

Acute encephalitis caused by *Streptococcus pneumoniae*: case report and review of the literature

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ABSTRACT:

Introduction: *Streptococcus pneumoniae* (pneumococcus), is a Gram-positive, spherical bacteria, member of the genus *Streptococcus*. It resides asymptotically in healthy carriers typically colonizing the respiratory tract, sinuses, and nasal cavity. However, in susceptible individuals with weaker immune systems, pneumococcus may become pathogenic and spread to other locations causing cardiorespiratory and bone diseases as well as meningitis. Encephalitis and brain abscesses caused by *Streptococcus pneumoniae* are rare entities and they account for less than 1% of all bacterial brain abscesses.

Purpose: We aim to present a case report of an acute encephalitis in a 16 years old female patient caused by *Streptococcus pneumoniae*, with review of the literature.

Case Report: A 16 years old, right-handed female, was hospitalized at the clinic due to impaired consciousness (coma) and decerebrate posturing. The symptoms started the previous days with vomiting, drowsiness, subfebrile temperature and were originally perceived as food poisoning. Laboratory blood analysis were normal at the beginning and despite supportive therapy, deterioration of the clinical condition occurred, followed by confusion, muscle weakness and collapse. These symptoms were initially addressed as a functional neurological symptom disorder and the patient was referred to a psychiatrist. However, the patient's condition got worse, with febrile symptoms, while the control laboratory blood examination showed signs of infectious syndrome. The patient was seen by infectologist and COVID-19 test was performed, with negative result. The analysis of CSF found bacterial infiltration, while the PCR test isolated *Streptococcus pneumoniae*. MRI of the brain (native and with contrast) showed bilateral multiple microabscesses, predominantly in the frontal and parietal regions. After the diagnosis was confirmed, the patient was treated promptly with antiedematous, antibiotic, neuroprotective and other symptomatic therapy for a period of 2 months. Her condition gradually improved completely, with amelioration of the state of consciousness and muscle weakness as well. Control laboratory blood analysis and CSF examination showed improvement as well, while the MRI of the brain displayed reduction of the previously described lesions and edema.

Conclusion: The atypical clinical picture may sometimes mislead the treating physician. Cases with encephalitis caused by *Streptococcus pneumoniae* have been rarely described in the literature, however, early recognition and adequate treatment are crucial for the positive outcome.

KEYWORDS: encephalitis, brain abscess, *Streptococcus pneumoniae*

SAŽETAK:

AKUTNI ENCEFALITIS UZROKOVAN *STREPTOCOCCUS PNEUMONIAE*: PRIKAZ SLUČAJA I PREGLED LITERATURE

Uvod: *Streptococcus pneumoniae* (pneumokok), je gram-pozitivna, sferna bakterija, pripadnik roda *Streptococcus*. Asimptomatski se nalazi u zdravih nositelja koji tipično koloniziraju respiratorni trakt,

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sinuse i nosnu šupljinu. Međutim, u osjetljivih osoba sa slabijim imunološkim sustavom, pneumokok može postati patogen i proširiti se na druga mjesta uzrokujući kardiorespiratorne i koštane bolesti, kao i meningitis. Encefalitis i moždani apscesi uzrokovani *Streptococcus pneumoniae* rijetki su entiteti i čine manje od 1% svih bakterijskih apscesa mozga.

Svrha: Cilj nam je prikazati prikaz slučaja akutnog encefalitisa u bolesnice stare 16 godina uzrokovanog *Streptococcus pneumoniae*, uz pregled literature.

