Primary Pyogenic Ventriculitis and Hydrocephalus Caused by Penicillin Non-Susceptible Streptococcus Pneumoniae Serotype 6B

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Abstract

Streptococcus pneumoniae (S. pneumoniae) can cause a range of infections, including community-acquired pneumonia, otitis media, sepsis and meningitis. Pyogenic ventriculitis, characterized by pus and ependymal inflammation in ventricular system, most commonly occurs as a complication of meningitis, brain abscess, or neurosurgical procedures. Primary pyogenic ventriculitis in adult is rare. We report an adult case of pyogenic ventriculitis and hydrocephalus presenting with fever and altered mental status. Penicillin non-susceptible S. pneumoniae was cultured in the cerebrospinal fluid (CSF) and confirmed as serotype 6B. She was treated with intravenous and intraventricular antibiotics and external ventricular drainage (EVD). Prompt diagnosis, surgical drainage and antibiotic treatment resulted in good neurologic outcome.

Keywords: Streptococcus pneumoniae, ventriculitis, hydrocephalus, penicillin non-susceptibility, intraventricular antibiotic

Introduction

Streptococcus pneumoniae (S. pneumoniae) is a Gram-positive, exclusive inhabitant in human oropharynx and nasopharynx. Over 100 serotypes are known. Colonization rates are higher in children under the age of two, the immunocompromised, and the elderly. We present a case of 67-year-old woman with diabetes, hypertension and negative vaccination history with an unusual presentation of primary ventriculitis. S. pneumoniae serotype 6B with penicillin non-susceptibility was isolated. To our knowledge, it is the first case of primary pyogenic ventriculitis and hydrocephalus secondary to penicillin non-susceptible S. pneumoniae (PNSP).

Case Report

A 67-year-old lady with a background of diabetes mellitus and hypertension presented to the emergency department with fever and agitation. She had no pneumococcal vaccination history. No headache or neck pain was reported. Her pupils were prompt and isocoric. There was no neck stiffness. Glasgow Coma Scale (GCS) was E4V2M5. Computed tomography (CT) of brain showed hydrocephalus. Urgent placement of external ventricular drainage (EVD) revealed turbid cerebrospinal fluid (CSF) at high pressure. Contrast CT-brain on the same day showed ependymal enhancement, and no intraventricular debris or brain abscess.
CSF assessment showed pleocytosis (White blood cells 43/cubic mm). The CSF grew PNSP by CLSI (Clinical and Laboratory Standards Institute) M100-Ed33 meningitis parenteral breakpoint. The isolate was serotype 6B. Intravenous ampicillin, metronidazole, ceftriaxone and vancomycin were given upon admission. The regimen was changed to intravenous cefotaxime and vancomycin on day 2 of admission when culture and sensitivity results were available. Intravenous vancomycin 10mg per day was given from day 2 to 8 of admission. Sterility of CSF was achieved on day 2 of admission. CSF mycobacterial culture was confirmed to be negative after standard 6-week culture. CSF protein decreased from 1.36 grams per litre on admission to 0.74 gram per litre on day 11. External ventricular drainage was removed on day 13 of admission. There was gradual neurological recovery that GCS was E4V4M6 on day 25 of admission. She was maintained on intravenous vancomycin and cefotaxime. There was transient rise in serum procalcitonin 3.03 nanogram (ng) per ml on day 25 of admission. She remained afebrile. CSF protein was 1.11 gram per litre and culture was negative. Cefotaxime was replaced with moxifloxacin 400mg every 24 hours and vancomycin was continued. The 6-week course of combination antibiotic treatment was completed. Post-ventriculitis hydrocephalus persisted on subsequent CT-scan. Ventriculo-peritoneal (VP) shunt placement was performed on day 80 of admission. CSF protein level upon VP shunt placement was 0.18 gram per litres. She was discharged home on day 101 with modified Barthel Index 62/100 and Glasgow Coma Scale 15/15.

Figure 1: Unenhanced computed tomography of brain shows dilated bilateral lateral, third and fourth ventricles.
Figure 2: Contrast CT-brain showed ependymal enhancement and hydrocephalus. No intraventricular debris was seen. Right EVD was placed.

