

解脲脲原体引起血流感染 1 例

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摘要: **目的** 分析安溪县医院 1 例流产后解脲脲原体引起的血流感染,及时为临床诊断及治疗提供依据。**方法** 回顾性分析该例解脲脲原体血流感染患者鉴定为解脲脲原体的整个诊断过程,收集了来自临床的基本资料、实验室诊断资料,包括血培养曲线特征、培养液瑞氏染色、支原体液体鉴定药敏及固体培养基菌落特征,以及靶向 DNA 测序结论。通过对上述资料的综合分析,优化血培养支原体的检测诊断流程及方法。**结果** 该例患者临床表现为术后发热 38.5 °C,CRP:14.85 mg/L,WBC:14.33×10⁹/L,NET:85.40%,PCT:0.12 ng/mL,IL-6:665.6 pg/mL。血培养 3 d 报阳,革兰染色未见菌体,瑞姬染色可见细沙样紫色菌体。接种于血平板、支原体固体、液体培养基,血平板培养 48 h 及 5 d 均未见菌落;支原体固体培养基上棕色油煎蛋状菌落边缘丝状;液体培养基上可鉴定为解脲脲原体。喹诺酮类、大观霉素耐药;大环内酯类、四环素类、林可霉素均敏感。后续靶向 DNA 测序结果一致也为解脲支原体。收到报告之前临床采用头孢曲松+甲硝唑常规经验抗感染覆盖阴性杆菌与厌氧菌,未对支原体进行针对性治疗,3 d 后患者体温恢复正常,炎症指标下降,患者要求出院。**结论** 目前解脲脲原体引起血流感染报道甚少,临床认识不足,容易造成误诊、漏诊。为了提高血培养支原体的检出率,需优化血培养的检测流程,为临床及时提供精准的诊疗依据。不过,从本例可以看出支原体血流感染病例属于自限性感染,对于免疫力正常的患者,不需要针对性治疗也可自行恢复,因而保护患者免疫力非常重要。

关键词: 解脲脲原体;流产后;血流感染

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One case of bloodstream infection caused by *Ureaplasma urealyticum*

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Abstract: **Objective** To analyze a case of bloodstream infection caused by *Ureaplasma urealyticum* after abortion in Anxi County Hospital, so as to provide basis for the clinical diagnosis and treatment. **Methods** The diagnosis of *Ureaplasma urealyticum* in this patient with bloodstream infection was retrospectively analyzed. The basic clinical data and laboratory diagnosis data were collected, including the characteristics of blood culture curve, Wright staining of culture medium, drug sensitivity of *Mycoplasma* liquid identification, colony characteristics of solid medium, and the conclusion of targeted DNA sequencing. Through the comprehensive analysis of the above data, the rapid diagnosis of this case can be realized by optimizing the detection and diagnosis process. **Results** The clinical manifestations of this patient were fever of 38.5 °C, CRP: 14.85 mg/L, WBC:14.33×10⁹/L, NET: 85.40%, PCT: 0.12 ng/mL, IL-6: 665.6 pg/mL, positive after 3 days of blood culture, no bacteria were found in Gram stain, and sand-like purple bacteria were observed after adding Wright's stain. After inoculation in blood agar, *Mycoplasma* solid and liquid medium, no colonies were grown in blood agar, after 48 h and 5 d. On *Mycoplasma* A7 agar, the edge of brown fried egg colony was striature, and it could be identified as *Ureaplasma urealyticum* with the *Mycoplasma* ID & AST panel, which was resistant to quinolones and spectinomycin, but sensitive to macrolides, tetracyclines and lincomycin. Subsequent targeted DNA sequencing results were also confirmed for *Ureaplasma urealyticum*. Before receiving the report, clinical experience treatment with ceftriaxone metronidazole was used to fight infection with negative bacilli and anaerobic bacteria. *Mycoplasma* was not treated with targeted treatment. After 3 days, the patient's body temperature returned to normal, inflammation index decreased, and the patient asked to be discharged. **Conclusions** At present, there are few reports of bloodstream infection caused by *Ureaplasma urealyticum*, and the lack of clinical understanding can easily lead to misdiagnosis and missed diagnosis. In order to improve the detection rate of *Mycoplasma* in blood culture, it is necessary to optimize the detection procedure of blood culture and provide accurate diagnosis and treatment basis for clinical practice. However, it is clear from this case that *Mycoplasma* bloodstream infection cases are self-limited infection and can recover by themselves without targeted treatment in patients with normal immunity. Therefore, it is very important to protect the immunity of patients.

