

ISSN 1220-8841 (Print)  
ISSN 2344-4959 (Online)

ROMANIAN  
NEUROSURGERY

Vol. XXXVI | No. 2 June 2022

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DOI: 10.33962/roneuro-2022-039



# Post ventriculoperitoneal shunting *S. Maltophilia* Meningitis. An uncommon case

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## ABSTRACT

**Background:** Leptomeningeal inflammation caused by *S. Maltophilia* is rare. It is inextricably linked with prior antimicrobial therapy; prolonged ICU stays and antecedent neurosurgical intervention.

**Case description:** We describe a case of a 5-year-old male child with posterior fossa medulloblastoma with obstructive hydrocephalus who underwent ventriculoperitoneal shunt followed by suboccipital midline craniotomy and later presented with *S. Maltophilia* meningitis.

**Conclusion:** The overall mortality in the cases reviewed was 17 per cent. Inherent resistance to a wide array of antimicrobial agents with a simultaneously increasing number of cases poses a therapeutic challenge. Trimethoprim/sulfamethoxazole is recommended as empirical and as a definitive treatment in patients with *S. Maltophilia* infection. The optimal duration of therapy for *S. Maltophilia* meningitis is similar to the treatment of gram-negative bacillary meningitis, which is usually 2 weeks after the culture has been negative.

## INTRODUCTION

After *P. Aeruginosa*, *Baumannii*, *S. Maltophilia* is the third most common isolated non-fermenting aerobic Gram-negative bacilli.<sup>[1]</sup> *S. maltophilia* rarely causes meningitis.<sup>[2]</sup> It is particularly common among critically ill / immunosuppressed patients and is inextricably linked with prior antimicrobial therapy, prolonged ICU stays, prematurity, intracranial hemorrhages, malignancies, and antecedent neurosurgical intervention. It has recently come into the limelight in the last two decades owing to its increased pathogenicity and also because of marked antibiotic resistance.<sup>[3]</sup> We describe a case of a 5-year-old male child with posterior fossa medulloblastoma with obstructive hydrocephalus who underwent ventriculoperitoneal shunt followed by suboccipital midline craniotomy and later presented with *S. maltophilia* meningitis.

## CASE REPORT

A 5-year-old male came to A&E with complaints of headache and vomiting (3-4) episodes since the last five days. There was no history of

## Keywords

*S. Maltophilia* Meningitis,  
nosocomial meningitis,  
neurosurgery



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ISSN online 2344-4959  
© Romanian Society of  
Neurosurgery



First published  
June 2022 by  
London Academic Publishing  
[www.lapub.co.uk](http://www.lapub.co.uk)

fever, loss of consciousness, seizures, visual impairment, hearing loss, motor or sensory deficit. On presentation, neurological examination revealed Glasgow coma scale of E4V5M6, the pupils were equal and reactive, cranial nerve IX & X were involved (uvula was in the midline but gag reflex was impaired), and cerebellar signs (ataxia and dysdiadochokinesia) on the right side were positive. Non-contrast CT scan head showed posterior fossa hyperdense lesion arising from the floor of the fourth ventricle causing upstream dilatation of third and bilateral lateral ventricle causing obstructive hydrocephalus. MRI brain showed intra-ventricular solid cystic lesion arising from the floor of the fourth ventricle with no restriction on diffusion weighted sequence and elevated choline peak with reduced N-acetyl aspartate suggestive of medulloblastoma. The patient underwent right ventriculoperitoneal shunt via right Keen's point under general anaesthesia in view of obstructive hydrocephalus, papilloedema on direct fundoscopy (Frisen's grade II), and clinical signs of raised intra-cranial pressure. CSF analysis revealed no signs of meningitis and CSF for malignant cytology revealed no malignant cells. The patient was discharged thereafter.

Four weeks later, the patient presented to the A&E with complaints of altered sensorium, increased drowsiness, and recurrent episodes of vomiting. The Glasgow coma scale was E4V4M6, and pupils were equal and reactive. The shunt chamber was compressible and recoil was good. However, a repeat CT scan showed an increase in the tumour size with peri-lesional edema. The patient underwent suboccipital midline craniotomy with tumor excision under general anesthesia. Postoperatively, the patient was shifted on mechanical ventilation. An extubation trial was given but was not successful. Tracheostomy was done on post-operative day two in view of anticipated prolonged ventilator requirement, impaired gag reflex and pooling of chest secretions.