Discussion

Pyogenic ventriculitis is usually caused by health-care related procedures, trauma, brain abscess or as a complication of meningitis. Hospital mortality of 30.6% and 61.8% of survivors with long-term neurological sequelae are observed. Currently, there is no consensus on the diagnostic criteria. Most reported cases are health-care related. Few cases of primary pyogenic ventriculitis have been described and this condition is supposed to be under-reported. The most common presenting features are fever and headache. Despite meningism being a common feature in meningitis, it is uncommon in primary ventriculitis. The complete triad of fever, neck stiffness and altered mental status was seen in only 31.6% of patients.

The common imaging features of pyogenic ventriculitis include intraventricular pus, ependymal enhancement and hydrocephalus. Diffusion restriction in the debris on diffusion-weighted MRI (Magnetic Resonance Imaging) is characteristic. The ventricular walls commonly show high T2 signal intensity. CT scans are still informative in patients who are unstable to undergo MRI. Irregular ventricular debris is especially characteristic for purulent material, in contrast to straight fluid level of intraventricular haemorrhage. The under-reported ‘lodge sign’ on CT is useful. Segmental dilation secondary to intraventricular adhesions and septae is another feature. Choroid plexitis, shown on contrast study as a swollen choroid plexus with poorly defined margin and enhancement, is sometimes shown. Periventricular calcifications almost never appear in pyogenic ventriculitis, though common in viral infections.

Reported causative organisms of primary pyogenic ventriculitis include Neisseria meningitidis, Staphylococcus aureus, Nocardia araoensis, Escherichia coli, Streptococcus pneumoniae, Methicillin resistant Staphylococcus aureus, Streptococcus intermedius, Listeria monocytogenes, Streptococcus agalactiae, Streptococcus acidominimus and Streptococcus suis.
The S. pneumonia capsule is an important virulence factor in pathogenesis through anti-phagocytosis and colonization promotion. It is also the basis of serotyping. Each capsular polysaccharide is antigenically unique. The virulence of each type differs from each other, differences in clinical outcomes and mortality rates are observed. Vaccine types and vaccination rates account for different predominant and common serotypes of S. pneumonia in different countries. Serotype 6b is a common pathogenic type and is covered in all pneumococcal vaccines. It is correlated to penicillin resistance. Penicillin resistance rates of S. pneumoniae range from 1.7-83.1% across the globe.

Antimicrobial drugs are not metabolized in CSF and their levels depend on penetration from serum. Meningeal inflammation facilitates entry of molecules from the serum to CSF. Third generation cephalosporins achieve good blood-brain barrier penetration and maintain prolonged-above-the- mean bactericidal concentration (MBC). The bactericidal activity of beta-lactam antibiotics is time-dependent. Studies showed that cefotaxime should be administered not longer than every 8 hours apart to maintain therapeutic level. Vancomycin is a hydrophilic glycopeptide which can be administered via several routes, intravenous, intraventricular and intrathecal. The bactericidal activity of vancomycin is both concentration- and time-dependent. Vancomycin can be used synergistically with other antibiotics for pneumococcal meningitis. The optimal vancomycin serum concentration is 15-20mg/L to improve CSF penetration. CSF sterility is achieved sooner with the use of intraventricular therapy and intravenous therapy together as compared to intravenous therapy alone. There are no confirmed adverse effects due to the intraventricular treatment. The recommended intraventricular dosage is 5-20mg daily.

CSF shunt valve occlusion was favoured by high perioperative CSF protein, particularly in tuberculosis meningitis. The optimal timing of VP shunt placement in consideration of CSF protein level, radiological features of hydrocephalus and clinical improvement will need to be studied. Potential confounding factors, such as shunt type, age and etiology, should be explored.

Conclusion

Primary pyogenic ventriculitis is a rare condition in immunocompetent adults. Antibiotic resistance and serology screening should be performed for diagnosis and initiation of appropriate treatment to prevent adverse outcomes. A guideline for primary pyogenic ventriculitis is to be developed. Clinicians should be aware of emerging penicillin non-susceptible Streptococcus pneumoniae CNS infection. Our goal is to increase awareness of this condition and to encourage vaccination against Streptococcus pneumoniae. Monitoring of serotype and antibiotic resistance of Streptococcus pneumoniae is warranted. The optimal timing of shunt placement and its relation to CSF protein level, clinical and radiological features of hydrocephalus need to be studied.

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References


