Annals of Clinical Case Reports

Case Report
Published: 19 Nov, 2022

An Adult Case Diagnosed with Group B Streptococcal Meningitis Using Metagenomic Next-Generation Sequencing

Deng J, Zhu H, Chen X, Chen Y, Liu M, Yu X and Chen P**

Department of Laboratory Medicine, The First Affiliated Hospital, Sun Yat-sen University, China

Abstract

Group B *Streptococcus* (GBS) is an important cause of invasive bacterial disease. Previous studies have shown a substantial and increasing burden of GBS infections among nonpregnant adults, particularly older adults and those with underlying medical conditions. Although GBS meningitis is frequently rapidly progressive with a high fatality rate, it can be difficult to diagnose. We present a 77-year-old male who was highly suspected of bacterial meningitis with negative Cerebrospinal Fluid (CSF) cultures. GBS meningitis was diagnosed by positive result from metagenomic Next-Generation Sequencing (mNGS) of CSF. The patient made a rapid clinical improvement, likely attributable to the fact that empiric antibiotic treatment was started soon after his admission, which provided the broad coverage and included non-resistant GBS coverage.

OPEN ACCESS

Correspondence:
Xuegao Yu, Department of Laboratory Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, 510080, China,
E-mail: 946931554@qq.com
Peisong Chen, Department of Laboratory Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, 510080, China,
E-mail: 980445642@qq.com

Received Date: *26 Oct 2022*
Accepted Date: *14 Nov 2022*
Published Date: *19 Nov 2022*

Citation:
Deng J, Zhu H, Chen X, Chen Y, Liu M, Yu X, et al. An Adult Case Diagnosed with Group B Streptococcal Meningitis Using Metagenomic Next-Generation Sequencing. Ann Clin Case Rep. 2022; 7: 2345.

ISSN: 2474-1655.

Background

Group B *Streptococcus* (GBS) is the most common cause of bacterial meningitis in neonates and infants, but is rarely the cause in adults. It usually affecting elderly patients and those with serious underlying disease, such as diabetics, cirrhosis, history of stroke, cancer, decubitus ulcer, and neurogenic bladder [1]. It is important to recognize and appropriately treat GBS meningitis, especially in the population greater than 65 years old due to its mortality rate approaching 56%, which is double the mortality of other types of bacterial meningitis [2,3]. Cerebrospinal Fluid (CSF) findings may not show evidence of infection early in GBS meningitis, and CSF culture may be negative due to the small number of bacteria and antimicrobial treatment before sample collection [4].

Next-Generation Sequencing (NGS) technology makes it possible to analyze large amounts of nucleic acid sequence data contained in samples in a single assay. Therefore, untargeted metagenomic NGS (mNGS) of clinical samples has been applied for the comprehensive diagnosis of infections, including viruses, bacteria, fungi, and parasites. It performs well in identifying rare, novel, difficult-to-detect and co-infected pathogens directly from clinical samples and presents great potential in resistance prediction by sequencing the antibiotic resistance genes, providing new diagnostic evidence that can be used to guide treatment options and improve antibiotic stewardship. Many physicians recognized mNGS as a last resort method to address clinical infection problems [5].

Here, we report a case of a 77-year-old male with a medical history of surgical excision of rectal carcinoma 14 years ago that had GBS meningitis revealed through mNGS. Initially he was started on broad spectrum antibiotics. After positive result from mNGS analysis of CSF was reported, antibiotic targeted for GBS infection was added. This case illustrates the importance of including mNGS analysis in diagnosis the specific pathogen causing the meningitis.

Case Presentation

A 77-year-old male presented to the Emergency Department (ED) of the First Affiliated Hospital of Sun Yat-sen University with a 7-day fever history to 39.5°C and unconsciousness. He underwent surgical treatment and chemotherapy for rectal carcinoma 14 years ago. On ED arrival, he presented with epilepsy for two minutes and was transferred to Intensive Care Unit (ICU). Due to his constellation of symptoms and physical exam findings, meningitis was initially suspected. Initial blood examination showed leukocytosis (18.89×10^9/L with 92% neutrophils), a C-Reactive Protein (CRP) level elevation of 303.98 mg/L, and an increased Procalcitonin (PCT) level of 36.3 ng/ml. A lumbar puncture examination of the CSF showed pleocytosis (1600×10^6/L with 70%

Table 1: Lab test results.

