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ORIGINAL PAPER

Infected Cemento-Osseous Dysplasia: Analysis of 66 Cases and Literature Review

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Abstract
The aim of this study was to describe a series with 66 cases of infected cemento-osseous dysplasia (COD) and to discuss the demographic distribution, clinicoradiographic features and treatment of this condition. A study looking back on the diagnoses made at a single Brazilian centre within a 28-year timeframe was performed. A literature review with searches across five databases was also conducted to identify reports on osteomyelitis/infected COD. Descriptive and statistical analyses were performed. The case series study showed a female/male ratio of 21:1. Affected individuals' mean age was 57.4 years. Mandible was the most affected site (95.5%) and florid subtype was the most frequent infected COD (62.1%). Tooth extraction was the main factor associated with the development of infection associated within a COD lesion. The literature review retrieved 30 studies reporting 46 cases of this condition. Asian women in their 40 s and 50 s were more affected. Surgery for removal/curettage of necrotic bone was acknowledged as an appropriate approach to the treatment of this infection. The clinicodemographic data of the study were similar to data collected across the literature. Clinicians, maxillofacial surgeons and oral rehabilitation providers should be alert to the diagnosis of COD, since infection is a frequent complication whose management is challenging.

Keywords Bone diseases · Osteomyelitis · Infection · Florid cemento-osseous dysplasia · Oral medicine · Oral diagnosis

Introduction

Cemento-osseous dysplasia (COD) is defined as a fibro-osseous lesion (FOL) usually associated with tooth areas of the jaws without any neoplastic component [1]. The first meticulous description of COD was provided by Melrose and colleagues 42 years ago [2]. However, Dr. Brophy, in 1915, had already described the lesion, known at the time as periapical cemental dysplasia [3]. Two decades later, in 1933, Dr. Stafne conducted a comprehensive analysis of the clinicoradiological and histopathologic features of 35 cases, denoted as periapical cementoma [4].

CODs are not rare and usually affect women in their 40 s and 50 s, who receive the diagnosis at oral and maxillofacial radiology services or during an appointment with a general practitioner [5–8]. In clinical and pathological studies worldwide, COD has been described as the most common lesion among the FOL of the jaws, with an estimated frequency of 30% to 70% [9, 10]. The categorization of the subtypes of COD is indeed an issue for oral health providers. The most recent World Health Organization (WHO) handbook of odontogenic and maxillofacial bone tumours [1] defines COD as periapical COD (PCOD), commonly associated with apical areas of the anterior mandible; focal COD (FCOD), linked to a particular posterior tooth; and florid COD (FLCOD) described as having a multifocal (multiquadrant) involvement.

The infection that occurs within a lesion of COD is the main complication that an individual with this condition might face [11–40]. These cases are often reported in the

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literature as osteomyelitis [11–14, 19, 21, 23, 25, 28–35, 37, 39, 40]. However, there are insufficient criteria to define which cases are infected COD or true osteomyelitis. Osteomyelitis is an inflammatory intra-osseous process including the cortex bone and the periosteum, which is characterized by progressive inflammatory bone resorption/formation [41–43]. The term osteomyelitis has been used to describe multiple entities that have distinct pathophysiology and clinical courses. Therefore, the literature can be confusing due to a non-uniform terminology [41, 43, 44]. The diagnosis is based on a combination of clinical course, i.e., history of relevant dental infection, pain, swelling, suppuration, and the presence of exposed bone, supported by certain radiographic findings and by laboratory as well as histological findings [41–46].

The etiopathogenesis of infected COD involves the access of oral bacteria to the COD and secondary inflammation. Trigger factors for the development of infection are chronic inflammatory periodontal disease, dental caries leading to pulp necrosis, tooth extraction, and minor irritation caused by dentures in edentulous areas [11–13].

