Bacterial Meningitis Caused by Hypervirulent *Klebsiella pneumoniae* Capsular Genotype K54 with Development of Granuloma-like Nodal Enhancement in the Brain during the Subacute Phase

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**Abstract**

A 72-year-old man was admitted to the emergency department due to coma. The cerebrospinal fluid cell count was 40,080 cells/μL, and *Klebsiella pneumoniae* was detected on culture. Stretching the bacterial colonies on an agar plate showed the formation of a viscous string with a length exceeding 5 mm, indicating hypervirulent *K. pneumoniae* (hv-KP). A genome analysis suggested hv-KP capsular genotype K54 with sequence type 29. Although no brain abscess was detected on contrast-enhanced computed tomography on Day 4 or on magnetic resonance imaging (MRI) on Day 7, contrast-enhanced MRI on Day 23 showed granuloma-like nodal enhancement on the surface of the left insula. Antibacterial therapy was continued until the enhancement disappeared on Day 40. MRI may help determine the duration required for antibacterial therapy. After six months, the patient was discharged and remained free from recurrence.

**Key words:** bacterial meningitis, sepsis, pseudoabscesses

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**Introduction**

A new hypervirulent type of *Klebsiella pneumoniae* (hv-KP) emerged. The frequency of infection by hv-KP is increasing in Asian and Western countries, and the disease is commonly observed in immunocompetent individuals with a poor prognosis (1). To differentiate hv-KP from classic KP, a string test, which examines the hypermucoviscosity on an agar plate, must be conducted (2). However, as the pathogenesis of hv-KP remains unclear, the guidelines for the diagnosis and treatment of this condition are not established (3).

Classic KP usually causes meningitis and is associated with a history of neurosurgery; however, meningitis caused by hv-KP (hv-KPM) is not associated with a history of neurosurgery. Although previous case reports have shown that classic KP meningitis cases have unusual brain radiological findings (4-6), nodal enhancement similar to cryptococcoma or tuberculoma is extremely rare (7, 8). We herein report a case of hv-KPM with granuloma-like nodal enhancement in the brain during the subacute phase.

**Case Report**

A 72-year-old Japanese man was admitted to our emergency department in a coma. He had experienced right-sided headaches 24 days before admission, and 5 days before admission, he was diagnosed with otitis media and underwent myringotomy; however, the discharge was not cultured. He had a history of hypertension, type 2 diabetes mellitus, cerebral hemorrhage without neurosurgical intervention, chronic pancreatitis, excessive alcohol consumption, and heavy smoking (20 cigarettes daily). On admission, his vital signs...
were as follows: blood pressure, 146/110 mmHg; heart rate, 117 beats/min; body temperature, 36.2°C; respiratory rate, 30 breaths/min; SpO₂, 96% (O₂ 3 L); and Glasgow Coma Scale, E4V1M4. His neck was not stiff, but jolt accentuation and Kernig’s sign were uncertain. Whole-body computed tomography (CT) did not indicate any foci of infection. His white blood cell count and C-reactive protein concentration were 22,500×10³ cells/μL and 18.05 mg/dL, which indicated severe inflammation. Lumbar puncture revealed turbid yellow cerebrospinal fluid (CSF) with a cell count of 40,080 cells/μL (normal range, <5 cells/μL). Gram staining of the CSF revealed gram-negative bacilli, on which a diagnosis of bacterial meningitis was based. Hence, ceftriaxone, vancomycin, and ampicillin administration were initiated.