Day of admission	1	2	3	4	5	6	7	9	12	13	16	18
CRP (0-10 mg/L)	303.98	243.54	172.93	100.15	96.79	63.37	45.89	21.66	76.49	50.35	15.69	/
WBC (4-10 × 10^9/L)	18.89	13.12	8.11	4.55	4.81	6.54	5.97	6.34	6.43	4.69	3.31	/
Neutrophil (0.46%-0.75%)	0.92	0.927	0.871	0.804	0.769	0.846	0.775	0.747	0.781	0.716	0.696	/
PCT (0-0.05 ng/ml)	36.3	19.4	11.2	6.68	3.57	2.08	1.38	0.69	0.26		0.11	/
Protein of CSF (120-600 mg/L)	1830			2392.8					1101.5			743
WBC of CSF (0-10 × 10^6/L)	1600			387					25			2
mNGS of CSF				GBS					GBS			Negative
Antibiotics	Meropenem (2g, q8h)					Meropenem (2g, q8h) + Linezolid (0.6g, q12h)						

polymorphonuclear cells), and an increased protein level of 1830 mg/L. This initial lab analysis confirmed our suspicion of bacterial meningitis. He was initially administered intravenous Meropenem (2g, q8h) for bacterial meningitis until further analysis was completed. On day 2 of admission, the patient started to have improvement in his inflammatory indicators, and continued to improve in the coming days (Table 1). On day 4 of admission, his vital signs normalized, and lumbar puncture was performed again to guide treatment (to diagnose the specific strain causing the bacterial meningitis and to target antibiotic therapy accordingly). The CSF analysis showed improvements as well (Table 1). CSF cultures were negative (showed no growth for 14 days), while mNGS returned positive for GBS from his CSF on day 6 of admission. Treatment was altered accordingly. In addition to Meropenem, intravenous Linezolid (0.6 g, q12h) was added to target antibiotic therapy for GBS. On day ten, the patient was transferred out of the ICU to the general medical floor. He received a total of 3 weeks of antimicrobial treatment and showed clinical improvement. He was discharged after confirmation of a continued normal temperature, no abnormalities on physical examination, and improved lab test results. At the time of discharge, the patient had not reported any hearing loss.

Discussion

Group B *Streptococcus* (GBS) or *Streptococcus agalactiae* is known as one of the leading etiological agents of neonatal sepsis following maternally derived infection during pregnancy.

Previous analysis shows that the incidence of invasive GBS infection among nonpregnant adults continues to rise, roughly tripling between 1990 and 2016 (from 3.6 to 10.9 cases per 100,000) [6,7].

Given the severity of invasive GBS (94.6% of cases were hospitalized, 27.3% of cases required intensive care unit admission, and 5.6% of cases were fatal in 2016), this rise represents a clinical and public health concern. There are no current strategies to prevent invasive GBS disease in adults. Reports of adult meningitis secondary to GBS remain rare, with an estimated incidence of 0.15 cases per 100,000 [8]. The majority of reported cases outside the peripartum period have been in elderly patients or those with chronic illness such as diabetes, cancer, pregnancy, acute renal or hepatic failure [2]. Bacterial meningitis can be difficult to diagnose. Less than 50% of adult patients who later test positive for the infection present with the classic triad of fever, neck stiffness and altered mental state [2]. The most common organisms causing bacterial meningitis vary depending on the age of the patient. For our purposes, the most common organisms (and their Attack Rate (AR) per 10,000 individuals) for our patient's age range include *Streptococcus pneumoniae* (AR: 1.5), *Listeria monocytogenes* (AR: 0.5), *Haemophilus influenzae* (AR: 0.2), GBS (AR: 0.2) and *Neisseria meningitidis* (AR: 0.1) [9]. It is important for physicians who suspect bacterial meningitis to assess the risk factors of the patient, not only in terms of the condition itself but also for which organism it could be. It is also critical that patients with suspected meningitis, especially in the elderly population, are initiated on recommended empiric antibiotic therapy based on their age and co-morbidities. A lumbar puncture should be routinely performed to diagnose the specific strain causing the bacterial meningitis and to target antibiotic therapy accordingly.

