Case Reports

Staphylococcal Septicaemia Associated with Peripheral Neuropathy in Three Different Clinical Settings

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Abstract
Among the various etiologies of peripheral neuropathy, S. aureus is a rare cause that is not even mentioned in standard textbooks. Here we like to report three clinical scenarios where patients with different manifestations of S. aureus infection developed peripheral neuropathy presenting as quadripareisis, which subsided gradually with control of infection and supportive care. No other known causes of peripheral neuropathy were present in these cases.

Introduction
Although Staphylococcus aureus (S. aureus) affects various organ systems of body, involvement of peripheral nerves is extremely uncommon and is virtually unknown.1 There are isolated case reports of Linezolid (commonly used in MRSA and VRSA infections) causing peripheral neuropathy but it is not an established adverse effect of this drug.2 Hence, peripheral neuropathy presenting as quadripareisis in three different settings of S. aureus infection could be a valuable learning in one’s clinical experience.

Case Report I
Presenting with high grade fever for ten days and vesiculo-bullous lesions all over the body (sparring mucous membranes) including palms and soles three days after appearance of fever, a 20-year-old male, developed sudden onset weakness of both lower limbs (proximal more than distal) which progressed to trunk and upper limbs on seventh day of fever. There were no history of sensory symptoms, bladder and bowel involvement, stiffness, flexor spasms, fasciculations, diurnal variation and cranial nerve involvement. Patient denied any history of similar illness in the past or any history of diarrhea or vaccination in the recent past. Family history was non-contributory.

General examination revealed a very-sick-looking febrile normotensive patient with tachycardia, tachypnea, mild pallor, icterus along with diffuse erythematous, vesico-bullous lesions with desquamation in some of them. CNS examination revealed preserved higher mental, cranial nerve, cerebellum and sensory function, as well as hypotonia with diminished motor power in all the four limbs with predominant affection of proximal (grade 3/5) group of muscles than distal (grade 4/5) ones and absent deep tendon reflexes with bilateral flexor plantar response. GI system examination revealed a soft tender 2cm enlarged liver with no evidence of splenomegaly or free fluid. Other relevant systemic examination findings were essentially normal.

Investigations revealed the following results: Hb 8.2 g/dl, TLC 25,500 (N83%, L14%, E2%, M1%, B0%), Mantoux test and antibodies to HIV-1 and 2, HBsAg, IgM anti-HCV and anti-GM1 antibodies were negative. Blood culture was positive for Staphylococcus aureus which was sensitive to vancomycin and linezolid only. CSF study showed 70 cells, 70% mononuclear and 30% polymorphs, protein 79 mg%, sugar 73 mg%, Cl- 123 meq/l. CSF culture (ordinary and BACTEC) showed no growth. Chest X-ray was normal. USG abdomen study was normal except for mild hepatomegaly. NCV showed absent F wave in tibial, peroneal and left ulnar nerves along with normal H reflex. EMG study revealed no spontaneous activity, normal interference, normal QMUP with reduced polyphasic amplitude in some of the sampled muscles suggestive of mixed neurogenic and myogenic pattern.

After hospitalization, patient’s general condition was poor and he was mildly dyspneic. Antibiotic combination of ceftriaxone (2 gm IV BD), amikacin (500mg IV BD) and linezolid (600 mg IV BD) was started soon after sending the blood and CSF cultures. Fever responded in about 10 days. Linezolid and ceftriaxone was continued in the same dose for another three weeks as per blood culture report. The rash started changing colour and consistency by the third day and took about four weeks to normalize. The power started improving by tenth day, however the DTRs were absent until six weeks. Incidentally his subsequent Hb was found to be 5.5 g/dl due to iron deficiency. He was transfused three units of packed cells and maintenance oral iron therapy was given. Repeat blood culture after two weeks of antibiotic therapy was found to be negative. He was discharged with a diagnosis of staphylococcal sepsis complicated with polyradiculoneuropathy and iron deficiency anemia.