The Glasgow coma scale of the patient was E3VtM6. He developed fever 102.3°F and neck stiffness on post-operative day three. All routine investigations including blood, urine, tracheal, CSF cultures, and pro-calcitonin were sent for this patient. The patient's blood and urine cultures yielded no sign of bacteria. However, analysis of CSF revealed sugar 2.1mmol/L, protein 0.23g/L, WBC count 0.53 x 10<sup>9</sup> cells /L (78% neutrophils, 10%

lymphocytes, 10% mononuclear). Pro-calcitonin was significantly positive for this patient (>10). CSF gram staining showed gram-negative bacilli. Antibiotics were upgraded to meropenem and vancomycin from ceftriaxone and amikacin. The patient fever and neck stiffness responded partially to the antibiotics.

However, the child later experienced an episode of the seizure (generalized tonic-clonic), and he was shifted on a continuous mode of mechanical ventilation in view of a dip in the Glasgow coma score (E2VtM5). Clinical examination showed that the shunt chamber was non-compressible and recoil was absent. Repeat CT scan revealed dilated ventricles with ventriculoperitoneal shunt in situ. The shunt was removed (in view of meningitis) followed by external ventricular drain insertion and the tip was sent for the culture. Tip culture yielded *S. maltophilia*; which showed sensitivity to trimethoprim/sulfamethoxazole, ciprofloxacin, and amikacin. Meropenem and vancomycin were discontinued. The minimum inhibitory concentration interpretive breakpoints of trimethoprim/sulfamethoxazole were susceptible,  $\leq 2/38$  g/mL; and resistant,  $\geq 4/76$  g/mL for *S. maltophilia*. Trimethoprim/sulfamethoxazole, 8-12 mg/kg/day administered intravenously every 6 hours was added to the antibiotic regimen. The patient's fever abated 4 days later and her stiff neck resolved. The next sample analysis of CSF from the drainage fourteen days after starting trimethoprim/sulfamethoxazole revealed the following profile: sugar 3.0 mmol/L, protein 0.1g/L, WBC count 0.1 x 10<sup>9</sup> cells /L (30% neutrophils, 55% lymphocytes, 15% mononuclear). Repeat culture was consistent with *S. maltophilia*; ciprofloxacin (15 mg/kg q12hr) was added to the treatment regime. The external ventricular drain catheter was changed and after 7 days of the combination therapy, CSF culture was sterile. Antibiotics were continued for fourteen more days, which was followed by a right ventriculoperitoneal shunt insertion. However, the patient later developed bilateral basal pneumonia three weeks after recovering from meningitis, which led to acute respiratory failure. The patient could not be resuscitated and died thereafter.

## DISCUSSION

Leptomeningeal inflammation caused by *S. maltophilia* is rare. Medline search was conducted with the phrase "*S. maltophilia*" which revealed 1660

published articles. Of these, only twenty-nine cases including the present case were linked with a prior neurosurgical procedure, whereas the rest accompanied community-acquired meningitis.<sup>[4]</sup> The incidence of neurosurgery-related meningitis is less, complicating less than 1% of craniotomies.<sup>[5]</sup> *S. maltophilia* being a multi-resistant organism, meningitis due to it is often insidious and protracted in course when compared to spontaneously occurring Gram-negative meningitis.<sup>[6]</sup>

Fever was the most common presenting symptom in these cases. In patients with neurosurgery-related meningitis, the average CSF cell count was  $0.434 \times 10^9$  cells/L (range, 0.014 –  $1.77 \times 10^9$  cells/L), glucose was 32.94 mg/dl (range, 4.9 – 77 mg/dl) and protein was 916 mg/dl (range, 76 – 3400 mg/dl). The average age was 49.85 years (range, 28 – 73 years) in adults, 4.29 months in infants (range, 2–6 months), and 4.5 years in children (range, 4–5 years). Of all the 29 cases, six patients had an intracerebral haemorrhage, five patients had hydrocephalus (out of which two had congenital hydrocephalus), four were diagnosed with the intracranial-extra-axial lesion, four had intraventricular haemorrhage on the CT scan, three cases had extracranial lesion with brain metastasis, three patients had aneurysm as their initial diagnosis, and rest included recurring cholesteatoma, subdural hematoma, subarachnoid haemorrhage, and a posterior fossa tumor with hydrocephalus (current case). Out of 29 cases associated with neurosurgery-related meningitis, nearly 50 per cent of them were due to ventriculoperitoneal shunt and prior craniotomy respectively. In the remaining, nearly one-third (28 per cent) cases occurred in patients who underwent prior craniectomy and had external ventricular drain in situ. The remaining included three cases that had ommaya reservoir in situ, two were linked with prior endoscopic third ventriculostomy, and one with stereotactic aspiration.