Keywords: *Ureaplasma urealyticum*; after abortion; bloodstream infections

解脲脲原体(*Ureaplasma urealyticum*, UU)是引起人类泌尿生殖系统感染的主要病原体之一,可定植于人体生殖道和呼吸道黏膜,与上皮细胞具有较强亲和性^[1],容易引起黏膜细胞损伤而造成泌尿生殖道感染,如非淋球菌性尿道炎、宫颈炎、阴道炎、绒毛膜羊膜炎、早产、自然流产和不孕症等^[2-8]。解脲脲原体一般可通过阴道和子宫颈上行感染宫腔^[9],也可在侵入性手术时意外引入,例如剖宫产、羊膜穿刺术、经皮胎儿血液取样、绒毛膜绒毛取样等泌尿生殖系统之外感染^[2],经查阅相关资料,有研究在妊娠孕妇血液、脐带血以及新生儿血液中分离到人型支原体和脲原体^[4],但解脲脲原体引起血流感染国内外的报道甚少。为临床诊疗提供相关依据,现将福建省安溪医院收治的1例流产后解脲脲原体引起的血流感染报道如下。

1 临床资料

患者,女,34岁,2021年8月28日16:34患者以“停经18周2d,阴道流血2d”为主诉入院。体格检查,体温T: 37.5℃,脉搏P: 104次/min,呼吸R: 20次/min,血压BP: 100/76 mmHg。心肺听诊未见明显异常,腹膨隆,如孕周,可触及胎肢及胎动,妇检:见一羊膜囊膨出?少量米黄色脓液流出,有异味,宫体如孕4+月大小,轻压痛,可闻及胎心165次/min,无宫缩,双附件未及异常包块,无压痛。8月28日彩超:宫内妊娠,单活胎,头位,双顶径4.4 cm,股骨长2.7 cm;胎盘0级;羊水最大深度5.2 cm,瞬时胎心率偏快,波动于169~174次/min。入院时诊断:(1)妊娠状态(G3P2孕18+2);(2)晚期难免流产;(3)妊娠合并绒毛膜羊膜炎?(4)妊娠合并宫颈功能不全?入院后完善生化全套、尿常规、凝血功能等检查未见明显异常。血常规,白细胞WBC:13.56×10⁹/L,中性粒细胞百分比NET:82.90%,降钙素原PCT:0.11 ng/mL,C反应蛋白CRP:12.08 mg/L;白带常规检查:清洁度IV°,未培养出B群链球菌。8月30日,阴道

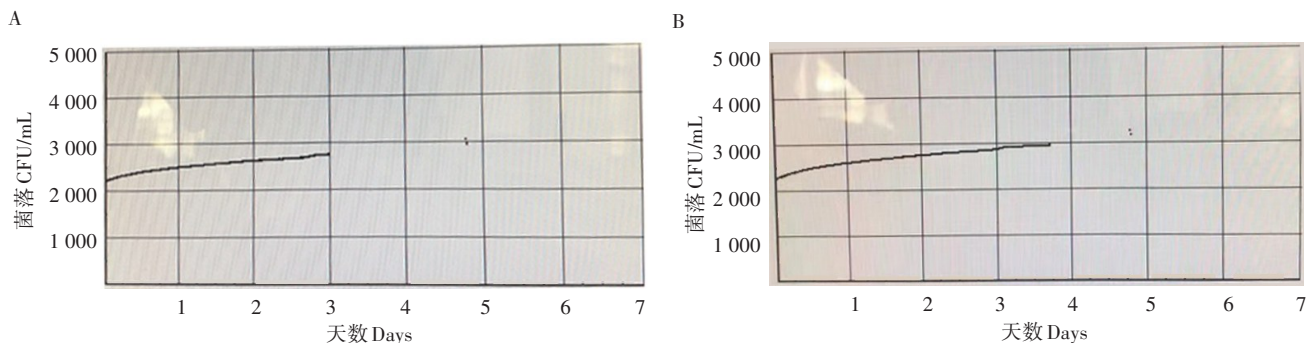
分泌物支原体培养,解脲脲原体:阳性≥10 000 ccu/mL,人型支原体:阴性,给予阿奇霉素1.0 g顿服。8月31日予以米非司酮+米索前列醇片口服引产,于12:20自娩一胚胎组织,产后阴道出血少,给予促宫缩处理,及头孢曲松+甲硝唑常规经验抗感染覆盖阴性杆菌与厌氧菌,随后出现寒战、发热,T:38.5℃,考虑宫腔内感染,立即复查血常规、CRP,采集双侧需氧血培养,物理降温,补液、继续予甲硝唑联合头孢曲松抗感染等处理。CRP:14.85 mg/L,WBC:14.33×10⁹/L,NET:85.40%,PCT:0.12 ng/mL,IL-6:665.6 pg/mL。金域检验回报沙眼衣原体(CT-DNA):阴性,淋球菌(NG-DNA):阴性。9月1日彩超提示:宫腔内中高回声病变(流产未净?)。临床观察其出血量在正常范围内,考虑是宫腔血块积聚,建议一周后B超复查。8月31日—9月2日患者体温基本正常,复查炎症指标下降,要求出院。9月3日,双侧需氧血培养报阳,电话回访,患者无发热及其他不适。9月5日,双侧需氧血培养检出解脲脲原体,下午患者返院,诉无发热,无腹痛,恶露少,无臭味,T:36.4℃,复查血常规、CRP、血培养,结果基本正常。