Prikaz slučaja: 16-godišnjakinja, dešnjakinja, hospitalizirana je u klinici zbog poremećaja svijesti (kome) i decerebracije. Simptomi su započeli prethodnih dana povraćanjem, pospanošću, subfebrilnom temperaturom i prvotno su percipirani kao trovanje hranom. Laboratorijske analize krvi u početku su bile normalne, a unatoč potpunoj terapiji došlo je do pogoršanja kliničkog stanja, konfuzije, slabosti mišića i kolapsa. Ovi simptomi su u početku tretirani kao poremećaj funkcionalnih neuroloških simptoma i pacijent je upućen psihijatru. Međutim, stanje bolesnika se pogoršalo, s febrilnim simptomima, a kontrolni laboratorijski pregled krvi pokazao je znakove infektivnog sindroma. Pacijenticu je pregledao infektolog i urađen test na COVID-19, s negativnim nalazom. Analizom likvora utvrđena je bakterijska infiltracija, dok je PCR testom izoliran *Streptococcus pneumoniae*. MRI mozga (nativni i s kontrastom) pokazao je bilateralne višestruke mikroapscese, pretežno u frontalnoj i parijetalnoj regiji. Nakon potvrde dijagnoze, pacijent je odmah liječen antiedematoznom, antibiotskom, neuroprotektivnom i drugom simptomatskom terapijom u trajanju od 2 mjeseca. Stanje joj se postupno potpuno popravljalo, uz poboljšanje stanja svijesti i slabost mišića. Kontrolna laboratorijska analiza krvi i pregled likvora također su pokazali poboljšanje, dok je MR mozga pokazao smanjenje prethodno opisanih lezija i edema.

Zaključak: Netipična klinička slika ponekad može dovesti u zabludu liječnika. Slučajevi s encefalitisom uzrokovanim *Streptococcus pneumoniae* rijetko su opisani u literaturi, međutim, rano prepoznavanje i adekvatno liječenje ključni su za pozitivan ishod.

KLJUČNE RIJEČI: encefalitis, apsces mozga, *Streptococcus pneumoniae*

INTRODUCTION

Encephalitis is an inflammation of the brain parenchyma that presents as diffuse and/or focal neuropsychological dysfunction. It primarily involves the brain, however, the meninges are frequently involved (meningoencephalitis). The cause of encephalitis is usually infectious in nature. Most cases are caused by viruses, although bacterial, fungal and autoimmune disorders can also produce encephalitis. *Streptococcus pneumoniae* (pneumococcus), is a Gram-positive, spherical bacteria, member of the genus *Streptococcus*. It resides asymptotically in healthy carriers typically colonizing the respiratory tract, sinuses, and nasal cavity. However, in susceptible individuals with weaker immune systems, pneumococcus may become pathogenic and spread to other locations causing cardiorespiratory and bone diseases as well as meningitis. Encephalitis and brain abscesses caused by *Streptococcus pneumoniae* are rare entities and they account for less than 1% of all bacterial brain abscesses (1).

CASE DESCRIPTION

We present a 16 years old patient, who was hospitalized due to consciousness impairment. On initial examination, she was comatous with Glasgow Coma Scale (GSC) of 3, with decerebrate posturing, deviated eyes to the right, without neck stiffness, with

negative meningeal signs. Babinski sign was positive bilaterally. Blood pressure was 160/90mmHg. ECG was with sinus rhythm and she had vesicular breathing. Her medical history was negative for any past diseases nor known allergies. The patient was COVID-19 negative, and she was not vaccinated. No other recent infections or immunizations were noted.

CLINICAL COURSE OF THE DISEASE

Several days before admission, the patient had symptoms of nausea, vomiting (several times), general weakness, headache and subfebrile temperature (37°C). Initially these symptoms were attributed to alimentary intoxication and she was treated with antibiotic and vitamin therapy. However, her condition progressed with impaired consciousness, disorientation and somnolence, muscle weakness, vomiting and collapse. Laboratory blood analysis showed increased leucocytes $26.40 \times 10^9/L$ (3.5-10), neutrophils $25 \times 10^9/L$ (1.2-6.8), lymphocytes $0.70 \times 10^9/L$ (1.2-3.2), monocytes $0.50 \times 10^9/L$ (0.3-0.8) and C-reactive protein (CRP)- 180.50 mg/L (0.0-6.0). Echosonography of the abdomen was normal. In the local urgent center the symptomatic therapy was continued, but the patient deteriorated with occurrence of disorganized movements and was sent for a psychiatric examination. But, the infectious

