

Deafness due to haemorrhagic labyrinthitis and a review of relapses in *Streptococcus suis* meningitis

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ABSTRACT

Deafness is a common and often permanent neurological sequel of *Streptococcus (S.) suis* meningitis. Suppurative labyrinthitis, rather than direct auditory nerve infection, has been found to be the site responsible for deafness. Neuroimaging is important to localise the site involved in hearing loss and to assess the feasibility of a cochlear implantation. *S. suis* is very sensitive to penicillin. Although a relapse of *S. suis* meningitis is uncommon, it can occur despite an adequate duration of appropriate antibiotic therapy. We describe a patient with *S. suis* meningitis, who developed permanent deafness from haemorrhagic labyrinthitis, as shown on magnetic resonance imaging. She suffered a relapse despite a seven-week course of intravenous antibiotics. A review on six cases of relapse reported in the literature shows that relapses occurred despite two to four weeks of antibiotics being administered to the patients. The clinical implications and treatment of relapse are discussed.

Keywords: deafness, meningitis, neuroimaging, relapse, *Streptococcus suis*

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INTRODUCTION

Streptococcus (S.) suis is a porcine bacteria that causes occasional human outbreaks. Human infection presents predominantly as acute septic meningitis or arthritis, but may also include pneumonia, endophthalmitis, endocarditis and fatal septicaemia. About half of the patients with *S. suis* meningitis develop characteristic sensorineural hearing loss. This is often bilateral, profound and permanent.^(1,2) Suppurative auditory neuritis was previously thought to cause post-meningitic deafness, but the cochlea has now been identified as the site of the lesion. Correct radiological localisation of the site involved is important so as to determine whether the patient would benefit from a cochlear implantation.



Fig. 1 Axial gadolinium-enhanced T1-weighted MR image shows abnormal cochlear enhancement on both sides (arrows).

We present the first case of *S. suis* meningitis with radiological features of haemorrhagic labyrinthitis and discuss the preventive measures for reducing the risk of post-meningitic deafness. *S. suis* is generally highly sensitive to penicillin, and a relapse of meningitis is uncommon. We perform a case review of relapses in *S. suis* meningitis and highlight the present case that relapsed despite receiving the longest course of antibiotics reported thus far.

CASE REPORT

A 70-year-old Chinese woman with hypertension and ischaemic heart disease presented with giddiness and lower back pain, followed by confusion and drowsiness of two days' duration. On examination, she was afebrile and disorientated, and had neck stiffness. Blood investigations showed leucocytosis ($12.6 \times 10^9/L$) and C-reactive protein (CRP) (263 mg/L). She was started on intravenous ceftriaxone 2 g 12-hourly. Computerised tomography of the brain was normal, and her family declined a lumbar puncture. Blood cultures subsequently yielded penicillin-sensitive *S. suis*, with a minimal inhibitory concentration of 0.064 mg/L. Her level of consciousness improved rapidly with treatment, and it then became apparent that she had developed bilateral hearing loss. Magnetic resonance (MR) imaging of the internal auditory meati revealed abnormal enhancement

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Fig. 2 Axial T1-weighted MR image without contrast shows abnormal patchy high signals in the cochlea (arrows) and vestibule (arrowheads) on both sides, suggestive of haemorrhage.

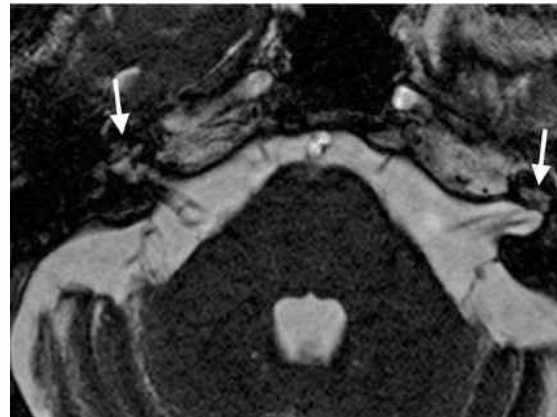


Fig. 3 Axial 3D FIESTA image shows reduced fluid signal in the cochlea bilaterally (arrows), suggestive of labyrinthine ossification.

of the cochlea and the labyrinthine apparatus on both sides, which was suggestive of bilateral labyrinthitis (Fig. 1). Patchy hyperintensity on the unenhanced T1-weighted images, suggestive of haemorrhage, was present in the cochlea and in the vestibule bilaterally (Fig. 2). No abnormal enhancement was seen along the course of the vestibulocochlear nerve complexes.