2 实验室检测

2.1 材料 试剂:血培养瓶(珠海迪尔生物工程有限公司),支原体固体和液体培养基(众爱生河北生物科技有限公司),哥伦比亚平板(广州迪景微生物科技有限公司),革兰氏染液(珠海恒屹生物科技有限公司),瑞姬染液(珠海贝索生物科技有限公司)。

仪器:法国梅里埃BacT-ALERT 3D240全自动血培养仪(迪尔血培养瓶),青岛海尔二氧化碳培养箱。

2.2 检测经过 2021年9月3日双侧需氧血培养3d报阳(未做厌氧瓶),曲线图基本相似,如图1。血培养瓶直接涂片,革兰染色未见菌体,加做瑞姬染色,可见浅紫色细沙样菌体,如图2。从血培养瓶分别各吸取50 μL接种于哥伦比亚血平板及支原体固体培养基,100 μL支原体液体培养基,放在5%~10%二氧化



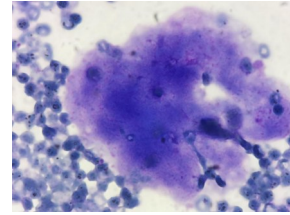
A. 左侧肘正中静脉采集之需氧血培养生长曲线;B. 右侧肘正中静脉采集之需氧血培养生长曲线图,均为3 d报阳,次日撤瓶。A is left side blood culture growth curves; B is right side blood culture growth curves; All positive reports were appear after 3 days.

图1 患者双侧肘正中静脉血培养

Fig. 1 Blood cultures were obtained from bilateral median cubital veins

碳培养箱^[4], 48 h后, 支原体固体培养基 100 倍镜下可见褐色条纹状菌落, 见图 3A。

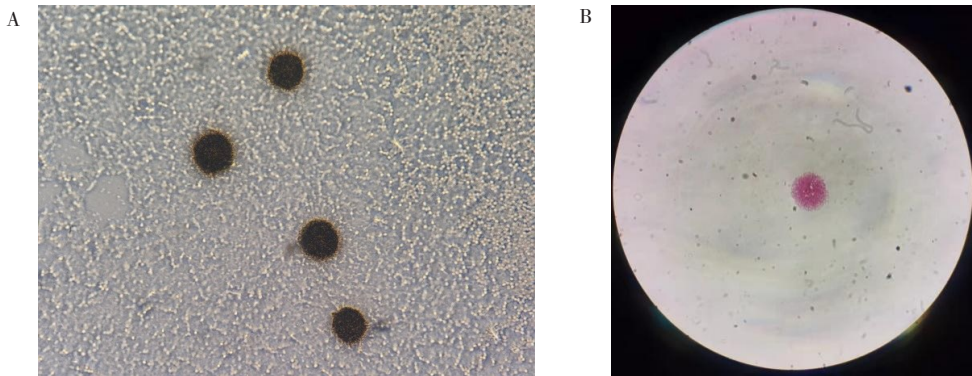
支原体液体培养基上鉴定为解脲脲原体, 其药敏结果喹诺酮类、大观霉素耐药; 大环内酯类、四环素类、林可霉素均敏感, 见图 4。哥伦比亚血平板放置 5 d 未见菌落生长。随后从固体培养基上刮下解脲脲原体菌落加到支原体液体培养基中, 在 CO₂ 培养箱中培养 48 h 后, 该菌液经 12 000 r/min (离心半径为 9.828 cm) 高速离心, 弃上清液后, 留下 20 μL 外检做靶向 DNA 测序, 经 Blast 比对显示, 结果为解脲脲原体, 与菌株 NR074762.2 相似度为 99.785%。