Case Report II
The second patient was 26-year-old male farmer who presented with pain, swelling and stiffness of the neck for ten days, high grade fever and headache for last seven days and weakness of all four limbs since last one day. The weakness started suddenly from left upper limb then right upper limb progressed to involve trunk and lower limbs in the same day and proximal involvement was more than distal.

There were no h/o recent vaccination, diarrhea, UTI, LRTI, skin rash, loss of consciousness and seizures. There were no h/o sensory symptoms or bladder bowel involvement, nor any h/o fasciculations, diurnal variation or cranial nerve involvement. There were no previous similar complaints and no significant family history.
General examination revealed a very-sick-looking normotensive febrile patient with tachypnoea, tachycardia and mild pallor. There was a diffuse tender, erythematous, inflamed swelling, soft-to-firm in consistency without any fluctuation at the right lateral aspect of the neck. Posterior pharyngeal wall was congested and tonsils were enlarged.

Relevant CNS examination findings revealed preserved higher mental, cranial nerve, cerebellum and sensory function, slightly dysarthric speech, neck rigidity and positive Kernig’s sign. There was no spinal tenderness or deformity but hypotonia with diminished motor power in all the four limbs with predominant affection of proximal (grade 3/5) group of muscles than distal (grade 4/5) ones. Planter was bilateral flexor and all the deep tendon reflexes were absent. Examination of other systems was essentially normal.

Investigations revealed Hb 11.1 g/dl, TLC 27,000 (N 92%, L 5%, E 2%, M 1%, B 0%). Fasting blood sugar, renal and liver function tests were normal. Mantoux test and antibodies to HIV-1 and 2, anti-GM1 antibodies were negative. Blood culture was positive for Staphylococcus aureus. Throat swab showed no growth in 48 hrs. CSF study showed 35 cells, 20% mononuclear and 80% polymorphs, protein 73 mg%, sugar 77 mg%. CSF culture (ordinary and BACTEC) showed no growth. CSF ADA was 9.88 U/L. Ultrasonography of abdomen and Chest X-ray was normal. NCV study was suggestive of mild acute demyelinating polyradiculoneuropathy. EMG study result was similar to the first case.

Soon after hospitalization, blood cultures, CSF and throat swab were sent and Linezolid 600mg IV BD and Ceftriaxone 2gm IV BD were started along with supportive measures. Neck swelling subsided by the first week and headache disappeared within a few days but continuous high grade fever was converted into an evening rise of temperature up to 100°F that persisted for next two weeks. Quadriplegia persisted for next one month and patient started improving with physiotherapy and supportive measures. He was discharged with a diagnosis of staphylococcal sepsis complicated with polyradiculoneuropathy presenting as quadriplegia.

Case Report III

A 19-year-old male was admitted with complaints of mid back pain for two weeks, weakness of both upper and lower limbs with urinary retention for 5 days and shortness of breath for two days. The patient was apparently well two weeks before admission when he developed dull aching pain in the mid back region with spinal tenderness around mid-dorsal spine. After about ten days following pain, he developed acute onset ascending type of weakness of both lower limbs and became bed-ridden in next two days accompanied by urinary retention and constipation. Two days before admission he had mild shortness of breath with wheezing, cough with scanty sputum and hoarseness of voice since day before admission. There were no history of fever, loss of consciousness, headache, vomiting or any cranial nerve involvement.

On examination, he was conscious and oriented. His pulse was 130/min, BP was 100/60, respiratory rate 34/min with regular shallow breathing. He was febrile with temperature of 100°F and mild pallor was present. On neurological examination, his higher mental functions and cranial nerves were found to be normal. Neck stiffness and Kernig sign were absent. Spine and cranium were normal except for tenderness over the D6 spine. Power was grade 1/5 on the left side and grade 3/5 on the right side with hypotonia. Plantar was bilaterally non-responsive with absent cremasteric, abdominal and lower limb deep tendon reflexes. Sensory and cerebellar examinations were normal.

Chest auscultation revealed bilateral coarse crackles and diminished vesicular breath sounds in all areas. Other systemic examinations were essentially normal.

