

天津市环湖医院2012-2017年神经梅毒流行病学特征分析

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【摘要】 目的 分析天津市环湖医院神经梅毒的流行病学特征。方法 回顾性分析天津市环湖医院2012-2017年诊断与治疗的138例神经梅毒患者的流行病学资料、实验室和影像学特征。结果 将138例神经梅毒患者分为无症状性神经梅毒(无症状组,32例)、间质性神经梅毒(间质组,46例)和实质性神经梅毒(实质组,60例)。实质组男性患者比例($\chi^2 = 9.623, P = 0.002$; $\chi^2 = 7.953, P = 0.005$)和年龄($t = 2.985, P = 0.004$; $t = 3.322, P = 0.001$)均高于无症状组和间质组;间质组($Z = 2.394, P = 0.024$)和实质组($Z = 2.937, P = 0.004$)快速血浆反应素试验滴度高于无症状组;实质组蛋白定量高于无症状组($t = 2.453, P = 0.017$)。无症状组患者影像学无特异性表现;间质组有22例影像学异常,主要表现为脑梗死;实质组有28例影像学异常,主要表现为脑缺血、脑白质变性和脱髓鞘、脑积水。结论 神经梅毒好发于男性和受教育程度较低人群,临床和影像学表现多样,应加强高危人群健康教育和行为干预措施,以降低神经梅毒发生率。

【关键词】 神经梅毒; 流行病学; 天津

Analysis of the epidemiological characteristics of neurosyphilis in Tianjin Huanhu Hospital from 2012 to 2017

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【Abstract】 **Objective** To analyze the epidemiological characteristics of neurosyphilis in Tianjin Huanhu Hospital. **Methods** The epidemiological data, laboratory examination results and neuroimaging features of 138 patients with neurosyphilis who were diagnosed and treated in our hospital from 2012 to 2017 were retrospectively analyzed. **Results** All patients were divided into asymptomatic neurosyphilis (asymptomatic group, N = 32), interstitial neurosyphilis (interstitial group, N = 46) and parenchymatous neurosyphilis (parenchymatous group, N = 60). The proportion of male patients ($\chi^2 = 9.623, P = 0.002$; $\chi^2 = 7.953, P = 0.005$) and age ($t = 2.985, P = 0.004$; $t = 3.322, P = 0.001$) of parenchymatous group were higher than those of asymptomatic group and interstitial group. The rapid plasma reagin (RPR) titers of interstitial group ($Z = 2.394, P = 0.024$) and parenchymatous group ($Z = 2.937, P = 0.004$) were higher than that of asymptomatic group. The protein quantification of parenchymatous group was higher than that of asymptomatic group ($t = 2.453, P = 0.017$). The imaging findings of patients in asymptomatic group showed no abnormalities. The imaging findings of 22 patients in interstitial group showed cerebral infarction, while the other one did not show abnormality. The imaging findings of 28 patients in parenchymatous group showed abnormalities such as cerebral ischemia, white matter degeneration, demyelination and hydrocephalus, while the other 7 patients did not show abnormality. **Conclusions** Neurosyphilis is more common in men and lower education people, which has complex and diverse clinical features and imaging manifestations. It is necessary to strengthen the measures of health education and behavior intervention in high-risk population, so as to reduce the incidence of neurosyphilis.

【Key words】 Neurosyphilis; Epidemiology; Tianjin

Conflicts of interest: none declared

梅毒系由梅毒螺旋体(TP)引起的性传播疾病,罹患梅毒患者是唯一传染源。根据感染时间,分为先天性和获得性两种类型。近年来,梅毒发病率逐年升高。流行病学调查显示,2000~2013年我国梅毒发病率年均增长13.37%,仅次于乙型肝炎和肺结核,成为重要的公共卫生问题^[1-2]。神经梅毒系梅毒螺旋体感染并侵犯中枢神经系统引起的一组临床综合征,是梅毒的严重并发症,可发生于梅毒的任何阶段。全球神经梅毒发病率0.16~2.10/10万^[3-4],且近年发病率显著升高。神经梅毒分为无症状性、间质性和实质性3种类型,其中,间质性神经梅毒包括脑膜梅毒、脊膜梅毒和血管梅毒,实质性神经梅毒包括麻痹性痴呆、脊髓痨、视神经萎缩和梅毒性树胶肿^[5]。研究显示,有13.5%~20.0%未经治疗的梅毒患者进展为神经梅毒,但仅4%~9%为症状性神经梅毒^[6-8],增加了临床诊断难度,易造成误诊或漏诊。本研究分析天津市环湖医院2012年12月至2017年12月收治的神经梅毒患者的流行病学特征,以为疾病的防控及临床诊断与治疗提供理论依据。

