Cavernous Sinus Thrombophlebitis in Children

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Eight Thai patients less than 15 years of age who were diagnosed with cavernous sinus thrombophlebitis at Ramathibodi Hospital, Bangkok, Thailand over the past 30 years were reviewed retrospectively. The predisposing infections and causative microorganisms were similar to previous reports in children and adults. Despite severe neurologic dysfunction during admission, including blindness, there was neither death nor severe permanent deficit found in the majority of the patients. Only one patient experienced mild hemiparesis caused by cerebral infarction, which was secondary to this condition. Early recognition of this condition, the appropriate selection of empirical antibiotic therapy, and the awareness of associated complication were the key factors leading to excellent outcome. © 2001 by Elsevier Science Inc. All rights reserved.


Introduction

Cavernous sinus thrombophlebitis, which was first reported by Duncan in 1821 [1], is an uncommon condition in pediatric patients. Infection is the common cause of this fatal disease. Mortality and morbidity rates associated with this disease were high, especially before the antibiotic era. There have been reports describing the epidemiology, clinical course, and outcomes in pediatric and adult patients [2-7]. A series reported by Shaw in 1952 [2] included 60 patients who demonstrated high mortality and morbidity rates in this condition. Another study in Indian adult and pediatric patients confirmed the same clinical course and outcomes [6].

The purpose of this article is to report our experience in pediatric patients with this devastating neurologic illness to ascertain a clinical course and outcomes for further clinical application.

Patients and Method

The medical records of pediatric patients less than 15 years of age with the diagnosis of cavernous sinus thrombophlebitis who were admitted to the Department of Pediatrics, Ramathibodi Hospital from 1969-1999 were reviewed. Cavernous sinus thrombophlebitis was diagnosed according to previously described clinical manifestations, which included dysfunction of the structures surrounding the cavernous sinus (CN II, III, IV, VI, V1, and/or V2) and the cavernous portion of the internal carotid artery. Predisposing cause, initial clinical presentation, investigation, isolated microorganism, treatment, hospital course, and the outcome were collected.

Results

There were eight patients, six males and two females ranging from 2 to 14 years of age, in this study. Table 1 lists the predisposing cause, initial clinical manifestation, site of initial infection, blood culture, cerebrospinal fluid (CSF) culture, and outcome obtained in each patient. The clinical courses of two patients were interesting and are presented in detail as follows.

Patient 3

A 14-year-old male who had active purulent discharge draining from an acne pustule for 4 days was brought to a provincial hospital because of high fever. Three days before he attempted to drain pus from the acne by using an unsterile needle. One day before admission, he experienced high-grade fever with swollen eyelids followed by blurred vision of the left eye. He was also drowsy and irritable. On admission, the patient was irritable with blindness in the left eye. It was noted that both eyes were swollen with proptosis, chemosis, and periorbital erythema; both pupils were sluggishly reactive to light, had
engorged retinal veins, ophthalmoplegia, and absent corneal reflexes. He then became unresponsive and required intubation. Initial lumbar puncture disclosed clear CSF with normal open pressure containing 6 leukocytes per mm$^3$, which were all mononuclear cell, normal CSF protein level, and normal CSF glucose-to-serum ratio. Cloxacillin and amikacin were empirically initiated. *Staphylococcus aureus* was obtained from his blood culture. Carotid angiography performed 7 days after admission demonstrated narrowing and irregular cavernous parts of both internal carotid arteries (Figs 1 and 2). Despite a life-threatening clinical presentation, he began to regain his consciousness with improving pulmonary function after intensive, specific, supportive treatments of the infection and brain swelling. He was extubated 2 days after admission. His vision in the left eye began to improve. Four days after treatment, he was able to count fingers. Visual acuity of his left eye was 20/20 at 3 weeks follow up. He was able to return home after a 42-day course of antibiotics. There has been no neurologic deficit observed on serial evaluations for total duration of 14 years.

**Patient 6**

This patient was an 8-year-old male who had injected right conjunctiva for 10 days before the admission. Oral antibiotic administration beginning on the first day of his illness did not improve the infection. Seven days later, his right eye became swollen. He then experienced double vision, fever, and was drowsy. His neck was supple. A swelling of the right eyelid with chemosis, injected conjunctiva, ptosis, and total ophthalmoplegia were present. Left lateral rectus palsy, facial weakness that was upper motor neuron

<table>
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Abbreviations:

- F = Female
- M = Male
- N/G = No growth for bacterial culture

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![Figure 1. Cerebral angiography demonstrates narrowing and irregular right internal carotid artery in Patient 3.](image-url)
type, impaired corneal reflex of the right eye, weakness graded 3/5 of the left upper and lower limbs, Babinski’s sign, and sustained ankle clonus of both sides were noted. A computed tomography scan of the head was performed on admission and revealed thrombosed bilateral cavernous sinuses, which was more severe on the right side. Infarction of the right internal capsule and area supplied by the right middle cerebral artery were also present. Magnetic resonance imaging (MRI) and magnetic resonance angiogram (MRA) performed 9 days later demonstrated subacute infarction of the right hemisphere affecting MCA and PCA territories with midline shift along with thrombosed bilateral cavernous sinuses and superior ophthalmic vein (Figs 3 and 4). Cloxacillin and gentamicin, dexamethasone, and intensive supportive therapy were initiated. His initial blood culture revealed *S. aureus*, which was sensitive to cloxacillin and vancomycin. Culture from CSF and urine were negative. One week after treatment he experienced progressive weakness and an allergic reaction to cloxacillin. Vancomycin and treatment with hyperosmolar solution (10% Glycerol [Glyceol]) were then initiated. Communicating hydrocephalus that occurred later was treated by serial lumbar punctures and administration of acetazolamide. After 21 days of vancomycin therapy and comprehensive supportive care, including physical therapy, his general condition improved. He was able to ambulate without support and was discharged from the hospital. Neurologic deficits that consisted of mild bilateral lateral rectus palsy, mild left facial palsy, and motor power of 2/5 at the left upper extremity were present on discharge. There was no ophthalmoplegia noted on examination 9 months later. Up to the date of this report, he still experienced mild ptosis of the right eyelid and mild facial weakness with normal and reactive papillary reflexes of both eyes. He was able to ambulate independently with motor power of 3/5 at the left arm and 4/5 at the left leg.

