Multi-Sites Infection Caused by Klebsiella pneumoniae After Hemopoietic Stem Cell Transplantation

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1. Introduction

Klebsiella pneumoniae is one of the most common pathogens (1, 2) and is often isolated from various specimens in inpatient (3), especially in those immunosuppressed patients. Here we report a case of multi-site infections caused by K. pneumoniae after hemopoietic stem cell transplantation, which was first isolated from the stool, then the blood, the sinuses, the throat swab, and the urine.

2. Case Presentation

A 22-year-old girl with complete remission after chemotherapy for her acute lymphoblastic leukemia was presented to the 2nd affiliated hospital of Zhejiang University for hemopoietic stem cell transplantation. She got a good check-up, however, her spirit was a little bad. Her primitive lymphocyte (0.06%) and total lymphocyte (27.05%) in the peripheral blood were in the normal range. She received a 224 mL stem cell transfusion including mononuclear cell (4.87 $\times$ 10$^8$/kg) CD34+ (0.6%) as well as reached the transplantation threshold of CD34+ cell (3 $\times$ 10$^6$/kg). Nine days after transplantation, there were no severe side effects except a little bit of vomit. However, the symptom of diarrhea appeared first. K. pneumoniae was isolated from the stool, then invaded into the blood, and caused sepsis. It disseminated and caused multi-sites infection.

Conclusions: It should be kept in mind that K. pneumoniae can translocate across the intestinal epithelium. It is important to pay attention to the bacterium isolated from the intestine in immunosuppressed patients.

Keywords: Multi-Sites Infection, Immunosuppressed Patient, Intestine, Klebsiella Pneumoniae
Figure 1. Clinical Course of the Patient After Hospitalization

| CRP (mg/mL) | PCT (ng/mL) | Day of Illness |
|-------------|-------------|---------------|
| 350         | 300         | 6             |
| 300         | 250         | 5             |
| 250         | 200         | 4             |
| 200         | 150         | 3             |
| 150         | 100         | 2             |
| 100         | 50          | 1             |
| 50          | 0           | 0             |

Abbreviations: AK, Amikacin; IMP, Imipenem; MEM, Meropenem; PB, Polymyxin B; SCF, Cefoperazone/Sulbactam; SMZ, Sulfamethoxazole; TEC, Teicoplanin; TGC, Tigecycline; VCZ, Voriconazole.

all positive for the \(bla_{KPC}\) gene (Figure 2A) and negative for \(bla_{SME}\), \(bla_{VIM}\), \(bla_{IMP}\), \(bla_{NDM}\), \(bla_{GIM}\), \(bla_{SPM}\), \(bla_{SIM}\), and \(bla_{OXA}\) genes (data not shown). The resistant gene was \(bla_{KPC-2}\) by sequencing. Pulsed field gel electrophoresis (PFGE) (6) demonstrated that the 5 \(K. pneumoniae\) isolates belonged to the same clone (Figure 2B).

3. Discussion

As we all know, \(K. pneumoniae\) is one of the most common and clinically important pathogens worldwide, causing abscess (especially liver abscess) (7, 8), and then invades into blood causing multi-sites infection. It can also cause an endogenous infection in diabetes mellitus patients (9-11) as well as cancer patients (12). However, the report of \(K. pneumoniae\) in the intestine invading into blood is rare. This is the first time to report a \(K. pneumoniae\) isolate invading into the blood from the intestine in a patient who was receiving hemopoietic stem cell transplantation and then causes multi-sites infection. As we know, due to immunosuppress, leukemia patients often received an opportunistic infection through a different pathway. Like the EB virus and \(Aspergillus\) infection through respiratory tract (13, 14), urinary tract infection caused by \(Escherichia coli\) (15) and derma infection is caused by Herpes Zoster (16). However, infection caused by intestinal microbiology is rare, just a report of intestinal dysbacteriosis (17). As Chun-Ru Hsu et al. (18) reported \(K. pneumoniae\) can translocate across the intestinal epithelium; the gut is always the epicentre of antibiotics resistance (19). Therefore, we need to pay attention to the bacteria isolated from the intestine in the immunosuppressed patients.