可见蓝紫色成堆存在的支原体菌体, 酷似蛋白凝块。着紫色表明细菌胞内存在有活性嗜天青颗粒, 与无生命凝块相鉴别。The presence of Lyons blue bacteria cluster of *Mycoplasma*, like protine clump; The purple color indicates the presence of azurophil granule in the bacterial cytosol to distinguish it from protine clump.

图2 血培养涂片镜检(瑞姬染色, ×1 000)

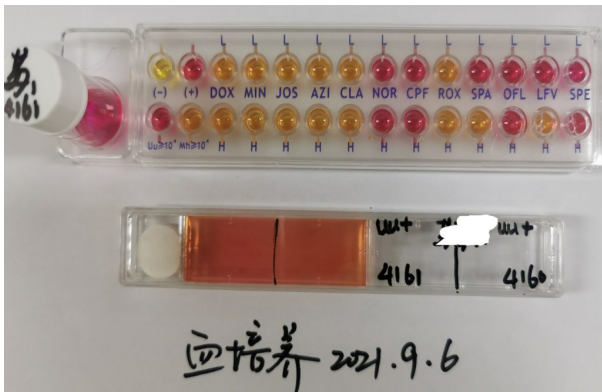
Fig. 2 Microscopic examination of blood culture smear (Wright's staining, ×1 000)



A. 支原体固体培养基×100, 镜下可见褐色条纹状菌落; B. UU 菌落革兰染色×1 000, 着色极浅, 无明显菌体。A is *Mycoplasma* A7 agar media (×100), *Ureaplasma urealyticum* is brown striature colony; B. Gram stain for *Ureaplasma urealyticum* is weak lavender, no obviously observed bacteria (×1 000).

图3 支原体固体培养

Fig. 3 Solid culture of *Mycoplasma*



支原体液体培养基 48 h, 鉴定为解脲脲原体, 药敏部分红色为耐药孔, 黄色为敏感孔。Mycoplasma A7 agar and Mycoplasma ID & AST panel, ID was *Mycoplasma urealyticum*, in AST part purple means resistant, and yellow means susceptible.

图4 支原体液体培养及其药敏结果

Fig. 4 Liquid culture of *Mycoplasma* and its drug sensitivity

3 讨论

解脲脲原体最早是在 1954 年被 Shepard 等从非淋菌性尿道炎 (nongonococcal urethritis, NGU) 患者的

尿道中分离发现的, 是一种无细胞壁的原核细胞微生物, 也是目前能在无生命培养基中繁殖的最小微生物^[10], 主要定植于泌尿生殖道和呼吸道中, 可在机体免疫抑制或器械检查、手术侵入等破坏宿主粘膜或组织而感染的条件致病微生物^[5, 11-13]。解脲脲原体主要传播途径为性接触传播和母婴传播, 最常引起泌尿生殖系统感染^[14-15], 该类病原体极少情况下能突破免疫屏障进入血液和无菌部位, 在早期的临床研究中也有发现有不洁性接触史后自关节液中检出支原体的报道^[16]。当解脲脲原体穿透免疫屏障而引起感染时, 在人体的血液、无菌体液或组织标本分离到解脲脲原体, 都有重要的临床意义^[4]。现在大多数商品化血培养基的多聚茴香磺酸钠做抗凝剂, 对支原体有一定抑制, 另外大多数厂家血培养基采用胰大豆肉汤作为基础培养基, 不适合支原体生长。再有尿道支原体产生 CO₂ 主要依靠分解尿素、精氨酸、胱氨酸等特定含氮化合物后产生的短链脂肪酸进一步分解产生。大多数支原体除了肺炎支原体外, 不利用葡萄糖, 因此无法从葡萄糖产生 CO₂, 导致代谢微弱无法被仪器探测

