论著·临床研究 doi:10.3969/j.issn.1671-8348.2022.12.010
网络首发 https://kns.cnki.net/kcms/detail/50.1097.R.20220427.1820.006.html(2022-04-28)

侵袭性肺炎克雷伯菌肝脓肿综合征 1 例并文献复习*

梁诚诚,卢家桀△,唐光敏
(四川大学华西医院感染性疾病中心,成都 610041)

[摘要] 分析侵袭性肺炎克雷伯菌肝脓肿综合征(IKLAS)的临床特征,以提高对该疾病的认识。回顾性分析该院收治的 1 例 IKLAS 患者的临床资料及诊疗过程,并复习相关文献。该例患者具有肺炎克雷伯菌肝脓肿,以及肺脓肿、左下肢软组织感染等肝外侵袭表现,符合 IKLAS 临床特征,糖尿病是其感染及转移的危险因素,患者经治疗好转出院。IKLAS 好发于糖尿病人群,应积极寻找原发灶并筛查肝外其他转移性感染病灶,早期诊断及治疗至关重要。

[关键词] 肺炎克雷伯菌;肝脓肿;侵袭综合征;病例报告
[中图法分类号] R575.4 [文献标识码] A [文章编号] 1671-8348(2022)12-2028-03

Invasive Klebsiella pneumoniae liver abscess syndrome: a case report and literature review*

LIANG Chengcheng, LU Jiajie△, TANG Guangmin
(*Infectious Disease Center, West China Hospital, Sichuan University, Chengdu, Sichuan* 610041, *China*)

[**Abstract**] To analyze the clinical features of invasion Klebsiella pneumoniae liver abscess syndrome (IKLAS) and raise awareness of the disease. The clinical data and diagnosis and treatment process of a patient with IKLAS admitted to this hospital were analyzed retrospectively, and the relevant literatures were reviewed. The patient had Klebsiella pneumoniae liver abscess and extrahepatic manifestations such as lung abscess and left lower extremity soft tissue infection, which accords with the clinical features of IKLAS. Diabetes mellitus was a risk factor for its infection and metastasis. The patient was discharged after treatment. IKLAS usually occurs in people with diabetes, and the primary lesion should be actively searched and other metastatic infection lesions outside the liver should be screened. Early diagnosis and treatment are very important.

[**Key words**] Klebsiella pneumoniae; liver abscess; invasive syndrome; case report

肺炎克雷伯菌(Klebsiella pneumoniae,KP)是医院和社区获得性感染的常见病原体之一,可致肺部、尿路、腹腔等机体多部位感染,也是肝脓肿的主要病原菌[1],因其血源性播散,部分肝脓肿患者可伴随严重的肝外感染,如肺脓肿、眼内炎、脑膜炎及坏死性筋膜炎等,临床上称为侵袭性肺炎克雷伯菌肝脓肿综合征(invasion Klebsiella pneumoniae liver abscess syndrome,IKLAS)。近年来,我国报道的 IKLAS 并不少见,但因其发病急、病情进展迅速、临床表现缺乏特异性等特点而致诊疗时机延误,患者预后较差。本文对近期收治的 1 例 IKLAS 患者的临床资料进行总结并结合文献分析,以期提高对该病的认识,有助于早期诊治及改善预后。

1 临床资料

患者,男,33 岁,因“发热 1 个月”于 2021 年 1 月 11 日入本院。患者 1 个月前出现发热,最高体温 41 ℃,伴寒颤、左下肢疼痛,外院给予左氧氟沙星、头孢哌酮舒巴坦抗感染及对症治疗后仍反复高热,伴左膝关节破溃、血性脓液外溢,为进一步诊治入本院。入院查体:体温 36.8 ℃,脉搏 106 次/分钟,呼吸频率 20 次/分钟,血压 124/80 mm Hg,心律齐,各瓣膜区未闻及杂音,右肺叩诊呈浊音,右下肺呼吸音粗,可闻及少许湿啰音。腹软,无压痛、反跳痛,肝脾肋下未扪及,肝区叩痛。左膝关节破溃伴少许血性脓液溢出。患者有支气管哮喘病史 5 年余。辅助检查:(1)血常规中白细胞(WBC)计数 12.35×10^9/L,中性粒细胞百分比 75.3%,中性粒细胞绝对值 9.30×10^9/L,血小板(PLT)计数 624×10^9/L;(2)降钙素原 0.16 g/mL,C 反应蛋白 81.30 mg/L,白细胞介素(IL)-6 13.20 g/mL;(3)生物化学指标中丙氨酸氨基转移酶(ALT)89 U/L,天冬氨酸氨基转移酶(AST)41 U/L,清蛋白 35.5 g/L;(4)糖化血红蛋白 7.1%,口服葡萄

