

中国首例输入性寨卡病毒病患者的 中西医结合治疗经验

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【摘要】 目的 寨卡病毒病是由寨卡病毒通过伊蚊叮咬传播的急性传染病。报告中国首例输入性寨卡病毒病患者的诊治经过, 探讨中西医结合的治疗作用。**方法** 江西省赣县人民医院于 2016 年 2 月 6 日收治了中国首例输入性寨卡病毒病患者, 经过 9 d 的隔离治疗痊愈出院。介绍临床诊治过程, 分析中药喜炎平注射液的抗病毒作用。**结果** 患者男性, 34 岁, 因“发热 9 d, 眼眶痛、皮疹伴瘙痒 4 d”于 2016 年 2 月 6 日入院。① 流行病学特征: 1 月 1 日患者前往委内瑞拉出差, 期间常被蚊虫叮咬, 当地正在流行寨卡病毒病。委内瑞拉当地时间 1 月 20 日患者曾出现头晕, 无发热, 自行购药(具体不详)服用后症状消失; 1 月 28 日稍感头晕、畏寒、低热, 呈阵发性发作, 无肌肉酸痛; 2 月 3 日颈部出现散在细小红色皮疹, 随后蔓延到前胸、四肢、躯干, 仍有低热、乏力、恶心, 耳后、眼眶开始出现阵发性针刺样疼痛, 期间一直未治疗; 2 月 4 日上述症状逐渐好转减轻。北京时间 2 月 5 日患者回到赣县后解黄色稀便 3 次, 体温正常, 颈部仍有散在皮疹, 无腹痛; 2 月 6 日在赣县人民医院诊治。② 临床表现: 入院体温 36.8℃, 脉搏 80 次/min, 呼吸频率 20 次/min, 血压 110/70 mmHg (1 mmHg = 0.133 kPa), 颈前区有散在淡红色细小皮疹, 全身浅表淋巴结无肿大, 双侧眼结膜充血明显, 生理反射存在, 病理反射未引出。③ 辅助检查: 2 月 6 日血常规正常, 活化部分凝血活酶时间 (APTT) 轻度延长 (38.6 s), 肝肾功能、心肌酶谱、电解质、血糖、C-反应蛋白 (CRP)、肌钙蛋白 I (TnI)、降钙素原 (PCT) 均正常。2 月 8 日胸部 CT 示左肺絮状阴影, 结合发热病史, 考虑炎症变和轻度肺气肿改变 (左下肺为主); 双肾结石。心电图及肝、脾、胰 B 超均未见明显异常。④ 病毒检测确诊过程: 2 月 6 日赣州市疾病预防控制中心 (CDC) 检测结果为登革病毒核酸阴性。2 月 7 日江西省 CDC 检测结果为寨卡病毒核酸阳性。2 月 9 日中国 CDC 检测结果为寨卡病毒核酸阳性。首次确诊后对密切接触者予以医学观察。⑤ 诊疗经过: 2 月 6 日收入隔离病房后给予对症治疗及每日静脉滴注 1 次喜炎平注射液 250 mg 抗病毒治疗。2 月 7 日无发热, 偶有畏寒, 颈部皮疹消失, 眼眶痛好转, 双侧眼结膜充血范围缩小变淡, 全身黏膜未见溃疡; 16:00 体温 37.5℃, 口服布洛芬 0.2 g, 每日 3 次。2 月 8 日无发热, 畏寒明显减轻, 无肌肉酸痛和皮疹, 眼眶痛及眼结膜充血进一步好转。2 月 9 日双侧眼角稍感刺痛, 眼角结膜少量充血, 无发热、畏寒, 因医院无重组人干扰素 α 滴眼液贮备, 故改用氯霉素滴眼液每日 2 次。2 月 11 日以后患者无不适感觉, 2 月 13 日江西省 CDC 和中国 CDC 均回报患者血、尿寨卡病毒核酸阴性, 符合出院条件, 患者于 2 月 14 日痊愈出院。**结论** 目前寨卡病毒病尚无特殊药物可以预防和治疗, 本例患者经过 9 d 对症治疗及中药喜炎平注射液抗病毒治疗后症状消失, 血、尿寨卡病毒核酸连续检测阴性, 痊愈出院。提示中西医结合治疗寨卡病毒病有一定优势。