Investigations revealed Hb – 9.8g/dl, ESR- 72 mm in 1st hour, TLC – 24,900 /cmm (86% polymorphs) on admission (which reduced to 10,000/cmm before discharge), platelet count – 400,000/ cmm. Renal and Liver function tests were normal as were serum electrolytes, lipid profile and urine routine examination. HIV 1 andII (ELISA), HBsAg, Sputum AFB and Mantoux test were all negative. Chest X-ray was suggestive of multiple pneumatoceles with fluid containing cavity in both the lung fields but more on the left side. CECT Thorax revealed similar finding (Figure 1).

Sputum Gram stain and Blood culture were positive for Staphylococcus aureus, sensitive to linezolid and vancomycin. CSF study, done after a week of admission, showed cell count of 10 with lymphocytes 90%, glucose 35 mg/dl, protein 80 mg/dl and ADA 18 U/dL.

Interestingly, the NCV study was suggestive of acute inflammatory demyelinating polyneuropathy; however MRI Dorsal spine revealed increased signal intensity of body of D6 vertebrae mainly in STIr image without any signal changes of adjoining disc, probably of infiltrative etiology (Figure 2).

Patient was started on Inj. Linezolid 600 mg I.V BD along with Inj. Ceftriaxone 2gm I.V. OD. He started improving after about two weeks of therapy, bladder function recovered earliest, shortness of breath diminished, chest findings improved and he slowly started to regain his power in his lower limbs.

A repeat MRI dorsal spine was done which showed resolution of the previous changes in the D6 vertebra with two weeks of anti-staphylococcal antibiotics (Figure 3).

He was discharged with a diagnosis of staphylococcal septicemia with diffuse pulmonary involvement and acute demyelinating polyradiculoneuropathy and is kept on regular follow-up.

**Discussion**

Although S. aureus infection can invade almost all organs including soft tissues, lungs, heart, gastrointestinal, musculoskeletal system and CNS, peripheral neuropathy due to S. aureus bacteremia is almost unknown. Only three cases of motor axonal neuropathy related to S. aureus endocarditis has been reported so far. The first case was of a 13-year-old boy with infective endocarditis caused by S. aureus in whom severe polyneuropathy developed during hospitalization.1 The second case was of a 65-year-old woman who had quadripareis and aseptic meningitis revealing S. aureus endocarditis. The third case is a recently reported case of a 74-year-old man who developed GBS following S. aureus endocarditis affecting aortic valve.7 Other case reports of Staphylococcus infection with neurological involvement include a case of isolated and transient splenial lesion of the corpus callosum associated with disseminated Staphylococcus aureus infection and acute transverse myelopathy associated to S. aureus septicemia.8

This case series depicting polyradiculoneuropathy, without any history of diabetes mellitus in three different clinical settings of staphylococcal septicemia are among the early few cases reported globally so far and may be the first so, from India. Pathophysiology underlying this unusual manifestation is not
yet clear, more detailed study of these cases are necessary in this aspect, but conjecture for peripheral motor neuropathy could be toxin mediated as shown in several research studies. Neurotoxicity has been shown to be property of alpha-hemolysin toxin causing demyelination of myelin sheath in both rabbit and murine models of infection with potential role of anti-staphylococcal beta-hemolysin antibodies in human model with neurological disease. More-than-one-month usage of Linezolid may be associated with peripheral neuropathy which is usually sensory and occasionally painful. But here in this case series, Linezolid was initiated after the onset of quadriplegia and the patients had pure motor neuropathy. All the three cases improved with antibiotic therapy and quadriplegia subsided with control of the infection. In the previously reported few cases, the neuropathy responded to control of infection which lead us to assume that staphylococcal toxin has a definitive role in the same.

Hence, in all probabilities, it can be assumed that the etiology of polyradiculoneuropathy in the above-reported cases is due to staphylococcal septicemia. Thus one should be aware of this rare complication of the common staphylococcal infection seen in our hospitals. Effective control of infection with antibiotics, preferably according to culture sensitivity reports, is important as prolonged use of Linezolid may further accentuate pre-existing peripheral neuropathy.

References