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CASE REPORT

Streptococcus suis meningitis in the Netherlands

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Summary We present four patients with *Streptococcus suis* meningitis identified during a 3.5-year prospective surveillance study in the Netherlands. All cases were associated with exposure to pigs. Patients presented with classic symptoms and signs of bacterial meningitis. Outcome was characterized by severe hearing loss. Physicians should be aware of occupational exposure with *S. suis* and risk of meningitis associated with this pathogen.
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Introduction

Streptococcus suis infection in humans is a zoonosis that has been mainly reported in pig-rearing and pork-consuming countries.[1] The most common manifestation of *S. suis* infection is meningitis.[1] In July 2005, a large outbreak of human *S. suis* infection occurred in China, showing the threatening potential of this emerging zoonotic agent.[1] In a recent study *S. suis* was the most common causative organism of bacterial meningitis in Vietnam.[2] Few cases have been described in the Western World.[1,3–5] In this report we provide a detailed description of four adults with *S. suis* meningitis from a prospective surveillance study on adulthood community-acquired bacterial meningitis in the Netherlands.

Methods

In the Dutch Meningitis Cohort Study, a nationwide observational cohort study in the Netherlands, 696 episodes of community-acquired acute bacterial meningitis were assessed prospectively.[6] All causative organisms were identified by cerebrospinal fluid (CSF) culture, which yielded *Streptococcus pneumoniae* in 352 episodes (51%), *Neisseria meningitidis* in 257 (37%), *Listeria monocytogenes* in 30 (4%), and other bacteria in 57 (8%). Inclusion and exclusion criteria have been described elsewhere.[6] In summary, eligible patients were >16 years old, had bacterial meningitis confirmed by culture of CSF, and were listed in the database of The Netherlands Reference Laboratory for Bacterial

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Meningitis from October 1998 to April 2002. For each patient, the treating physician was contacted, and informed consent was obtained from all participating patients or their legally authorized representatives. The Dutch Meningitis Cohort Study was approved by the ethics committee. Data registration was started at the time of inclusion. The study was undertaken in accordance with Dutch privacy legislation, and information was obtained via a case-record form. Patients receiving immunosuppressive drugs and patients with diabetes mellitus, alcoholism, asplenia, liver cirrhosis, end-stage renal disease, or HIV infection were judged to be immunocompromised. Patients underwent a neurological examination at discharge, and outcome was graded with the Glasgow Outcome Scale. This measurement scale is well validated, with scores varying from 1 (death) to 5 (good recovery). Focal neurological abnormalities were divided into focal cerebral deficits (aphasia, monoparesis, or hemiparesis) and cranial nerve palsies.

Results

Among the 696 episodes of community-acquired acute bacterial meningitis, four episodes of *S. suis* meningitis were identified in four patients (Table 1). The calculated annual incidence was 0.01 cases/100,000 adults. All four cases were associated with exposure to pigs or meat of pigs. None of the patients had other predisposing conditions for acquiring bacterial meningitis.

Three patients had symptoms for more than 24 h before presentation; none had received pre-hospital treatment with antibiotics. Patient 4 presented with more acute and severe disease, reflected by a shorter period of symptoms and a lower score on the Glasgow Coma Scale, as compared with the other patients. Three patients presented with a change in mental status (defined as a Glasgow Coma Score < 14). The triad of classic symptoms of bacterial meningitis, fever (defined as body temperature $> 38.5\,^{\circ}$C), neck stiffness, and a change in mental status was present in only one patient; none of the patients presented with rash. Two patients had hearing loss on presentation.

All patients underwent a lumbar puncture and results of CSF analysis were abnormal in all. There were a strong neutrophil predominance, and high CSF protein levels. Serum investigations showed abnormal platelet counts in three patients; two had a platelet count of $<100{,}000/mm^3$. Although C-reactive protein concentrations were high (normal value < 10 mg/L) in all, ESR was only mildly elevated in three patients. Gram stain of CSF showed Gram-positive cocci in all.

During clinical course, two patients developed focal neurologic deficits (Table 2). None of the patients suffered from severe septic shock with cardiorespiratory failure. At discharge the most common neurologic sequelae was hearing loss, occurring in three patients. Hearing loss was severe in all and resulted in a score of 4 on the Glasgow Outcome Scale (moderate disability).

Initial therapy consisted of monotherapy amoxicillin or penicillin in three patients; one patient was initially treated with ceftriaxone, and therapy was stepped-down to penicillin after results of culture became available. All patients received a 14-day course of antimicrobial therapy; none was treated with adjunctive dexamethasone.

