Treatment of Cavernous Sinus Thrombosis

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Cavernous sinus thrombosis is a life-threatening severe condition and its treatment is controversial. The outcome is fatal in approximately 30%, and residual sequelae are seen in 23-50% of cases [1,2]. Despite adequate intensive care, 44-86% of survivors remain with chronic sequelae, including cranial nerve lesions, hemiparesis and hypopituitarism. Most of the survivors suffer weakness of the extraocular muscles, impaired vision or blindness [3].

Patient Description
A 20 year old previously healthy man presented to the emergency room with complaints of severe headache of 3 days duration, acute onset of periorbital swelling of the right eye, fever, photophobia and malaise. The onset of symptoms occurred 2 weeks following an upper respiratory tract infection. Physical examination confirmed a patient with neck rigidity, fever of 39°C, periorbital swelling, chemosis, ptosis and external ophthalmoplegia of the right eye. Rhinoscopy revealed purulent discharge unexpectedly in the left side of the nasal cavity. Cerebrospinal fluid obtained by lumbar puncture demonstrated elevated protein level, normal glucose rate and three neutrophils.

Contrast-enhanced axial computerized tomography of the orbit on admission showed left pansinusitis, right-sided orbital diffuse cellulitis with intracranial phlegmon, no fluid collection, dilated superior orbital vein, and an enlarged right cavernous sinus containing hypodense filling defects.

The patient was initially treated empirically with ceftriaxone 4 g/day and subcutaneous injections of low molecular weight heparin sodium 5,000 U/day. No organisms were grown from CSF, blood, urine and sputum cultures. Under the same treatment 4 days later his condition deteriorated with the onset of respiratory distress. Chest X-ray and subsequent chest CT showed septic pulmonary emboli. CSF from a repeat lumbar puncture demonstrated normal glucose rate; protein level remained elevated, and no cells were found. Lack of clinical response of the right orbital symptoms prompted a repeat CT scan 6 days later, which showed an organized intracranial abscess, laterally and cranial to the optic nerve. The superior orbital vein and cavernous sinus were unchanged. A small (1.5 cm) abscess was seen in the cerebellum at the level of mid-pons.

Magnetic resonance imaging performed on the same day showed the above mentioned orbital and brain findings. In addition, two well-defined subdural empyemas were seen, one at the right temporal pole and the second around the right lower frontal lobe.

The finding of an organized right orbital abscess prompted surgical intervention. On the 7th day of hospitalization, a left endoscopic sinus surgery and incision and drainage of the orbital abscess were performed. Both sinus pus and orbital abscess cultures grew Streptococcus group C, sensitive to penicillin, ampicillin and erythromycin. Treatment was switched to crystalline penicillin 16,000,000 U/day, metronidazole 4 g/day, and heparin 24,000-30,000 U/day. A few days later the anticoagulation treatment was changed to warfarin sodium and steroids (dexamethasone) were added. The patient was discharged in good condition on the 44th day of admission. Residual diplopia disappeared 2 months later.

Axial contrast-enhanced CT image obtained one month following the surgery showed resolution of the orbital and cerebellar abscesses. The right cavernous sinus was of normal width and shape, without filling defects; no subdural empyemas were noted.

Comment
Staphylococcus aureus is isolated in two-thirds of cases of septic cavernous sinus thrombosis, followed by pneumococci, streptococci, gram-negative bacteria and anaerobes [4]. Immediate empiric antibiotic coverage must include gram-positive, gram-negative and anaerobic bacteria. Later treatment can be narrowed, adjusted to cultures and sensitivities. Surgical drainage of affected sinuses should be considered [2-4].

There are insufficient data regarding the indication of anticoagulant therapy for CST because the condition is rare. It was found that antibiotics in conjunction with anticoagulant therapy used early in the course of CST reduced residual morbidity [2].

CST = cavernous sinus thrombosis

Gadolinium-enhanced axial T1-weighted magnetic resonance image through the lower third of the orbits: left-sided sphenoiditis and ethmoiditis with enhanced mucus and fluid in the sinuses (arrowheads), enlarged right cavernous sinus filled with hypointense filling defects (short wide arrow), subdural empyema at the right temporal pole (short arrow), fusiform intracranial fluid collection in the right orbit (open arrow), leptomeningeal enhancement coating right 7-8 complex (long arrow).
Mortality was lower among patients who received heparin treatment, 14% vs. 36% [3]. Early administration of heparin may serve to prevent spread of thrombosis to the other cavernous sinus as well as to the inferior and superior petrosal sinuses. Intravenous heparin (maintaining the partial thromboplastin time or thrombin clot time at 1.5 to 2 times that of the control) must be continued until the patient is stable for at least several days. Empirically, warfarin sodium (maintaining the prothrombin time at 1.3–1.5 times the control) could then be started and continued for 4 to 6 weeks to allow adequate collateral channels to develop. Steroid therapy is universally used in abscesses treated non-surgically [5]. This does not prove that corticosteroids influence the morbidity or mortality rates of CST, but their use may have partially prevented cranial nerve dysfunction caused by inflammation [3].

CST as a complication of sinusitis is a rapidly progressive and dangerous condition that requires immediate initiation of intensive treatment, including broad-spectrum antibiotics, surgical drainage of the source of infection, anticoagulants and possibly steroids. Early MRI is necessary for the accurate diagnosis of extension of intracranial complications.

References

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Capsule

Hematopoietic stem cells participate in the pathogenesis of atherosclerosis

Excessive accumulation of smooth-muscle cells (SMCs) has a key role in the pathogenesis of vascular diseases. It has been assumed that SMCs derived from the outer medial layer migrate, proliferate and synthesize extracellular matrix components on the luminal side of the vessel. Although much effort has been devoted to targeting migration and proliferation of medial SMCs, there is no effective therapy that prevents occlusive vascular remodeling. Sata et al. show that in models of post-angioplasty restenosis, graft vasculopathy and hyperlipidemia-induced atherosclerosis, bone marrow cells give rise to most of the SMCs that contribute to arterial remodeling. Notably, purified hematopoietic stem cells differentiate into SMCs in vitro and in vivo. The findings indicate that somatic stem cells contribute to pathologic remodeling of remote organs, and may provide the basis for the development of new therapeutic strategies for vascular diseases through targeting mobilization, homing, differentiation and proliferation of bone marrow-derived vascular progenitor cells.

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How neutrophils recognize bacteria

Cyclic ADP-ribose is believed to be an important calcium-mobilizing second messenger in invertebrate, mammalian and plant cells. CD38, the best-characterized mammalian ADP-ribose cyclase, is postulated to be an important source of cyclic ADP-ribose in vivo. Using CD38-deficient mice, Sanchez et al. demonstrate that the loss of CD38 renders mice susceptible to bacterial infections due to an inability of CD38-deficient neutrophils to directionally migrate to the site of infection. They show that cyclic ADP-ribose can directly induce intracellular Ca++ release in neutrophils and is required for sustained extracellular Ca++ influx in neutrophils that have been stimulated by the bacterial chemoattractant, formyl-methionyl-leucyl-phenylalanine (FMLP). Finally, they demonstrate that neutrophil chemotaxis to FMLP is dependent on Ca++ mobilization mediated by cyclic ADP-ribose. Thus, CD38 controls neutrophil chemotaxis to bacterial chemoattractants through its production of cyclic ADP-ribose, and acts as a critical regulator of inflammation and innate immune responses.

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