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Mediastinitis of odontogenic origin. A serious complication with 80 years of history

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Keywords: Mediastinitis•Descending necrotizing mediastinitis•systematic review,• Treatment and Evolution

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Abstract

We performed a systematic review of the literature about Descending Necrotizing Mediastinitis (DNM) of odontogenic origin. In parallel, a retrospective review of this pathology was carried out in an Oral and Maxillofacial Surgery Service of a reference hospital for a population of 1,100,000 inhabitants. The main objectives were to determine changes in mortality and prevalence of this serious complication. The systematic review included 51 articles with eighty nine patients and our study seven patients. The period of time with the highest number of cases was between 2000-2009 (38 patients). The percentage of mortality

observed was 20.2% in diffuse DNMs and 4.9% in localized DNMs . Thirty-one patients with DNMs in our review were admitted for more than 41 days. Despite evidence of a decrease on DNMs cases, publications have increased over the years, but it does not appear to be due to an increase in those that have an odontogenic origin. The survival of DNMs has improved since 1998, remaining stable since then. Despite the low prevalence of this disease, multicenter control studies are needed to achieve a better evidence about this entity.

Keywords: *Mediastinitis, Descending necrotizing mediastinitis, systematic review, Treatment and Evolution*

Introduction

Mediastinitis is a rare but severe infection defined as an inflammation of the connective tissues and structures within the mediastinum. It can be caused by a range of different etiologies including deep sternal wound infection following sternotomy, oesophageal perforation and descending necrotizing mediastinitis (DNM), which is often secondary to an oropharyngeal abscess.[1] The first description of mediastinitis was made by Hermman Boerhaave in 1724. He described the clinical case of Baron Von Vassenaer, who suffered a esophagus posthemhetic perforation (Boerhaave Syndrome).[2]

DNM diagnosis criteria established by Estrera et al.[3] include: (1) severe infection clinical manifestations; (2) demonstration of characteristic roentgenographic features; (3) documentation of the necrotizing mediastinal infection at surgery or post-mortem examination, or both; (4) establishment of the relationship of oropharyngeal or cervical infection, with the development of the necrotizing mediastinal process.

DNM can be caused by odontogenic (36%-47%), pharyngeal (33%-45%) or cervical (15%) infections.[1,4,5] This disease is often a polymicrobial infection and the most frequent microorganisms isolated are Streptococcus spp. (43-62%) and anaerobic microbial flora (typical of dental abscesses) (46-78%).[1,6]

DNM can be classified into Type I (localized), Type IIa (diffuse, extending into the lower anterior mediastinum) and Type IIb (diffuse extending into both the anterior and posterior lower mediastinum).[7] This classification is important to prognosis, but it is not used enough among clinicians.

Eighty one years passed since Pearse[8] disclosed the first series of patients with mediastinitis with *cervical suppuration*. This review included 110 patients with mediastinitis, and only 21 could be considered etiologically as DNM. According to this author, the mortality rates were 85% in patients whom conservative treatment was chosen and 35% in patients who underwent to a surgically treatment. Since then, there have been immeasurable changes in medicine, pharmacology, microbiology and surgery. It is also assumed that the oral health of the population has experienced a significant improvement in developed countries. Therefore, it would be reasonable to think that nowdays, DNM of odontogenic origin has a different epidemiological characteristics. In this situation, the queries that justify our work would be: Has the number of cases of DNM with odontogenic origin decreased over the years? Has the survival of these patients increased?

Material and method

Systematic review of the literature

This systematic review was planned following the PRISMA system (Preferred Reporting Items for Systematic Reviews and Meta-analyzes). We performed a search at the PubMed, MEDLINE and EMBASE electronic databases using the terms “Descending necrotizing mediastinitis“ OR ”Mediastinitis" AND "Infection" AND "Tooth" OR "Mediastinitis" AND "Focal Infection, Dental" OR "Odontogenic infection" AND "Mediastinitis".