资料与方法

一、临床资料

1. 纳入标准 (1)均符合2010年美国疾病预防控制中心(CDC)制定的神经梅毒诊断标准^[9],并经血清梅毒螺旋体特异性抗体和快速血浆反应素试验(RPR)证实。(2)均为获得性梅毒。(3)本研究经天津市环湖医院道德伦理委员会审核批准,所有患者或其家属均知情同意并签署知情同意书。

2. 排除标准 (1)先天性梅毒患者。(2)人类免疫缺陷病毒(HIV)感染患者。(3)中枢神经系统肿瘤患者。(4)其他原因致神经系统症状患者。(5)妊娠期和哺乳期女性。

3. 一般资料 选择2012年12月至2017年12月经天津市环湖医院预防保健科疫情上报的神经梅毒患者共138例,男性94例,女性44例,男女比例为2.14:1.00;年龄25~86岁,平均(48.36 ± 11.78)岁;职业分别为农民36例(26.09%),工人25例(18.12%),无业人员21例(15.22%),家政人员13例(9.42%),干部和职员10例(7.25%),个体户10例(7.25%),教师3例(2.17%),离退休人员10例(7.25%),职业不详10例(7.25%);受教育程度高中及以下83例(60.14%),大专及以上55例(39.86%);婚姻状况为已婚99例(71.74%),未婚26例

(18.84%),离异13例(9.42%);传染途径为婚内不洁性接触史20例(14.49%),婚外异性不洁性接触史23例(16.67%),同性性接触史4例(2.90%),吸毒史1例(0.72%),否认不洁性接触史82例(59.42%),传染途径不详8例(5.80%)。

二、研究方法

1. 病史采集 收集所有患者的流行病学资料,包括性别、年龄、职业、受教育程度、婚姻状况和传染途径等。

2. 实验室检查 (1)血清学检查:本组138例患者均于入院时采集肘静脉血2 ml,采用化学发光免疫分析[HISCL-5000型化学发光免疫分析仪,希森美康医用电子(上海)有限公司]检测血清梅毒螺旋体特异性抗体,行RPR试验(上海科华生物工程股份有限公司),酶联免疫吸附试验(ELISA)检测HIV(Bio-Rad 680型酶标仪,北京华大吉比爱生物技术有限公司)。(2)脑脊液检查:腰椎穿刺取脑脊液1~3 ml,手工计数白细胞并测定蛋白定量水平。白细胞计数 $\geq 10 \times 10^6/L$ 为白细胞计数升高,蛋白定量 $> 500 \text{ mg/L}$ 为蛋白定量升高。

3. 影像学检查 所有患者均于入院时采用荷兰Philips公司生产的Brilliance iCT扫描仪行头部CT检查,以及德国Siemens公司生产的Skyra 3.0T超导型MRI扫描仪行头部MRI检查。脑缺血、脑白质变性和脱髓鞘、脑积水等均为非特异性影像学改变。

4. 统计分析方法 采用SPSS 22.0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 检验或秩和检验。等级资料的比较采用秩和检验。呈正态分布的计量资料以均数 \pm 标准差($\bar{x} \pm s$)表示,采用单因素方差分析,两两比较行LSD-t检验。以 $P \leq 0.05$ 为差异具有统计学意义。