syndrome (febrile temperature – 38.5°C) persisted, the patient became soporous and was finally sent to an infectologist. Several investigations were performed, such as rapid antigen test for COVID-19 which was negative, Rtg of the lungs and brain CT were normal (Figure 1). On lumbar puncture purulent CSF was noted, Pandy positive, with 6300 elements, 0.10 lymphocytes, 17,6 mmol/L (1,2-2,1) lactates, 10,4 g/L (0,12-0,60) albumins, sacharides- 1,1 mmol/L (2,2-3,9). M-Real time PVR discovered *Streptococcus pneumoniae* and diagnosis of acute bacterial encephalitis was established. Since the clinic for infectious disease was a COVID center at the time, the patient was transferred to

the clinic of neurology where she was hospitalized. After several days magnetic resonance of the brain (native and with contrast) was performed, that showed multiple, hypersignal lesions in the white matter as well as subcortically, distributed dominantly in the frontal and parietal regions, as well as temporally and occipitally, with presence of perifocal oedema, in both hemispheres (Figure 2). Electroencephalography (EEG) was performed after 2 weeks and it showed that the basic brain activity is symmetric and reactible, with occasional asynchronous and diffuse isolated spikes and sharp waves, without clear lateralization and location of the changes (Figure 3).

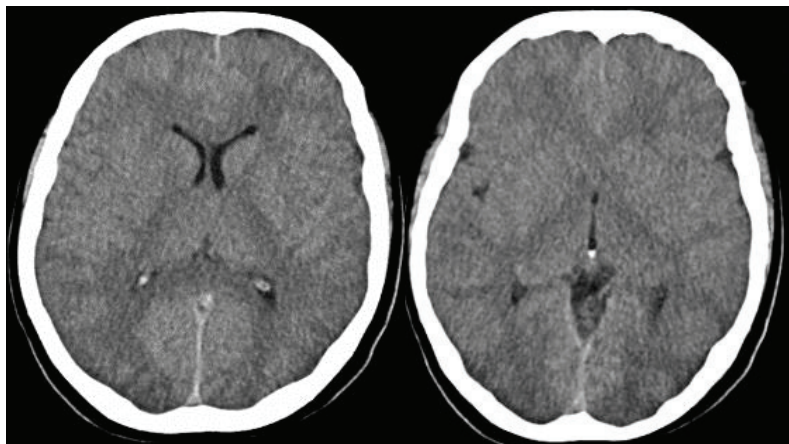


Figure 1. Initial brain CT scan, with normal findings

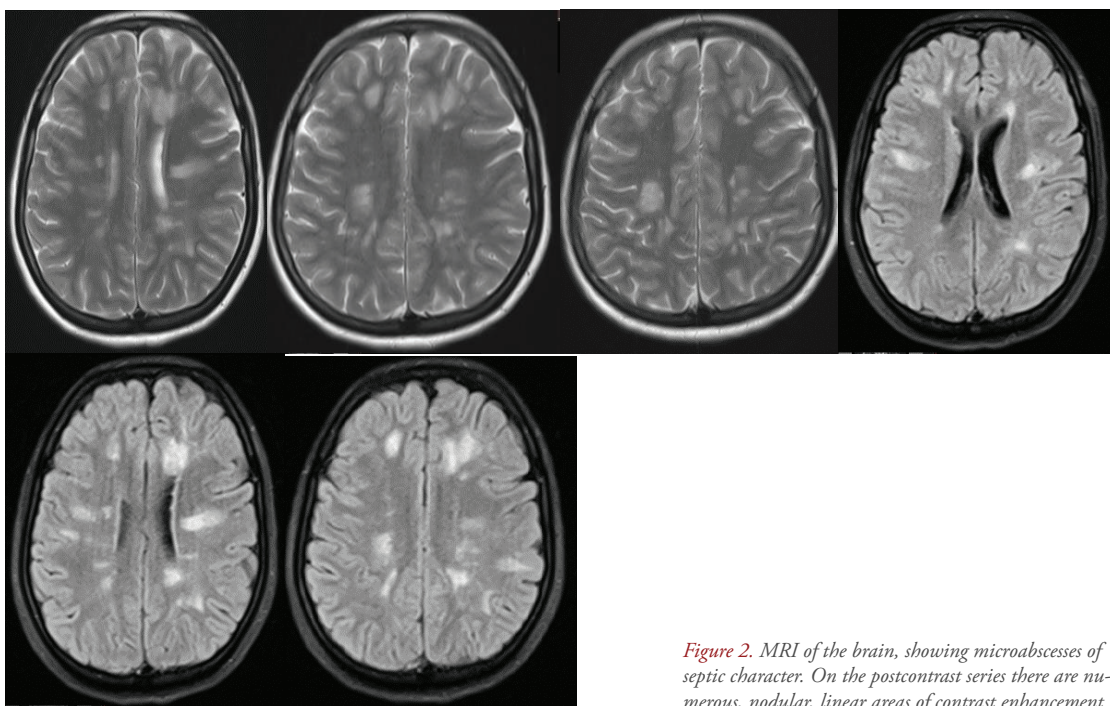


Figure 2. MRI of the brain, showing microabscesses of septic character. On the postcontrast series there are numerous, nodular, linear areas of contrast enhancement.