The following inclusion criteria were considered:

- All selected articles must be written in English.
- Articles related to DNMs with a exclusively dental and/or periodontal origin (according to the criteria established by Estrera et al.[3]).
- Adult patients (over 18 years of age).
- Search period of time: January 1990 to December 2018.

The variables analyzed were: number of patients, age, sex, medical history, origin of the infection (odontogenic origin), imaging studies, microbiological cultures, treatment performed, hospital admission time and evolution of mediastinitis. All articles included were read in their entirety

Our Hospital Case Series

Simultaneously, a retrospective study was carried out in the Oral and Maxillofacial Surgery Service of our hospital (reference for a population of 1,100,000 inhabitants). We included all the patients diagnosed and treated for DNMs of a odontogenic origin between 1987 and 2018. The variables analyzed were the same as the articles included in the literature review. This study was not required approval by the Research and Ethics Committee because it was a retrospective study.

Results

Systematic review of the literature

The initial search in PubMed, MEDLINE and EMBASE databases identified a total of 1,138 articles. After the application of the inclusion criteria and subsequent screening at the title and abstract 1,083 articles were excluded. The full manuscripts of the remaining 55 articles were read. Another 5 were excluded because they did not included relevant information about this pathology. After reviewing the bibliography of the selected articles 1 article was included. Finally, 51 papers were fulfilled all inclusion criteria. (Fig. 1) (*see: complementary data*). We did not find randomized controlled trials or clinical practice guidelines published on the diagnosis and treatment of DNM. Most of the studies reviewed included a single case or series of a few patients.

The 51 articles (89 patients in total) were grouped according to their year of publication in three periods (years: 1990-1999; 2000-2009; 2010-2018). The period of time with the highest number of cases was between 2000-2009 (38 patients). It was significantly higher than the period between 1990-1999 (26 patients) and the period between 2010-2018 (25 patients). The mean age of patients was 41.5 years (range: 18-89 years) with male predominance (66 patients). More than half of patients (59 patients) had not relevant medical history. The most frequent medical conditions were alcoholism (11.2%), smoking (10.1%) and diabetes (7.9%). In 43 of the 89 patients studied (48.3%) a dental pyogenic focus could not be established. Of the remaining 46 patients, the origin was the third molar in 28 cases (60.8%) followed by the lower second molars in 17 cases (36.9%) *(see: complementary data)*. The final number of cases reviewed was not obtained from any registry of notifiable diseases.

A total of 219 imaging studies were requested in the 89 patients under review. Computed tomography (CT) was the most common method (116 CTs: 74 for diagnosis and 42 to control). The second most used was a simple chest x-ray (52 simple x-rays: 41 for diagnosis and 11 to control). Only 11 of the 89 patients were diagnosed exclusively by orthopantomography *(see: complementary data)*.

In relation to the microbiological study, 55 cases (61.8%) provide information on this topic. A total of 156 microorganisms were isolated, 150 were bacteria (96.1%) and 6 were fungi (3.9%). Table 1, details this information. In order to keep the airway patent, it was necessary to perform a tracheostomy in 18 patients and orotracheal intubation in 4 patients, one of them finally needed a tracheostomy. In the remaining 67 patients, It was not specified if they needed auxiliary techniques to keep the airway permeable.

Drainage of the purulent collections was performed on 83 of the 89 patients (93.3%), according to the following distribution: thoracotomy (49 patients), cervicotomy (24 patients) and mediastinoscopy-videothoracoscopy (4 patients). Dividing the hospital admission time into 20-day ranges, the distribution shown in figure 2 was obtained. Thirty-one patients with DNMs in our review were admitted for more than 41 days (39.24%). In 10 patients no information was provided on this variable.

Nowadays mortality remains high, 18 patients died: 20.2% in diffuse DNM and 4.9% in localized DNM. Seventy patients evolved satisfactorily with the established treatment and in only one patient the data are not conclusive about the evolution of the disease. Septic shock

and the DNM type (localized or diffuse) were risk factors that correlated with a poor prognosis.