【关键词】 寨卡病毒病; 喜炎平注射液; 中西医结合治疗

Experience of integrated traditional Chinese and Western medicine in first case of imported Zika virus disease in China Deng Yichu, Zeng Liping, Bao Wen, Xu Pinghua, Zhong Gongrong

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【Abstract】 Objective Zika virus disease is an acute infectious disease caused by Zika virus transmitted through *Aedes* mosquitoes. To explore the therapeutic effect of integrated traditional Chinese and Western Medicine for Zika virus disease, the treatment process of the first imported case in China was reviewed. **Methods** The first imported Zika virus disease in China was admitted to Ganxian People's Hospital in Jiangxi Province on February 6th, 2016, and the patient received isolation treatment for 9 days and cured later. The effect of antiviral treatments including Xiyanping injection was evaluated based on clinical diagnosis and treatment process of the patient. **Results** A 34-year old male patient was admitted with chief complaint of fever for 9 days, orbital pain and itching rash for 4 days on February

6th, 2016. ① Epidemiological characteristics: the patient was bitten by mosquitoes during his business trip in Venezuela since January 1st, where Zika virus disease was spreading. On January 20th he had dizziness without fever, and the symptom disappeared after taking medicines without details. Paroxysmal dizziness, chills and mild fever without myalgia was experienced on January 28th. On February 3rd small red rash appeared in the neck, spreading to anterior part of chest, limbs and trunk, and the fever, fatigue, nausea was continued, and a new symptom of paroxysmal pain in back of ears and orbits appeared, during which he had not go to hospital. The symptoms relieved on February 4th. He returned to Ganxian County on February 5th, he had yellow stool 3 times with normal temperature, without abdominal pain, and red rash still appeared in the neck. He went to Ganxian People's Hospital on February 6th, 2016. ② Clinical manifestation: the vital signs showed a temperature of 36.8 °C, a pulse rate of 80 bpm, a respiratory rate of 20 bpm, and a blood pressure of 110/70 mmHg (1 mmHg = 0.133 kPa). It was showed by physical examination that red rash appeared in the neck, and no superficial enlarged lymph nodes were found. Bilateral conjunctival congestion was obvious, physiological reflex existed and pathological reflex was not found. ③ Auxiliary lab test and examination: no abnormal finding were revealed throughout examination and laboratory tests, including routine blood test, liver function, renal function, serum myocardial enzyme, electrolyte, blood sugar, C-reactive protein (CRP), troponin I (TnI), and procalcitonin (PCT), except slight prolongation in activated partial thromboplastin time (APTT, 38.6 s) on February 6th; and slightly dense shadow in left lung in lung CT scan, considering inflammatory changes and slight emphysema (especially in the left lower lung) as well as bilateral renal calculus on February 8th. No significant abnormalities were found in electrocardiogram and B ultrasound test of liver, spleen, and pancreas. ④ Virus confirmation: Zika virus nucleic acid was positive reported by Jiangxi Province Center for Disease Control and Prevention (CDC) on February 7th and Chinese CDC on February 9th, respectively, though Dengue virus were negative reported by Ganzhou CDC on February 6th. Right after the first diagnosis, anyone who had been in close contact with the patient received medical monitoring. ⑤ Treatment process: on February 6th, symptomatic treatment was prescribed since admitted into the infectious isolation wards and daily intravenous drip of Xiyanping injection 250 mg was prescribed for antiviral therapy. On February 7th, the patient had no fever, with occasional chills, neck rash was disappeared, orbital pain relieved and bilateral conjunctival hyperemia range was paler and narrowed, and his condition improved. Ibuprofen was administered for defervescence 3 times a day when his temperature reached to 37.5 °C at 16:00. On February 8th, the patient had no fever, times of chills was significantly reduced, without myalgia and rash, orbital pain and conjunctival hyperemia further recovered. On February 9th, bilateral eyes slightly tingling, mild conjunctival congestion, no fever chills or other discomfort was found. The chloramphenicol eye drops was prescribed for relieving sting pain with conjunctival congestion twice a day as recombinant human interferon alpha eye drops was out of store. The patient was comfortable from February 11th to February 13th. Blood and urine test for Zika were reported negative by the Chinese CDC and Jiangxi Province CDC. Because all the discharge criteria were satisfied, the patient was discharged on February 14th. **Conclusions** At present, there is no specific effective drug to prevent and treat Zika virus disease effectually. After receiving symptomatic treatment and antiviral treatments including Xiyanping injection, the patient's symptoms were relieved. Zika virus nucleic acid in blood and urine was negative. The patient was discharged. Combination of traditional Chinese medicine and Western medicine maybe a good method to prevent and treat Zika virus disease.