Footnotes

Authors' Contribution: Lin Huang collected the data, contributed to the design, and draft of the work. Yan Yan Hu and Rong Zhang contributed to the drafting of the work and critically revising the work for important intellectual content.

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Table 1. Minimum Inhibitory Concentration of Antibiotics

| Antibiotics          | MIC, µg/ml |
|----------------------|------------|
| Ampicillin           | ≥ 32       |
| Cefazolin            | ≥ 64       |
| Gentamicin           | ≥ 16       |
| Tobramycin           | ≥ 16       |
| Cefepime             | ≥ 64       |
| Ceftriaxone          | ≥ 64       |
| Cefotixin            | ≥ 64       |
| Imipenem             | ≥ 16       |
| Ertapenem            | ≥ 8        |
| Amikacin             | ≥ 64       |
| Ciprofloxacin        | ≥ 4        |
| Levofloxacin         | ≥ 8        |
| Trimethoprim/sulfamethoxazole | ≥ 16/304 |
| Amoxicillin/clavulanate | ≥ 32/6  |
| Piperacillin/tazobactam | ≥ 12/4  |
| Tigecycline          | 2          |
| Aztreonam            | ≥ 64       |
| Polymyxin B          | 0.5        |

References

1. Sewify M, Nair S, Warsame S, Murad M, Alhubail A, Behbehani K, et al. Prevalence of Urinary Tract Infection and Antimicrobial Susceptibility among Diabetic Patients with Controlled and Uncontrolled Glycemia in Kuwait. *J Diabetes Res*. 2016;2016:657325. doi: 10.1155/2016/657325. [PubMed: 26844231].

2. Chuang C, Fan WC, Lin YT, Wang FD. The emergence of Klebsiella pneumoniae liver abscess in non-diabetic patients and the distribution of capsular types. *Gut Pathog*. 2016;8:46. doi: 10.1186/s13099-016-0128-y. [PubMed: 27777630].

3. Calbo E, Garau J. The changing epidemiology of hospital outbreaks due to ESBL-producing Klebsiella pneumoniae: the CTX-M-15 type consolidation. *Future Microbiol*. 2015;10(6):1063–75. doi: 10.2217/fmb.15.22. [PubMed: 26059626].

4. Freire MP, Pierrotti LC, Filho HH, Ibrahim KY, Magri AS, Bonazzi PR, et al. Infection with Klebsiella pneumoniae carbapenemase (KPC)-producing Klebsiella pneumoniae in cancer patients. *Eur J Clin Microbiol Infect Dis*. 2015;34(2):277–86. doi: 10.1007/s10096-014-2233-5. [PubMed: 25169967].

5. Iraz M, Ozad Duzgun A, Sandalli C, Doymaz MZ, Akkoyunlu Y, Saral A, et al. Distribution of beta-lactamase genes among carbapenem-resistant Klebsiella pneumoniae strains isolated from patients in Turkey. *Ann Lab Med*. 2015;35(6):595–601. doi: 10.3343/arm.2015.35.6.595. [PubMed: 26354347].

6. Gouby A, Neuwirth C, Bourg G, Bouziges N, Carles-Nurit MJ, Despaux E, et al. Epidemiological study by pulsed-field gel electrophoresis of an outbreak of extended-spectrum beta-lactamase-producing Klebsiella pneumoniae in a geriatric hospital. *J Clin Microbiol*. 1994;32(2):301–5. [PubMed: 8150918].

7. Ma LC, Fang CT, Lee CZ, Shun CT, Wang JT. Genomic heterogeneity in Klebsiella pneumoniae strains is associated with primary pyogenic liver abscess and metastatic infection. *J Infect Dis*. 2005;192(1):27–28. doi: 10.1086/430689. [PubMed: 15942901].