Our Hospital Case Series

In the retrospective study done in our department we have collected 7 patients, which we divided into two chronological periods (Tables 2 and 3).

Between 1987 and 1999 four cases were identified with a mean age of 25 years, significantly younger than those observed in the systematic review of the literature. During this period there was only one death (case 1). The hospital admission time of the three patients who survived was 31.6 days (Table 2).

Between 2000 and 2018 the number of patients diagnosed and treated for an odontogenic origin DNM in our hospital was three. In the last five years, no cases were collected. The mean age of the patients was 37.6 years. No patient in this period of time died as a result of this complication (Fig. 3). The mean hospital admission time was 38.3 days (Table 3). The mortality rate due to odontogenic origin DNM was 14.2%.

Discussion

In the present study the methodology used to answer the query, "has mediastinitis decreased over the years?" must be viewed with caution. The final number of cases reviewed was not obtained from any registry of notifiable diseases. It is reasonable to assume that an undetermined number of patients with odontogenic mediastinitis have not been documented in scientific literature. However, the comparison between different historical periods can provide interesting information. Under this perspective, different

authors postulate an increase in the number of cases of DNMs (odontogenic and non-odontogenic) over the years.[5,9,10] Between the years 1938 and 1997, 152 cases of mediastinitis (usually) were collected in the literature. Between 1998 and 2008, 278 patients were published and between 2009 and 2014 480 patients were reported, of which 163 were of odontogenic origin.[5]

However, in the present review, focused on the odontogenic origin of the infection, the results are not so clear. We have observed a significant increase in the number of cases in the period between 2000-2009 (38 patients) compared to the years 1990-1999 (26 patients), but since 2010 the number of published cases seems to remain stable.[5,9-12]

There are no prospective studies about the incidence of odontogenic DNMs. Deu Martín et al[9] reported in their retrospective study that the incidence established in Catalonia (Spain) between 1996-2006 was 5.1 cases per 1,000,000 inhabitants/year. This incidence is much higher than we observed in our territory (Asturias, Spain) for the same period of time and in subsequent years. In the last five years no new DNMs cases of odontogenic origin were registered in our department.

The other objective of the present study was to assess whether the survival of this complication has increased over the years. Between 1938-1997, the mortality rate recorded in the literature was 37% (range 23-51%). From 1998 to 2014 it decreased significantly, reaching an average value of 19.5% (range 9-23%). [5,8,11-14] Our review shows that mortality has decreased from 1998 to 2014, but has remained stable in the last ten years. Mortality in cases of DNM of odontogenic origin was higher compared to overall mortality (25% vs 18%).

[5,13] However, the level of evidence is low. In the study by Sumi et al[14], there were no differences regarding the causative etiology (odontogenic vs non-odontogenic) in the four patients who died.

One of the secondary objectives of the present study was to identify the origin of the infection (causal tooth). Most are lower molars, particularly third molars followed by second molars. However, it is surprising that in the systematic review carried out, 48.3% of the patients did not show the exact location of the dental focus, despite being the origin of the infection. In addition, only 11 of the 89 patients with DNM of odontogenic origin had undergone a diagnostic orthopantomography. In many of the studies it was not detailed if the extraction of the causative teeth (only documented in 31 of the 89 patients) was performed acutely (in the context of surgery), was delayed or was not performed (see: supplementary data). Since 1960, the advantages of one or the other approach have been discussed.[15] For some authors, tooth extraction in the acute phase would reduce hospitalization.[16] In three patients of our serie, tooth extraction was performed simultaneously with cervical drainage, although it was not followed by a lower hospitalization time for these patients.