【Key words】 Zika virus; Treatment of traditional Chinese medicine and Western medicine; Xiyanping injection

寨卡病毒病是由寨卡病毒引起的急性传染病,主要通过伊蚊(*Aedes mosquitoes*)叮咬传播。寨卡病毒病属自限性疾病,感染寨卡病毒后只有约 20% 的人有症状,病程通常持续不到 1 周,典型症状包括突发低热、斑丘疹、关节疼痛(主要累及手、足小关节)、结膜炎;其他症状包括肌痛、头痛、眼眶痛及无力;少见症状包括腹痛、恶心、呕吐、黏膜溃疡和皮肤瘙痒;需要住院治疗的严重病情并不常见。2013 年和 2015 年,在法属波利尼西亚和巴西寨卡疫情期间就有报道称寨卡病毒病可能会造成神经和自身免疫系统并发症^[1-3]。2016 年 2 月 1 日,世界

卫生组织(WHO)召开紧急会议,决定把寨卡病毒感染列为国际紧急卫生事件。目前还没有药物可以预防和治疗寨卡病毒病^[4]。本院 2016 年 2 月 6 日收治中国首例输入性寨卡病毒病患者,经采用密切隔离和中西医结合方法治疗,效果满意,患者已于 2 月 14 日痊愈出院,现将诊疗经过报告如下,以期中西医结合治疗寨卡病毒病提供一些思路。

1 病例资料

1.1 流行病学史及发病经过:患者男性,34 岁,因“发热 9 d,眼眶痛、皮疹伴瘙痒 4 d”于 2016 年 2 月 6 日入院。2016 年 1 月 1 日患者前往委内瑞拉出差,

期间常有蚊虫叮咬,当地正在流行寨卡病毒病。患者主诉于委内瑞拉当地时间1月20日曾出现头晕,无发热,自行购药(具体不详)服药2片后症状消失;1月28日稍感头晕、畏寒、低热,呈阵发性发作,无肌肉酸痛,自觉体温达 38.0°C ;2月2日仍有低热、乏力,头晕加重,呈持续性;2月3日颈部出现散在细小红色皮疹,随后蔓延到前胸、四肢、躯干,皮疹未突出皮肤,仍感低热、乏力,耳后、眼眶开始出现阵发性针刺样疼痛,稍感恶心,食欲有所减退,期间一直未处理;2月4日上述症状逐渐减轻、好转。北京时间2月5日回到赣县后解黄色稀便3次,体温正常,颈部仍有散在皮疹,无腹痛;2月6日来本院诊治,以“发热待查”收入感染性疾病科隔离病房。病程中患者精神、睡眠可,二便正常,未出现肢体活动受限及听力异常情况。既往有轻度肺气肿病史(左下肺为主)。

