

·病例报告·

中国首例输入性裂谷热危重症病例的救治及随访

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【摘要】目的 探讨我国首例输入性裂谷热危重症病例的救治。**方法** 对本院收治的我国首例输入性裂谷热危重症病例的临床资料、诊疗经过及预后进行回顾性分析。**结果** 本例裂谷热危重症患者为45岁男性,在非洲务工两年回国,当地无裂谷热疾病流行。主要临床表现为发热、头痛、周身肌肉酸痛,进行性尿量减少。实验室检查提示肝、肾功能重度损伤。入院第3天,经中国疾病预防控制中心报裂谷热病毒核酸阳性,其他病原核酸均为阴性,确诊为裂谷热。经持续血液净化、保肝、稳定细胞膜以及对症支持治疗后,患者尿量逐渐增加,肝肾功能逐渐恢复正常,痊愈出院。门诊随访半年,肝肾功能均正常,视力无异常。**结论** 裂谷热作为一种人畜共患病,传入我国的风险逐渐增加。急性肾功能衰竭、急性肝功能损伤是危重症裂谷热的主要表现,经过积极治疗,病情可有效控制。

【关键词】 输入性传染病;裂谷热;危重症;肾功能衰竭、急性;肝功能损伤、急性

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【Abstract】Objective To investigate the treatment of the first case of rift valley fever in China. **Methods** The clinical data, treatments, prognosis and follow up data of the first case of rift valley fever in China were analyzed, retrospectively. **Results** This case of rift valley fever critically ill patient was male, 45 years old, living in Angola for 2 years, there were no rift valley fever epidemic. The main clinical manifestations were fever, headache, abdominal muscle pain, progressive reduction in urine output. Laboratory tests suggested severe liver and kidney function damage. On the third day of admission, the rift valley fever virus was reported positive by the Chinese CDC, and other pathogens were negative and rift valley fever was confirmed. After continuous blood purification, liver protection, stable cell membrane and symptomatic support treatment, the urine output was gradually increased, liver and kidney function gradually recovered. Outpatient follow-up for six months, liver and kidney function of the case were normal, and the patient was discharged. **Conclusions** As a zoonotic disease, the risk of rift valley fever incoming to China is gradually increased. Acute renal failure and acute liver injury are the main manifestations of critical rift valley fever, it could be effectively controlled after treatment.

【Key words】 Imported transmitted diseases; Rift valley fever; Critically ill; Acute renal failure; Acute liver injury

裂谷热(rift valley fever, RVF)是由裂谷热病毒(rift valley fever virus, RVFV)引起的急性传染病,又称作里夫谷热,是一种由病毒引起的人畜共患病,主要流行于非洲^[1]。临床表现为发热、头痛、疲劳、关节和肌肉疼痛,

伴有恶心、呕吐,部分患者会出现结膜炎;严重者可能会导致出血、休克、脑炎或肝炎,严重患者会出现死亡^[2-5]。2016年7月23日国家卫计委通报,中国确诊首例输入性裂谷热病例,为重症病例,存在急性肾功能衰竭和严重肝功能损伤^[6]。该患者于本院抢救治疗后痊愈出院,出院6个月后随访,患者肝、肾功能和视力正常。本文特对该病例的抢救经过进行报道。

一、患者的临床资料

患者汤某某,男性、45岁,主因“发热6 d,无尿3 d”门诊以发热待查于2016年7月21收入院。患者在安哥拉罗安

DOI: 10.3877/cma.j.issn.1674-1358.2018.01.020

基金项目:新发突发传染病研究北京市重点实验室资助课题(No. D09050703560908; DTKF-2016-04);北京市医院管理局重点医学专业发展计划-新发突发传染病(No. ZYLX201602);感染病科国家重点专科建设项目;感染性疾病重症医学(No. ZYLX201827)

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达工作两年,期间未回国,未到过外地。从事铲车司机工作,每日工作约6 h,无高温工作史,驾驶室有空调,此次发病前有大量蚊虫叮咬史。无牛羊等动物接触史。6天前在安哥拉工作期间出现发热,体温最高达38.3℃,伴有头痛、周身肌肉酸痛,无畏寒、寒战,无咳嗽、咯痰,无腹痛、腹泻,无皮疹关节痛。在当地医院按疟疾治疗后无改善。3天前开始出现恶心、进食少、无尿。1天前再次出现发热,伴有恶心,为进一步诊治回国。