On Day 2, K. pneumoniae was identified, and positive results were obtained on the “string test”; a viscous string with a length exceeding 5 mm indicates a positive result when bacterial colonies are stretched on an agar plate (2) (Fig. 1). Whole-genome sequencing was performed on the isolates. The sequencing library was prepared using a Nextera XT DNA Sample Prep Kit (Illumina, San Diego, CA, USA), and sequencing was performed with a MiSeq sequencer (Illumina) in a 2×300-bp paired-end run. Capsular genotyping and multilocus sequence typing using a wzc genotyping system and the MLST 1.8 website, respectively, confirmed that the isolate was capsular genotype K54 with sequence type 29 (9). In addition, an analysis of whole-genome sequencing data with blastn (https://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE_TYPE=BlastSearch) revealed that the isolate carried virulence genes rmpA, terA, iroN, and iucA (10-12). We therefore concluded that the isolate was a hypervirulent strain. The strain was found to be susceptible to gentamicin, cefazolin, ceftriaxone, flomoxef, meropenem, and levofloxacin, but resistant to ampicillin and piperacillin; we therefore changed the regimen to treatment with ceftriaxone alone, based on the results of antimicrobial susceptibility testing.

On Day 4, contrast-enhanced CT did not indicate any abscess formation in the brain, liver, or any other organs. However, residual otitis media was suspected; on Day 6, we performed myringotomy and inserted a tympanic ventilation tube, but a culture of the exude fluid was negative. On Day 7, the patient remained in a deep coma, and we therefore performed contrast-enhanced MRI. Diffusion-weighted images (DWIs) showed multiple high-intensity areas of the leptomeninges (Fig. 2), but contrast-enhanced MRI did not detect any brain abscesses. On Day 9, the CSF cell count was 1,029 cells/μL. On Day 23, follow-up contrast-enhanced MRI showed a 5-mm nodal enhancement in the left pia region of the insula (Fig. 3a), but DWIs did not indicate a high-intensity signal in the same area (Fig. 3b), suggesting subacute inflammation. MRA did not show any evidence of an infectious aneurysm. Although his general condition and level of consciousness improved, we continued antibacterial therapy without surgery. On Day 40, the high-intensity area was not observed on MRI (Fig. 3c), and antibacterial therapy was discontinued. Finally, on Day 55, his level of consciousness improved to E4V4M6 and he was transferred to another hospital for rehabilitation. After six months, he was discharged and remained free from recurrence.

**Discussion**

The present case illustrates two significant clinical findings for patients with hv-KP. First, hv-KP formed a granuloma-like focal lesion, similar to cryptococcoma and tuberculosis, during the subacute phase. Second, this lesion became undetectable during the course of antibacterial therapy.

To our knowledge, only one previous report has described the MRI findings in a case of hv-KP (13). In that case, MRI showed cord-like structures in the subarachnoid space, while our case showed granuloma-like focal lesions. Brain abscess caused by classic KP infection can be monoloculated or multiloculated (14); hence, further case series are needed. Previous studies have suggested that hv-KP forms...
colonies in the intestines and migrates to the liver where it forms abscesses. The infection then becomes systemic and may cause endophthalmitis, meningitis, and brain abscesses (15, 16). However, in the present case, the entry portal for infection was unknown. Since no liver abscesses were observed, hv-KP may not have originated in the intestines in our case. Another possibility is that hv-KP meningitis may have developed as a result of the spread of the pathogen from the ear (17); the patient might have become infected via the ear, since he complained of a persistent headache and had otitis media.

In the present case, we were unable to perform biopsy because the lesion was small. We ruled out an infectious aneurysm using MRA, narrowing the differential diagnosis to infectious granuloma and cold abscess. In patients with cryptococcoma, antifungal treatment is continued until the lesion resolves on MRI (7). Therefore, we continued antibiotic therapy and determined the therapeutic duration for the treatment of meningitis based on the MRI findings. K. pneumoniae serotype K54 with sequence type 29 (18), a longer period of antibacterial therapy might be necessary. Serial MRI scans and the patient’s level of consciousness may help determine the required duration of antibacterial therapy.

In the present case, hv-KP caused by K. pneumoniae serotype K54 with sequence type 29 formed granuloma-like focal lesions similar to those of cryptococcoma or tuberculosis. The lesion emerged during the sub-acute phase and was resolved with antibiotic therapy alone. We therefore believe that serial MRI scans may help determine the required duration of antibacterial therapy.

Written informed consent was obtained from the patient and his family for the publication of this case report and the accompanying images.