In the systematic review and in our serie, clindamycin was one of the most widely used antibiotics. Although clindamycin use is admitted in complicated DNM cases (with a toxic Streptococcal syndrome),[17-19] different authors postulate a slower evolution in those patients who have received clindamycin as the first antibiotic (e.g. alergicals to penicilins).[20] Although 15% of patients hospitalized in the head and neck surgery department have a penicillin allergy, only 10% of them are truly allergic.[21] On the other hand, although recent

studies indicate that only 5% of the empirical antibiotic therapy initiated will be modified after microbiological isolation in cultures[22], the severity of this pathology requires the performance of specific cultures and antibiograms.

Lastly, the percentage of patients who require admission to ICU due to an odontogenic infection has increased, from 7% to 24%, as well as the admission time.[23] In our review 59 patients with DNM stayed in ICU over 21 days. Health costs derived from odontogenic infections (complicated or not) is increasing. At the present time is necessary to create predictive models to control the evolution of any odontogenic infection after hospital admission. [1,16]

In conclusion, we did not find any randomized controlled trials or clinical practice guidelines on the diagnosis and treatment of MNA of odontogenic origin. The evidence of our study was obtained from 96 patients collected from the available literature, which provides a level of evidence III on the scale of Shekelle et al.[24,25] The number of published articles on mediastinitis has increased in the last 80 years, although it does not appear to be due to an increase in those of odontogenic origin. Survival of odontogenic DNMs has improved since 1998, remaining practically stable since then. Despite the low prevalence of this disease, multicenter control studies are needed to achieve better evidence on this entity.

Conflict of Interest

No conflicts of interest for all authors

Ethics statement/confirmation of patient permission

Ethics approval is not required. Patient permission/consent is not required

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LEGENDS

FIGURES:

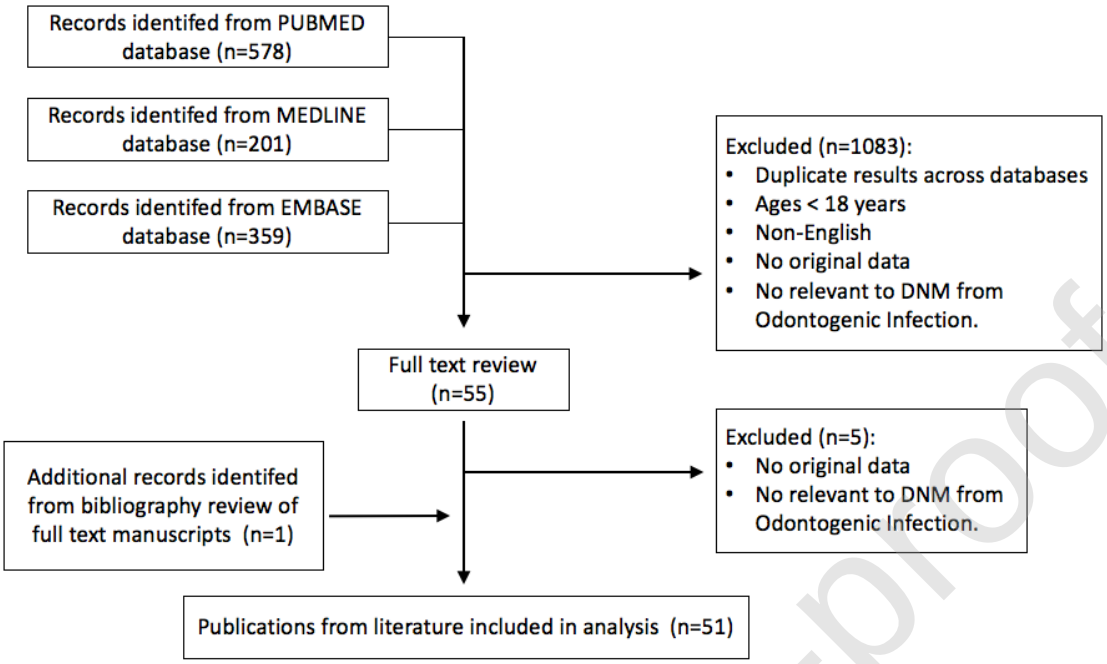

Figure 1. Flowchart of the evaluation and inclusion process.