**Discussion**

Cavernous sinus thrombophlebitis is a serious neurologic complication of infection [7]. Although it is not a common
illness, it can cause severe neurologic deficits and death. In the past the mortality and morbidity rates were high; in 1961, Yarington [3] demonstrated a mortality rate of 72.8% and a morbidity rate of 65.3%. Patients who suffer from this condition may experience double vision caused by oculomotor weakness, blindness, motor dysfunction, or hypopituitarism [5,8].

This condition occurred either after uncontrolled infection of the medial third of the face, which was most common primary focus, or from direct infection of the orbit, such as orbital cellulitis [9]. Sphenoid sinusitis and dental caries with root abscess may be complicated by this condition, although the latter has been much less common [6,7,9-11]. The predisposing infections found in our study, which were infection of face such as acne and cellulitis, were in line with previous reports. Other locations of infection, such as dental root abscess, however, also may be the primary site of infection.

Differential diagnosis of this condition includes orbital abscesses, which may mimic this condition and may be complicated by cavernous sinus thrombosis. However, with strict diagnostic criteria according to accepted clinical manifestations along with the presence of meningeal irritation signs, one should be able to differentiate these two conditions [1,5-7,12]. Absent corneal reflex is more often present in cavernous sinus thrombosis than in simple orbital abscess [4,9]. Occasional weakness of the opposite arm and leg or even both sides has been found in some patients [5].

Because this condition may cause severe neurologic deficits and high mortality, in this study, early recognition was the key factor leading to good outcomes. In a full-blown case the diagnosis was a straightforward issue, which might not need any further investigation. However, there were some variations among patients that were probably affected by the duration from the time of onset before the diagnosis given and the previous antibiotic treatment. In some patients in which neurologic dysfunction might not be typical in the early stage of the illness, the initial diagnosis might not be easy and further investigation for a definite diagnosis needed. However, this investigation would delay treatment and might cause serious complication. Therefore, awareness of this condition is crucial, and initial treatment of this condition must be initiated as soon as possible.

Certain tests, such as CT scan, cerebral angiography, MRI, and MRA of the brain were performed in our patients. Although CT scan is not as sensitive and specific as MRI in this situation, it may be able to reveal irregular filling defects inside cavernous sinus, erosion of bony structure around cavernous sinus or dilatation, and tortuosity of superior ophthalmic vein [13-16]. High-resolution CT scanning is more sensitive than conventional CT [13,14,16]. MRI is an excellent tool in identifying the structures around cavernous sinus [7,17,18]. MRI along with MRA of the brain would be able to disclose any secondary complications, such as internal carotid artery occlusion, dural sinus thrombosis, or secondary vasculitis of the affected vessels such as observed in one of our patients (Patient 6) [7,14,19,20]. Cerebral angiography might also be helpful in establishing the diagnosis, such as was revealed in two of our patients, including Patient 3 [21]. These two patients were diagnosed before the availability of MRI in our institution. However, it was an invasive procedure and difficult to perform in young children. Gallium scintigraphy was also useful in the diagnosis of cavernous sinus thrombosis; however, it is not available in some institutions [22].

*S. aureus* was the most common causative microorganism detected in our patients, as found in other reports [4,23]. Blood cultures were also able to detect these bacteria in five patients who demonstrated infection around the facial area. One patient (Patient 2) with chronic mastoiditis had *Morganella morganii* identified in CSF culture. Dental caries was the other predisposing infection found in one patient. Thus selection of antibiotic therapy should be made according to predisposing risk or to the site of infection.

Apart from antibiotic and intensive supportive therapy that were still the mainstay treatment of this condition, the other mode of treatment, that is, anticoagulation therapy with coumadin or heparin, was still controversial. Coumadin was included to the regimen without statistical support to justify its use [3,4]. Early anticoagulant therapy within 7 days of the clinical course was reported to reduce the morbidity in the adults who had this condition twofold [17]. Administration of low-molecular-weight heparin was demonstrated to be effective in improving outcomes of venous thrombosis [24]. However, there is no information regarding its usefulness in secondary thrombosis from infective process. Complications of anticoagulant therapy, such as hemorrhage from venous infarctions or from necrotic walls of the cavernous portion, must be considered [7]. At present there is no scientific consensus regarding this issue. Despite receiving no anticoagulant therapy, almost all of our patients experienced complete recovery, including the male patient who was blind on referral (Patient 3). The only patient (Patient 6) who had cerebral infarction caused by secondary thrombosis of the internal carotid artery inside cavernous sinus still had motor dysfunction. With proper antibiotic therapy along with treatment of brain edema with hyperosmolar solution and intensive supportive care, he was able to return home and was able to walk independently with normal vision.

According to our study, we would like to emphasize that a pediatrician’s awareness of this illness, early recognition, investigation, including high-quality radiographs demonstrating thrombosis of cavernous sinus and narrowing of the internal carotid artery, appropriate administration of antibiotics against causative bacteria before definitive identification of bacteria could be reached, early intervention of associated complications, and proper supportive cares were the key factors leading to the good
outcomes of cavernous sinus thrombophlebitis in our patients.

References