* 基金项目:四川省科技厅重点研发项目(2017FZ0062)。 作者简介:梁诚诚(1993—),住院医师,硕士,主要从事细菌的免疫预防研究。
△ 通信作者,E-mail:10955415@qq.com。

糖耐量试验(OGTT)空腹血糖 5.10 mmol/L,餐后 2 h 血糖 12.05 mmol/L;(5)痰培养肺炎克雷伯菌阳性(琼脂平板培养检出);(6)多次血培养及膝关节分泌物培养肺炎克雷伯菌阳性(血培养瓶及琼脂平板培养检出)。胸腹部 CT(图 1、2):双肺散在结节及团块影,部分团块内见空洞,较大者位于右肺上叶尖段,大小约 4.1 cm×2.6 cm;肝脏多发稍低密度结节及团块影,边界欠清,考虑感染性病变。小腿及膝关节增强 CT(图 3):左膝关节囊可疑少许积液,左膝软组织肿胀,考虑感染病变可能。下肢动静脉彩超(图 4):左小腿胫前上段胫骨周围弱回声区,考虑炎性伴脓肿形成。入院诊断 IKLAS,先后给予哌拉西林舒巴坦、头孢哌酮舒巴坦联合左氧氟沙星抗感染及保肝、控制血糖、止痛等对症治疗,后因患者在输入左氧氟沙星过程中出现过敏性休克,故停用左氧氟沙星,继续予头孢哌酮舒巴坦抗感染治疗。住院期间多次请骨科会诊均建议继续抗感染治疗,暂无穿刺引流指征。住院 7 周后患者体温正常,复查肺、肝、膝关节影像学提示病灶明显好转,血常规、炎性指标恢复接近正常,改为头孢地尼胶囊口服抗感染治疗,好转出院。

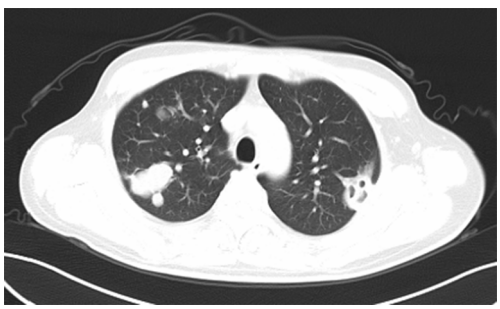

图 1 患者胸部 CT 影像图

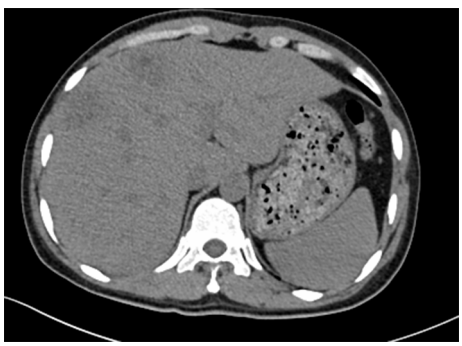

图 2 患者腹部 CT 影像图

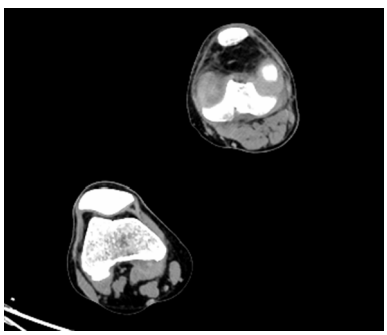

图 3 患者小腿及膝关节增强 CT 影像图

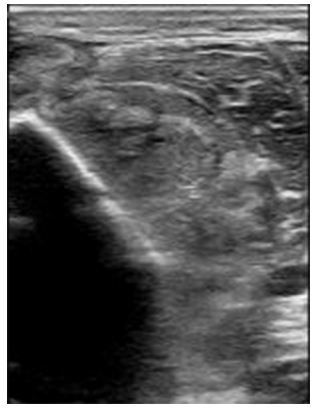

图 4 患者下肢动静脉彩超图

2 讨 论

IKLAS 最初在新加坡、韩国等亚洲多地被报道,近 30 年来全球多地区报道病例日益增加。IKLAS 主要好发于亚裔人群,其原因可能与亚洲人群肠道更易定植 KP 相关。既往研究表明,亚洲 IKLAS 患者分离出的 KP 与其他地区相比在遗传学和表型上存在明显差异,表现出更强的毒力及侵袭力[2]。该病多由高毒力血清型 KP 引起,如荚膜血清型 K1、K2 等,这类血清型常伴有 magA 和 rmpA 基因,可增强高黏液表型的毒力及抗巨噬细胞的吞噬作用,从而增加肺、眼、脑、肾等肝外部位转移感染的风险[3]。本文报道的该例患者具有肺炎克雷伯菌肝脓肿及肝外侵袭表现,并发肺脓肿及左下肢软组织感染,临床表现符合 IKLAS。

