Original Research

Cervicofacial Cellulitis: The Impact Of Non-Steroidal Anti-Inflammatory Drugs

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ABSTRACT
Aim: The aim of the study was to determine the impact of NSAIDs on the evolution of CFC.
Material and methods: The cases incorporated in the series comprised individuals who were hospitalised due to the severeness of the presenting symptoms and were admitted to the emergency department. There were sixty instances of CFC in this category.
Results: NSAIDs were utilised by 80% of patients, either through self-medication or by prescription from a community physician, dentist or chemist. The molecules that occurred most frequently were diclofenac and tiaprofenic acid. In the majority of instances, CFC extension was limited to the maxillary and/or ipsilateral subhyoid region; however, there were four catastrophic cases of lower cervical extension and one case of mediastinal involvement.
Conclusion: CFC is a critical and potentially fatal infection that signifies an urgent need for both diagnostic and therapeutic interventions. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) is often cited as a risk factor; thus, these drugs should be utilised with extreme caution, if at all, in cases of head and neck infections, particularly those of an odonto-stomatological nature.
Keywords: Gravida; Gestational diabetes mellitus; Maternal factors; Obese

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INTRODUCTION

Cervicofacial cellulitis (CFC) is a highly severe and recurrent infectious emergency affecting the head and neck region. Mortality remains significant despite advancements in diagnosis and treatment. It primarily originates from the oropharyngeal (20%) or orodental (70%) regions of the cellulo-adipose spaces of the head and neck.[1,2] While the majority of cases are localised acute forms devoid of symptoms of severity (such as serous and suppurating forms) that resolve rapidly with appropriate medical and surgical treatment, others can be fatal due to their rapid dissemination, which can result in extensive necrosis or cellulitis that may even affect the mediastinum. Necrotizing fasciitis, in particular, can be fatal, characterisedby extensive necrosis.[2] From a nosological standpoint, "necrotizing fasciitis" is a generic term used in English to refer to all varieties of cellulitis. However, the medical term "cellulitis" encompasses a significantly broader spectrum of pathologies, including extensive necrosis (referred to as fasciitenécrosante in French).[3,4] Incomplete or inappropriate treatment (antibiotherapy not adapted to bacteriology, inadequate surgical resection of necrotic tissue, for instance) or an underlying predisposition that compromises the organism's immune system (diabetes, congenital or acquired immune deficiency) may contribute to severe forms.[5]In addition to the aforementioned established risk factors, complications in CFC have been frequently attributed to the overprescription of nonsteroidal anti-inflammatory medications (NSAIDs), although the causal relationship has yet to be conclusively established.

We routinely observed a high incidence of NSAID use among hospitalised patients presenting with CFC in our practice. As a result, the current study was undertaken

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to assess the effects of non-steroidal anti-inflammatory medications on cervicofacial cellulitis.

PATIENTS AND METHODS

A prospective study was conducted within the hospital's department of head and neck surgery. Included were patients who were hospitalised as a result of the severeness of their presenting symptoms and were admitted to the Emergency Department with CFC. Numerous cases that were amenable to outpatient management were omitted due to organisational considerations such as data missing, loss to follow-up and so forth.

Data were collected on a form detailing, among other points:

- Probable or proven origin of infection (dental, oral, oropharyngeal, adenitis, etc.)
- NSAID consumption prior to the onset of CFC: molecule, dose, duration of treatment, and prescription modalities (self-medication,specialist or non-specialist medical prescription)
- risk factors: diabetes, long-course corticotherapy, other immune deficiency factors
- Pre- and post-admission assessment: blood tests, bacteriology, contrast-enhanced CT, and management after admission(surgery, intensive care)

Assessment

Systematically, a complete blood count, electrolyte analysis and screening for glycemic variability and concomitant hydroelectrolytic disorder constituted the standard biological assessment. In cases where a purulent assemblage was detected, bacteriological samples were obtained, including from patients who were prescribed antibiotics prior to their admission. In nine instances (15 percent), multibacterial flora consisting of cocci and Gram-negative bacilli was identified.

Contrast-enhanced CT was systematically performed on 51 patients who underwent pantomography to detect purulence and evaluate profound extension.

Pre-admission treatments

An NSAID regimen was initiated by 48 patients or 80% of the total. The two molecules that were prescribed with the highest frequency were tiaprofenic acid and diclofenac, sometimes prescribed together. Prior to emergency admission, all patients had been prescribed one or more antibiotics by their community physician (n = 18), dentist (n = 17), specialist (n = 1), or self-medicated with one or more antibiotics (n = 24), in addition to nonsteroidal anti-inflammatory drugs (NSAIDs). Associated metronidazole-spiramycin, metronidazole, amoxicillinclavulanic acid, ciprofloxacin, and ofloxacin were the most prevalent molecules.

