

Complicated Pneumoniae and Disseminate Infection Caused by *Streptococcus constellatus* in two Children from Turkey

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Abstract

Streptococcus constellatus is a member of *Streptococcus anginosus* (SAG) group. They are members of oropharyngeal, gastrointestinal and genitourinary flora, however they can be pathogenic. These microorganisms cause pyogenic invasive infections with their tendency to abscess formation. The infections due to these organisms may be more serious than other streptococcus species. A significant number of SAG infections are polymicrobial and frequently associated with gastrointestinal flora and obligatory anaerobes. Two children who developed necrotizing pneumonia and disseminated infection due to *S. constellatus* were presented in this case report. Both cases were treated with long term antibiotic treatment and surgical interventions. In cases of *S. constellatus* growth it should not be considered as a part of normal flora. Given the tendency for dissemination of this microorganism, the patients should be screened for other foci of infection. Since infections are frequently polymicrobial and associated with anaerobes, antibiotics effective against anaerobes should be used as a part of the treatment regime. Surgical intervention in addition to antibiotic therapy is frequently required for treatment of infections. Since they may cause abscess formation, a longer duration of antibiotic treatment is required.

Keywords: *Streptococcus constellatus*; children; sinusitis; pneumoniae

Introduction

S. anginosus group bacteria (also known as *Streptococcus milleri* group) include *S. anginosus*, *S. intermedius* and *S. constellatus*. They are members of oropharyngeal, gastrointestinal and genitourinary flora, however they may cause adjacent or distant infections following mucosal injury. The infections due to these organisms may be more serious than other streptococcus species. The most important feature of this group of microorganisms is that they may cause pyogenic infections in association with abscess formation [1-3].

Two children from Aegean region of Turkey who were referred to a university hospital with necrotizing pneumonia and disseminated infection due to *S. constellatus* were presented in this case report.

Case Reports

Case 1

Fourteen-year-old male admitted with the complaints of fever for the last one week, erythema and swelling in both eye lids. The patient had complaint of cough for 1 month, however erythema and swelling of both eye lids and fever started after he hit his head. Antibiotic and analgesic were given in out-patient service. The patient admitted to our hospital since his complaints didn't improve and somnolence was added.

He had no known disease, prior medical history was unremarkable. Physical examination revealed 39,6°C of fever, somnolence and his oropharynx was hyperemic. There were swelling and erythema of both eyelids. He had neck stiffness.

Laboratory examination was as follows; WBC: 21,400/mm³ (neutrophile predominance), Hb: 10,3 g/dL, platelet: 297,000/mm³, CRP:171 mg/L (0-5 mg/L), ESR: 73 mm/hr. Blood biochemistry was normal. Lumbar puncture was traumatized. A glucose level of 62 mg/dL

(blood glucose: 99 mg/dL), total protein 72 g/dL, leucocyte count $10/\text{mm}^3$, erythrocyte count $2880/\text{mm}^3$ (traumatized) were found on CSF examination. Ceftriaxone and vancomycin treatment was started. Paranasal and orbital CT examinations showed periorbital soft tissue swelling and pansinusitis (Figure 1a). Brain MR imaging revealed epidural collections located at left frontotemporal extraaxial space 1 cm at the thickest part with peripheral contrast enhancement (Figure 1b). MR angiography revealed thrombosis of superior sagittal sinus and sinus rectus and extensive collateral vascular structures (Figure 1c). Bilateral peripherally enhanced periorbital collections with central liquefaction were seen on orbital MRI (Figure 1d).