目前 IKLAS 发病机制尚不明确,可能的相关因素包括胃肠道定植菌易位、口咽定植菌吸入、直接血源性或胆源性播散、免疫功能缺陷等。其中,宿主和细菌毒力在疾病发生、发展中起重要作用。肺炎克雷伯菌肝脓肿患者多合并糖尿病,且糖尿病患者转移性眼内炎的发生率明显高于其他疾病患者或健康人群[4]。高血糖可促进革兰阴性菌的生长繁殖,抑制白细胞趋化和吞噬功能,因此糖尿病是 IKLAS 发生的独立危险因素。脂肪肝和高血压病等代谢性疾病或其他免疫受损患者也易并发 IKLAS[5]。细菌毒力是另一重要因素,高毒力肺炎克雷伯菌株利用荚膜、铁载体、脂多糖等作用机制增加其致病性及躲避宿主免疫反应,在健康患者中引起严重的转移性感染[6]。此外,既往肝脓肿病史和尿路结石、脓肿大小、血小板减少、初始治疗使用头孢唑啉而非广谱头孢菌素等因素亦可能与转移性感染相关,而遗传因素尚未得到证实[7-8]。本报道病例在此次发病后发现血糖升高,临床诊断为 2 型糖尿病,故存在肺炎克雷伯菌感染及转移的危险因素。

IKLAS 起病隐匿,症状缺乏特异性,常表现为发热、寒战、肝区疼痛,可先引起单一部位的脓肿,多发于肝右叶,早期可通过血源性播散累及各个部位,眼、肺和中枢神经系统是常见的肝外侵袭部位[9]。临床上可因突发的眼内炎表现起病,眼部症状早于肝脓肿

的全身症状，预后较差，多数造成失明[10]。而并发脑膜炎、脑脓肿、肺栓塞者也往往显示高病死率[11-12]。KASSAM 等[13]报道了坦桑尼亚首例 IKLAS 病例，其主要表现为发热、双下肢进行性肿胀，与本报道病例临床表现类似，侵袭了肺及下肢软组织。对于以肝外转移性感染为首发表现的患者，应积极寻找肺炎克雷伯菌病原学证据，高度警惕是否存在肝脓肿及其他受累脏器部位，以免延误诊治。

病原微生物培养是确诊 IKLAS 的主要依据，目前尚无明确的治疗指南，亚洲主要选择头孢类抗菌药物，美国倾向于联合抗菌治疗。高毒力肺炎克雷伯菌菌株可通过质粒传播方式获取超广谱 β-内酰胺酶或 AmpC β-内酰胺酶等耐药基因，从而获得抗生素耐药性，可能对临床治疗提出挑战[14]。但目前 IKLAS 对大多数常用抗菌药物治疗仍较敏感，其原因可能与高毒力 KP 菌株多为社区获得性相关。一般经验性治疗先选取第 3 代头孢菌素类、喹诺酮类、碳青霉烯类等，其后可根据药敏试验及疗效调整用药。抗感染治疗的疗程为 4～6 周，病情危重者应适当延长治疗疗程，直至临床症状消失、炎症指标恢复正常及影像学证实脓腔消失等可考虑停用抗菌药物。此外，对于充分液化、直径大于 3 cm 的肝脓肿可选择穿刺抽脓，较大者置管引流，对药物、引流效果不佳及脓肿破裂者可行腹腔镜手术治疗[15]。而转移性眼内炎的治疗还会涉及玻璃体腔内注药和玻璃体切除术等[16]。本病例以全身药物治疗为主，选用了第 3 代头孢菌素加酶抑制剂联合喹诺酮类药物抗感染治疗，但期间因过敏反应而停用喹诺酮类药物，治疗 7 周后患者好转出院。

综上所述，IKLAS 在临床上日益增多，其起病隐匿，症状非特异，预后较差。临床应加强糖尿病筛查，对不明原因发热或突发眼内炎的糖尿病患者需警惕 IKLAS 的发生，通过病原菌培养及影像学检查等，积极寻找原发灶并筛查肝外其他转移性感染病灶，尽早明确诊断，给予早期、足量、足疗程的抗菌治疗或肝脓肿穿刺引流，严格控制血糖，以改善临床不良预后。

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(下转第 2036 页)

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(收稿日期:2021-11-19 修回日期:2022-02-23)

(上接第 2030 页)

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(收稿日期:2021-11-26 修回日期:2022-03-03)