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Review article

Septic cerebral venous sinus thrombosis

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ABSTRACT

Septic cerebral venous sinus thrombosis, once a common and deadly disease, has fortunately become rare now. Not only that the incidence has fallen significantly after the antibiotic era, the morbidity and mortality has also decreased substantially. Cavernous sinus thrombosis is by far the commonest form of septic cerebral venous sinus thrombosis. Due to its rare occurrence, a lot of current generation clinicians have not encountered the entity in person. Despite all the advances in diagnostic modalities, a high index of clinical suspicion remains the mainstay in prompt diagnosis and management of this potentially lethal condition. Keeping this in view, the authors have reviewed the subject including the old literature and have summarized the current approach to diagnosis and management.

Septic cavernous thrombosis is a fulminant disease with dramatic presentation in most cases comprised of fever, periorbital pain and swelling, associated with systemic symptoms and signs. The preceding infection is usually in the central face or paranasal sinuses. The disease rapidly spreads to contralateral side and if remains undiagnosed and untreated can result in severe complications or even death. Prompt diagnosis using radiological imaging in suspected patient, early use of broad spectrum antibiotics, and judicial use of anticoagulation may save the life and prevent disability. Surgery is used only to treat the nidus of infection.

Contents

1. Introduction

Cerebral venous and sinus thrombosis (CVT) is an uncommon disease and accounts for <1% of all strokes [1,2]. Multiple predisposing factors have been associated with CVT among which only few are reversible. Some of the predisposing conditions associated with CVT

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include thrombophilias, irritable bowel disease, head trauma, oral contraceptive use, pregnancy, dehydration and infection [1]. Cerebral venous thrombosis varies widely in its presentation, predisposition, neuroimaging, outcomes and prognosis [3]. The exact incidence and prevalence of CVT is unknown due to lack of population based data. Although no age is exempt from cerebral venous thrombosis; in pediatric population, neonates are most affected, and in adults the highest incidence is in the third decade with female preponderance [2]. Diagnosis of cerebral venous thrombosis is still overlooked or delayed despite the advances in its understanding and the availability of diagnostic tools. It remains a diagnostic and therapeutic challenge [4].

2. Infection related/septic cerebral venous sinus thrombosis

Infection related/septic cerebral venous sinus thrombosis has decreased dramatically in incidence after the widespread use of antibiotics for infections. Infection used to be the main cause of CVT before the era of antibiotics [5]. Due to rarity of occurrence, septic CVT may be misdiagnosed or remain undiagnosed which can result in treatment delay in this potentially life threatening condition [5]. It is more common in children compared to adults. Cavernous sinuses are the most commonly involved sinuses in septic CVT, and usually follow the infection of paranasal sinuses, dental abscesses, otitis media and orbital infections [6]. Infection as a possible cause or trigger of cerebral venous thrombosis is very common in children, with almost half of the patients having recent infection prior to the diagnosis of cerebral venous thrombosis [7,8]. Facial infections contributed to the largest number of cases of cavernous sinus thrombosis in the pre-antibiotic and early antibiotic era [9]. Ethmoid and sphenoid sinusitis had become common preceding infection in the antibiotic era [9], whereas middle ear infections, and mastoiditis remain other preceding infections.

3. Anatomy and pathophysiology

The cavernous sinuses which are the most commonly affected sinuses in septic cerebral venous thrombosis, are paired sinuses located in the base of skull, superolateral to the sphenoid air sinuses. These are separated from sphenoid air sinuses by thin bone, or sometime only by soft tissue, if the bone is not fully formed [6]. Oculomotor, trochlear, and the superior 2 divisions of trigeminal nerve travel adjacent to cavernous sinus, while abducens nerve and carotid artery pass through the cavernous sinus [9] (Fig. 1). The cavernous sinuses receive most of the venous return from the face via ophthalmic veins, and drain in the internal jugular veins through superior and inferior petrosal sinuses [6] (Fig. 2). The dural sinuses and cerebral veins lack valves. This lack of valves make the blood flow pressure dependent, and blood can flow in either direction depending on the pressure gradient [5,6]. These anatomic peculiarities, as well as extensive direct and indirect vascular connections of the centrally located cavernous sinuses make them susceptible to infections involving the facial structures, and adjacent paranasal sinuses [12]. These sinuses are trabeculated and may act like sieves to entrap bacteria, emboli or thrombi [12]. In the preantibiotic era, majority of septic CVT resulted from facial infections [6,9]. Middle ear, pharynx and teeth can be other sources of septic cavernous sinus thrombosis. The lateral sinus thrombosis is mostly associated with middle ear infection or mastoiditis [10,11]. Superior sagittal sinus is uncommonly involved in septic CVT and is mostly in relation to meningitis. Orbital infections are rarely complicated by septic thrombosis of cavernous sinuses despite the direct drainage of ophthalmic veins in the cavernous sinuses [5,6,12].