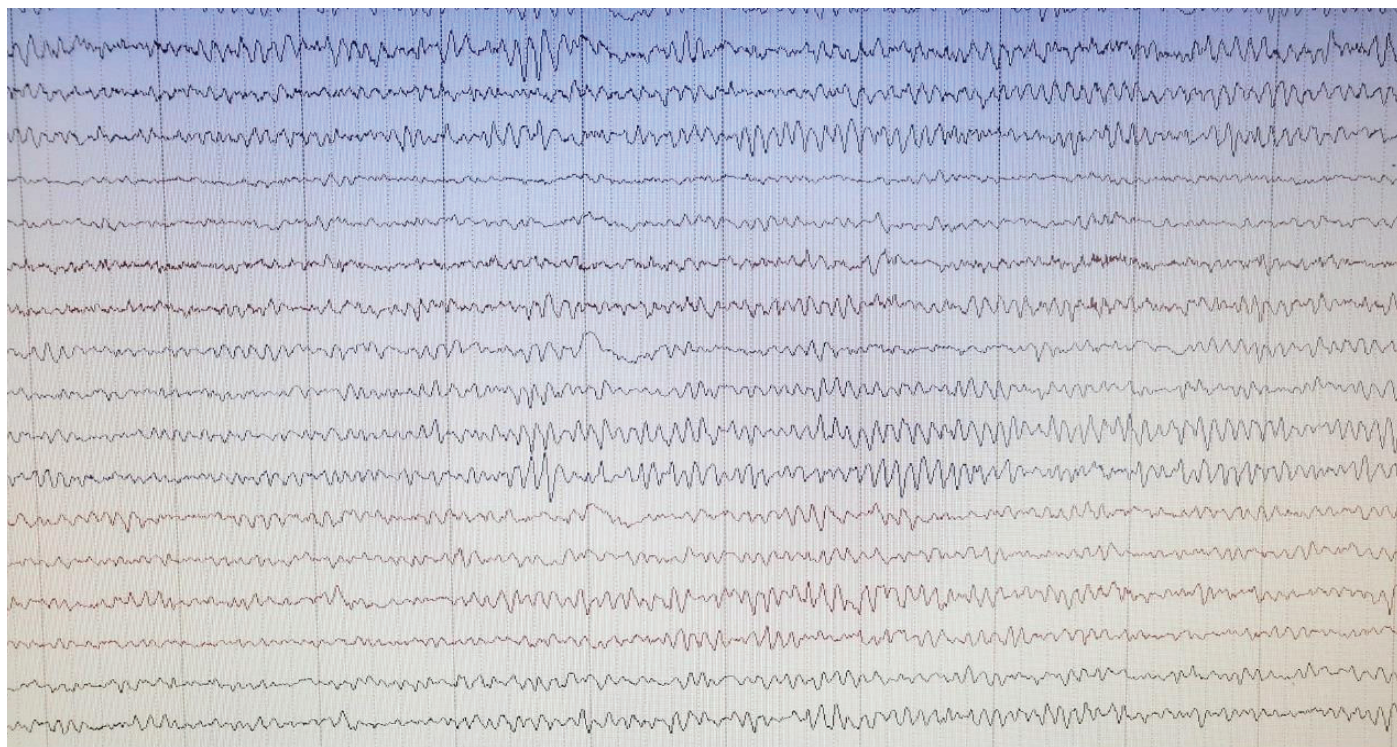


Figure 3. EEG findings

Table 1. CSF characteristics of different types of encephalitis

CSF analysis	Bacterial	Tuberculosis	Viral	Fungal	Aseptic
Color	cloudy	Cloudy	clear	clear	clear/cloudy
Glycosis	increased	Decreased	decreased	normal	decreased
Proteins	increased	Increased	normal	normal	normal
Elements	increased neutrophil dominant	increased lymphocytes dominant	increased lymphocytes dominant	increased lymphocytes dominant	Increased neutrophil dominant

Treatment of the patient included antiedematous therapy (manitol, corticosteroids) and intravenous antibiotic therapy according to protocol : Metronidazol (for a period of 3 weeks) and Ceftriaxone with Vankomycin (for a period od 6 weeks). Afterwards, treatment with Meropenem was continued for 2 weeks. Neuroprotective treatment with infusions Amantadine sulfate was provided for a period of 2 weeks, and peroral treatment with MLC901 was started and recommended for a period

of 3 months. Control laboratory blood analysis as well as CSF analysis showed improvement, with gradual normalization of the values (Leucocytes - 21...15...14...9.2 10^9 L (with neutrophylic domination); CRP- 162...154...10...4...0.6mg/dL; D-dimer- 804...3025...286...300). Control MRI of the brain showed signs of regression of the changes with decreased number and reduction of the perifocal edema. The physical and neurological condition of the patient gradually improved during the hospitali-

zation period of 2 months. She regained her consciousness, and has no residual motor nor cognitive deficit.

DISCUSSION

