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REVIEW ARTICLE

Cavernous Sinus Thrombosis focusing on odontogenic causes: a narrative review

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Abstract:

Cavernous Sinus Thrombosis (CST) is an uncommon neurological infection that affects the cavernous sinus of the dura mater, which can lead to death. When untreated, odontogenic infections can cause CST, since facial veins do not have valves. The diagnosis consists of the clinical characteristics added to imaging exams such as computed tomography (CT) and magnetic resonance imaging (MRI). The effectiveness of antibiotic therapy in significantly reducing mortality has been proven, but therapy with anticoagulants and corticosteroids remains unknown in the literature. Objective: The purpose of the study is to make a literature review on etiology, paraphysiology, symptoms, complementary exams, diagnosis and outcome of patients who presented CST as a result of an odontogenic infection. Materials and methods: a literature review was carried out, using articles from the Pubmed, Lilacs and Cochrane databases, from the last 10 years in the English language and reference articles to complement. The Mesh terms used were 'Cavernous Sinus Thrombosis', 'Cavernous Sinus Thrombosis AND Odontogenic Infections' and 'Cavernous Sinus Thrombosis AND Dental Infection'. Conclusion: CST motivated by odontogenic infections is a rare but extremely dangerous disorder that must be discovered early in order for the patient's prognosis to be favorable. It is necessary to pay attention to the clinical signs and to the analysis of the imaging exams so that the differential diagnosis is made.

Keywords: "Cavernous sinus thrombosis"; "Odontogenic infections"; "Venous trombosis"

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INTRODUCTION

Cavernous Sinus Thrombosis (CST) is an uncommon neurological infection that affects the cavernous sinus of the dura mater[1,2], It can lead to death[3]. CST can be derived from traumatic or infectious causes, odontogenic infections may be one of the possible causes of their occurrence, although it is one of the most unlikely factors[4, 5, 6]. This is due to the anatomy and venous drainage of the face that generate probability of a multidirectional venous flux[7, 2]. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are the most frequently performed exams to arrive at diagnosis, which may help in the early recognition of the disease and, possibly, in a better prognosis[8,9]. The management of the infection consists in the control of the disease through medicines that sensitize the causative agent and prevent the spread of infection[1]. Despite the increased survival of the patients, most present sequelae affect, above all, the muscles of the eyes. The purpose of the study is to make a literature review on etiology, paraphysiology, symptoms, complementary exams, diagnosis and outcome of patients who presented CST as a result of an odontogenic infection.

MATERIALS AND METHODS

The databases used in this narrative review with convenience sampling were "Pubmed" (MEDLINE), "Cochrane" and "Lilacs", and the survey was conducted in April 2021. The criteria chosen for the research were the articles published in these databases of the last 10 years in English. The Terms Mesh used were The Cavernous Sinus Thrombosis', The Cavernous Sinus Thrombosis AND Odontogenic Infections' and The Cavernous Sinus Thrombosis AND Dental Infection'. As a result, 38 articles were selected, in which we excluded CST associated with Lemierre syndrome, leaving 29 articles. The other selected articles are considered a reference in the subject or filled gaps necessary to complete the reasoning.

LITERATURE REVIEW AND DISCUSSION

Cavernous sinus thrombosis (CST) usually has an infectious origin, but is also reported due to traumas[4] and idiopathic issues. The infection may develop locally in facial soft tissues, nasosinusal cavities, or adjacent orbits[10]. However, the most affected region is usually inserted in the dangerous triangle of the face, being the highest occurrence in relation to sinusitis of the paranasal sinuses. Infections of odontogenic origin are associated with 10% of the cases, a considerable percentage given the severity of the disease. Individuals with systemic impairments are more vulnerable to the evolution of the infectious condition to septicemia[11, 12].

Odontogenic infections can manifest in the tooth or in tissues surrounding it[13] (fig 1). They may originate from caries, periodontal disease, abscesses, tooth extractions and traumatic surgery[4]. Depending on the anatomical region and virulence of the bacterium, the infection may become confined or spread[12].

