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CASE REPORT

A rare case of acute transverse myelitis associated with *Staphylococcus aureus* bacteremia and osteomyelitis

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INTRODUCTION: Direct intramedullary infections are considered very rare. Only few reports of *Staphylococcus aureus* myelitis have been published.
CASE PRESENTATION: Our patient, a 79-year-old male, presented with a 2-day history of high-grade fever and high inflammatory markers and progressively developed tetraplegia during hospitalization. Lumbar puncture revealed cerebrospinal fluid pleocytosis and a spinal cord MRI revealed transverse myelitis at the level of C3–C5 and possible osteomyelitis of C5–T1. Two blood cultures were positive for methicillin-sensitive *S. aureus*. Despite control of the infection, there was no neurologic improvement.
DISCUSSION: The morbidity of infectious myelitis can be severe. Considering the rarity of *S. aureus* myelitis, experience gained from case reports is important. A brief review of the available literature is provided.

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INTRODUCTION

Acute transverse myelitis is a rare disease with a reported estimated annual incidence ranging from 1.34 to 6.2 per million.[1] The morbidity of the disease is significant, with ~30–50% of affected patients having poor neurologic outcome.[1–4] Back pain, rapid progression of symptoms and severe initial symptoms are poor prognostic factors.[2–4] In many cases, a cause for the disease is not identified (idiopathic transverse myelitis).[2,4] A history of antecedent infection is common.[1] Diseases associated with secondary transverse myelitis include infections, systemic inflammatory/autoimmune diseases (for example, systemic lupus erythematosus, Sjogren syndrome, antiphospholipid syndrome and systemic sclerosis), neurosarcoidosis, demyelinating disorders (multiple sclerosis, neuromyelitis optica, ADEM) and paraneoplastic syndromes. Other causes of myelopathy that may mimic transverse myelitis clinically include compressive myelopathy, vascular diseases (for example, spinal cord infarct), radiation myelitis, trauma and nutritional deficiencies (for example, dorsal column degeneration with B12/vitamin E/copper deficiency).[2,4,5]

A long list of pathogens have been reported in association with acute myelitis.[5] Typically, myelitis occurs after the resolution of the initial infection,[5] which suggests an immune-mediated effect. Direct bacterial myelitis is considered very rare. Examples of pathogens associated with transverse myelitis are herpes viruses, enteroviruses, flaviviruses, HIV, mycoplasma, *Borrelia burgdorferi* and *Mycobacterium tuberculosis*. We found only few published case reports describing acute myelitis associated with *Staphylococcus aureus* infection, which are summarized later in the discussion section (Table 2).

Experience gained from case reports/series is important for the recognition and management of very rare diseases. Here we describe a case of acute transverse myelitis associated with *S. aureus* bacteremia and osteomyelitis.

CASE REPORT

A 79-year-old male presented to the emergency department with a 2-day history of high-grade fever, for which he was prescribed cefuroxime. He also mentioned an acute upper back and neck pain 5 days before, for which he had visited the on-call emergency department and for which he was prescribed analgesics. The patient reported a history of hypertension, dyslipidemia and hyperuricemia. His medications included valsartan/hydrochlorothiazide, lercanidipine, atorvastatin and allopurinol.