Bacterial encephalitis and/or brain abscess caused by *Streptococcus pneumoniae* is an extremely rare condition. Our case was defined by positive M-Real time PVR for *Streptococcus pneumoniae* isolated from CSF and MRI findings that demonstrated lesions compatible with the radiological features of a brain abscess. There are only few cases described in the literature. Jorens et al. (2) reported on three adult patients with meningoencephalitis caused by *Streptococcus pneumoniae*. In all three, CT and MRI revealed widespread brain lesions, suggesting extensive parenchymal injury. Diffusion-weighted MRI showed lesions with restricted diffusion, reflecting local areas of ischaemia with cytotoxic oedema secondary to an immunologically mediated necrotising vasculitis and thrombosis. High levels of markers of neuronal, glial and myelin damage were found in the cerebrospinal fluid. Their patients were treated with pulse doses of glucocorticoids which resulted in dramatic clinical improvement and an excellent final neurological recovery.

The same author (3) also reported another case of a 7-month-old child with meningoencephalitis caused by *Streptococcus pneumoniae*. Peculiar, widespread and unique signal abnormalities were found on MRI with extensive central nervous white matter injury as well as evidence of thrombosis of the lateral transverse sinus. These changes were observed very early in the course of the illness, presumably reflecting widespread cytotoxic edema, vasculitis and acute demyelination. These lesions occurred despite appropriate antibiotic and anti-inflammatory (glucocorticoid) therapy started very early in the course of the disease.