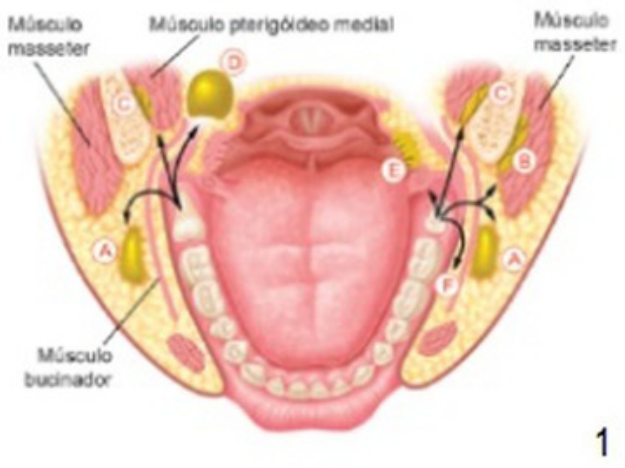

Fig 1. Facial spaces in which odontogenic infection can spread to tissues adjacent to erupted and semi-impacted molars. A. Submandibular space. B. Masserium space. C. Pterygomandibular space. D. Retropharyngeal space. F. Oral space.29. PRADO, Roberto; SALIM, Martha Alayde Alcantara. Cirurgia bucomaxilofacial: diagnóstico e tratamento. 2. ed. Rio de Janeiro: Guanabara Koogan, 2018. 712 p.

About 90% of these infections are caused by bacteria Staphylococcus aureus, Streptococcus sp. and gram-negative organisms. However, they can still be fungal, parasitic and

virotic source[4,14]. These microorganisms have the ability to go through the hematogenous pathway[1], mainly through facial and ophthalmic veins[15], reaching the cavernous sinus. The anatomy and drainage of the face contribute to the spread of this infection, thus affecting other areas.

The cavernous sinuses are at the central base of the skull, located in the region near the sella túrcica, previously limited by the superior orbital fissure and later by the petrosal bone of the temporal[13]. They are responsible for the drainage of the skull, orbit, face, and neck[14] into the pterygoid venous plexus and then into the internal jugular vein[16]. The cavernous sinuses are in close connection with important components such as the pairs of cranial nerves Oculomotor (III), trochlear (IV), ophthalmic and maxillary branches of the trigeminal (V) and abducent (VI), ethmoid paranasal sinuses and sphenoid, Internal carotid artery and brain structures of the middle cranial fossa[4] (fig 2.).

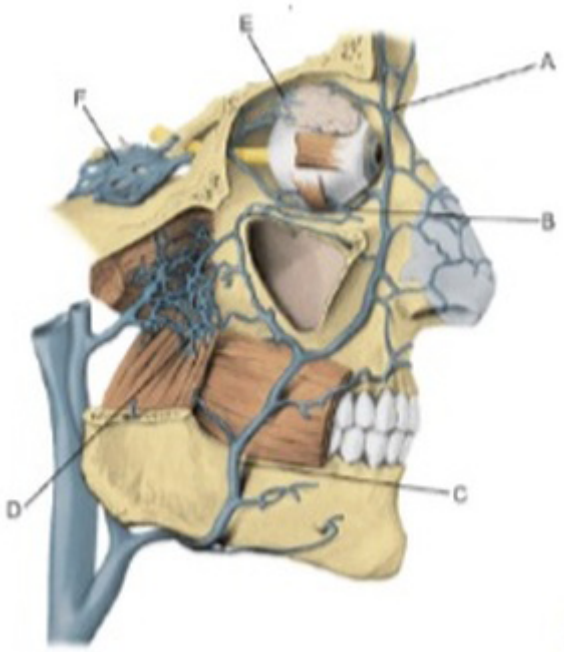

Fig 2. Anatomical structure responsible for the dissemination of odontogenic infection to the cavernous sinus of the dura mater. A. Angular vein. B. Inferior ophthalmic vein. C. Facial vein. D. Pterygoid plexus. E. Superior ophthalmic vein. F. Cavernous sinus.29. PRADO, Roberto; SALIM, Martha Alayde Alcantara. Cirurgia bucomaxilofacial: diagnóstico e tratamento. 2. ed. Rio de Janeiro: Guanabara Koogan, 2018. 712 p.