Our patient also had a similar risk factor profile as reported earlier, i.e. neurosurgical procedures (ventriculoperitoneal shunt and craniotomy), ICU stays, exposure to broad-spectrum antimicrobial treatment (ceftriaxone, amikacin, meropenem, and vancomycin). The overall mortality rate in the cases reviewed was 17 per cent. Although up to 50 per cent of cases of shunt infections can be treated by using antibiotics alone, many authors recommend

removal of the prosthetic device followed by immediate or delayed insertion at a later stage.<sup>[7]</sup> Clinical data are limited regarding optimal therapy for infections caused by *S. maltophilia*. Nicodemo *et al.* suggested trimethoprim/sulfamethoxazole as the empirical choice for clinically suspected *S. maltophilia* infections and as the treatment of choice for culture-proven infections by this agent.<sup>[3]</sup>

It has been found that *S. maltophilia* is generally resistant to quinolones, aminoglycosides, and third-generation cephalosporins. Inducible beta-lactamase activity (a zinc-containing penicillinase [L1] and a cephalosporinase [L2]), efflux mechanism, aminoglycoside-modifying enzyme activity, biofilm formation, and expression of an outer membrane protein (OMP54) are responsible for its resistance to multiple antibiotics. Contemporary literature shows that resistance to trimethoprim/sulfamethoxazole is on the rise.<sup>[3]</sup> Tigecycline has demonstrated good in vitro activity against *S. maltophilia* strains.<sup>[3]</sup> New fluoroquinolones such as clinafloxacin, levofloxacin, moxifloxacin have shown superior in vitro activity compared to earlier quinolones. Gesu *et al.*, in an in vitro study comparing levofloxacin and ciprofloxacin against *S. maltophilia* 124 strains, confirmed the susceptibility rates of 85.5 and 58.9%, respectively, to levofloxacin and ciprofloxacin.<sup>[8]</sup> Although, ticarcillin-clavulanic acid combination demonstrated susceptibility against *S. maltophilia* above 70%,<sup>[3]</sup> further in vitro studies showed incomplete growth suppression followed by regrowth, mandating the requirement of additional controlled studies to further establish the true potential of this combination in *S. maltophilia* infections.<sup>[9]</sup> As per Zelenitsky *et al.*, combination therapy with ceftazidime, gentamicin, tobramycin, and ciprofloxacin showed a significant bactericidal effect when compared with the trimethoprim/sulfamethoxazole monotherapy alone.<sup>[10]</sup>

However, it is difficult to infer the treatment for *S. maltophilia* due to limitations in the number of strains tested, wide variety of antimicrobial combinations, and different method used in the in vitro studies. Although the synergistic action between drug combinations is evident, it is difficult to achieve the synergism in clinical drug concentrations.<sup>[3]</sup> The median duration of antibiotic therapy was 13 days (range 10–28 days). The optimal duration of therapy for *S. maltophilia* meningitis is

not known but we believe it to be similar to the treatment of gram-negative bacillary meningitis, which is usually 2 weeks after culture have been negative.<sup>[11]</sup>

### CONCLUSION

*S. maltophilia* is an evolving gram-negative bacilli with an armamentarium of antimicrobial resistance. Inherent resistance with a simultaneously increasing number of cases poses a therapeutic challenge. It is associated with prior neurosurgical procedures, long ICU stays, and previous exposure to antibiotic treatment. Empirical treatment should consist of vancomycin plus a third-generation cephalosporin (ceftazidime or cefepime) for 48-72 hours. Clinicians should be alerted for *S. maltophilia* in whom empirical therapy fails or in those with the risk factors mentioned earlier. Trimethoprim/sulfamethoxazole is the treatment of choice for culture-proven infections by this agent. Further in vivo studies are necessary to better delineate the efficacy of individual antimicrobial agents, combination therapy, and to establish the therapeutic outcomes for *S. maltophilia* meningitis.

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