Analyses of a significant number of COD cases are sparse in the literature [2, 6, 15, 47, 48]. Furthermore, the existing epidemiological investigations of FOL of the jaws conducted in Asia, Europe, Africa and South America have reached divergent conclusions with respect to the occurrence and clinicopathological profile of CODs [8, 9, 15, 47–51]. As far as we know, no summary of data on the clinicoradiographic features and appropriate management of infected COD has been conducted. Thus, the aim of this study was to describe a series of 66 cases of Brazilian individuals with infected COD from a single reference centre and to discuss the clinicoradiographic features, treatment options, prognosis, and predictive factors of this condition.

Materials and Methods

Patients and Ethical Approval

An analysis of 66 individuals with infected COD was conducted. The guidelines to strengthen the description of observational studies (STROBE) were followed [52]. This study consisted of individuals who were referred to the service of oral and maxillofacial pathology of the School of Dentistry of Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Brazil, between 1990 and 2017. Participants had been evaluated and clinical information had been compiled by various providers with experience in oral diagnosis during this 28-year timeframe. This study is part of a previous investigation conducted by this research group [8], in which 383 cases of FOL of the jaws were analysed. Permission of the Ethics Board of UFMG (No. 52652016.2.0000.5149) was obtained. Following the Statement of Helsinki, participants agreed that their cases could be published.

Data Collection

The following data were compiled: participant gender, age, skin colour (non-white/white), anatomical location (maxilla/mandible), symptomatology (symptomatic/asymptomatic), swelling (yes/no), radiographic features (radiolucent/radiopaque/mixed), recurrence of the lesion (yes/no), trigger factors (e.g., tooth extraction or trauma by denture), treatment provided, and COD subtype.

The CODs were classified according to the WHO handbook [1]. The clinicoradiographic diagnosis of infected COD was made based on the presence of suppuration, fistula, pain, odour, bone sequestration with/without bone exposure in the oral cavity, as well as radiographic features [13, 53]. The collected radiographs were reviewed by a specialist in oral and maxillofacial radiology (C.N.A.O.K.). The most common radiographic images obtained were plain films (particularly panoramic views) and periapical radiographs. The histopathological records of all participants from the university's oral pathology laboratory were also reviewed in order to microscopically confirm the cases of infected COD. A senior lecturer (R.A.M.) in oral and maxillofacial pathology assisted with the ratification of the cases. Necrotic bone, intense inflammatory infiltrate and bone reabsorption, alongside the typical characteristics of COD were observed on the microscope slides. The exclusion criterion was missing information regarding sociodemographic data and the clinical characteristics of the disease.

Literature Review

A literature review of reports of cases or series of cases of individuals with osteomyelitis/infected COD was carried out in September 2018. Searches with no restriction regarding geographic area where the study was conducted or date when the article was published were conducted across five electronic databases: PubMed, Medline Ovid, Web of Science, Scopus and LILACS. Table 1 outlines the search strategies employed for each electronic database.

A manual search screening of the list of references of the selected articles was also performed in order to retrieve studies susceptible of having been overlooked at the time of the electronic searches. Additionally, a search in Google Scholar, restricted to the evaluation of the first one hundred references that had come through was carried out. If necessary, contact with authors was made in order to obtain additional information. The EndNote software (Clarivate Analytics, Philadelphia, US) was used. References that came in duplicate were deleted.

Table 1 Search strategy for each searched electronic database

Database	Search strategy
PubMed	Cemento-osseous dysplasia OR osseous dysplasia OR fibro-osseous dysplasia OR focal cemento-osseous dysplasia OR periapical cemento-osseous dysplasia OR periapical cemental dysplasia OR periapical cementoma OR florid cemento-osseous dysplasia OR gigantiform cementoma OR multiple cemento-ossifying fibroma OR sclerosing osteitis OR multiple exostosis OR sclerotic cemental masses AND osteomyelitis
Medline	Same as PubMed
Web of science	Same as PubMed
Scopus	"Cemento-osseous dysplasia" OR "osseous dysplasia" OR "fibro-osseous dysplasia" OR "focal cemento-osseous dysplasia" OR "periapical cemento-osseous dysplasia" OR "periapical cemental dysplasia" OR "periapical cementoma" OR "florid cemento-osseous dysplasia" OR "gigantiform cementoma" OR "multiple cemento-ossifying fibroma" OR "sclerosing osteitis" OR "multiple exostosis" OR "sclerotic cemental masses" AND osteomyelitis
LILACS	Cemento-osseous dysplasia OR focal cemento-osseous dysplasia OR periapical cemento-osseous dysplasia OR florid cemento-osseous dysplasia AND osteomyelitis