发病以来神志清楚,精神正常,大便正常。入院查体:体温37℃,脉搏68次/min,呼吸19次/min,血压113/63 mmHg (1 mmHg = 0.133 kPa)。神志清楚,急性病容,全身皮肤黏膜中度黄染,心肺无异常,腹软无痛,四肢活动正常。入院后血液查未见疟原虫。CD4⁺ T淋巴细胞 154/μl,其余化验详见表1。肺腹部CT扫描提示双侧肺炎,胸腔积液,胆囊炎和少量腹水。头部CT扫描未见异常。超声心动图显示左心室射血分数为60%,心脏结构无明显差异。

入院诊断:发热黄疸待查:病毒性肝炎?疟疾?黄热病?登革热?急性重度肝功能损伤、急性肾功能衰竭、代谢性酸中毒、低蛋白血症。

二、治疗过程

因患者持续无尿,转重症医学科抢救治疗。转入后行深静脉穿刺,开始血液滤过透析治疗,维持内环境和水电解质平衡。因为存在呕吐及胰腺炎,予以禁食,同时静脉营养支持。同时给予保肝、稳定细胞膜以及对症支持治疗。入院第3天中国疾病预防控制中心报裂谷热病毒核酸阳性,其他病原核酸均为阴性,确诊为裂谷热。经持续血液净化治疗8 d后,患者尿量逐渐增加,改为间断血液净化治疗,病程第17

天,尿量达到2 000 ml,停用血液净化,观察肌酐水平稳定下降,肝功能逐渐好转。2016年8月7日患者开始出现多尿,每日尿量在5 000 ml以上,电解质稳定,肾功能好转,肌酐稳定下降至233 μmol/L,病情明显好转。2016年8月11日转普通病房继续治疗,2016年9月5日痊愈出院。出院后半年随访,患者肝肾功能正常,无异常发现,视力正常。

讨论 裂谷热(RVF)是由裂谷热病毒,也称立夫特谷热病毒(RVFPV)引起的急性传染病^[1]。裂谷热是一种病毒性人畜共患病,主要感染动物,但也能感染人。受到裂谷热感染的牲畜会出现死亡和流产,可造成重大经济损失^[7-9]。在非洲和阿拉伯半岛发生过大规模的裂谷热疫情,最近在南非、肯尼亚、苏丹、沙特阿拉伯、坦桑尼亚和也门等地区也有发生^[10-14]。研究表明,近年来人类裂谷热疫情的暴发是病毒遗传突变和基因组重组造成,裂谷热病毒株变异增加了对人类的威胁,导致潜在的公共卫生和社会经济威胁^[9]。

国外报道的人间裂谷热大多数是由于直接或间接接触受感染动物的血液或器官造成的。病毒可通过在宰杀、帮助接生、兽医操作而传染给人。因此,某些职业群体的感染风险较高,如牧民、农民、屠宰工人和兽医^[15]。有证据显示,人若摄入被感染的动物的奶,也有可能染上裂谷热。受感染蚊子叮咬也会导致人际感染。2015年一例来自马里的肾移植受者在法国诊断为裂谷热,在脑脊液和血液中检测到RVFPV特异性IgM和IgG,在尿液和精液中检测到RVFPV基因组RNA,提示裂谷热可通过血液传播^[16]。

关于裂谷热的发病机制至今尚未完全阐明。研究表明,裂谷热病毒进入机体后,首先在侵入的局部组织中复制,通过淋巴系统转移至局部淋巴结而进一步复制,继而

表1 患者住院期间实验室检查结果

指标	7月21日	7月22日	7月23日	7月26日	8月19日	8月29日
WBC (× 10 ⁹ /L)	6.77	5.91	2.47	9.09	8.52	7.81
NE (%)	71.50	66.00	80.00	68.00	61.8	57.60
血色素 (g/L)	155.40	137.00	143.00	129.00	94.00	89.00
血小板 (× 10 ⁹ /L)	99.00	104.00	81.00	85.00	335.00	261.00
ALT (U/L)	5 910.00	5 360.00	1 968.00	857.00	194.00	42.00
AST (U/L)	7 570.00	686.00	612.00	124.00	90.00	29.60
TBil (μmol/L)	83.80	96.00	59.00	46.00	16.00	10.00
DBil (μmol/L)	71.80	85.00	52.00	37.00	11.00	5.00
白蛋白 (g/L)	36.80	31.60	30.90	28.90	49.00	43.00
尿素氮 (mmol/L)	35.19	37.00	19.00	18.00	8.00	5.03
肌酐 (μmol/L)	1 005.70	097.00	540.00	397.00	139.00	86.00
肌酸激酶同工酶 (ng/ml)	86.00	70.00	26.00	25.00	20.00	15.00
C-反应蛋白 (mg/L)	18.50	16.30	7.20	8.20	5.00	0.50
降钙素原 (ng/ml)	71.78	50.50	34.00	1.00	0.22	< 0.05
血脂肪酶 (U/L)	58.10	122.00	468.00	192.00	30.00	20.00
血淀粉酶 (U/L)	132.00	65.90	284.00	67.00	50.00	45.00