1.2 住院后查体:体温 36.8°C ,脉搏80次/min,呼吸频率20次/min,血压110/70 mmHg(1 mmHg= 0.133 kPa),意识清楚,急性面容,全身皮肤、黏膜无黄染,颈前区散在淡红色细小皮疹,压之不褪色,未高出皮肤,无融合成片,其余皮肤未见色素沉着,无出血点,全身浅表淋巴结无肿大,双侧眼结膜充血明显、无脓点,视力正常,双耳、鼻、口腔未见异常,颈软;双肺、心脏听诊未闻及异常;腹平软,无压痛及反跳痛;脊柱、四肢无畸形,运动无障碍,关节无红肿,双下肢无水肿;生理反射存在,病理反射未引出。

入院后接诊医师考虑患者来自南美洲,属于寨卡病毒病流行疫区,有蚊虫叮咬史,故警惕为寨卡病毒病,分别向科主任、院感科、医务科汇报,院感科向县疾病预防控制中心(CDC)汇报,当即成立了院内专家组集体讨论,一致认为不能排除寨卡病毒病,需与登革热鉴别,将血标本送至江西省CDC和中国CDC检测,并对病房进行严格灭蚊消毒,同时完成辅助检查。

1.3 辅助检查:2月6日查血常规正常:白细胞计数(WBC) $4.3\times 10^9/\text{L}$,中性粒细胞比例0.577,淋巴细胞比例0.288,红细胞计数(RBC) $4.96\times 10^{12}/\text{L}$,血红蛋白(Hb)159 g/L,血细胞比容0.439,血小板计数(PLT) $224\times 10^9/\text{L}$;凝血指标:凝血酶原时间(PT)13.2 s,国际标准化比值(INR)1.06,活化部分凝血活酶时间(APTT)38.6 s,凝血酶时间(TT)12.8 s,纤维蛋白原(Fib)2.36 g/L,提示APTT轻度升高;肝肾功能、心肌酶谱、电解质、血糖、C-反应蛋白(CRP)均

正常,肌钙蛋白I(TnI) $0.04\text{ }\mu\text{g/L}$,降钙素原(PCT) $<0.05\text{ }\mu\text{g/L}$,提示TnI及PCT正常。21:00赣州市CDC回报登革病毒核酸阴性,目前可排除登革热,但需要警惕寨卡病毒病。

1.5 治疗经过

1.5.1 2月6日:患者入院后即进行了严密隔离,并给予对症治疗及中药喜炎平抗病毒治疗(250 mg 静脉滴注,每日1次)。

1.5.2 2月7日:08:00查房患者无发热,偶有畏寒(持续时间5 min左右、间隔时间5 h左右),颈部皮疹消失,无色素沉着,眼眶痛好转,双侧眼结膜充血范围缩小变淡,全身黏膜未见溃疡,病情好转。在等待上级专家组指导诊断和排除过程中,密切观察患者病情变化,同时做好隔离和防蚊、灭蚊工作以及家属的医学监测。**16:00**患者体温 37.5°C ,给予布洛芬0.2 g口服,每日3次。**13:00**江西省CDC回报寨卡病毒核酸检测阳性,考虑不排除寨卡病毒病。在对患者进一步加强治疗的同时,每日留取患者和家属的空腹血液标本5 mL、尿液20 mL送江西省CDC进行流行病学监测,每日16:00前向赣州市CDC报告患者病情及家属医学监测情况。

1.5.3 2月8日:08:00查房患者无发热,畏寒明显减轻,无肌肉酸痛,皮疹消退,眼眶痛好转,二便、食欲正常,无腹痛;眼结膜充血较前好转。继续给予布洛芬对症及喜炎平抗病毒治疗。**13:00**省、市卫生计生委领导和专家组联合会诊后诊断为疑似寨卡病毒病,排除登革热。要求严密观察和控制患者症状的发展,同时做好隔离和密切接触者的医学监测,双眼结膜给予重组人干扰素 α 滴眼液。由于医院无重组人干扰素 α 滴眼液贮备,故改用氯霉素滴眼液。同时完善胸部CT检查,结果提示:左肺絮状阴影,结合发热病史,考虑炎性变,轻度肺气肿改变,以左下肺为主(图1A~1B);双肾结石。心电图未见异常。B超:肝、脾、胰未见明显异常。