At presentation to the emergency department, a brief neurologic examination revealed left-arm weakness and ataxic broad-based walking. A brain CT was normal and lumbar puncture was performed. The cerebrospinal fluid (CSF) analysis revealed 298 white blood cells (58% lymphocytes), glucose 71 mg dl^{-1} (reference range 45–80 mg dl^{-1}) (with a concurrent serum glucose of 160 mg dl^{-1}) and total protein 1738 mg dl^{-1} (reference range 20–40 mg dl^{-1}). Blood chemistry revealed a very high C-reactive protein (32 mg dl^{-1}) (normal < 0.5 mg dl^{-1}). He was initially treated empirically for meningoencephalitis with a combination of intravenous dexamethasone, ceftriaxone, vancomycin, ampicillin and acyclovir pending blood cultures and CSF cultures and PCR. During the following 48 h, the patient progressively developed flaccid tetraplegia, a bilateral C3 sensory level and respiratory failure (shallow breathing and inefficient cough) all pointing to acute cervical spinal cord injury. The patient was fully oriented and cranial nerve functions were intact. MRI of the brain and spinal cord were performed and revealed increased T2 signal of the spinal cord at the level of C3–C5, findings compatible with transverse myelitis, and possible osteomyelitis of C5–T1 with inflammation of the perivertebral soft tissues (Figure 1). The brain MRI revealed bilateral nonspecific white matter lesions suggestive of chronic microvascular ischemic disease. The patient satisfied the previously described criteria for acute transverse myelitis and high-dose IV methylprednisolone (1 g daily) was started,[6] but no response was seen. The CSF cultures and PCR were negative (see Table 1 for a summary of the investigations performed). The first two blood cultures came back positive for methicillin-sensitive *S. aureus* (MSSA). At day 4, after the above results were available, the initial empiric treatment was

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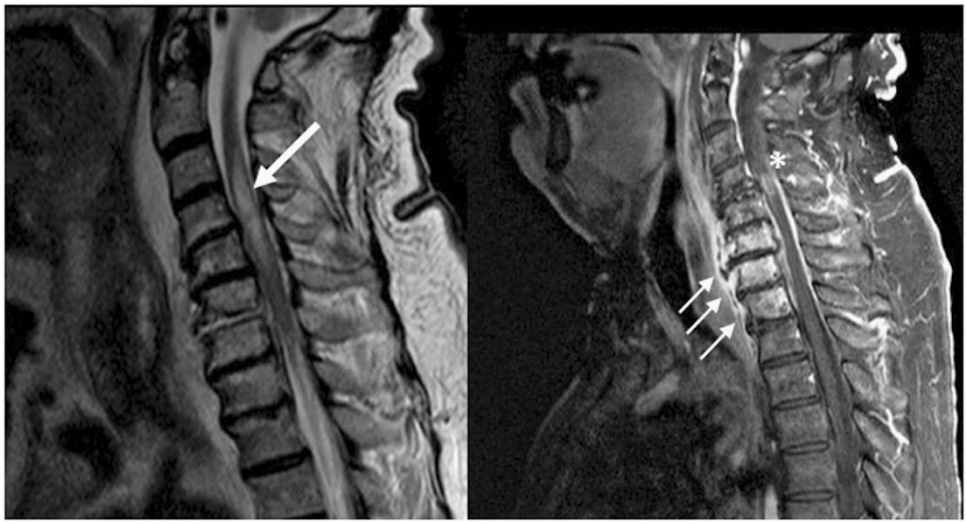

Figure 1. MRI demonstrating cervical myelitis and osteomyelitis. Left: T2-weighted image depicting a swollen spinal cord with increased intramedullary signal (arrow). Right: T1-weighted image with gadolinium showing gadolinium enhancement of the spinal cord (asterisk) and of the vertebral bodies and prevertebral tissue (arrows).