到,所以血液很难分离到解脲脲原体^[4]。鉴于对支原体无菌部位及血流感染的重视,我们调整了检验流程,增加了对血培养支原体的常态化检测,2020年7月—2022年1月在妇产科、胸外科、骨科等血培养中,成功培养出8例人型支原体及1例解脲脲原体,与靶向DNA测序结果高度一致。我们进行了如下检验流程的调整:当血培养3 d左右报阳,曲线较为平缓,血培养瓶直接涂片,革兰染色未见菌体时,应加做瑞姬染色,若见浅紫色细沙样菌体或者未见明显易辨识菌体时,可从血培养瓶分别各吸取50 μ L接种于哥伦比亚血平板及支原体固体培养基,100 μ L接种于支原体液体培养基,放在5%~10%二氧化碳培养箱^[4],每天2次,观察液体培养基颜色变化,48 h后,在显微镜100 \times 镜下观察支原体固体培养基上的菌落形态,解脲脲原体呈褐色条纹状菌落,人型支原体为饱和而扩散的油煎蛋状菌落。在支原体液体培养基鉴定药敏板上尚可初步鉴定解脲脲原体和人型支原体出具药敏结果。解脲脲原体在哥伦比亚血平板不生长也有助于鉴别人型支原体^[4],这样调整流程后可以避免血培养报阳后,革兰染色查不到菌体时,疑是报“假阳”而造成漏诊^[7]。血流感染是最严重的感染之一,是导致患者感染相关死亡的主要因素。而血培养又是诊断血流感染和脓毒症的金标准,故提高血培养阳性检出率势在必行,实践证明我们的流程调整对于降低特定微生物的漏诊有意义。

本例患者双侧血培养与流产前阴道分泌物支原体培养的结果一致,药敏结果是米诺环素、多西环素、交沙环素、阿奇霉素、克拉霉素、罗红霉素均敏感,司帕沙星、左氧氟沙星中介,诺氟沙星、环丙沙星、氧氟沙星、壮观霉素均耐药,推测是流产时定植在阴道的解脲脲原体逆行引起血流感染。流产前阴道分泌物培养解脲脲原体时,临床给予阿奇霉素1.0 g顿服,流产后发热,给予促宫缩处理及考虑可能合并阴道阴性杆菌与厌氧菌感染继续给予头孢曲松+甲硝唑,5 d后双侧血培养培养出解脲脲原体时,患者返院复查,T:36.4 $^{\circ}$ C,血常规、CRP、血培养,结果基本正常。本例患者流产后血培养培养出解脲脲原体时,临床未再针对解脲脲原体抗感染治疗,这可能是流产前给予阿奇霉素顿服进行预防性治疗解脲脲原体有效,因解脲脲原体是一种无细胞壁的原核细胞微生物^[5],对作用于细胞壁的抗生素不敏感,例如 β -内酰胺和万古霉素等,这些药物又是临床最常使用的经验用药^[12],还有大环内酯类、四环素类等抗生素的广泛应用,不合理联用等现象,使支原体多重耐药性菌株在临床上不断增多^[6,11],故及时准确地分离病原微生物与药敏试验,

是临床精准诊疗最有效的保障。

从本例以及我们之前遇到的案例,发现支原体血流感染还是具有一些独特之处的。主要表现在:支原体菌血症相较于一般细菌感染其免疫应答要弱得多,原因就是该类微生物缺乏细胞壁,没有LPS与胞壁酸作为免疫系统的识别位点,所以脓毒症反应不会非常强烈,PCT、CRP、IL-6、甚至白细胞总数可能都不高。从本案例的疾病转归分析,我们也能看出,抗生素并不是唯一的影响因素,很多报道的支原体血流感染,在不进行针对性治疗的前提下,依靠自身免疫力也能恢复。免疫状态受抑制与否与免疫能力的强弱才是感染清除的关键,对于免疫正常的患者不采取针对性抗生素治疗大多数也能康复,说明局部正确处理及保护免疫功能,避免皮质激素等免疫抑制剂的滥用有利于患者的康复。支原体细胞膜上的脂蛋白抗原变异系统改变了支原体细胞表面的结构有助于微生物的免疫逃逸,感染的扩散和迁延,并同时造成了临床表现的不典型^[16]。另外,该类微生物缺少细胞膜,对消毒剂不耐受,常规皮肤消毒剂如乙醇、异丙醇、含碘消毒剂均可快速杀菌,因此极少因消毒不严污染血培养。

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