Inclusion/Exclusion Criteria

Studies reporting cases or series of cases of individuals with osteomyelitis/infected COD with enough clinical and radiological features confirming the diagnosis were included. Articles in English, French, Spanish or Portuguese were considered. In vitro studies, reviews and letters were excluded unless cases of individuals with this condition with sufficient data on radiological and clinical features had been reported within.

Data Extraction and Analysis

The authors (J.A.A.A. and C.N.A.O.K.) independently evaluated data using specially designed data extraction forms. In cases of divergence of opinion, a senior lecturer in oral and maxillofacial pathology (R.A.M.) was consulted to confirm inclusion or exclusion. Data of the selected studies were collected as follows: identification of the authors, year of publication, country and continent where the case(s) had been reported, number of individuals whose cases had been reported, patient gender and age, skin colour (non-white/white), time during which the lesion had taken place prior to diagnosis, and anatomical site (mandible/maxilla). Information about clinical features and symptomatology, radiological characteristics, i.e., image with radiolucency, masses with radiopacity, and combined image (radiolucency and radiopacity), COD subtype, trigger factors, treatment performed, and follow-up period (in months) was also extracted and analysed descriptively.

The Statistical Package for the Social Sciences (SPSS) software (IBM Corp., version 23.0, Armonk, US) was used for the analysis of the relationship between the subtypes of infected COD (periapical, focal and florid) and predictor variables (socio-demographic, clinical and radiological data). The ANOVA test and Fisher's exact test were applied to determine significant differences between the categorical variables considering $p < 0.05$.

Results

Case Series

The overall information for the 66 cases is displayed in Table 2. The most frequent subtypes of COD associated with infection were FLCOD (62.1%), followed by FCOD (27.3%), and PCOD (10.6%). Infection within a COD lesion most frequently occurred among females (63 cases, 95.5%). The female/male ratio was 21:1. Affected individuals' mean age at the time of the diagnosis was 57.4 years (± 10.1) (range 40 to 83 years). Female individuals' mean age was 57.6 years (ranging between 40 and 83 years). Male individuals' mean age was 55.3 years (range 46 to 61 years). Individuals in their 60 s were the most affected (n = 20, 31.2%), followed by individuals in their 50 s (n = 18, 28.1%) and individuals in their 40 s (n = 16, 25%). Non-white individuals (n = 58, 93.5%) were more affected. Most lesions were diagnosed in the mandible (n = 63, 95.5%). A total of 48 patients showed signs and symptoms for any length of time before the diagnosis, and swelling was observed in 28 subjects (42.4%) (Fig. 1a).

Radiographically, most regions of infected COD cases exhibited mixed density (77.2%), followed by radiopaque (17.5%) and radiolucent (5.3%) densities. All infected COD areas were surrounded by an osteolytic area with or without formation of a bone sequestrum. Figure 1b illustrates the radiographic features of the most common infected COD (florid) observed in the present study, showing irregular and diffuse mixed images in the mandible.

