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Case Report

A Rare Case of Orbital Cellulitis with Tolosa-Hunt Syndrome Caused by Methicillin-Resistant *Staphylococcus aureus* (MRSA): a Case Report

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ABSTRACT

Background: Orbital cellulitis is an active infection of the orbital soft tissue posterior to the orbital septum, which can cause Tolosa-Hunt Syndrome (THS) complication. **Purpose**: We reported a child with orbital cellulitis with THS complication caused by methicillin-resistant *Staphylococcus aureus* (MRSA). **Case**: A two-year-old girl complained of swelling and pain in the left eye accompanied by fever. In nasal region and left eye showed multiple erythema patches with geographic shape, size 1x2cm - 4x5cm, unclear border, erosion with sizes 0.5x1cm - 1x1.5 cm size covered with blackish crusts. After several days of hospitalization, she complained of proptosis and pain in moving her eye. We did the magnetic resonance imaging (MRI) scan examination, which showed a mass size of 2.2 x1.1 x 0.9 cm in a left intraconal orbital and dilation of the left-sided cavernous sinus. The blood culture showed MRSA bacteria. She was diagnosed with orbital cellulitis with THS complication and showed a good response with Meropenem, Methylprednisolone, cendo lyteers eye drops, levofloxacin eye drops, and gentamicin eye ointment. **Discussion**: Orbital cellulitis presents as ill-defined erythema, edema, warmth, and pain around the nasal and the orbital region and is more often found in children. The THS complication is characterized by ophthalmoplegia, unilateral orbital or periorbital pain, unilateral headache, and leukocytosis. Orbital cellulitis management includes antibiotic intravenous, corticosteroid, and eye care. **Conclusion:** THS is a rare complication of orbital cellulitis. Early diagnosis and management of orbital cellulitis are essential to prevent THS complication.

Keyword: orbital cellulitis, Tolosa-Hunt syndrome, methicillin-resistant *Staphylococcus aureus,* infectious disease.

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BACKGROUND

Orbital cellulitis is an active infection of the orbital soft tissue which is located posterior to the orbital septum. Clinical features found include fever, leukocytosis, proptosis, chemosis, inhibition of eyeball movement and pain in eye movement. Delay in treatment will result in the progression of infection and the development of orbital apex syndrome or cavernous sinus thrombosis. Complications that may occur include blindness, cranial nerve palsy, brain abscess, and even death.[1,2,3]

Between 2001-2014, orbital cellulitis hospitalized up to 14.5% of the total 671,324 eye disease patients in the United States. Data on orbital cellulitis cases in Indonesia are not available. However, at Sanglah General Hospital Denpasar in the 2016-2020 period, data on the number of issues showed two patients with cellulitis in the eye area and one patient with orbital cellulitis were hospitalized.[4]

Treatment of orbital cellulitis consists of the administration of intravenous antibiotics in adequate doses. However, in some cases, there was a failure of therapy with antibiotics due to various factors. Recent

research states that infection with methicillin-resistant *Staphylococcus aureus* (MRSA) has become the most common cause of orbital cellulitis, especially in children, as reported in a retrospective study in Houston, Texas, which stated that MRSA infection was in 73% of all reported cases of orbital cellulitis.[6,7,8] There was a report of orbital cellulitis caused by MRSA with Tolosa-Hunt Syndrome (THS) complication. THS is a rare condition characterized by ophthalmoplegia pain due to idiopathic inflammation of the cavernous sinus, orbital crest, or superior orbital cleft, resulting in paralysis of the third, fourth, and or sixth cranial nerves. The incidence in United States is one case per one million people each year, with an average onset of age ranging from 16 to 41 years.[9] We reported a child with left orbital cellulitis with THS complication caused by MRSA. This case is reported to increase understanding of clinical manifestations, diagnosis, and appropriate treatment.