The patient's backache worsened, and she subsequently developed lower limb weakness and areflexia. MR imaging of her lumbosacral region showed a L3/4 epidural abscess with discitis and paravertebral infection. She underwent spinal decompression with lumbar laminectomy. The acute infective markers normalised with two weeks of ceftriaxone followed by penicillin-G at 3 mega-units six-hourly. She remained profoundly deaf in both ears and was incapacitated by persistent vertigo and gait instability. The absence of wave I bilaterally on her brainstem evoked response (BAER) was consistent with an extra-axial auditory lesion. There was no cochlear ossification on MR imaging three weeks after the disease onset, and plans for a cochlear implantation were therefore made. In the meantime, she was started on betahistine and vestibular rehabilitation.

However, two months after the initial illness, while still receiving her fifth week of intravenous penicillin, the patient suffered a relapse with the development of myoclonic seizures in the left leg. She was afebrile, with an erythrocyte sedimentation rate of 69 mm/hr and a CRP of 12 mg/L. MR imaging of the brain showed a bilateral medial frontal leptomeningeal enhancement with oedema of the right superior frontal and medial parietal cortex, suggestive of acute meningoencephalitis. Lumbar puncture revealed sterile cerebrospinal fluid with normal opening pressure, leucocytosis of 28

white cells, 10 red blood cells, protein 0.8 g/L and glucose 3.2 mmol/L. Blood cultures were negative and a lumbosacral MR imaging showed post-surgical changes with no evidence of an ongoing infection. There was no clinical or radiological evidence of an infective focus elsewhere. The patient received an additional two weeks of ceftriaxone, followed by eight weeks of oral cephalexin. This rapidly led to a further reduction of the CRP and an uneventful clinical recovery.

Seven months after the onset of the illness, a reduced fluid signal was seen in both cochleas on MR imaging, in keeping with labyrinthine ossification (Fig. 3). The patient underwent a right cochlear implantation successfully, despite a partial obliteration of the labyrinths. With rehabilitation, she was eventually able to walk independently.

DISCUSSION

S. suis usually affects healthy adults who have an occupational exposure to pigs or raw pork,^(3,4) with outbreaks reported in pig farming industries. *S. suis* infection among housewives is not unusual, despite an apparent absence of occupational exposure. In a Hong Kong case series, five out of nine women who were infected were housewives who had no obvious cutaneous injury prior to the illness.⁽¹⁾ In patients presenting with meningitis, *S. suis* should be considered regardless of the patient's occupational background if the characteristic features of prominent and early hearing loss are present. The organism, a beta-haemolytic streptococcus, is generally highly sensitive to penicillin. Thus, the prompt treatment of *S. suis* meningitis with appropriate antibiotics has been found to lead to a favorable outcome and a low mortality rate of 7%.⁽¹⁾ However, half of the patients with *S. suis* meningitis will acquire hearing

Table I. Cases of relapse in *Streptococcus (S.) suis* meningitis.

Case no.	Age (years), gender, occupation	Past medical history	<i>S. suis</i> MIC and MBC to penicillin (mg/L)	Antibiotic, dosage, duration	Type of relapse	Further intervention
1 ⁽¹⁵⁾	52, M, poultry worker	None	0.06	Penicillin, 3 mu 6 hourly, 4 weeks	Clinically, bacteriologically in CSF	Penicillin, 6 mu 6 hourly, 2 weeks
2 ⁽¹⁵⁾	65, M, NS	NS	0.06	Penicillin, 6 mu 6 hourly, 2 weeks	Clinically, bacteriologically in CSF	Penicillin, 6 mu 6 hourly, 4 weeks
3 ⁽¹⁾	51, M, cook	NS	0.06	Penicillin, 12–24 mu/day, 2 weeks	NS	Penicillin, 12–24 mu/day, 4 weeks
4 ⁽¹⁾	65, M, retired	NS	0.06	Penicillin, 12–24 mu/day, 4 weeks	NS	Penicillin, 12–24 mu/day, 2 weeks
5 ⁽²⁾	47, F, butcher	Alcohol consumption, ½ bottle/day	NS	Penicillin, dose NS, 8 days	NS	Penicillin same dose as initial therapy, 8 days
6 ⁽¹⁶⁾	60, M, pig-meat factory worker	Heavy drinker	MIC 0.015 mg/L, MBC > 2 mg/L	Chloramphenicol, 4 days; penicillin, 18 mu/day, 3 weeks	Clinically, bacteriologically in CSF	Penicillin, 18 mu/day, 4 weeks plus chloramphenicol 1st week; gentamicin, 3 weeks
7(current)	70, F, housewife	Hypertension, hyperlipidaemia, ischaemic heart disease	MIC 0.064 mg/L, MBC not tested	Ceftriaxone, 2 g 12 hourly, 2 weeks; penicillin, 3 mu 6 hourly, 6 weeks	Clinically, radiologically	Ceftriaxone, 2 g 12 hourly, 2 weeks; cephalexin, 500 mg tid, 8 weeks