结 果

一、临床资料的比较

本组138例患者根据临床表现分为无症状性神经梅毒组(无症状组,32例)、间质性神经梅毒组(间质组,46例)和实质性神经梅毒组(实质组,60例)。3组患者临床资料比较,性别($P = 0.003$)和年龄($P = 0.000$)差异具有统计学意义,其中实质组男性患者比例($\chi^2 = 9.623, P = 0.002$; $\chi^2 = 7.953, P = 0.005$)和年龄($t = 2.985, P = 0.004$; $t = 3.322, P = 0.001$)均高于无症状组和间质组;而职业、受教育程度、婚姻状况和

表1 无症状组、间质组与实质组患者临床资料的比较**Table 1.** Comparison of general data among asymptomatic, interstitial and parenchymatous groups

| Item | Asymptomatic (N = 32) | Interstitial (N = 46) | Parenchymatous (N = 60) | Statistic value | P value | Item | Asymptomatic (N = 32) | Interstitial (N = 46) | Parenchymatous (N = 60) | Statistic value | P value |
|-------------------------------|--------------------------|--------------------------|----------------------------|--------------------|---------|---|--------------------------|--------------------------|----------------------------|--------------------|---------|
| Sex [case (%)] | | | | 11.588 | 0.003 | Education [case (%)] | | | | 3.425 | 0.180 |
| Male | 17 (53.13) | 27 (58.70) | 50 (83.33) | | | High school and below | 15 (46.88) | 28 (60.87) | 40 (66.67) | | |
| Female | 15 (46.88) | 19 (41.30) | 10 (16.67) | | | College degree and above | 17 (53.13) | 18 (39.13) | 20 (33.33) | | |
| Age ($\bar{x} \pm s$, year) | 43.12 ± 14.20 | 44.25 ± 9.83 | 51.61 ± 12.31 | 7.254 | 0.000 | Marriage [case (%)] | | | | 3.873 | 0.144 |
| Occupation [case (%)] | | | | 4.222 | 0.121 | Married | 19 (59.38) | 33 (71.74) | 47 (78.33) | | |
| Farmer | 10 (31.25) | 8 (17.39) | 18 (30.00) | | | Unmarried | 8 (25.00) | 9 (19.57) | 9 (15.00) | | |
| Worker | 6 (18.75) | 7 (15.22) | 12 (20.00) | | | Divorced | 5 (15.63) | 4 (8.70) | 4 (6.67) | | |
| Unemployed person | 5 (15.63) | 10 (21.74) | 6 (10.00) | | | Route of infection [case (%)] | | | | 2.486 | 0.289 |
| Housekeeper | 3 (9.38) | 2 (4.35) | 8 (13.33) | | | Marital unclean sexual contact history | 5 (15.63) | 8 (17.39) | 7 (11.67) | | |
| Official staff | 2 (6.25) | 3 (6.52) | 5 (8.33) | | | Extramarital unclean sexual contact history | 5 (15.63) | 10 (21.74) | 8 (13.33) | | |
| Self-employed person | 2 (6.25) | 6 (13.04) | 2 (3.33) | | | Homosexual contact history | 1 (3.13) | 1 (2.17) | 2 (3.33) | | |
| Teacher | 1 (3.13) | 1 (2.17) | 1 (1.67) | | | Drug abuse history | 0 (0.00) | 0 (0.00) | 1 (1.67) | | |
| Retiree | 2 (6.25) | 3 (6.52) | 5 (8.33) | | | Denial of unclean sexual contacts | 19 (59.38) | 26 (56.52) | 37 (61.67) | | |
| Unknown | 1 (3.13) | 6 (13.04) | 3 (5.00) | | | Unknown | 2 (6.25) | 1 (2.17) | 5 (8.33) | | |

Two-independent-sample *t* test for comparison of age, χ^2 test for comparison of sex and education, Kruskal-Wallis test for comparison of others