CASE REPORT

The patient was consulted by the Pediatric department with complaints of swelling in the left eye which had been felt three days ago. Her mother said five days ago that the patient complained of an ulcer on her nose, then she scratched and drained pus. The nose has become swollen and reddish since three days ago. The swelling spread to the left eye and caused the eyelid to swell, causing redness and pain when she moved her eyes. Besides that, the patient also complained of redness around the nose and eyes, with fever and enlarged eyeball since four days ago. She was given ceftriaxone for three days but there was no improvement.

A physical examination showed redness in both eyes. Dermatological status in the nasal region and left eye showed multiple erythema patches with geographic shape, size 1x2 cm - 4x5 cm, and unclear border. There was also considerable erosion, with sizes ranging from 0.5x1 cm - 1x1.5 cm covered with blackish crusts. On fluorescence examination in figure number 1, there was an erosion of the cornea. Other physical examinations were within the normal limit.

After several days of hospitalization, she complained of enlargement of the eye and painful sensation during movement of the eye. We did the blood test, culture, computed tomography (CT) scan, and magnetic resonance imaging (MRI) examination. The blood test result showed leukocytosis and increased erythrocyte sedimentation rate (ESR), and blood culture found the MRSA bacteria that resistant to cefadroxil, cefuroxime, cephalothin ceftriaxone, and cefepime. The bacteria still sensitive to azithromycin, gentamicin, ciprofloxacin, moxifloxacin, ofloxacin, erythromycin, clindamycin, linezolid, vancomycin doxycycline, tetracycline, tigecycline, rifampicin, trimethoprim, meropenem and sulfamethoxazole.

The CT scan examination in figure number 2 showed a mass with soft tissue density, lobulated, relatively firm boundaries, size ± 2.2 x1.1 x 0.9 cm in the left intraconal orbital, and substantial contrast enhancement in some masses. There is also dilation of the left-sided cavernous sinus. MRI examination in figure number 5 showed infection of the cavernous sinus and was indicated by the presence of a granulomatous appearance in the left cavernous sinus

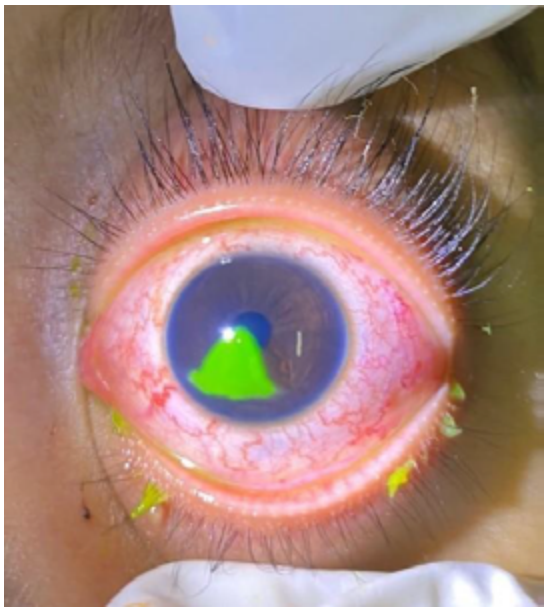

Figure 1. Fluorescence test showed corneal ulceration on the left eye.

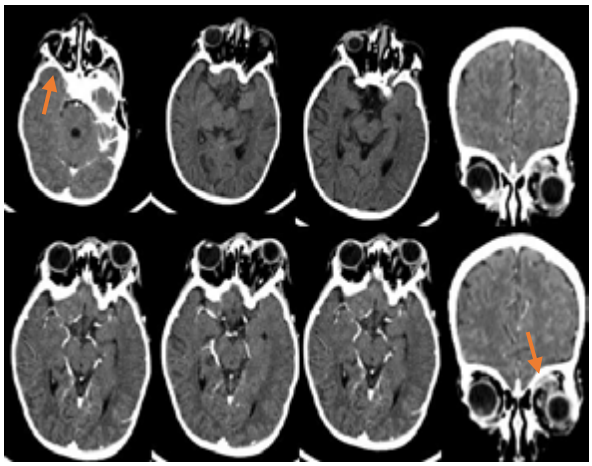

Figure 2. Computed tomography (CT) scan showed a mass that caused the ocular bulb's proptosis to the anterolateral side. There is also dilation of the left-sided cavernous sinus.