Regarding the causes of infection associated within a lesion of COD, tooth extraction (63.6%), followed by unspecified trauma due to wearing complete dentures

Table 2 Demographic and clinicoradiological features of individuals with infected cemento-osseous dysplasia (COD) from our service

Variables	COD subtype			p value
	Periapical	Focal	Florid	
Individuals	7	18	41	
Age (decades) mean ± SD (years)[c] (n = 64)	62.7 ± 8.2	56.6 ± 8.8	56.9 ± 10.9	0.347[a]
40–49	1	3	12	0.096[b]
50–59	0	7	11	
60–69	6	6	8	
70–79	0	2	7	
80–89	0	0	1	
Gender (n = 66)				
Female	7	17	39	0.999[b]
Male	0	1	2	
Skin colour[c] (n = 62)				
White	0	2	2	0.721[b]
Non-white	6	15	37	
Anatomical location (n = 66)				
Maxilla	0	0	3	0.677[b]
Mandible	7	18	38	
Symptomatology[c] (n = 62)				
Symptomatic	4	11	33	0.155[b]
Asymptomatic	1	7	6	
Swelling[c] (n = 34)				
Yes	2	7	19	0.347[b]
None	1	0	5	
Radiographic features[c] (n = 57)				
Radiolucent	1	1	1	0.053[b]
Radiopaque masses	3	4	3	
Mixed	3	12	29	
Trigger factors[c] (n = 33)				
Tooth extraction	3	3	15	0.760[b]
Trauma by denture	2	3	7	
Treatment[c] (n = 59)				
Surgical removal of necrotic bone	5	18	36	0.077[b]
Recurrence[c] (n = 64)				
Yes	1	2	5	0.999[b]
No	6	16	34	

SD standard deviation

[a]ANOVA test

[b]Fisher's exact test

[c]Data were not available in some cases

(36.4%) were the main trigger factors. Surgical removal/curettage of necrotic bone was the most common treatment (89.4% of cases). In 56 cases (84.8%), no recurrence was reported. No significant association was observed between trigger factors, anatomical location, treatment, or recurrence of patients with infected COD ($p > 0.05$).

A gross section of necrotic bone was represented by irregular, hard and brownish-yellow material of variable size. Microscopic evaluation of H&E-stained slides revealed necrotic tissue characterized by loss of osteocytes and bone marrow replaced by amorphous material and an inflammatory infiltrate (Fig. 1c–f).

Literature Review

During the electronic searches, 531 references were collected. Two-hundred references in duplication were deleted and 331 references were scrutinised by applying the inclusion and the exclusion criteria. Four references that fulfilled the inclusion/exclusion criteria were singled out in the