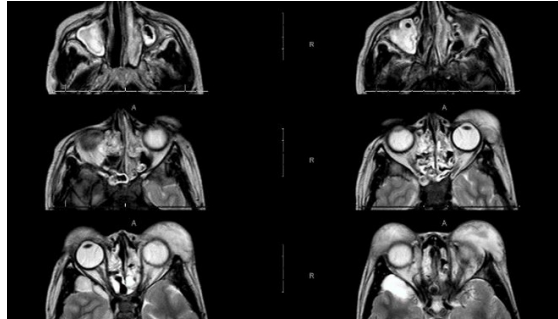


Figure 1a: Periorbital soft tissue swelling and pansinusitis on paranasal and orbital CT

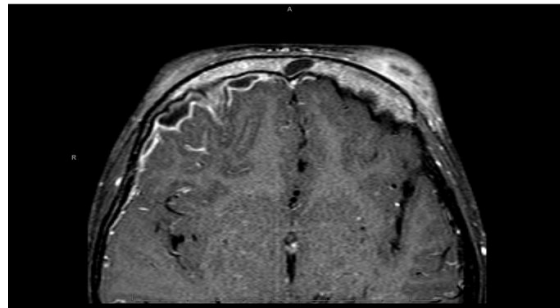


Figure 1b: Peripherally enhanced epidural and subdural collections at extraaxial space on contrast enhanced cranial MRI

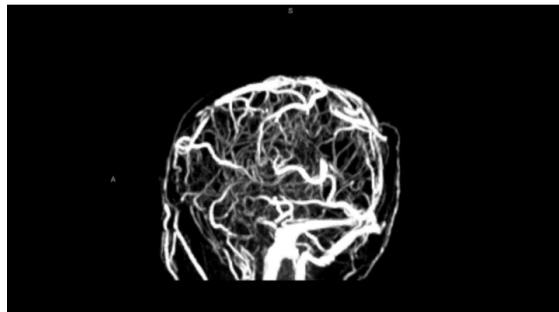


Figure 1c: Thrombosis of superior sagittal sinus and sinus rectus and extensive collateral vascular structures on MR angiography

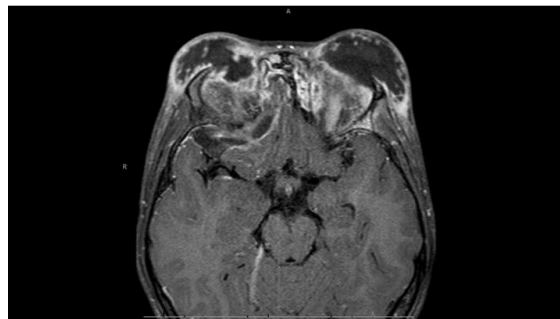


Figure 1d: Bilateral peripherally enhanced periorbital collections with central liquefaction on orbital MRI

Subdural and epidural empyema was drained by neurosurgery and purulent collection on each eyelid was drained by ophthalmology. Metronidazole and clexan were added to patient's therapy. *Streptococcus constellatus* grew on cultures of samples of epidural and subdural empyema and vancomycin treatment was stopped and ceftriaxone and metranidazoel treatment continued. The isolates were identified to the species level using Vitek 2 GN cards by VITEK 2 Compact system (bioMerieux,France). It was not possible to study sensitivity test for the patient because of absence of Etest in the laboratory at that time.

There was no growth on blood and CSF cultures. A chest radiogram obtained to investigate infection source in other regions revealed consolidation at left upper lobe. Thorax CT showed cavitary pneumonia at apicoposterior segment of right upper lobe, bilateral pleural effusions and compressive atelectatic changes (Figure 2). Abdominal ultrasonography and echocardiography were normal. Anti HIV and tests for immune deficiency were negative.



Figure 2: Thick walled, 3X3 cm cavitation with air-fluid levels at apicoposterior segment of upper lobe of right lung, bilateral pleural effusion and compressive atelectatic areas on thorax CT

On follow up of patient fever subsided on the 6th day of treatment, acute phase reactants and leucocyte count decreased, following 6 weeks of intravenous treatment patient was discharged with oral amoxicillin-clavulanate treatment.

Cranial MRI was performed 2 months later to ensure that the preexisting lesions were completely resolved. There was minimal subdural hemorrhage and no pathological enhancement and there was regression of the thrombus with permission to flow in superior sagittal sinus, sinus rectus and both transverse sinuses compared to previous examination and clexan was stopped. A chest radiogram was normal. Oral amoxicillin-clavulanate treatment was stopped 2 months later. Patient has been followed for 2 years in outpatient clinics with no problem. Informed consent was received from the family for publication.