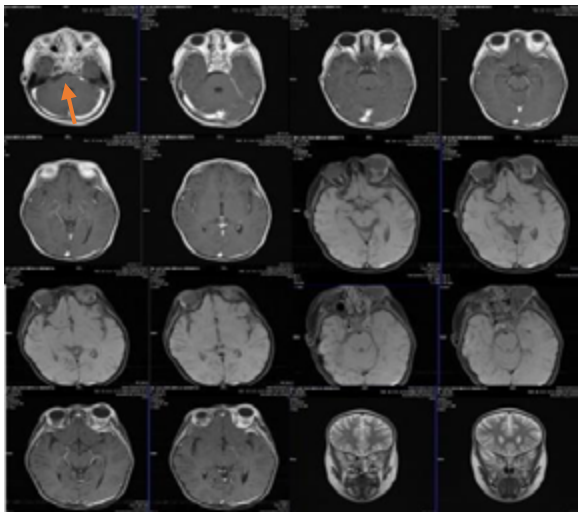

Figure 3. Magnetic resonance imaging (MRI) showed infection of the cavernous sinus and this was indicated by the presence of a granulomatous appearance in the left cavernous sinus.

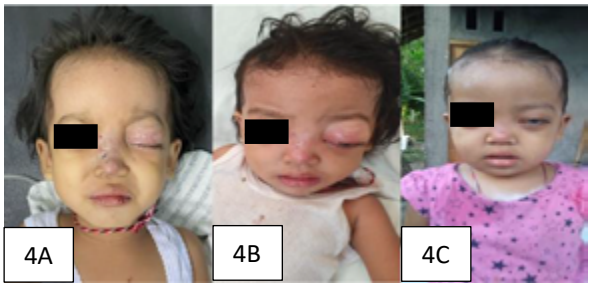

Figure 4. A. Patient's condition before treatment **B.** Proptosis on day 3 of treatment **C.** Seven days of treatment.

The patient was diagnosed with orbital cellulitis with THS complication caused by MRSA infection. She was given meropenem 400 mg intravenously every 24 hours a day for seven days, intraoral methylprednisolone 4 mg taken every 12 hours for five days, and a NaCL 0.9% compress on the nose. Besides, the patient was also given cendo lyteers eye drops 6x1 drops, levofloxacin eye drops 6x1 drops, and gentamicin eye ointment for three days on both eyes. There was an improvement in the patient's condition after seven days of treatment.

DISCUSSION

Classic cellulitis presents as an ill-defined erythema and edema and is often warm and painful. Cellulitis in the facial area is more common in children than in adults. Preseptal (periorbital) cellulitis and orbital cellulitis are cellulitis that occurs around the nasal and orbital region. Orbital cellulitis, on the other hand, is a posterior infection of the septum with overt orbital involvement. It is often caused by sinusitis, but also can be caused by a focal infection in the area around the nose or eyes. In cutaneous findings, symptoms can be found almost similar to periorbital cellulitis (manifest as erythema, swelling of the palpebral, and pain in the periorbital), but in orbital cellulitis we can also find proptosis (bulging eyeball), edema in the bulbar conjunctiva, ophthalmoplegia, decreased visual acuity, fever, increased leukocytes, and headache. There may be complications in orbital cellulitis in the form of permanent vision loss or spread of posterior infection to the brain.[3,5]

The differential diagnosis of orbital cellulitis is between preseptal cellulitis and retrobulbar tumor. In retrobulbar tumors, symptoms are similar to those of orbital cellulitis, such as proptosis, eye discomfort, dizziness, blurred vision, and limited eye motion. Eyeball enlargement in retrobulbar tumors tends to be slower than the proptosis, which occurs in cases caused by infection. Blood tests did not reveal leukocytosis or an increase in markers of infection. In addition, there is no pain in retrobulbar tumors, and a different CT scan image is obtained compared to orbital cellulitis. CT scan results on retrobulbar tumors showed a well-defined, homogeneous, and round mass.[7]