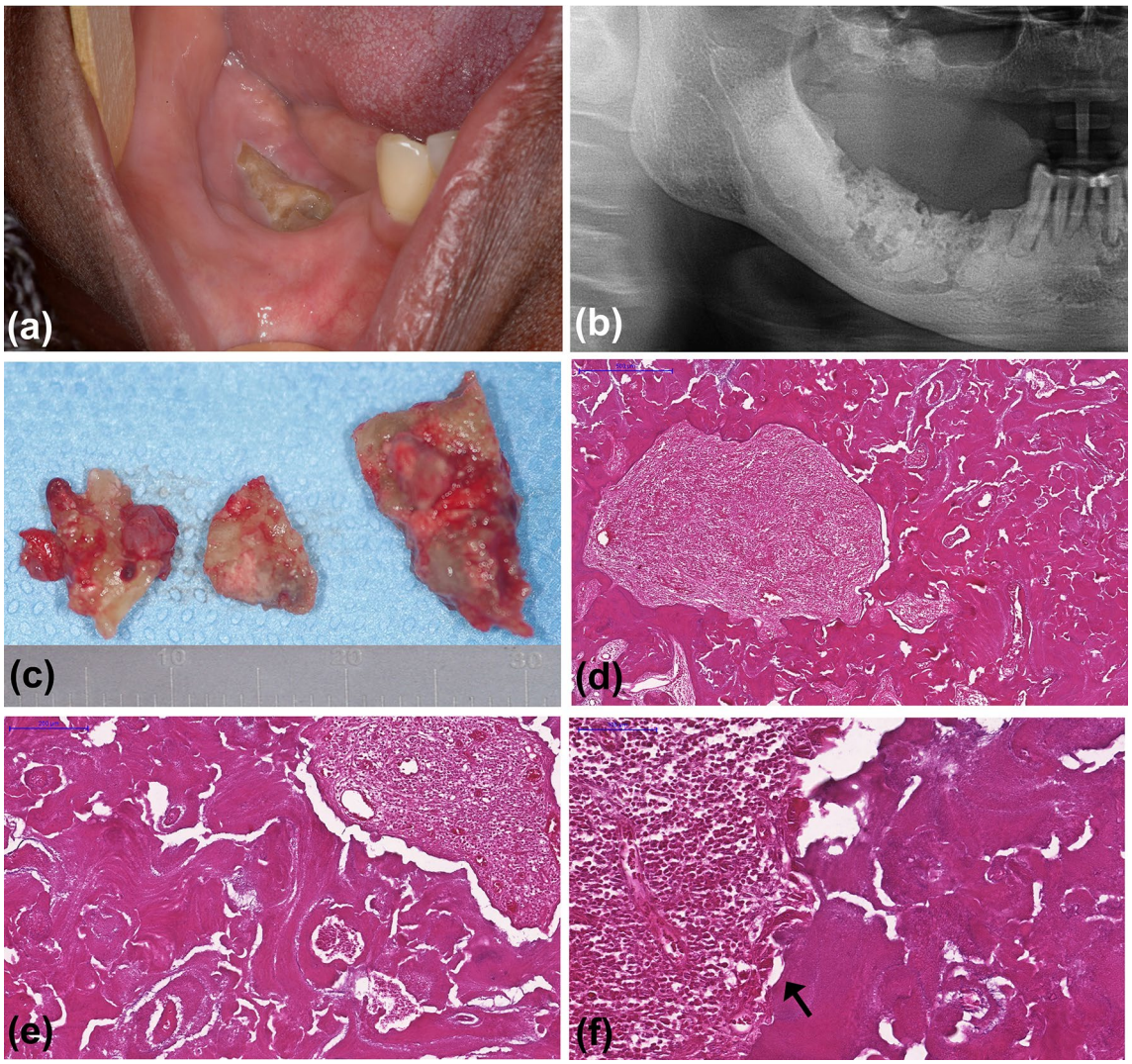

Fig. 1 Clinicoradiographic and histopathological features of the most common infected cemento-osseous dysplasia (COD) in the current study. **a** Clinical presentation of a 65-year non-white female with exposed yellowish bone masses in the right alveolar ridge of the posterior mandible. **b** Panoramic radiograph of infected florid COD showing an irregular and diffuse mixed image above the mandibular canal measuring approximately 4.0 cm in the right posterior edentulous mandible. **c** Surgical specimen of the infected cemento-osseous tissue including the sequestrum showing brownish-yellow and grossly fragmented irregular areas. **d**, **e** Compact bone tissue with medullar spaces replaced by loss and vascularized connective tissue with an inflammatory infiltrate or an amorphous and eosinophilic mass (necrotic tissue). Also, there were no osteocytes (H&E staining, × 5 and × 10 magnification, respectively). **f** Intense chronic inflammatory infiltrate in medullar spaces (osseous resorption, black arrow) (H&E staining, × 20 magnification)

manual search and in the Google Scholar search. Efforts were made to contact the authors of one study [54]; however, the article could not be retrieved. A total of 30 articles reporting 46 cases of osteomyelitis/infected COD were selected [11–40]. The countries where most cases were reported were Singapore in Asia, the Netherlands in Europe, the United States and Brazil in the Americas, and Nigeria in Africa.

Forty-four affected individuals were females (95.7%) and two were males (4.3%) (Table 3). The female/male ratio was 22:1. As regards COD subtype, FLCOD (93.5%) was the most frequent, followed by FCOD (4.3%), and PCOD (2.2%). Affected individuals' mean age was 53.3 years (± 10.5) (range 33 to 79 years). Female individuals' mean age was 53.8 years and male individuals' mean age was 43 years. With respect to skin colour, 21 individuals were white (51.2%) and 20 were non-white (48.8%). Mandible was the site most frequently affected by lesions (87.8%). Individuals showed pain (88.8%), swelling (53.3%), and fistulation with pus discharge (46.6%). Symptoms lasted between 5 days and 192 months (median: 3 months).