Clinically, GBS meningitis is indistinguishable from meningitis caused by other pyogenic bacteria, with an acute onset and a high incidence of neurological dysfunction. However, GBS meningitis is frequently rapidly progressive with a higher proportion of patients with GBS presenting within 24 h of the onset of symptoms than those with other forms of bacterial meningitis [10]. In addition, the case fatality rate associated with GBS meningitis is considerably higher than that associated with meningococcal meningitis, at around 25% [1]. Although rare, GBS should be a part of a patient's differential when initiating antibiotics in adults with chronic illnesses. Our patient did present with risk factors for GBS meningitis, including his age as well as having a medical history of rectal carcinoma. A lumbar puncture was performed and broad-spectrum antibiotics were started after bacterial meningitis was suspected. Several lumbar punctures were performed to diagnose the specific strain causing the bacterial meningitis and to guide antibiotic therapy. After mNGS of CSF reported positive for GBS, targeted antibiotic was added. This case illustrates the importance of including GBS in the differential of chronically ill patients, especially those with concern for meningitis.

mNGS is increasingly being applied in clinical laboratories for unbiased culture-independent diagnosis. mNGS analysis of CSF is advantageous for diagnosing meningitis in patients with negative CSF cultures. According to a study by Wilson et al. [11], mNGS identified pathogens in CSF from 13 (22%) of 58 patients with meningitis/encephalitis that were not identified by conventional clinical testing. PCR is also used as a molecular diagnostic method and has advantages, in terms of sensitivity, for diagnosing meningitis in patients with negative CSF culture [12]. mNGS appears to be more suitable as a diagnostic procedure, because it does not rely on the pre-selection of targeted pathogens, but rather is able to detect many potential infectious agents in a single assay. In our patient, GBS meningitis was diagnosed by mNGS analysis. mNGS analysis is expected to become a standard diagnostic test for CSF samples, replacing conventional diagnostic procedures.

References

1. Farley MM. Group B streptococcal disease in nonpregnant adults. Clin

Infect Dis. 2001;33:556-61.

2. Thigpen MC, Whitney CG, Messonnier NE, Zell ER, Lynfield R, Hadler JL, et al. Bacterial meningitis in the United States, 1998-2007. N Engl J Med. 2011;364(21):2016-25.
3. Domingo P, Barquet N, Alvarez M. Group B streptococcal meningitis in adults: Report of twelve cases and review. Clin Infect Dis. 1997;25(5):1180-7.
4. Troendle M, Pettigrew A. A systematic review of cases of meningitis in the absence of cerebrospinal fluid pleocytosis on lumbar puncture. BMC Infect Dis. 2019;19(1):692.
5. Han DS, Li ZY, Li R, Tan P, Zhang R, Li JM. mNGS in clinical microbiology laboratories: on the road to maturity. Crit Rev Microbiol. 2019;45(5-6):668-85.
6. Skoff TH, Farley MM, Petit S, Craig AS, Schaffner W, Gershman K, et al. Increasing burden of invasive group B streptococcal disease in nonpregnant adults, 1990-2007. Clin Infect Dis. 2009;49(1):85-92.
7. Watkins LKF, McGee L, Schrag SJ, Beall B, Jain JH, Pondo T, et al. Epidemiology of invasive group B streptococcal infections among nonpregnant adults in the United States, 2008-2016. JAMA Intern Med. 2019;179(4):479-88.
8. Jackson LA, Hilsdon R, Farley MM. Risk factors for group B streptococcal disease in adults. Ann Intern Med. 1995;123(6):415-20.
9. Schrag SJ, Zywicki S, Farley MM, Reingold AL, Harrison LH, Lefkowitz LB, et al. Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis. N Engl J Med. 2000;342(1):15-20.
10. Dunne DW, Quagliarello V. Group B streptococcal meningitis in adults. Medicine. 1993;72(1):1-10.
11. Wilson MR, Sample HA, Zorn KC, Arevalo S, Yu G, Neuhaus J, et al. Clinical metagenomic sequencing for diagnosis of meningitis and encephalitis. N Engl J Med. 2019;380:2327-40.
12. Morrissey SM, Nielsen M, Ryan L, Al Dhanhani H, Meehan M, McDermott S, et al. Group B streptococcal PCR testing in comparison to culture for diagnosis of late onset bacteraemia and meningitis in infants aged 7-90 days: A multi-centre diagnostic accuracy study. Eur J Clin Microbiol Infect Dis. 2017;36(7):1317-24.