Discussion

S. suis is a rare cause of bacterial meningitis in the Netherlands. In this prospective study four patients were identified over the 3.5-year period. All of these cases were associated with exposure to pigs. In the period subsequent to Dutch Meningitis Cohort Study, from April 1 2002 to December 31 2007, five additional patients with *S. suis* meningitis were identified by the Netherlands Reference Laboratory for Bacterial Meningitis (personal communication, L. Spanjaard). A previous study reported an estimated annual risk of developing *S. suis* meningitis among Dutch abattoir workers and pig breeders of approximately

Table 1 Presentation of four patients with *S. suis* meningitis

	Year	Age	Sex	Exposure to pigs	Other predisposing factors	Fever	Headache	Neck stiffness	Rash	Score on GCS	Focal cerebral deficits	Cranial nerve palsies
Patient 1	2000	64	M	Pig farmer	No	No	Yes	Yes	No	8	No	N.VII, N.VIII
Patient 2	2000	58	M	Pig farmer	No	No	Yes	Yes	No	12	No	No
Patient 3	2001	49	M	Pig farmer	No	No	Yes	Yes	No	15	No	N.VIII
Patient 4	2001	33	F	Butcher	No	Yes	Yes	Yes	No	5	No	No

	Serum WBC (10^9/L)	Platelet count (/mm^3)	ESR (mm/h)	CRP (mg/L)	CSF WBC (mm^3)	%PML	CSF protein (g/L)	CSF glucose (mmol/L)	CSF gram stain	Blood culture	CT head before LP
Patient 1	6.6	141,000	29	84	2341	90	5.8	1.7	Positive	Positive	ND
Patient 2	8.8	47,000	27	312	1200	96	7.7	0.6	Positive	Positive	Normal
Patient 3	23.7	84,000	70	318	213	97	2.3	1.5	Positive	Negative	ND
Patient 4	19.8	287,000	19	ND	4049	>99	3.0	3.1	Positive	Negative	Cerebral oedema

GCS, Glasgow Coma Scale; N., cranial nerve; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; CSF, cerebrospinal fluid; PML, polymorph leukocytes; CT, computed tomography; and ND, not done.

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Table 2 Clinical course and outcome of four patients with *S. suis* meningitis

	Deterioration of consciousness	Seizure	Cardiorespiratory failure	Focal neurologic deficits	Hearing loss	Degree of hearing loss	CT during admission	Score on GOS discharge	Sequelae discharge
Patient 1	No	Yes	No	Yes	Yes	Bilateral 70 dB	Normal	4	Hearing loss, palsy N.VI and N.VII
Patient 2	No	No	No	No	Yes	80 and 120 dB	Normal	4	Palsy N.VI, deafness
Patient 3	No	No	No	No	Yes	Not assessed	Normal	4	Hearing loss
Patient 4	No	No	No	No	No	—	Cerebral oedema	5	No sequelae

CT, computed tomography; GOS, Glasgow Outcome Scale; and N., cranial nerve.

3 per 100,000.[7] This risk is 3000 times higher than the incidence of *S. suis* meningitis in our nationwide cohort study.[6]

Patients with *S. suis* meningitis in our cohort presented with classic signs and symptoms of bacterial meningitis; although three patients presented without fever. All patients had CSF abnormalities with elevated CSF WBC and high protein levels. None of the patients presented with subcutaneous haemorrhages, but three patients had low platelet counts. A recent prospective case series described 151 Vietnamese patients with *S. suis* meningitis.[2] In this Vietnamese study, patients presented signs and symptoms of bacterial meningitis: headache in 94%, neck stiffness in 94%, fever (defined as $\geq 38\ ^\circ C$) in 98% and a decreased level of consciousness (defined as a score on the Glasgow Coma Scale < 15) in 69% of included patients. Only 9 of 151 (6%) patients had skin abnormalities.

Most striking was the high rate of severe hearing loss among our four patients. Three patients were discharged with moderate disability due to hearing loss or complete deafness. In the large Vietnamese cohort study, 93 of 140 (66%) evaluated patients with *S. suis* meningitis developed hearing loss.[2] The high rate of hearing loss in patients with *S. suis* meningitis has also been described in retrospective studies, with rates varying between 11 and 67%.[1,8–10] The rate of hearing loss is much higher compared with other causes of community-acquired bacterial meningitis.[6] The reason for this high rate is unknown. Animal models of *S. suis* meningitis should be developed to further elucidate the inflammatory processes in *S. suis* meningitis.

None of our four patients received adjunctive dexamethasone treatment. Recently, a randomized study comparing adjunctive dexamethasone therapy and placebo including 435 Vietnamese patients over the age of 14 years who had suspected bacterial meningitis was published.[11] A high proportion of included patients had meningitis due to *S. suis* (27%). A significant benefit in mortality by dexamethasone was seen in patients with confirmed bacterial meningitis (relative risk 0.43, 95% confidence interval 0.2—0.94). Overall, dexamethasone was associated with reduced deafness ($P = 0.02$) and this effect on hearing loss was most apparent in those with *S. suis* meningitis (7 of 57 patients given dexamethasone [12%], as compared with 20 of 53 given placebo [38%]; $P = 0.003$). Since the publication of the results of the European Dexamethasone Study,[12] guidelines recommend the routine use of adjunctive dexamethasone therapy in adults with suspected bacterial meningitis.[13,14]

A limitation of the current cohort study is that all patients underwent lumbar puncture. Lumbar puncture will be postponed in patients with septic shock and subcutaneous haemorrhages, both relatively common features of *S. suis* infection.[1] In these patients empirical antimicrobial therapy will be started and this will decrease the likelihood of culturing *S. suis*. None of our patients had typical subcutaneous haemorrhages and therefore, the incidence of *S. suis* meningitis might be underestimated.

In conclusion, physicians should be aware of the potential for occupational exposure with *S. suis*. The presentation of *S. suis* meningitis is similar to that of *S. pneumoniae* meningitis. This disease is associated with high rates of hearing loss and patients will benefit from adjunctive dexamethasone therapy.

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