In this case, it was found that there was a complaint of redness in the nose that spread to the eye area, which began with swelling of the palpebral and was progressively accompanied by a protruding eyeball and involvement of the cranial nerves III and IV. The patient also complained of difficulty in moving the left eye, especially towards the right and left, a fever, and an increased number of leukocytes from blood tests. From CT scan and MRI examination, there was also no evidence of tumor mass, so that it excluded the differential diagnosis and the diagnosis of orbital cellulitis was made.

The most common risk factors for orbital cellulitis are sinusitis, especially those that occur in the ethmoid sinus, infection in the location around the orbital, for example, dacryocystitis; folliculitis around the nose or eyes; trauma and surgery; but can also be caused by the expansion of infection in preseptal cellulitis in patients who are not receiving adequate therapy.[8,9,10] Other systemic or epidemiological risk factors include obesity, kidney or liver disease, connective tissue disease, and malignancy. Immune deficiency (including iatrogenic or systemic conditions such as HIV or diabetes) remains controversial as a predisposing factor for routine cellulitis. Important local risk factors are damage to the skin barrier or the underlying lymphovascular system and may result from lymphedema, toe infections, inflammatory dermatoses, peripheral vascular disease, or iatrogenic causes, including placement of an intravenous line, the site of surgical intervention (which can interfere with the skin barrier and underlying lymphovascular

system), as well as post-radiation changes.[1] In this case, before orbital cellulitis occurred, the patient complained of having an ulcer on the nose which was scratched and then drained of blood and pus, which subsequently caused swelling and redness of the eyelids and caused complaints of proptosis, interference with eye movement, fever, and leukocytosis in accordance with clinical orbital cellulitis.

Microbial pathogens can reach the inner dermis and subcutaneous tissue through damage to the skin, spreading to the lymphatics, blood vessels, and interstitial spaces. The portal of entry for infection was identifiable in 62% of patients. Group A beta-hemolytic streptococci (*Streptococcus pyogenes*) and staphylococci (especially *S. aureus*) are the most commonly identified pathogens.[1,9,11] The incidence of orbital cellulitis increases with the increase in the incidence of MRSA in the community. Recent research states that infection with MRSA bacteria has become the most common cause of orbital cellulitis, especially in children, as reported in a retrospective study in Houston, Texas, which stated MRSA infection accounted for 73% of all reported cases of orbital cellulitis.[11,12,13,14] In this case, the patient showed no improvement after being given ceftriaxone 500 mg intraorally every 12 hours for four days, and the results of the gram culture showed *Staphylococcus aureus* infection which was resistant to cefadroxil, cefuroxime, cephalotin, ceftriaxone, and cefepime. Therefore, it can be concluded that the germs causing infection in this patient were MRSA bacteria.

Complications of orbital cellulitis include permanent vision loss, diplopia, ophthalmoplegia, optic neuropathy, central retinal artery occlusion, cavernous sinus thrombosis, meningitis, intracranial abscess formation, septic embolism, neurological disorders, and even death. A case of MRSA orbital cellulitis in healthy adults was first reported in the United States in 2005, accompanied by complications of cavernous sinus thrombosis. Cavernous sinus thrombosis is characterized by fever, leukocytosis, disturbances and/or pain in eye movement, especially eye movements supplied by cranial nerves III, IV, and/or VI, swelling of the eyelids, diplopia, and unilateral headache. The cavernous sinus thrombosis diagnosis can be enforced from history, physical examinations, and supporting examinations, namely CT scan. CT scan showed a picture of proptosis, widening of the left superior ophthalmic vein, and soft tissue inflammation.[12,13]