CSF: cerebrospinal fluid; F: female; M: male; MBC: minimal bactericidal concentration; MIC: minimal inhibitory concentration; mu: mega-units; NS: not specified

loss with or without vestibular dysfunction. In contrast, only about 10% of other bacterial meningitis survivors develop deafness. The deafness was previously thought to be attributed to direct infection of the auditory nerves or brainstem encephalitis. More recently, animal experiments⁽⁵⁾ and human electrophysiological studies⁽⁶⁾ have identified the cochlea as the site of the lesion. *S. suis* is believed to enter the perilymph via the cochlear aqueduct through the lytic actions of exotoxins.^(5,7,8)

In patients with bilateral profound post-meningitic hearing loss, the correct localisation of the site involved is crucial so as to determine whether a cochlear or auditory brainstem implant would be beneficial. In addition, the feasibility of a cochlear implantation should be explored early, before secondary cochlear ossification and obliteration occur. BAER can differentiate an extra-axial cause from a brainstem cause of hearing loss but may not discriminate between a cochlear involvement and an auditory nerve involvement. Neuroimaging, in particular, MR imaging of the cochlea and auditory nerve, has emerged as an important tool in the evaluation of cochlear implant candidates. It is able to localise the site of the lesion, show the underlying pathology

and assess the severity of cochlear ossification.⁽⁹⁾ The signal changes in our patient's initial MR imaging were suggestive of bilateral labyrinthine haemorrhage, likely secondary to the underlying infective and inflammatory processes. To the best of our knowledge, this is the first case report of haemorrhagic labyrinthitis due to *S. suis* meningitis evident on MR imaging.

Can the adjuvant use of corticosteroids decrease the risk of post-meningitic permanent deafness? A meta-analysis in 2007 showed that corticosteroids reduced the incidence of deafness in children with bacterial meningitis and decreased the mortality rate and short-term neurological sequelae in adults.⁽¹⁰⁾ Corticosteroids are therefore recommended to be used in conjunction with the first dose of antibiotics in patients with meningitis. However, a recent study of *S. suis* meningitis conducted specifically in adults at the time of discharge from the hospital, showed that dexamethasone therapy was associated with severe deafness.⁽¹¹⁾ This suggests that the benefit of corticosteroid therapy in reducing post-meningitic neurological sequelae does not apply to *S. suis* meningitis. A more important determinant of the reversibility in hearing loss may lie in prompt diagnosis

and early antibiotic treatment within the first few days of infection of bacterial meningitis, as was shown in a study of children with bacterial meningitis.⁽⁶⁾

Apart from deafness, patients with post-*S. suis* meningitis may be permanently incapacitated by vertigo and gait instability due to vestibular dysfunction. During the acute phase, a short course of vestibular suppressants, preferably non-sedating (e.g. betahistine), can be given for symptomatic relief.⁽¹²⁾ This should immediately be followed by vestibular rehabilitation which will improve the patient's independence in daily activities via the facilitation of central vestibulospinal compensation.^(13,14)

The vast majority of patients with *S. suis* meningitis recover after a two- to four-week course of penicillin, ampicillin or cephalosporin. This is expected in view of the high sensitivity of *S. suis* to penicillin. However, a relapse of *S. suis* meningitis has been reported in six cases (Table I).^(1,2,15,16) In these cases, the organisms were sensitive to penicillin but demonstrated different levels of susceptibility. Relapses may occur despite a high level of penicillin susceptibility, as was shown in Cases 1 to 4, which had low minimal bactericidal concentration (MBC) values (Table I). Patients relapsed despite receiving 12 to 24 mega-units of benzyl penicillin for two to four weeks (except for Case 5, who was treated for only eight days). The relapse occurred within a week of the antibiotic cessation, with no evidence of an intracranial abscess formation or occult systemic foci of infection. Complete eradication was then achieved by extending the duration of penicillin therapy to a total of six weeks. Our patient was unusual as she relapsed despite a seven-week course of antibiotics that the organism was sensitive to. The MBC was not tested, and we believe an undetermined poor susceptibility to penicillin may have contributed to her relapse.

We suggest that patients with *S. suis* meningitis be monitored for signs of relapse after the cessation of an adequate course of appropriate antibiotics. In the event of a relapse, the occult infective foci should be looked for and the organism's susceptibility to antibiotics re-tested. Meanwhile, penicillin may be resumed and continued for another two weeks if no systemic focus is found

and the organism remains highly susceptible. A larger observational study is needed to identify the subgroup of patients at high risk of a relapse. These patients should be treated with a longer course of antibiotics.

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