表2 无症状组、间质组与实质组患者RPR滴度的比较[例(%)]**Table 2.** Comparison of RPR titers among asymptomatic, interstitial and parenchymatous groups [case (%)]

| Group | N | RPR | | | | | | |
|----------------|----|-----------|------------|------------|------------|-----------|-----------|----------|
| | | 1 :1 | 1 :2 | 1 :4 | 1 :8 | 1 :16 | 1 :32 | 1 :64 |
| Asymptomatic | 32 | 6 (18.75) | 2 (6.25) | 12 (37.50) | 9 (28.13) | 1 (3.13) | 1 (3.13) | 1 (3.13) |
| Interstitial | 46 | 2 (4.35) | 5 (10.87) | 15 (32.61) | 11 (23.91) | 4 (8.70) | 2 (4.35) | 3 (6.52) |
| Parenchymatous | 60 | 0 (0.00) | 12 (20.00) | 12 (20.00) | 15 (25.00) | 6 (10.00) | 6 (10.00) | 5 (8.33) |

Z = 4.254, P = 0.016。RPR, rapid plasma reagin, 快速血浆反应素试验

传播途径,3组间比较差异无统计学意义(均P > 0.05,表1)。

二、实验室检查

1. 血清学检查 本组138例患者均检测血清梅毒螺旋体特异性抗体并行RPR试验,血清梅毒螺旋体特异性抗体均呈阳性;RPR滴度1:1~128,其中,8例(5.80%)为1:1,19例(13.77%)为1:2,39例(28.26%)为1:4,35例(25.36%)为1:8,11例(7.97%)为1:16,9例(6.52%)为1:32,9例(6.52%)为1:64,8例(5.80%)为1:128;3组患者RPR滴度差异有统计学意义($P=0.016$),其中,间质组($Z=2.394, P=0.024$)和实质组($Z=2.937, P=0.004$)RPR滴度高于无症状组,而间质组与实质组差异无统计学意义($Z=0.480, P=0.632$;表2)。

2. 脑脊液检查 本组89例患者行腰椎穿刺脑

脊液检查,37例(41.57%)白细胞计数 $> 10 \times 10^6 / L$,26例(29.21%)蛋白定量 $> 500 \text{ mg/L}$ 。3组患者脑脊液白细胞计数差异无统计学意义($P > 0.05$);蛋白定量差异有统计学意义($P = 0.048$),其中,仅实质组蛋白定量高于无症状组($P = 0.017$;表3,4)。

三、影像学检查

本组有62例患者行头部CT和(或)MRI检查。无症状组(4例)患者影像学无特异性表现;间质组(23例)有22例影像学表现异常,主要表现为脑缺血,余1例未见明显异常;实质组(35例)有28例影像学表现异常,主要表现为脑缺血、脑白质变性和脱髓鞘、脑积水,余7例未见明显异常。

讨 论

在本研究中,男性多于女性,男女比例高达

表3 无症状组、间质组与实质组患者脑脊液检查的比较($\bar{x} \pm s$)**Table 3.** Comparison of CSF test results among asymptomatic, interstitial and parenchymatous groups ($\bar{x} \pm s$)

| Group | N | WBC ($\times 10^6/L$) | Protein (mg/L) |
|--------------------|----|-------------------------|-----------------|
| Asymptomatic (1) | 8 | 25.12 ± 10.36 | 437.51 ± 186.90 |
| Interstitial (2) | 32 | 30.36 ± 14.78 | 633.69 ± 257.12 |
| Parenchymatous (3) | 49 | 29.01 ± 13.26 | 686.87 ± 276.29 |
| F value | | 0.621 | 3.135 |
| P value | | 0.479 | 0.048 |

WBC, white blood cell, 白细胞计数

表4 无症状组、间质组与实质组患者脑脊液蛋白定量的两两比较**Table 4.** Paired comparison of protein quantification results in CSF test among asymptomatic, interstitial and parenchymatous groups

| Paired comparison | t value | P value |
|-------------------|---------|---------|
| (1) (2) | 2.012 | 0.052 |
| (1) (3) | 2.453 | 0.017 |
| (2) (3) | 0.852 | 0.397 |