The signs and symptoms of complications observed in general are the result of venous obstruction and paralysis of cranial nerves, mainly VI par[14]. Headache, fever, periorbital edema and changes in vision and/or eye movement are the most reported complaints. The spread of this infection can be caused by the connection of the oral space with the infraorbital and periorbital tissues[17]. This fact justifies the symptom of periorbital edema so common in patients with cavernous sinus thrombosis, motivated by odontogenic infections. There are also reports of other conditions that affect vision, such as chemosis, ptosis, proptosis, and photophobia, as well as neurological issues related to altered mental status, ocular pressure, and intracranial problems[18].

The most common risk factors are pro-thrombotic conditions, such as genetic or acquired thrombophilia, pregnancy, and the use of oral contraceptives[2, 19]. In addition, neurovascular abnormalities and malformations, inflammatory disorders, immunosuppressive, hematological and systemic diseases[4, 19].

The diagnosis is made by means of imaging tests, such as computed tomography (CT) and magnetic resonance imaging (MRI)[8]. In these examinations, it is possible to verify expansion, convexity of the lateral wall and lack of enhancement of the cavernous sinuses. In addition, obstructions or narrowing of the veins, dilation of the superior ophthalmic vein, exophthalmos, edema of soft tissues and thrombosis in veins or sinuses of the face, which in turn are tributaries of the cavernous sinus, may also be observed. MRI enables differential diagnosis in relation to some similar comorbidities, indicating the cause and extent of the disease[14]. In addition, laboratory tests are done, such as complete blood count, comprehensive metabolic panel and coagulation exam that allow to analyze if there are factors. Bacterial culture is a hematological test that enables the discovery of the causative agent of infection[20]. This is important to determine the type of treatment that will be performed

to combat the microorganism. The diagnosis may be slow, because it requires the distinction of CST compared to other diseases[9].

Since generally the causative sources are bacteria and fungi, in most cases, the individual receives intravenous broad-spectrum antibiotics, such as the third generation of cephalosporins, penicillins and carbapenems, for the purpose of sensitization of the pathogen by medication[9]. The most commonly used anticoagulants are low molecular weight heparin and heparin, indicated in some cases in association with antibiotics, to reduce the possibility of thrombosis[21] and the spread of thrombosis to other sythions[22, 9]. Surgical intervention can be used in cases where the infection is uncontrolled [1, 5], as in the existence of abscesses, and can be surgically drained to avoid septicemia[8]. If the infection is odontogenic, it may be necessary to remove the teeth that caused the problem. In addition, the use of steroids for nerve tissue repair[6,23].

The determination of the severity of odontogenic infections also depends on the relationship that the muscle has with the space in which the bacteria overcome, acting as a barrier and, thus, hindering the propagation to the fascial spaces, which could result in CST. Generally, odontogenic infections spread more easily through the vestibular region of the maxilla, since the cortical bone is less thick[12]. However, Jones and Arnold presented a case on a CST resulting from an odontogenic infection in the mandibular region, in which it is suggested that the dissemination of the infection was by the retrograde flow of the retromandibular vein and pterygoid plexus[24].

There is a relationship between CST and cranial nerves, mainly with the sixth nerve, since it passes medially through the cavernous sinus, with the third and fourth pairs being less impacted because they are located more laterally. According to Okamoto et al, approximately 20% of individuals have maxillary and ophthalmic nerve dysfunction. Verma et al. reported a case of a 50-year-old patient who had CST as a complication of a dental abscess. In this case, CST generated paralysis of the lower half of the patient's face, being caused by compression of the branches of the facial nerves[7], an uncommon occurrence compared to the other symptoms in the studied cases, in which the most seen clinical characteristics were fever, pain and ophthalmology[4].