Table 1. Summary of the laboratory tests and imaging studies performed

Diagnostic tests/imaging	*Results*
Complete blood count and blood chemistry at first ED visit	9200 WBC, 7800 neutrophils per μl, 600 lymphocytes per μl, 0 eosinophils per μl, CRP not available
Complete blood count and blood chemistry at admission	WBC 8400 μl, 6700 neutrophils, 10.9% lymphocytes, 10 μl^{-1} eosinophils, hematocrit 34, hemoglobin 11.5 g dl^{-1}, platelets 234 000 μl^{-1}, CRP 32 mg dl^{-1}, ESR 108, glucose 166 mg dl^{-1}, urea 65 mg dl^{-1}, creatinine 1.11 mg dl^{-1}, total bilirubin 0.4 mg dl^{-1}, direct bilirubin 0.16 mg dl^{-1}, SGOT 45 U l^{-1}, SGPT 59 U l^{-1}, ALP 135 U l^{-1}, γ-GT 50 U l^{-1}, Na 135 mmol l^{-1}, K 4.2 mmol l^{-1}, normal urinalysis
CSF fluid analysis	298 WBC (58% lymphocytes, 35% polymorphonuclears, 7% monocytes), glucose 71mg dl^{-1} (with a concurrent serum glucose of 160 mg dl^{-1}) and total protein 1738 mg dl^{-1}
CSF cytology	Negative
CSF Gram stain and culture	Negative—two separate lumbar punctures
CSF PCR (National Reference Center for Meningitis in the National School of Public Health)	Negative for VZV, HSV1, HSV2, Neisseria meningitis, *Streptococcus pneumoniae*, *Haemophilus influenza* type b, *Listeria monocytogenes*, *Streptococcus* spp, *Haemophilus influenza* (non b), *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *M.tuberculosis*
Blood cultures	The first two blood cultures were positive for MSSA
Serology	EBV VCA IgG(+) IgM(−), CMV IgG(+) IgM(−), HSV1 IgG(+) IgM(−), HSV2 IgG− IgM−, anti-HIV(−), anti-HBsurface (−), anti-HBcore (−), HBsAg (−), anti-HCV (−), Coxsackie B IgG(−), IgM weakly positive, Echovirus IgG(−) IgM(−), Parvo IgG(−) IgM(−), *B. burgdorferi* IgG(−) IgM(+), *Rickettsia conorii* IgG(−) IgM(−), *Mycoplasma pneumonia* IgG(−) IgM(−)
Other lab tests	All normal: ACE level, ANA, C3c, C4, RF, serum protein electrophoresis and immunofixation, B12, IgG, IgA, IgM
Mantoux test	'0' mm
Brain MRI	Bilateral small deep white matter lesions (T2 hyperintense lesions without gadolinium enhancement) suggestive of ischemic microangiopathy
Spinal cord MRI	C3–C5 myelitis, C5–T1 osteomyelitis, perivertebral phlegmon (Figure 1)
Other imaging	Transesophageal ultrasound at day 8 negative for endocarditis, abdominal ultrasound without pathological findings. No findings suggestive of sarcoidosis from chest CT

Abbreviations: ACE, serum angiotensin-converting enzyme level; ANA, antinuclear antibodies; CMV, cytomegalovirus; CRP, C-reactive protein; CSF, cerebrospinal fluid analysis; EBV, Epstein–Barr virus; ESR, erythrocyte sedimentation rate; HSV1 and 2, herpes simplex virus 1 and 2; MSSA, methicillin-sensitive *S. aureus*; VZV, varicella zoster virus; WBC, white blood cells.

stopped and IV cloxacillin 2 g every 4 h was started and continued for 6 weeks.

Abdominal ultrasound and transesophageal echocardiography did not reveal a source for the infection. Because of the lack of neurological improvement and suspicion of paraspinal abscess by a second MRI of the spinal cord (at day 10), neurosurgical consultation was obtained. Surgical drainage was attempted (at day 14). However, no abscess was found after surgical exploration of the area. Tissue from the inflammatory paravertebral space and affected bones was obtained. Culture of the tissue was negative. The biopsy of the bone was compatible with osteomyelitis. Despite control of the MSSA infection (as evidenced by resolution of fever, rapid blood culture sterilization, negative culture of the paravertebral tissue and fall of inflammatory markers), there was no neurological improvement. Two months later, the patient remained tetraplegic, although a follow-up MRI at 1 month showed significant reduction of the pathologic intramedullary signal. He died a few months later.