Infection in the cavernous sinus thrombosis can have clinical symptoms resembling THS. THS is a rare condition characterized by ophthalmoplegia and pain due to idiopathic inflammation of the cavernous sinus, orbital crest, or orbital cleft superior, resulting in third, fourth, and or sixth cranial nerve palsies. There was also unilateral orbital or periorbital pain, unilateral headache, and leukocytosis. MRI examination found the presence of granulomatous in the cavernous sinus, which was shown by a convex-shaped hypodense lesion located to the left of the cavernous sinus. THS incidence in the United States is one case per million people each year, with an average onset of age ranging from 14 to 41 years. Only 18 cases of THS have been reported in children in America, and its treatment and therapy are still controversial.[17] In this case, leukocytosis, left unilateral orbital pain, and ophthalmoplegia so that the patient had difficulty moving the eyeballs, and the CT scan image showed cavernous sinus thrombosis. Whereas on the MRI image, infection of the cavernous sinus is indicated by the presence of a granulomatous appearance in the left cavernous sinus according to the diagnostic criteria and symptoms of THS.

The gold standard therapy in cases of cellulitis with MRSA is the administration of intravenous antibiotics, whereas in the case of THS, although there is no gold standard treatment yet, many experts and studies have stated that there is a progression in subjects treated with the administration of intravenous antibiotics and corticosteroids.[16] The dose of corticosteroid given to patients with THS is still controversial, but in general, the dose given is a high-dose intravenous route for 5-7 days and will be slowly tapered off. Administration of corticosteroids to patients with THS is expected to reduce inflammation quickly so that it can reduce the likelihood of worse complications in the brain.[18,19] In this case, the patient was treated with Meropenem 400mg intravenously given for 7 days, even though her blood culture showed there was no Meropenem, but Meropenem can be used to treat infantile orbital cellulitis that caused by community-MRSA.[20] When the patient was discharged, she was given intraoral methylprednisolone 4 mg twice a day for 5 days. In addition, while the patient was hospitalized, the patient was also given levofloxacin ointment, which was applied to the orbital area twice a day; gentamycin ointment, applied twice a day; cendo lyteers eye drops, which are given once a day, as much as 1 drop. The patient also received 2% sodium fusidate ointment which was applied to the nose every 12 hours, and an erosion compression was performed on the nose suspected of being a port de entry using gauze and NaCl 0,9%.

The prognosis of orbital cellulitis with THS given intravenous antibiotic therapy and corticosteroids is excellent. The prognosis of patients can be seen by

calculating the pain scale of the patient every day during treatment.[17] In this case, there was a significant improvement in the patient's condition after receiving intravenous antibiotic therapy and methylprednisolone after seven days of antibiotics and five days of steroid administration. Based on the patient's pain scale, there was a decrease in the pain scale every day while the patient was treated, which indicates an improvement in the patient's condition in general. However, to determine the patient's prognosis, other evaluations are still needed, such as funduscopic examination, visual examination, and a repeat CT-scan or MRI to determine the improvement in the patient's condition.

We reported a case of orbital cellulitis with Tolosa-Hunt Syndrome caused by methycillin-resistant *Staphylococcus aureus* bacteria. Diagnosis of our case is based on proptosis, pain when she moved her eyes, and from MRI imaging showed a mass in her left cavernosus sinus, and involment of nervus III, IV and VI. Her blood culture showed she was infected with MRSA. Patients were given systemic antibiotic therapy with meropenem 400 mg intravenously every 24 hours a day for seven days, intraoral methylprednisolone 4 mg taken every 12 hours for five days, and NaCL 0,9% compress on the nose. Generally, healing of this disease takes longer than that of orbital cellulitis. This is supported by the causative pathogen in this patient being MRSA bacteria and accompanied by THS complications.

Further investigations are needed to validate the role of CT-scan and MRI on brain tumors to differentiate infection and tumor cases and give an early diagnostic for cases like this. The limitation for this case report is that we cannot compare about the imaging of the brain tumor mimicking the Tolosa-Hunt Syndrome.

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