Treatments in hospital

When small, all purulent accumulations were expelled via perforation; for larger ones, drainage was employed. A Sebilleau incision was utilised in three instances, followed by meticulous necrosectomy and lavage utilising oxygenated water and povidone-iodine. In two instances, a thoracotomy-guided mediastinal approach was utilised to perform extensive drainage.

Parenteral antibiotherapy was continued until oral antibiotics could be substituted or there was clinical relief in symptoms.

Antibiotherapy related to:

- amoxicillin + clavulanic acid100 mg/kg/day in3 fractions, IMgentamicin 3 mg/kg/day: n = 34 patients;
- amoxicillin + clavulanic acid and gentamicin at the above doses associated to metronidazole 1 g/day: n = 10 patients;
- ceftriaxone 8 mg/kg/day: n = 10 patients;
- moxifloxacin 400 mg/day: n = 6 patients

The mean length of hospitalisation was six days (range: three to twelve days); however, three patients who necessitated ICU admission for mediastinal extension of CFC perished despite receiving intensive care and surgical debridement that extended to the mediastinum.

RESULTS

60 patients were recruited: 38 male, 22 female; age ranging from 10 to 67 years old (median age 31 years).

Table 1: distribution of patients according to age and gender

	N (60)	%
Age	10-67 years	
Gender	Male- 38 Female - 22	63.3% 36.6%

60 patients were recruited for the study. Out of them 38 were males and 22 were females; age ranging from 10 to 67 years old (median age 31 years).

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Table 2: distribution according to History

History	N (%)
Type-2 diabetes	25(41.6%)
CFC revealed the diabetes	15(25%)
Long-course corticotherapy	0
Congenital or acquired immune deficiency	0

At admittance, all 25 patients (41.6%) with type-2 diabetes had inadequate glycemic control (glycemia> 2 g/dL). In fifteen patients, diabetes was identified by the CFC. Long-course corticotherapy and congenital or acquired immune deficiency did not occur in any cases..

Table 3: distribution according to origin of cervicofacial cellulitis

Origin	N (%)
Dental origin	51(85%)
Tonsillar	3(5%)
Complication of adenitis	1(1.6%)
Origin was undetermined	5(8.3%)

In the case of 51 patients (85%), the patient reported dental pain or treatment during the interview or at admission, which indicated that CFC originated in the mouth. In patients without dental presenting symptoms, this was confirmed clinically by the presence of tooth caries or residual root, and/or radiologically by a systematic pantomogram revealing dental origin. Tonsillar origin was postulated for CFCs in three instances. In one case, adenitis was implicated. Determination of origin was absent in five instances.

Table 4: distribution according to sign and symptoms

Signs and symptoms	N (%)
Dental pain	45(75%)
Limitation of mouth opening	41(68.3%)
Edema of the floor of the mouth	11(18.3%)
Dysphagia	4(6.6%)

A total of 45 patients were experiencing dental discomfort. Mouth opening was restricted in forty-one patients (68.3% of the total series and 75% of CFCs of dental origin); eleven patients presented with edoema of the floor of the mouth, and four patients experienced mild dysphagia. In every instance, the effect on overall health status was moderate.In 51 patients, CFC was limited to the superolateral cervical and maxillary regions (85%). In 20 cases, tumefaction was pre-collected without skin inflammation; in 35 cases, it fluctuated with skin inflammation. Tumefaction was rigid. In two cases, extension occurred in the temporal region, while in four cases, it occurred in the inferolateral cervical region. One patient who had been prescribed nonsteroidal anti-inflammatory drugs (NSAIDs) developed mediastinal involvement, which proved fatal despite intensive care.

DISCUSSION

While the precise causal relationship between NSAIDs and CFC is not known, numerous series, including the current one, suggest that they may contribute to or exacerbate CFC, if not directly cause it. In a series of 45 patients admitted with CFC, Mathieu et al[2] identified 44% of cases involving NSAID use. Similar to the current results, Merle et al[3] identified a 76.46% NSAID rate as a promoter of CFC in a smaller series of 17 patients presenting with odontogenic CFC; of these, 8 presented with mediastinitis, 4 had been prescribed NSAIDs, and 7 perished. NSAID use was reported in 80% of patients in a larger series of 94 CFC patients admitted to intensive care between 1995 and 2005, according to Shaikh et al[4]. In a number of additional studies, an association between NSAID use and cellulitis complicated by odontogenic mediastinitis was also documented. There have been reports of cellulitis other than cervicofacial, and the progression of fatal necrotizing fasciitis has been linked to the use of nonsteroidal anti-inflammatory drugs (NSAIDs).[5] This correlation might be accounted for by the anti-inflammatory mechanism of action of nonsteroidal anti-inflammatory drugs (NSAIDs), which is, in essence, a broad-spectrum defence mechanism against microbial invasion. Nonsteroidal anti-inflammatory drugs (NSAIDs) impede the cyclooxygenase pathway-mediated degradation of cellular arachidonic acid, thereby impeding the synthesis of prostaglandin and thromboxane A2, both of which are critical for cellular chemotaxis. Polynucleate cells and macrophage migration and phagocytosis are therefore inhibited by NSAIDs. Additionally, they diminish the initial indications of inflammation, which consequently