2.14 :1.00,且实质组男性比例高于无症状组和间质组,提示男性是神经梅毒的高危人群,且梅毒晚期患者多见于男性,与文献报道相一致^[6],考虑是由于男性发生婚外性行为比例和性需求高于女性所致。实质组患者年龄明显高于无症状组和间质组患者,考虑是由于实质组神经梅毒潜伏期较长,患者感染梅毒螺旋体后3~30年才发病^[10]。受教育程度以高中及以下为主,占60.14%(83/138),主要是由于受教育程度较低人群对性传播疾病防控知识了解甚少甚至缺乏,自我保护意识较差,而且罹患梅毒后由于心理压力等原因,不能及时就医,从而进展为神经梅毒。职业以农民、工人和无业人员为主,占59.42%(82/138),考虑是由于其受教育程度普遍较低,发生不安全性行为的概率较高,且京津冀地区外来务工人员密集,均增加梅毒的发病风险。因此,上述高危人群是梅毒防控与治疗的重点,应加强健康教育和行为干预。

尽管梅毒的传播方式以性传播为主,但本组有59.42%(82/138)患者否认不洁性接触史,可能是由于患者对梅毒的危害性认识不足,为保护个人隐私而隐瞒真实情况,故临床诊断时不洁性接触史仅作为参考依据。本组有14.49%(20/138)患者有婚内不洁性接触史,16.67%(23/138)患者有婚外异性不洁性接触史,可能是由于随着经济水平和生活质量

的提高,性能力保持良好,而且部分人群道德观念发生变化,嫖娼现象屡见不鲜,从而增加梅毒的发病风险^[11]。

神经梅毒临床表现多样、无特异性,是一种误诊率很高的疾病^[12]。本组有无症状性神经梅毒患者32例(23.19%),有症状性神经梅毒患者106例(76.81%)。无症状性神经梅毒患者尚未发生神经系统病变或发生较小病变,但可代偿且无临床症状,是神经梅毒的最初阶段,亦是最佳治疗阶段,因此需要实验室指标的证实^[13]。本组患者血清梅毒螺旋体特异性抗体和RPR试验均呈阳性,与既往研究结果一致^[14]。有研究显示,早期梅毒患者由于血清梅毒螺旋体特异性抗体滴度较低,易呈假阴性结果,造成漏诊。因此,临床应结合其他检测方法,避免漏诊或误诊^[15]。李宇等^[16]的研究显示,由于神经梅毒患者在疾病后期RPR可转为阴性,因此高度怀疑神经梅毒时可进一步检测脑脊液梅毒螺旋体特异性抗体和进行RPR试验进行筛查。

神经梅毒是感染性疾病,发病后脑脊液白细胞计数和蛋白定量异常改变^[17]。本组9例患者行腰椎穿刺脑脊液检查,37例(41.57%)白细胞计数 $\geq 10 \times 10^6/L$,26例(29.21%)蛋白定量 $> 500 \text{ mg/L}$,且实质组脑脊液蛋白定量高于无症状组,与文献报道相一致^[6],表明在排除其他细菌、病毒和并发感染的基础上,脑脊液白细胞计数和蛋白定量升高提示神经梅毒的可能。

神经梅毒影像学表现缺乏特异性,不同类型患者可以表现为脑膜炎、中枢神经系统血管炎、脱髓鞘疾病和肿瘤等影像学表现^[18-20]。MRI表现为脑萎缩、脑水肿、颅内动脉炎症性改变、脑缺血或腔隙性梗死等。脑膜神经梅毒和脑膜血管神经梅毒病灶通常位于双侧颞叶、顶叶和基底节区,呈散在分布,增强扫描病灶不强化,可累及皮质和神经核团^[21]。本组有62例患者行头部CT和(或)MRI检查,50例(80.65%)呈异常表现,主要表现为脑梗死、脑缺血、脑白质变性和脱髓鞘、脑积水。周畅等^[22]对脊髓痨患者进行影像学检查,未发现脊髓和脊神经根异常,表明影像学表现无特异性不能作为诊断神经梅毒的直接证据,但可以作为辅助诊断依据。

综上所述,神经梅毒好发于男性和受教育程度较低人群,应加强对上述高危人群的健康教育和行为干预;神经梅毒临床表现复杂,应强调实验室检查并予以早期治疗,防止疾病进一步发展。由于本

研究样本量较小,且患者入组前可能已接受治疗,且仅部分患者进行脑脊液和影像学检查,可能对结果有一定影响,尚待进一步深入研究。

利益冲突 无

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