Table 3 Demographic and clinical features of the cases of osteomyelitis/infected cemento-osseous dysplasia (COD) retrieved in the present literature review

Variables	n (%)
Gender	
Female	44 (95.7)
Male	2 (4.3)
Ratio	22:1
Age (decades)	
30–39	3 (6.5)
40–49	15 (32.6)
50–59	14 (30.4)
60–69	11 (24)
70–79	3 (6.5)
Skin colour[a] (n = 41)	
Non-white	20 (48.8)
White	21 (51.2)
Evolution time[a] (median, min–max) (n = 18)	3 months, 5 days–192 months
Anatomical location[a] (n = 41)	
Mandible	36 (87.8)
Maxilla	5 (12.2)
COD subtype	
Florid	43 (93.5)
Focal	2 (4.3)
Periapical	1 (2.2)
Radiographic features	
Mixed	33 (71.7)
Radiopaque masses	13 (28.3)
Trigger factors[a] (n = 21)	
Tooth extraction	11 (52.3)
Trauma by denture	7 (33.3)
Endodontic therapy	1 (4.8)
Tooth restauration	1 (4.8)
Tooth extraction and trauma by denture	1 (4.8)
Treatment[a] (n = 36)	
Surgical removal of the necrotic bone/curettage	9 (25)
Surgical removal of the necrotic bone/curettage associated with antibiotics/analgesics	23 (63.9)
Antibiotics/analgesics	3 (8.3)
Radical surgery (partial mandibulectomy)	1 (2.8)
Follow-up period[a] (n = 13) (median, min–max)	12 months, 15 days–120 months

SD, standard deviation

[a]Data were not available in some cases

As regards radiographic features of osteomyelitis/infected COD, most cases exhibited mixed density (71.7%) with a bony sequestrum image, followed by radiopaque masses (28.3%). Bone expansion was reported in seven cases. Treatment included surgical removal and/or curettage of necrotic bone associated with antibiotics and/or analgesics (63.9%), followed by surgical removal/curettage of necrotic bone alone (25%). Three articles reported the use of systemic antibiotics associated or not with analgesic drugs. The main antibiotics used were clindamycin (dosage range 250 to 300 mg) and amoxicillin (500 mg) combined or not with clavulanic acid (125 mg). In one case, surgical removal of necrotic bone was supplemented with antibiotics and hyperbaric oxygen. In one case report, partial mandibulectomy was performed. Among the 13 individuals who had been followed through, the mean time of follow-up was 12 months (ranging between 15 days and 120 months), and one case reported recurrence of the lesion. Three cases were lost during follow-up.

Discussion

In this series, 66 cases of infection occurring within a lesion of COD have been added to the literature. Our literature review demonstrated that this condition has been seldom addressed, with only 46 cases reported worldwide thus far. Based on the most recent WHO handbook [1], similarity was observed between the findings of the case series and the present review regarding the occurrence of infection occurring within a lesion of FLCOD, FCOD or PCOD. There is no consensus about the worldwide prevalence of COD. Retrospective studies in North and South America have demonstrated that PCOD is the most frequent subtype [6, 49, 50]. However, de Noronha Santos Netto et al. [9] reporting 65 cases of FLCOD and Owosho et al. [48], reporting 17 cases, stated that this subtype was the most frequent in their surveys. In addition, an international multicentre study involving five institutions of the Americas and Africa also provided a large series of 82 patients affected by FLCOD [47]. These findings may reflect the fact that cases of FLCOD are more often reported as symptomatic outcomes than the other COD subtypes. Interestingly, Asia was the continent where a significant number of cases was detected. Among the 46 cases retrieved in the present review, 20 cases of osteomyelitis/infected COD were reported in Singapore, India, Iran, South Korea and China.