进入血循环形成病毒血症,一般持续4~7 d,出现发热等感染中毒症状,并可引起多脏器局灶性感染,以肝脏受累为著^[2,17-18]。动物实验证明,组织器官发生病变的部位和病毒复制部位一致,细胞损伤可能通过溶解效应造成,同时还可能与免疫损伤有关^[19-22]。严重病毒血症和受染细胞的广泛坏死导致促凝物质释放,毛细血管内皮细胞受损,纤维素沉着,纤维降解产物增加,促进血小板聚集、消耗,引起弥漫性血管内凝血^[23-24]。

裂谷热的病理表现主要为皮肤、皮下组织和内脏器官表面浆膜广泛出血;肝脏肿大,存在广泛坏死灶,镜下可见肝细胞灶性坏死,可相互融合,病变广泛,多见于肝中带,肝细胞内可见嗜酸性变^[25-27]。肾皮质可见充血和点状出血,肾实质可见出血和肾小球毛细血管纤维素沉着,以肾小管病变为著;肾小球毛细血管和近曲小管内可出现纤维素沉着,尿中出现红细胞、白细胞、管型、少尿甚至肾功能衰竭;脑组织和脑膜呈灶性细胞变性炎症浸润^[18,28-29]。

裂谷热感染后大多无症状,发病者症状多轻微,如流感样症状,发热、肌肉疼痛、关节疼痛和头痛等。少数人可发展成严重感染,出现眼部疾病、脑膜炎或出血热。约1%的裂谷热病例合并严重的出血^[30]。出血热一般在发病2~4 d后出现,表现为严重肝功能损伤、出血倾向,如皮肤紫癜或瘀斑、鼻或牙龈出血、静脉穿刺部位出血等,严重者出现呕血、便血。发生严重出血的患者病死率高,约50%,多在出血症状3~6 d后死亡^[22,31-32]。

急性肾功能损伤和急性肝功能损伤是裂谷热最为常见和致命的并发症。苏丹的一项研究表明,2007年9月和2008年1月,194例裂谷热患者中存在肾损伤者占60%,其中90%需要透析治疗。急性肾功能衰竭患者病死率为31%;肝肾综合征患者病死率为25%。该研究表明在当地裂谷热仍然是急性肾衰竭的主要原因,且病死率高,早期肾脏替代治疗可以改善患者的生存率^[33]。苏丹另外一项共计18例患者的临床资料表明,裂谷热的主要临床特征包括肝功能衰竭6例(33.3%),急性肾功能衰竭4例(22.2%),出血5例(27.8%),视力障碍6例(33.3%)。死亡的主要原因是肝、肾功能衰竭,以及出血引起的贫血^[34]。

本例患者因发热和无尿入院,临床表现和实验室检查提示存在急性肾功能衰竭和急性重度肝功能损伤。入院后经中国疾病预防控制中心实验室检查裂谷热病毒核酸阳性,明确了裂谷热的诊断^[35-36]。本例患者主要损伤的脏器为肾脏和肝脏,存在急性肾功能衰竭和急性重度肝功能损伤,而无明显的出血表现,与国外的报道相同。在住院期间及院外随访中,均未发现存在眼部病变。对于同时存在肝、肾功能严重损伤的患者持续肾脏替代治疗是较好的治疗方法,可以患者维持机体内环境稳定和水电解质平衡,同时可以清除小分子物质如尿素氮、肌酐、胆红素等,是

广义人工肝治疗的模式。此患者在持续肾脏替代治疗后,黄疸亦呈进行性下降趋势,可能与此治疗模式有一定关系。

综上,裂谷热作为一种传染性较强的人畜共患病,随着国际交流的不断增加,裂谷热传入我国的风险逐渐增加。本例是我国首例输入性裂谷热病例,虽然病情危重,但经过积极稳妥的抢救治疗,病情较快得到控制,为我国裂谷热的防控和治疗经验的积累提供临床依据。

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- (收稿日期: 2017-02-27)
(本文编辑: 孙荣华)

熊号峰, 李传胜, 谭建波, 等. 中国首例输入性裂谷热危重症病例的救治及随访[J/CD]. *中华实验和临床感染病杂志(电子版)*, 2018,12(1):98-101.