DISCUSSION

We described a case of acute cervical myelitis associated with *Staphylococcus aureus* bacteremia and osteomyelitis. Despite

Table 2. Summary of previous case reports of *S. aureus* myelitis

	Patient	*Microbiology*	*Site of infection*	*CSF analysis*	*Treatment regimen*	*Outcome*
Our case	Male, age = 79 years	MSSA from two blood cultures. Negative CSF culture and PCR (patient already on cefuroxime for 2 days)	C3–C5 myelitis+C5–T1 osteomyelitis+perivertrebral phlegmon	WBC 298 μl^{-1} (58% neu, 35% lym, 7% monocytes), glu 71 mg dl^{-1}, serum glu 160 mg dl^{-1}, TP 1738 mg dl^{-1}	Main regimen: IV cloxacillin 2 gx6 for 6 weeks. See text for other antibiotics during hospitalization	Minimal neurological improvement
He *et al.*[9]	Male, age = 34 years	MRSA from pus, blood and CSF culture.	Psoas abscess, C2–C3 myelitis	WBC 5000 μl^{-1}, glu 11 mg dl^{-1}, TP 500 mg dl^{-1}	Abscess drainage+vancomycin for 10 days, followed by oral linezolid for 6 weeks	Partial neurologic improvement
Eduwu *et al.*[8]	Female, age = 26 years	MRSA from sputum and blood culture. Vancomycin Etest MIC = 2 mcg ml^{-1}. Negative CSF culture (day 4: patient on vancomycin)	Pneumonia, C3–T2 myelitis +prevertebral phlegmon+C5–T1 osteomyelitis	WBC 58 μl^{-1} (58% neu), glu 55 mg dl^{-1}, serum glu 136 mg dl^{-1}, TP 537 mg dl^{-1}	Initially vancomycin+levofloxacin, switched to daptomycin+linezolid at day 8 because of persistent bacteremia+gentamicin added at day 18 because of persistent bacteremia. Gentamicin was discontinued at 2 weeks and linezolid at 4 weeks. Daptomycin was continued for 8 weeks.	Complete response
Saini *et al.*[12]	Female, age = 79 years	MSSA from blood and CSF culture.	No primary site of infection. T11 myelitis	RBC 39, WBC 813, 95% neu, 5% lym, glu 75 mg dl^{-1}, serum glu 108 mg dl^{-1}, TP 280 mg dl^{-1}	IV crystalline penicillin.	No improvement
Kulkarni *et al.*[10]	Male, age = 12 years	MRSA from blood and abscess culture.	Pneumonia. C2–C4 myelitis, T1 osteomyeltis, cervical and thoracic paraspinal pyomyositis	WBC 470, 95% neu, 5% lym, glu 55 mg dl^{-1}, TP 400 mg dl^{-1}	Vancomycin for 6 weaks	Complete recovery
Kalkan *et al.*[14]	Female, age = 13 years	MRSA from bronchoalveolar lavage	Pneumonia. Diffuse myelitis	Not available	Myelitis symptoms developed during treatment with linezolid and responded to steroid therapy	Improvement
Friess *et al.*[15]	Female, age = 41 years	*S. aureus* from blood culture	C2–C7 myelitis. Brain abscesses	Not obtained	Gentamicin+oxacillin	Improvement

Abbreviations: CSF, cerebrospinal fluid; glu, glucose; lym, lymphocytes; MSSA, methicillin-sensitive *S. aureus*; MRSA, methicillin-resistant *S. aureus*; Neu, neutrophils; RBC, red blood cells; TP, total protein.

control of the infection with antibiotics, our patients showed minimal neurological improvement.