The authors state that they have no Conflict of Interest (COI).

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References
1. Shon AS, Bajwa RP, Russo TA. Hypervirulent (hypermucoviscous) Klebsiella pneumoniae: a new and dangerous breed. Virulence 4: 107-118, 2013.
2. Hadano Y. String test. BMJ Case Rep 2013: bcr2012008328, 2013.
3. Khan FY, Abukhattab M, AbuKamar M, Anand D. Adult Klebsiella pneumoniae meningitis in Qatar: clinical pattern of ten cases. Asian Pac J Trop Biomed 4: 669-672, 2014.
4. Costerus JM, van de Beek D, Brouwer MC. Nosocomial meningitis caused by gas producing Klebsiella pneumoniae. BMJ Case Rep 2012: bcr1120115137, 2012.
5. Doula MS, Grimes-Zeppigno R, Molina E, et al. A k2A-positive Klebsiella pneumoniae causes liver and brain abscess in a Saint Kitt’s man. Int J Med Sci 6: 301-304, 2009.
6. Nagase T, Wada S, Nakamura R, et al. Magnetic resonance imaging of multiple brain abscesses of the bilateral basal ganglia. Intern Med 34: 554-558, 1995.
7. Saleh M, Saeedi AA, Ali Pooran A. Brain tuberculosis: a case report. Jundishapur J Microbiol 7: e11252, 2014.
8. Hagan JE, Dias JS, Villasboas-Bisneto JC, Falcao MB, Ko AL. Ribeiro GS. Puerperal brain cryptococcoma in an HIV-negative woman successfully treated with fluconazole: a case report. Rev Soc Bras Med Trop 47: 254-256, 2014.
9. Larsen MV, Cosentino S, Rasmussen S, et al. Multilocus sequence typing of total-genome-sequenced bacteria. J Clin Microbiol 50: 1355-1361, 2012.
10. Yu WL, Ko WC, Cheng KC, et al. Association between rmpA and maaA genes and clinical syndromes caused by Klebsiella pneumoniae in Taiwan. Clin Infect Dis 42: 1351-1358, 2006.
11. Bachman MA, Oyler JE, Burns SH, et al. Klebsiella pneumoniae yersiniabactin promotes respiratory tract infection through evasion of lipocalin 2. Infect Immun 79: 3309-3316, 2011.
12. Tang HL, Chiang MK, Liou WJ, et al. Correlation between Klebsiella pneumoniae carrying pLVPK-derived loci and abscess formation. Eur J Clin Microbiol Infect Dis 29: 689-698, 2010.
13. Takahashi K, Miura A, Yamaguchi T, Kanematsu M. Novel cord-like structures on MRI in a case of hypervirulent Klebsiella pneumoniae. Intern Med 54: 355-356, 2015.
14. Chang WN, Huang CR, Lu CH, Chien CC. Adult Klebsiella pneumoniae meningitis in Taiwan: an overview. Acta Neurol Taiwan 21: 87-96, 2012.
15. Fung CP, Lin YT, Lin JC, et al. *Klebsiella pneumoniae* in gastrointestinal tract and pyogenic liver abscess. Emerg Infect Dis 18: 1322-1325, 2012.

16. Chung DR, Lee H, Park MH, et al. Fecal carriage of serotype K1 *Klebsiella pneumoniae* ST23 strains closely related to liver abscess isolates in Koreans living in Korea. Eur J Clin Microbiol Infect Dis 31: 481-486, 2012.

17. Yilmaz G, Aydin K, Bektas D, Caylan R, Caylan R, Koksal I. Cerebellar abscess and meningitis, caused by *Shewanella putrefaciens* and *Klebsiella pneumoniae*, associated with chronic otitis media. J Med Microbiol 56: 1558-1560, 2007.

18. Chuang YC, Lee MF, Yu WL. Mycotic aneurysm caused by hypermucoviscous *Klebsiella pneumoniae* serotype K54 with sequence type 29: an emerging threat. Infection 41: 1041-1044, 2013.

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