Magnus et al. (4) reported an exceptional case of a 4-month-old boy with meningoencephalitis caused by *Streptococcus pneumoniae*. CT and MRI examinations of the brain showed bilateral symmetrical necrosis involving the lentiform and caudate nuclei, as well as the thalamus. T1-weighted MR images showed patchy areas of increased signal intensity, consistent with hemorrhagic transformation of the lesions. Autopsy revealed widespread necrosis of the basal ganglia with clear signs of vasculitis.

Bakar and Hakki Tekkok (5) described a 56-year-old man presented with blurred vision. Two days after uneventful surgery, the patient became hyperpyrexia which progressed to confusion and lethargy within 48 hours. Spinal fluid cultures revealed *Streptococcus pneumoniae*. The patient was treated appropriately and made an uneventful recovery. MR images showed persistent changes within both frontal lobes. This case further suggests that peri-operative antimicrobial chemoprophylaxis may not save the patient from serious surgical infections.

Belodu et al. (6) have described a man who presented with the signs and symptoms of a mass lesion which was localized to the temporal lobe. The clinical examination and computerized

tomography revealed the diagnosis of a temporal abscess. The loculated mass was tapped and it was sent for histopathology, which confirmed the presence of an organizing abscess. A laboratory investigation of the pus revealed *Streptococcus pneumoniae*. The treatment included total excision and the administration of prolonged antibiotics, which led to a good outcome in the patient.

According to the recommendations, until the arrival of the results of the diagnostic investigations, empirical treatment of the encephalitis should be started, which is based on the clinical picture and epidemiological factors (7). Also, 1-2 weeks after the treatment, a control MRI of the brain should be performed for evaluation of the condition. In cases where the number of abscesses is increased, neurosurgical intervention is recommended (aspiration/excision of the abscess).

When should we think of encephalitis? We need to obtain good anamnesis (heteroanamnesis) with precise data regarding type and onset of symptoms and presence of previous infections. Clinical presentation consists of headache, vomiting, increased body temperature, impaired consciousness and epileptic seizures. Diagnostic investigations that should be performed and included in the differential diagnosis are infectious (bacterial, viral, parasites), autoimmune (ADEM, NMDAR, AMPAR, GABA_BR, LGI1, CASPR2), toxins/metabolic (hyper/hypoglycemia, hyponatremia, uremia, Wernicke encephalopathy), vascular (ischemic/hemorrhagic stroke, cerebral sinus venous thrombosis, subarachnoidal haemorrhage), neoplastic and psychiatric examinations.

CSF investigation in bacterial encephalitis show cloudy (pyogenic) appearance, with increased level of glycosis, proteins and elements (Table 1).

EEG is an important diagnostic and monitoring tool to consider in the management of different types of encephalitis. There is no pathognomonic EEG pattern for any type of encephalitis. In general, viral encephalitis has slow background rhythms along with the presence of focal epileptogenic discharges.

MRI of the brain does not show specific characteristics in encephalitis, only presence of edema and increased T2 signal. In case of abscess, there is hypersignal in T1 and hyposignal in DWI with surrounding oedema. ADEM can be considered as a differential diagnosis of encephalitis, where there are multifocal hyperintense changes in T2 sequence, localized supra and infratentorially with involvement of structures in the grey matter, especially thalamus and basal ganglia.

PROGNOSIS

Despite timely recognition and treatment, mortality in bacterial encephalitis with abscesses is high (20%) and it increases with

the expanding of the number of abscesses. If intraventricular rupture of the abscess occurs, the mortality is increasing. Mortality in these pathologies is also associated with age, comorbidities and haematogenic dissemination of the infection. In 40% of the survivors, there are permanent neurological consequences, such as symptomatic epilepsy and neurological and cognitive deficits (behavioural changes, cognitive impairment, disturbed memory).

CONCLUSION

Early recognition and prompt treatment of acute encephalitis caused by *Streptococcus pneumoniae* are needed in order to provide favourable outcome of the patients.

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