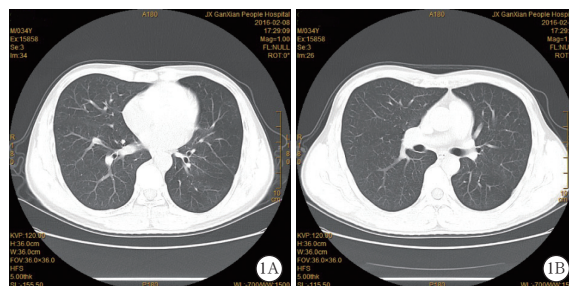


图1 中国首例输入性寨卡病毒病患者2016年2月8日胸部CT检查结果(A、B)提示左肺絮状阴影

1.5.4 2月9日:08:00 查房患者精神明显好转,无发热畏寒等不适,双侧眼角稍感刺痛,双侧眼角结膜少量充血(图 2A~2B),给予氯霉素滴眼液 2 滴滴眼,每日 2 次。期间中国 CDC 回报寨卡病毒核酸检测阳性。

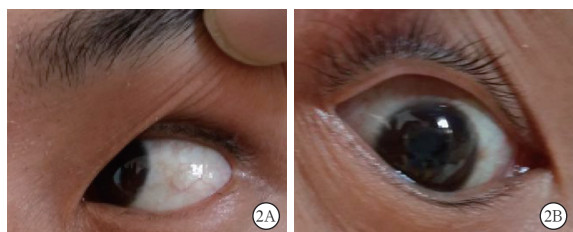


图 2 中国首例输入性寨卡病毒病患者 2016 年 2 月 9 日左侧(A)、右侧(B)眼角结膜少量充血

1.5.5 2月10日:08:00 查房患者未诉任何不适,左侧眼角结膜少量充血,继续使用氯霉素滴眼液。

1.5.6 2月11日以后患者已无不适感觉,继续在院隔离观察,等待血、尿寨卡病毒检测结果,以决定出院时间。2月13日江西省 CDC 和中国 CDC 均回报患者血、尿寨卡病毒核酸检测阴性,符合出院条件,故 2月14日患者痊愈出院。

2 喜炎平注射液用于寨卡病毒病治疗的临床思路

由于目前没有特殊药物可以预防和治疗寨卡病毒病,只能采取对症支持治疗。喜炎平注射液是一种经国家中药指纹图谱检测标准批准上市的新型中药制剂,为穿心莲提取物,其成分为水溶性穿心莲内酯总酯磺化物,主要包括穿心莲内酯、异穿心莲内酯、新穿心莲内酯、去氧穿心莲内酯、脱水穿心莲内酯及穿心莲甙等成分,具有抗病毒、抗菌、增强机体免疫力、清热解毒的作用^[5]。药理研究表明,穿心莲可通过直接破坏内毒素结构或抑制其诱导释放的炎性细胞因子活性而有效拮抗内毒素,可广泛用于感染性和非感染性疾病^[6]。还有研究表明,喜炎平注射液用于治疗手足口病^[7]、带状疱疹^[5]、小儿上呼吸道感染^[8-9]、小儿轮状病毒性腹泻^[10]等都有明显的疗效;对腺病毒、呼吸道合胞病毒和流感病毒也有较强的灭活作用^[11]。本例患者同样为病毒感染,且无特殊治疗药物,因此我们采用喜炎平注射液 250 mg + 5% 葡萄糖注射液 250 mL 静脉滴注、每日 1 次治疗,取得了较为满意的效果。说明了中西医结合治疗传染性发热疾病有一定优势。

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