少了其向III期梅毒的转变,并且导致梅毒树胶样肿的发生率大为降低^[5]。

神经梅毒的临床表现多变,症状无特异性,几乎涵盖各种神经系统疾病中的症状及体征^[6]。其中不典型的无症状型神经梅毒在临床已较少见。本组29例神经梅毒患者仅有2例以无症状型神经梅毒为首发症状,比较容易忽视。容易误诊的症状如四肢末梢闪电样持续疼痛^[7]却有2例为首发症状,神经梅毒可以表现为无症状或者是影响到大脑或脊髓后出现中风或脑膜脑血管性梅毒,这些症状可以在感染后数周内出现,例如梅毒性脑膜炎患者,或者经过数十年演变为脊髓痨^[8,9]。

对神经梅毒侵犯颅神经的病例做文献复习,有报道患者以头疼及复视为首发症状,神经系统查体右侧外展神经麻痹及共济失调,余无明显神经系统阳性体征,血清学实验TPHA定量1:32,证实为神经梅毒,该患者普通CT见右侧小脑半球低密度影及右侧颞叶不规则低密度影,增强CT可见右侧颞叶靠近硬脑膜的同样大小的椭圆形增强区域。MRT1像示右侧小脑半球,右侧小脑脚中部及右侧颞叶呈低信号,T2像这些区域为高信号^[10]。另有51岁女性患者轻度眩晕6周加重2天入院,伴有双侧听力下降及面部感觉障碍,查体可见双侧面部神经麻痹,电测听示双侧严重听力丧失,脑脊液VDRL结果阳性证实为神经梅毒侵犯前庭蜗神经损伤,作者指出可以通过对该类患者行磁共振增强显示前庭蜗神经及迷路,然而面神经合并前庭蜗神经

的病历比较罕见^[1]。

为降低误诊率需重视病史询问以提高对神经梅毒疾病的诊断率。尤其应该注意一些病人不能主动提供冶游史或者刻意隐瞒冶游史,其中一部分年轻患者以精神异常或痴呆起病,头CT及头MRI提示脑内多发异常信号及弥漫性脑萎缩,排除高血压病、糖尿病、各种免疫疾病及大量吸烟、饮酒史后也应该警惕神经梅毒的可能,这些因素对于神经梅毒的诊断或者明确排除都是难题。

本组29例患者诊断的参考标准包括流行病史、临床症状与体征以及实验室TRUST和TPPA的检测结果。神经梅毒的诊断尚无明确金标准,相关的实验室检查的敏感性和特异性不强,其诊断价值有争议。国内朱建明等^[2]的观点为:神经梅毒的诊断需要综合考虑病史、临床表现、梅毒血清学、脑脊液、影像学等的改变,而患者的非婚姻性生活史、血清和脑脊液的梅毒螺旋体血球凝集试验(TPHA)、快速血浆反应素试验(RPR)检测是确诊梅毒的关键。本组29例患者血清梅毒全部阳性,血TRUST阳性19例,血RPR阳性4例,血TPPA阳性4例,脑脊液RPR阳性2例,脑脊液TPPA阳性2例,脑脊液压力升高1例,脑脊液糖及氯化物升高4例,脑脊液梅毒抗体阳性1例,脑脊液蛋白升高9例,脑脊液免疫球蛋白升高12例,脑脊液细胞数升高10例。

2006年Castro等研究表明神经梅毒中脑脊液TPPA敏感性为100%,迄今为止仍公认梅毒血清学检测及脑脊液梅毒螺旋体抗体检测占首位^[3]。

在一项回顾性研究中,Mitsonis等人调查了1965-1984年和1985-2005年的81例表现为神经梅毒的病人,调查其发病的典型特征,比如脊髓痨、进行性麻痹性痴呆和脑血管梅毒。在后期经典的特征性表现比在前期出现的少,原因是抗生素的广泛应用以及更好的筛选方法的应用^[4]。Costiniuk等报导的3例神经梅毒病人均没有瞳孔改变,心血管系统和皮肤检查也没有明显发现^[5]。

仅以癫痫发作为首发症状的神经梅毒并不少见,且缺少特异性,此外影像表现也不典型。因此,我们推荐每一个临床表现为癫痫发作的病人应进行梅毒方面的血液检测,所有血清学检测为阳性的病人都应进一步化验脑脊液。Man-Li Tong等对一组169例病人的研究表明,13例病人以癫痫发作为唯一表现,2例病人癫痫发作伴病毒性脑膜炎,5例病毒性脑膜脑血管病,6例麻痹性痴呆;癫痫的表现包括简单部分发作、复杂部分发作伴继发泛化,以及全身性癫痫发作,癫痫发作的临床特征没有典型特点^[6]。神经梅毒由于临床症状多种多样、缺乏典型特点,大部分病人无症状或仅有非特异性表现,临床上很难确诊^{[6][8]}。在我们之前的研究中,我们分析过21例以缺血性卒中为首发表现的情况,除了4例有缺血性卒中病史的病人,其余17例均以缺血性脑卒中急诊发病^[7]。感染导致的血管炎可以引起大脑和小脑梗塞,造成结构和功能改变,比如病灶周围皮质重构、交通神经元回路、膜性能改变和并行轴突生长。神经元损害的位置和范围由其电活动决定,这些病人的癫痫发作的临床表现与以前的报道相似^[19]。

到现在为止,没有一种化验能检测出所有的神经梅毒,神经梅毒的诊断通常根据临床表现和血清、脑脊液化验结果^[20]。

根据疾病预防和控制中心的结果,脑脊液VDRL检测的特异性高,敏感度大约22-69%,表明脑脊液VDRL检测阳性反应可以诊断为神经梅毒而阴性反应不能排除诊断^[21]。尽管脑脊液苍白密螺旋体试验敏感性高,欧洲疾控中心仍推荐脑脊液VDRL或脑脊液RPR作为神经梅毒的诊断标准,因其特异性高。相反,脑脊液TPPA或荧光螺旋体抗体吸收测试的敏感性高,可以用来排除神经梅毒诊断可能;然而,反过来却不能成立,因此我们的研究中依靠综合方法确诊^[22]。

总之,近年神经梅毒的发病率呈逐年上升,其诊断复杂,临床表现多样,应引起临床医生重视,尽快行血清及脑脊液的梅毒抗体检查,运用综合手段提高对神经梅毒的诊断及治疗水平,争取早期诊断、早期治疗,以改善预后。

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