Case 2

A 16 year-old male admitted with complaints of cough for 20-25 days, nasal discharge, fever and respiratory distress for the last 2-3 days.

Medical history revealed that he has been followed with the diagnosis of autism since he was 6 years old, cardiopulmonary resuscitation was applied for cardiac arrest due to electric shock 3 years ago, right lower lobe lobectomy was done for necrosis of right lower lobe, tracheostomy tube was inserted and percutaneous endoscopic gastrostomy (PEG) tube was placed and he lived bedridden for 3 years.

Fever was 39 °C of fever, general condition was moderate, he was conscious, cachectic and he had tracheostomy and PEG tube, tachypneic (respiratory rate 45/minute) on his physical examination. No respiratory sound was heard on right lung and there were wide spread secretion rales at left lung. He had motor and mental retardation and had contractures at hands and foot. At his laboratory examination revealed that WBC: 17,500/mm³ (neutrophile dominance), Hb: 8, 5 g/dL, platelet count 263,000/mm³, CRP: 322.1 mg/L (N: 0-5 mg/L), BUN: 24, 4 mg/dL, creatinine: 0, 57 mg/dL, other blood biochemistry and blood gas analyses were normal. Right costaphrenic sinus was blunted and there was pleural effusion at right side on PA chest radiogram. Thorax CT confirmed right pleural effusion and 1700 mL purulent material was drained by thoracentesis and a chest tube was inserted (Figure 3). Ceftriaxone and vancomycin treatment was started and patient was admitted to pediatric intensive care unit. There was no growth on blood and urine cultures, *Streptococcus constellatus* grew on pleural fluid culture. The isolate was identified to the species level using Vitek 2 GN cards by VITEK 2 Compact system (bioMerieux,France). The MICs of penicillin, cefotaxime, erythromycin, clindamycin, tetracycline, cefotaxime, levofloxacin, and linezolid were determined by Etest method (bioMerieux, France). Because it was resistant to cefotaxime, ceftriaxone was stopped and meropenem was started.

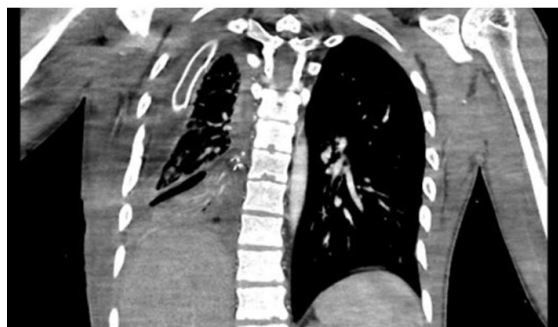


Figure 3: Atelectatic changes at right lung, superior basal segment of lower lobe and pleural effusion at right hemithorax on thorax CT

Following removal of chest tube, respiratory distress developed (on day 15) and pneumothorax was detected and bronchopulmonary fistula repair was performed by thoracotomy. No additional source of infection was found on abdominal ultrasonography, echocardiography and cranial imaging findings. During follow up fever and acute phase reactants subsided and following 6 weeks of parenteral therapy patient was discharged with oral clindamycin treatment (it was sensitive to clindamycin). Patient has been followed for 12 months in outpatient clinics with no complaints. Clindamycin was stopped 1 month later. Informed consent was received from the family for publication.

Discussion

S. constellatus cause serious pyogenic invasive infections with their tendency to abscess formation and dissemination [1,2,3]. Although the exact mechanism of their tendency to form abscess is unknown, it is reported that they cause tissue necrosis and abscess formation by their polysaccharide capsule, extracellular enzymes (hyaluronidase, deoxyribonuclease, chondroitin sulphatase) secreted by them and their synergistic effect with anaerobic bacteria [4-6].