In general, studies reporting cases of COD have demonstrated a marked predilection for descendants of Eastern Asia or Africa populations [55, 56]. An important issue that should be taken into account; however, is miscegenation worldwide. Brazilians, for instance, are people characterised by their heterogeneity as a result of more than 500 years of miscegenation involving Europeans, Amerindians, Africans, Levantines, and East Asians [57]. In this context, it is challenging to assign individuals to particular ethnic groups. Herein, the affected individuals were described as white or non-white. In the present series, we did not identify any individuals with an Asian background. Non-white individuals were more affected, in agreement with retrospective studies on COD published elsewhere [6, 9]. In addition, no difference regarding skin colour was observed in the current review.

Equivalent to this review, the case series demonstrated that osteomyelitis/infected COD has a strong predilection for female individuals, with marked occurrence of this condition among individuals in their 60 s, 50 s and 40 s. Likewise, studies about FOLs of the jaws, including COD cases have exhibited a female predilection [9]. Additionally, in a recent investigation [6] in which COD cases were assessed by cone beam computed tomography, 71 women (86.6%) were affected. Conversely, the authors of a Japanese study [58] reported that CODs more frequently affect men of more advanced ages and hormonal factors were suggested to be associated with sex predilection. As regards osteomyelitis of the jaws, individuals of any age may be susceptible and a slight male predilection exists [59]. Based on the findings of the present case series, women seem to be more likely to develop infection occurring within a lesion of COD than men. However, due to the limited number of cases with osteomyelitis/infected COD described in the literature within the last three decades (as shown in Fig. 2), the question concerning which sex is most affected by this condition is yet to be fully answered.

The incidence of osteomyelitis of the jaws has plummeted [41, 42, 60]. The reasons might be associated with the use of more sophisticated medical and dental technology, economic improvement and adoption of an adequate lifestyle [61]. However, individuals affected by CODs may be susceptible to such an outcome, as observed in Fig. 2. The results of the present review show that the occurrence of osteomyelitis/infected COD has increased twofold since 2007. The classification of FOL of the jaws has been an issue over time and different classification systems have emerged [5, 55, 56]. Possibly, cases of infection occurring within a lesion of COD have been under-reported over time due to misdiagnosis.

The management of an infection occurring within a lesion of COD is challenging for clinicians and maxillofacial surgeons [13] due to the lower vascularization and increased bone hardness, predisposing the affected area to necrosis [62]. In agreement with the present review, our case series demonstrated that the main predictive factors for the development of osteomyelitis were tooth extraction and the wearing of complete dentures. However, the

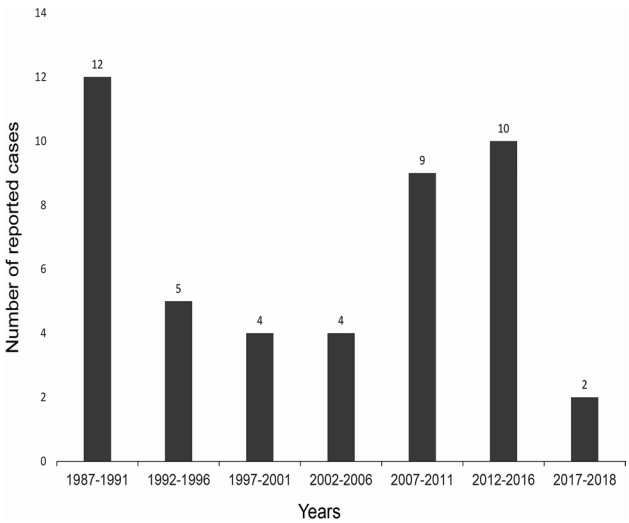

Fig. 2 Distribution of reported cases of osteomyelitis/infected cemento-osseous dysplasia over time

patients had been referred to our service, which precluded the retrieval of information about how the extraction was performed. Hence, oral health care providers should avoid submitting individuals with COD to any sort of surgery, including those for the positioning of temporary skeletal anchorage devices (mini-screws and mini-plates) or orthodontic traction [7]. Edentulous adults and elderly individuals wearing complete dentures should also be under strict surveillance to mitigate the chances of trauma to the COD jaw area [11, 12].