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postpones the need for consultation.[6,7] Experimentary studies, such as the one conducted by Solberg et al[8] on phenylbutazone, which demonstrated impaired granulocyte activation, phagocytosis, and intracellular elimination of streptococci and staphylococci in vitro, corroborated the detrimental effects of NSAIDs on infection. The Centres for Disease Control and Prevention (CDC) in the United States of America advised against the prescription of nonsteroidal anti-inflammatory drugs (NSAIDs) for the treatment of uncontrolled infections, or at the very least, against failing to perform a systematic assessment within 48–72 hours to monitor evolution.[1] CFC has a broad age range of manifestation, with an average age of 40 years at onset.[9,10] The mean age in the current series was 31 years, which can be attributed to the younger age pyramid. Paediatric varieties are considerably uncommon; the current series comprises a mere seven individuals aged 8–15 years. This could potentially be attributed to the lack of specific CFC risk factors, including alcohol consumption and smoking. Several instances of extensive CFC in minors, including mediastinal extension, have been reported.[11] Certain forms of mediastinal extension may be primary if they are particularly aggressive (caused by NSAID use or impaired diathesis) or if they are treated belatedly or inadequately. It is enabled by the convergence of cervical aponeuroses into infection pathways. The last mandibular molars have the potential to introduce infection into the cervical and para-tonsillar regions (also referred to as the anterior subparotid or pterygopharyngeal). These areas are critical for the transmission of the infection to other cervical spaces and the mediastinum through the detachable Reinke's space and vascular pathway. CFC affects males more than females. Umeda et al[12], in a review of 125 cases, reported a sex ratio of 3:1; in the present series there was likewise male predominance. In the present series, the main Beyond NSAIDs, diabetes constituted 41.6% of CFC risk factors. A significant proportion of these patients exhibited inadequate glycemic control. Diabetes is recognised as a contributor to immune dysfunction[12,13], which increases the susceptibility to non-specific infections. In addition to infections affecting the extremities, cellulitis is a prevalent infection among individuals with diabetes, particularly when infection sites include dental apical granuloma and tooth caries. Additional risk factors associated with the immune system encompass liver cirrhosis, HIV infection, kidney failure, and cardiac failure, all of which were not detected in the current series.[14] The predominant origin in the current study was dental (85%), which is marginally higher than the rate reported in the literature. Low socioeconomic status or inadequate oral and dental hygiene may contribute to this. As previously emphasised, extensive CFC is a contagious infection that spreads via the fasciae and nerves of the face and neck. Necrosis begins with tissue that is less oxygenated and vascularized, such as fascia, and progresses to tissue that is more vascularized, including subcutaneous fat and muscle.[14] An infection is frequently caused by a combination of aerobic and anaerobic microorganisms that operate in concert: the oxidative defences of immune cells (macrophages, granulocytes, and monocytes) are depleted by aerobic bacteria, which promotes the growth of anaerobic bacteria. Although Streptococcus pyogenes is the most prevalent pathogen, the following strains have been identified: Enterobacter, Fusobacterium, Bacteroides, and Staphylococci. One study identified eleven distinct strains in a single patient.[15] Nine samples in the current series contained multibacterial coccus and Gram-negative flora. Possible explanations for the remaining negative results include the use of antibiotics prior to admission. Awaiting bacteriology and the antibiogram, early broad-spectrum probabilistic antibiotherapy is of particular interest due to the multimicrobial character of CFC. However, medical intervention in isolation is not curative due to the isolation of purulent aggregates within necrotic tissue from the vascular system, which impedes the diffusion of antibiotics, even when administered parenterally. Primary broad-spectrum probabilistic antibiotherapy was utilised in the current series, supplemented with drainage and nearly complete surgical debridement as needed. According to the literature, mortality ranges from 19 to 40%.[16,] demonstrating the severe severity of this infection; the cure rate in the current series was 98.59 percent. After extensive mediastinal involvement, 3 fatalities ensued.

CONCLUSION

Cervicofacial cellulitis is a critical infectious emergency that demands prompt and specialised treatment. Anti-inflammatory drugs that do not require prescriptions inhibit the function of the immune system and obscure the clinical presentation, thereby postponing the diagnosis and comprising a genuine aggravation risk factor. It is important to emphasise that while the current series did demonstrate a robust correlation between nonsteroidal anti-inflammatory drugs (NSAIDs) and CFC, this does not establish causation (due to potential recruitment bias and the routine prescription of NSAIDs). However, it should be regarded as a mitigating circumstance, in accordance with the precautionary principle. Therefore, numerous health organisations, such as the Centres for Disease Control and Prevention (CDC), advise the cautious substitution of nonsteroidal anti-inflammatory drugs (NSAIDs) with conventional analgesics and antipyretics.

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