The main risk factors for SAG infection are dental procedures, congenital anomalies, diabetes, inflammatory bowel disease, immunosuppression and trauma. However, infection can also occur in healthy people. Risk factors for SAG were present in only 18% of 180 children with SAG infection between April 1992 - December 1998 and trauma was present in 3% of patients [1]. There was a history of head trauma in our first patient and disseminated infection might have been occurred by trauma. The other patient was a bedridden child with malnutrition, and he had tracheostomy and PEG. Complicated pneumonia developed probably secondary to aspiration of oropharyngeal secretions in this patient.

SAG organisms cause suppurative infections in all anatomic regions. In the studies evaluating the correlation between anatomic location of infection and species, it was shown that *S. intermedius* was more common in central nervous system and hepatic infections, *S. constellatus* was more frequent in pulmonary infections, *S. anginosus* was isolated frequently in blood, gastrointestinal, genito-urinary infections and soft tissue infections. However, this association was not detected in all studies [1,2,7,8]. Complicated pneumonia was the only finding in common in our cases. However, the first case had disseminated *S. constellatus* infection. In literature review, there was no case having complicated sinusitis and necrotizing pneumonia due to *S. constellatus* in the child group with no underlying disease, with these features our first case is unique in literature.

Sinusitis bacteriology has been changed with application of pneumococcal vaccine. SAG is the most common bacterial pathogen (28%) reported in childhood rhinosinusitis cases with intracranial complication. It was reported that sinusitis due to SAG caused more severe intracranial complications and more frequent neurological deficits, associated with more neurosurgical interventions and required longer antibiotic therapy compared to other bacterial pathogens causing sinusitis [9-11]. The first case had sinusitis with both periorbital and orbital and intracranial complications compatible with literature. Abscesses at eyelids and empyema at epidural and subdural spaces were drained and long term intravenous antibiotic therapy was given. Fortunately no neurological sequelae developed in the patient.

In a study evaluating CT findings and clinical features in 15 children with pleural pulmonary infection due to SAG microorganisms, it was found that CT frequently showed complex pleural effusions and pulmonary abscess, invasive procedures were usually required for effective treatment and such patients had prolonged hospitalization [12]. Complicated pneumonia was present in both of our cases similar to literature. There were necrotizing pneumonia and pleural effusion in the first case and patient recovered by medical therapy without any intervention. Pleural empyema was present in the second case and the patient underwent surgical intervention initially for empyema and later for bronchopleural fistula developed during follow up.

It has been reported that a significant number of SAG infections (12.5-51%) was polymicrobial. Organisms encountered together with SAG are frequently gastrointestinal flora and obligatory anaerobes. SAG infections with anaerobes was found to have more severe course [1,2,8]. Since the association of SAG microorganisms with anaerobes is frequent, antibiotics which are effective against anaerobes should be used in the treatment of infections caused by these organism. We also used anaerobic antibiotics to treat both patients (metronidazole, meropenem).

Although sensitivity may change from country to country, even in different regions of the same country, SAG is usually sensitive to penicillin, ampicillin and ceftriaxone, sensitivity to tetracycline, clindamycin and erythromycin is variable [1,2,8]. All of the 78 SAG microorganisms isolated in Poland between 1996-2012 were sensitive to penicillin whereas 9% was resistant to macrolides and majority were resistant to tetracycline [13]. Infective endocarditis cases due to penicillin resistant *S. constellatus* were reported in adults [14,15]. In addition, penicillin resistance was not reported in children with SAG infection [1]. Sensitivity could not be studied in our first case. *S. constellatus* was resistant to penicillin and cefotaxime in the second case. To the best of our knowledge, a case of cefotaxime resistant *S. constellatus* has not been previously reported. Therefore, therapy should be guided by the results of culture and antimicrobial susceptibility testing.

In conclusion, in cases of *S. constellatus* growth it should not be considered as a part of normal flora. Given the tendency for dissemination of this microorganism, the patients should be screened for other foci of infection. Surgical intervention in addition to antibiotic therapy is frequently required for treatment of infections. Since they may cause abscess formation, a longer duration of antibiotic treatment is required. Because infections are frequently polymicrobial and associated with anaerobes, antibiotics effective against anaerobes should be used for treatment. Antimicrobial susceptibility testing is helpful in guiding therapy.

Conflict of interest. None of declare.

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