Whether the myelitis was the result of direct *Staphylococcus aureus* intramedullary infection or the result of another pathogenetic mechanism is unclear. The detection of MSSA in two sets of blood cultures, the clinical presentation of acute high-grade fever and the resolution of fever and inflammatory markers with antibiotic treatment suggest with a high level of certainty that the patient truly had an MSSA infection. The presence of osteomyelitis (confirmed by imaging and biopsy) close to the site of myelitis suggests the possibility of contiguous spread of the infection, although the affected vertebrae (C5–T1) were at a lower level than the level of myelitis (C3–C5). On the other hand, MSSA was not isolated from CSF (both CSF cultures and PCR were negative) or culture of the tissue biopsies (which, however, were taken late in the course of antibiotic treatment), which points to alternative mechanisms (for example, parainfectious immune-mediated myelitis[1,5]).

Alternative causes of myelopathies were ruled out. Compressive myelopathy was excluded by MRI imaging and neurosurgical consultation and surgical exploration. A spinal cord infarct would have a more acute, rather than progressive, presentation and a vascular distribution of neurological findings on clinical examination (anterior spinal artery syndrome and posterior spinal artery syndrome), although atypical cases have been described. There was no evidence in favor of the systemic diseases associated with transverse myelitis. MRI imaging of the brain and spinal cord and the clinical presentation were not compatible with CNS demyelinating disorders. Findings from lab tests and imaging are summarized in Table 1.

Few cases of myelitis associated with *S. aureus* have been previously published.[7–15] Table 2 summarizes findings from previous case reports. Of note is the fact that *S.aureus* myelitis has been described even without contiguous spread (for example, ref 12). As in our case, in most other cases the cervical spinal cord was involved. High protein in the CSF was noted in all cases with available CSF analysis ($>400\ mg\ dl^{-1}$ in three of four cases). Our patient had a much higher CSF protein. Other causes of very high CSF protein include some cases of purulent meningitis, tuberculous meningitis, CNS tumors and blocked CSF flow (usually due to compression by tumors or abscess).[16] All the above causes were ruled out in our patient (negative CSF PCR for tuberculosis, no suggestion of CNS tumor or abscess by imaging, negative CSF cytology). A block of the normal CSF flow due to severe spinal cord and meningeal swelling, and inflammation in combination with a herniated disk may explain the finding in our patient.

Our patient had a very poor neurologic outcome. Considering the rapid sterilization of blood cultures, the lack of isolation of MSSA from the prevertebral phlegmon, and the resolution of fever and inflammatory markers, the lack of improvement is unlikely to be due to antibiotic treatment failure, although inadequate eradication of an intramedullary focus of infection cannot be excluded. Potential explanations for the lack of response to antibiotics are the following: (1) Delayed initiation of appropriate antibiotic treatment with irreversible spinal cord damage. The patient had presented to the on-call emergency department 5 days before admission to our hospital. The only clues for infection from the available laboratory tests at that time was a neutrophilic predominance and severe eosinopenia (similar findings at presentation to our hospital). A CRP measurement was not available at the first visit; (2) our patient was much older than previously described successfully treated patients; (3) Immune-mediated transverse myelitis is possible, although there was no response to high-dose IV methylprednisolone; and (4) Cloxacillin has poor lipid solubility and CSF penetration may be insufficient.[17] Furthermore, poor penetration of cloxacillin into abscesses of the central nervous system has been previously described.[18] Failure of IV crystalline penicillin was also noted in a previous report of MSSA myelitis,[12] supporting the hypothesis that penicillins may be a poor choice as monotherapy for bacterial myelitis. Nevertheless, successful treatment of MSSA central nervous system infections with high-dose cloxacillin has been described.[19]

In conclusion, myelitis associated with *Staphylococcus aureus* has been very rarely reported. Because of the potential significant morbidity of the disease associated with poor neurologic outcome, experience gained from case reports is important. Because of their poor CNS penetration, penicillins may not be an appropriate choice for monotherapy, as demonstrated by our case and a previous case of MSSA myelitis. Agents with better central nervous system penetration such as linezolid, levofloxacin and daptomycin,[20] may be a better choice. Treatment regimens previously used successfully in *S. aureus* myelitis are shown in Table 2.

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COMPETING INTERESTS

The authors declare no conflict of interest.

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