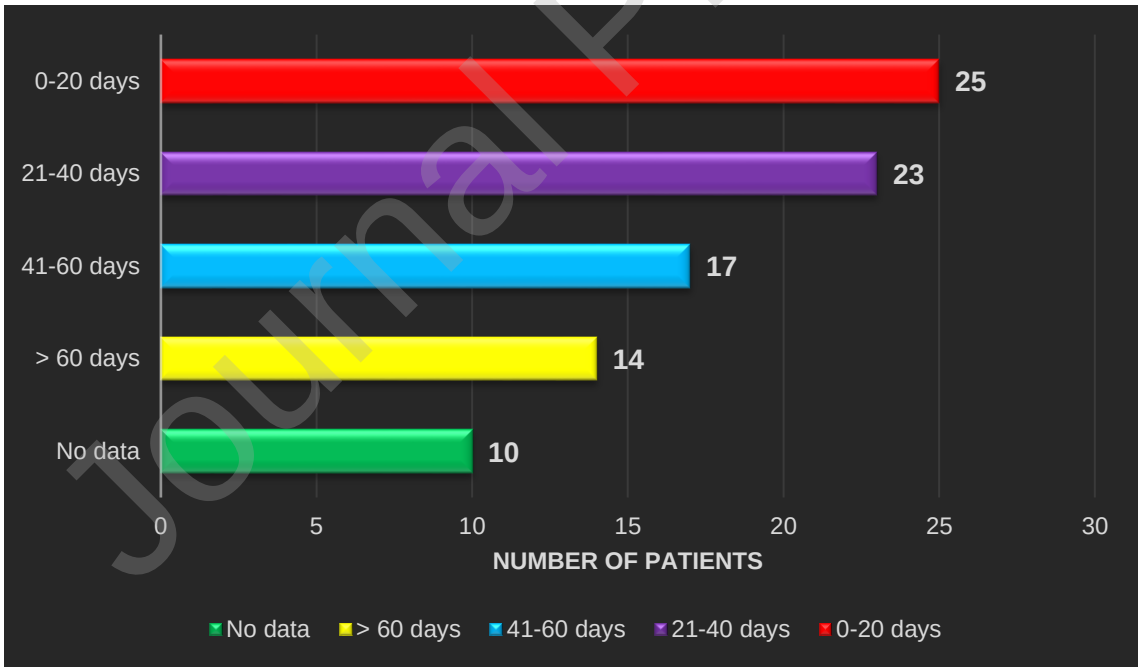

Figure 2. Hospital admission time for patients in our review.

Figure 3. TC, axial view (case 7) which shows a collection of liquid gas specks inside and peripheral enhancement surrounding the aortic arch as well as a slight reticulation of prevascular anterior mediastinal fat with predominatly right bilateral pleural effusion.

TABLES:

Table 1. Pathogenic microorganisms in the descending necrotizing mediastinitis of our review.

Table 2. Odontogenic mediastinitis. Our hospital case series, years 1987-1999.

Table 3. Odontogenic mediastinitis. Our hospital case series, years 2000-2018.

TYPE OF BACTERIUM (GENDER)	SPECIES
STREPTOCOCCUS (n=49)	Unspecified: 11 S. intermedius: 6 S. Salivarius: 2 S. Milleri: 4 S. Faecalis: 1 S. Coagulase negative: 1 S. Viridans: 9 S. Constellatus: 5 S. Cralis: 3 S. Mitis: 1 S. Sanguinis: 1 S. Anginosus: 3 S. b-hemolytic: 2
STAPHYLOCOCCUS (n=16)	Unspecified: 2 S. Aureus: 7 S. Epidermis: 6 S. Lugdunensis: 1
PSEUDOMONAS (n=12)	Unspecified: 2 S. Aeruginosas: 10
PREVOTELLA (n=11)	Unspecified: 3 P. Intermedia: 2 P. Buccae: 3 P. Melaninogenica: 2 P. Oris: 1
PEPTOSTREPTOCOCCUS (n=11)	Unspecified: 7 P. Micros: 3 P. Intermedius: 1
BACTEROIDES (n=9)	Unspecified: 2