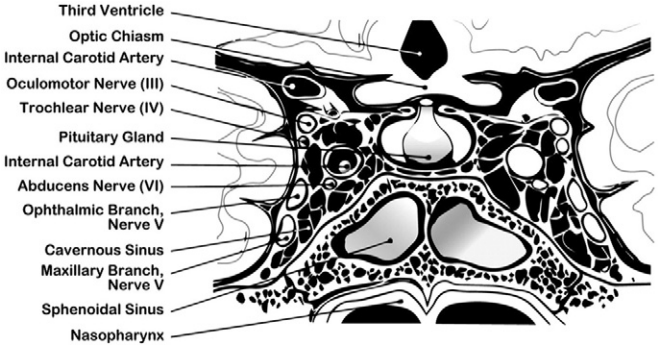

Fig. 1. Coronal section of schematic diagram of cavernous sinuses showing the contents of cavernous sinuses, as well as adjacent structures.

The exact mechanism of septic thrombosis is yet unclear. Infection may trigger thrombosis directly by causing septic thrombosis or indirectly by precipitating thrombosis in patients already at risk of thrombosis due to predisposing thrombophilia [5]. The infection may spread within veins (thrombophlebitis) or as septic emboli that get trapped within the trabeculations of cavernous sinuses [13]. Bacteria are potent inducers of thrombosis and thrombus in turn is a great growth medium for bacteria [13]. Bacteria trapped in the deeper layers of thrombus may be protected from antibiotic penetration and can become source of infection [13]. Intracranial infections like meningitis, subdural abscess, empyema can be source of direct spread of microorganisms to the cerebral venous sinuses [10].

The autopsy reports have shown bilateral involvement in most cases with extension of thrombosis to other venous sinuses [9]. Other abnormalities included leptomeningitis, brain abscesses, subdural empyema as well as cerebral infarcts [9].

4. Microbial etiology

Bacterial infections are by far the commonest cause of septic CVT, however, viral, parasitic and fungal etiologies have been well described (see Table 1). *Staphylococcus aureus* is the most commonly identified organism, followed by streptococcal species, gram negative organisms, and anaerobes [6,12]. Cytomegalovirus, herpes simplex, measles, hepatitis, and HIV all have been attributed to the development of CVT [5,10]. Fungal infections including aspergillus, mucormycosis, and coccidiodomycosis all have been reported to contribute to septic CVT [5]. Parasitic infections including malaria, trichinosis, and toxoplasmosis have also been reported [10].

5. Septic cerebral venous thrombosis in special situations

There is no clear evidence that chronic immunocompromised status predisposes to septic CVT. There are only few reports of septic CVT in patients with chronic infections like human immunodeficiency virus (HIV) and tuberculosis. Patients with HIV possibly are more likely to have venous thrombotic events; cerebral venous thrombosis is rather uncommon in this population. Most of the published reports describe aseptic CVT rather than septic CVT in patients diagnosed with acquired immunodeficiency syndrome (AIDS) [14,15]. Few reports of septic CVT in patients with HIV had not been proven to be directly caused by HIV itself. It is probable that the combination of coagulopathy and opportunistic infections are the main culprit of septic CVT in HIV patients, rather than the HIV itself [5,16].

Despite affecting central nervous system (CNS) frequently in the form of meningitis and CNS tuberculosis (TB), tuberculosis has rarely been reported in association with septic CVT, mostly in the patients who had disseminated disease [17,18].

There is a report of CVT after a bee sting, in which the culture yielded *Staphylococcus aureus* and *Streptococcus pyogenes* [19]. The authors have proposed several mechanisms how a bee sting could have precipitated infection of the cavernous sinuses.

A number of neoplastic conditions lead to prothrombotic or hypercoagulable state. Chemotherapy has been associated with slight increase in the risk of cerebral arterial or venous thrombosis [20].