Strict anaerobic bacteria predominate in odontogenic infections[12], differing from the species most commonly found in CST that are anaerobic facultatives[4]. Fungi are the second most common causative agent, and Aspergillus fumigatus is the most common. These organisms reach the most susceptible individuals, such as those who have comorbidities or who, for some reason, are immunosuppressed[1]. Sources of dental and sinus infections should not be neglected in patients with a low immune system[24]. Regarding systemic diseases, diabetes mellitus is the most frequently found in patients with serious dental infections[17]. In patients with a compromised immune system, bacteremia can become a septicemia[12], aggravating the case and making treatment more difficult.

Kasim et al. presented a case of a man who, after the extraction of the first right and left upper molars, showed edemaciated face, vision reduction and diplopia. It was also found that the patient had been contaminated by SARS-COV-2 for three months, but did not present any case of comorbidity. After the discovery of CST, by means of contrast-enhanced computed tomography, the condition was complicated, indicating a state of severe sepsis and, after 72 hours, the patient died. Indications indicate that, due to the state of infection by SARS-COV-2, hypercoagulation was aggravated, which would cause disseminated intravascular coagulation, leading to the death of the patient[25].

Idiculla et al. performed a comparative analysis of the two most commonly used examination modalities, CT and MRI. CT provides high resolution images and is usually required for simpler case diagnoses. The exam is done quickly and has a lower chance of presenting radiographic artifacts in the result[2]. In addition, it is important to emphasize that individuals who use

devices as pacemakers can perform it. MRI is a more complex and sensitive examination, has a good detailing capacity and does not expose the patient to ionizing radiation[2]. According to Weerasinghe et al, the most commonly performed imaging studies is MRI, followed by CT[1]. Venography by MRI and common MRI are highly sensitive, enabling the most accurate diagnosis. CT may fail to show the anomalies present[7]. Aggarwal et al. explain the similarity between CST and orbital cellulitis. In this context, MRI assists in the differential diagnosis[22]. According to Idiculla et al, angiography is the gold standard for the diagnosis of CST[2]. However, Okamoto et al. state that the cavernous sinus is not well visualized in this type of examination, besides being able to increase the spread of infection[9].

According to Verma et al, as soon as the diagnosis of CST is proven, the patient should start using a broad spectrum antibiotic. However, when the results of the examination of the culture of microorganisms are ready, the medication should be rethought[7]. Weerasinghe et al advise knowing the agent causing the infection before choosing the appropriate therapy. These authors demonstrated that, in most cases, beta-lactam antibiotics were choices[1]. Anticoagulant therapy is still controversial in the literature. Clinical studies on CST suggest that the use of anticoagulants considerably reduces mortality and the incidence of neurological problems when combined with antibiotics[4]. However, there are still indications that its effect occurs only when the disease is at the begin[7, 26, 27].In addition, its use may cause intracranial and systemic hemorrhage, while its benefit has not yet been evidenced[9]. Steroid therapy is still contradictory in the literature. According to Colbert et al., the benefits of corticosteroids in the treatment of CST have not yet been substantiated[21]. However, Tsai states that steroids can be used for their anti-inflammatory effect, having the ability to repair neural tissue[18].

The use of antibiotics has considerably reduced the mortality of patients with CST[8], but this disease is still worry[13,22]. The CST is severe and has a poor prognosis, since, generally, the diagnosis is not early. Despite the existence of reports in the literature of patients who survived this disease, most of these individuals present some immediate or late sequelae, such as vision problems and ophthalmopplegia[14], besides the involvement of the cerebral artery, which may cause hemifacial paralysis[24]. In addition, the possibility of intracranial aneurysms even after treatment[13]. However, it has been seen in the literature cases in which visual sequelae regressed[9].

CONCLUSION:

A CST can occur in clinical practice as a severe complication derived from an odontogenic infection that can lead to death. In this sense, knowledge of the subject by the medical and dental community is important in order to diagnose the disease early and, as a consequence, improve the treatment and prognosis of the patient.

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