	B. Melaninogenicus: 4 B. Intermedius: 1 B. Uniformis: 1 B. Fragilis: 1
ESCHERICHIA (n=7)	E. Coli: 7
ENTEROBACTER (n=6)	Unspecified: 3 E. Cloacae: 3
FUSOBACTERIUM (n=6)	Unspecified : 4 F. Necroforum: 2
ACINETOBACTER (n=4)	Unspecified: 2 A. Baumannii: 2
GEMELLA (n=3)	G. Haemolysans: 1 G. Morbillorum: 2
ENTEROCOCOS(n=3)	Unspecified: 2 E. Faecium: 1
VEILLONELLA (n=2)	Unspecified : 2
SERRATIA (n=2)	S. Marcescens: 2
KLEBSIELLA (n=2)	K. Pneumoniae: 2
LACTOBACILLUS (n=2)	L. Catenaformis: 1 L. Jensenii:1
HAEMOPHILUS (n=1)	H. Aphorophilus: 1
PROTEUS (n=1)	P. Mirabilis: 1
RALSTONIA (n=1)	R. Pickettii: 1
PROPINEBACTERIUM (n=1)	P. Acnes: 1
CORINEBACTERIUM (n=1)	Unspecified: 1

TYPE OF FUNGUS (GENDER)	SPECIES
CANDIDA (n=6)	Unspecified: 1 C. albicans: 3 C. parapsilosis: 1 C. krusei: 1

Table 1. *Pathogenic microorganisms in the descending necrotizing mediastinitis of our review.*

	CASE 1	CASE 2	CASE 3	CASE 4
Gender	Male	Female	Male	Male
Age (Years)	25	24	15	36
Medical History	No	Alcohol + HIV	Asthmatic	No
Tooth origin of the infection	4.7	3.5 , 3.6 y 3.7	3.6 y 3.7	3.7
Medical Treatment	Penicilin G	Clindamycin + gentamicin	Amoxicillin/Clavulanic acid + Imipenem	Amoxicillin/Clavulanic acid + gentamicin
Surgical Treatment	Tracheostomy+ cervical drainage	Cervical drainage + thoracic intubation	Cervical and thoracic drainage + nasotracheal intubation	Cervical drainage+ nasotracheal intubation
Microbiology	No information	Haemophilus S. faecalis	Gemella haemolysans	Staphylococcus coagulase negative
Evolution and Length of Hospitalization	Exitus	Resolution 35 admission days	Resolution 32 admission days	Resolution 28 admission days

HIV= Human Immunodeficiency Virus

S= STREPTOCOCCUS

Table 2*. Odontogenic mediastinitis. Our hospital case series, years 1987-1999.*

	CASE 5	**CASE 6**	**CASE 7**
Gender	Male	Male	Male
Age	38	43	32
Medical History	No	Diabetes mellitus (type II)	No
Tooth origin of the infection	4.8	4.5, 4.6 y 4.7	Mulitple foci
Medical Treatment	Clindamycin + gentamicin	Clindamycin + Imipenem	Amoxicillin/clavulanic acid + Imipenem
Surgical Treatment	Cervical drainage + tracheostomy + tooth extraction	Cervical and thoracic drainage +nasotracheal intubation	Cervical and thoracic drainage + tracheostomy
Microbiology	S. salivaris	Staphylococcus Klebsiella	S. Constellatus F. Necrophorum
Evolution and Length of Hospitalization	Resolution 60 admission days	Resolution 15 admission days	Resolution 40 admission days

Table 3*.Odontogenic mediastinitis. Our hospital case series, years 2000-2018*

S. = Streptococcus
F. = Fusobacterium