8. Fung CP, Siu LK. Virulence of Klebsiella pneumoniae serotype K3 should not be underestimated in K. pneumoniae liver abscess. *Clin Jundishapur J Microbiol*. 2017;10(8):e12933.
9. Nagai T, Inoue C, Tonouchi K, Tonooka N, Imamura M, Kaneko K, et al. Multiple organ failure followed by intrauterine klebsiella pneumoniae infection associated with diabetes mellitus. Kitakanto Med J. 2009;59(2):351-5. doi: 10.2974/kmj.59.151. [PubMed: 19868886].

10. Liao HR, Lee HW, Leu HS, Lin BJ, Juang CJ. Endogenous Klebsiella pneumoniae endophthalmitis in diabetic patients. Can J Ophthalmol. 1992;27(3):343-7. [PubMed: 1586886].

11. Sawada A, Komori S, Udo K, Suemori S, Mochizuki K, Yasuda M, et al. Case of endogenous endophthalmitis caused by Klebsiella pneumoniae with magA and rmpA genes in an immunocompetent patient. Infect Chemother. 2013;4(2):326-9. doi: 10.1007/s10156-012-0468-6. [PubMed: 22992835].

12. Lin YT, Liu CJ, Fung CP, Tseng CH. Nosocomial Klebsiella pneumoniae bacteremia in adult cancer patients-characteristics of neutropenic and non-neutropenic patients. Scand J Infect Dis. 2011;43(8):603-8. doi: 10.3109/00365548.2011.577800. [PubMed: 21539500].

13. Mori N, Yamashita Y, Tsuzuki T, Nakayama A, Nakazawa M, Hasegawa Y, et al. Lymphomatous features of aggressive NK cell leukemia/lymphoma with massive necrosis, haemophagocytosis and EB virus infection. Histopathology. 2000;37(4):363-71. doi: 10.1046/j.1365-2559.2000.00916.x. [PubMed: 1012744].

14. van Burik JA, Carter SI, Freifeld AG, High KP, Godder KT, Papanicolau GA, et al. Higher risk of cytomegalovirus and aspergillus infections in recipients of T cell-depleted unrelated bone marrow: analysis of infectious complications in patients treated with T cell depletion versus immunosuppressive therapy to prevent graft-versus-host disease. Biol Blood Marrow Transplant. 2007;13(12):1487-98. doi: 10.1016/j.bbmt.2007.08.049. [PubMed: 18022579].

15. Hari MD, Soetaryo PK. The risk factor of urinarytract infection in patient with leukemia. Berbala Ilmu Bedokteran. 2009;41(4):378-82.

16. Demircioglu S, Aydogdu I, Kaya E, Kuku I, Erkurt MA. Atypical presentation of herpes zoster infection following fludarabine treatment for chronic Lymphocytic leukemia: A case report. J Inonu Univ Med Faculty. 2011;18(4):281-3.

17. Tomoda T, Nakano Y, Kageyama T. Intestinal candida overgrowth and candida infection in patients with leukemia: Effect of bifidobacterium administration. Bifidobacteria Microflora. 1988;7(2):71-4. doi: 10.12938/bifidus1982.7.2_71.

18. Hsu CR, Pan YJ, Liu YJ, Chen CT, Lin TI, Wang JT. Klebsiella pneumoniae translocates across the intestinal epithelium via Rho GTPase-and phosphatidylinositol 3-kinase/Akt-dependent cell invasion. Infect Immun. 2015;83(2):769-79. doi: 10.1128/IAI.02345-14. [PubMed: 25452552].

19. Carlet J. The gut is the epicentre of antibiotic resistance. Antimicrob Resist Infect Control. 2012;1(1):39. doi: 10.1186/2047-2994-1-39. [PubMed: 2388506].

Infect Dis. 2007;45(1):1530-1. doi: 10.1086/523007. [PubMed: 17990243].

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