The mandible was affected in almost 90% of the individuals of the case series and of the present review. Indeed, COD usually takes place adjacent to lower teeth above the inferior alveolar canal. The position and the cementum-like material that usually forms indicate that COD may have its origin linked to the periodontal ligament [56, 63]. Despite the close proximity to the periodontal ligament, in most cases this structure remains visible and intact [58]. In general, FCOD and FLCOD affect the posterior area of the mandible, whereas PCOD exhibits a predilection for the anterior mandible [9, 15, 50, 64, 65]. Awareness of the anatomical distribution of COD is important, particularly for the differential diagnosis with other oral and maxillofacial diseases.

Moreover, previous investigations have indicated that COD is for the most part asymptomatic and may be accidentally diagnosed during oral radiographs taken routinely [6, 9]. However, Kawai et al. [58] showed that nearly 60% of the 54 individuals evaluated in their research presented symptoms or signs of inflammation. The results of the cited case series demonstrated that most affected individuals were symptomatic and showed swelling of the affected region. These finding were confirmed by the current literature review, in which more than 90% of the individuals reported pain. Therefore, pain, swelling and presence of pus formed the profile of the individuals with an infection occurring within a lesion of COD.

Radiographic examination is an effective method for the detection of osteomyelitis/infected COD. A mixed radiopaque/radiolucent appearance is the most common finding. Well-defined irregular radiopaque masses with radiolucent rims confined to the alveolar bone have been observed at the intermediate stage of COD maturation. At this point, there is an increased mineralization of the lesion and consequent damage to local vascularization, favouring secondary infection [48]. Mixed feature is determined from osteolysis of the inflammation. Likewise, a similar radiographic aspect has been observed among individuals with other bone conditions such as Paget's disease and osteopetrosis [14, 49]. Osteosarcomas of the jaws and metastatic carcinomas of other parts of the body should also be included in the list of conditions with similar characteristics during the differential diagnosis, particularly when osteomyelitis/infected COD occurs at the mandibular angle and ramus [9, 49, 64, 65].

An efficient diagnosis is mandatory for the clinician choosing an appropriate treatment strategy for the management of infected COD. The literature has indicated different treatment approaches for osteomyelitis of the jaws, regardless of the association with COD. Segmental resection, transport of bone, reconstruction in two stages, treatment with antibiotics and hyperbaric oxygen, as well as soft tissue grafting have been reported [12, 28, 41–45, 59–61, 66, 67]. Since bacterial biofilms are resistant to antibiotic therapy, antibiotics play an adjuvant role by possibly preventing the formation of new biofilms by killing bacteria before they attach to the necrotic bone [67]. The current literature review revealed that there was no consensus regarding the most appropriate therapy for infected COD lesions, but curettage/surgery for removal of necrotic bone was acknowledged as an appropriate approach to the treatment of such a condition, as reported in 88.9% of cases. In line with the literature review, in our institution, 89.4% of cases were similarly treated. Therapy with antibiotics/analgesics was reported in 23 cases (63.9%). In addition, the literature has also recommended antibiotic prophylaxis prior to surgical procedures, to avoid the risk of infection [2, 20, 35, 36, 40]. The limited available data do not allow us to state whether antibiotics or adjuvant therapies are supportive or not for this condition. The knowledge gained with this study confirms that in the initial phases of infection, the diagnosis of this condition largely relies on clinicoradiographic assessment rather than histopathological exams. Therefore, periodic radiographic monitoring is encouraged for affected individuals [6].

The findings of this case series and literature review should be viewed with caution. The first limitation regards missing data, an issue inherent to the retrospective nature of the study. Keeping in mind that no standardization of the treatment for infection associated within a lesion of COD exists, mainly because of the variability in the regimen of antibiotic and analgesics used, further investigations, particularly multicentre studies, are needed for a more evidence-based management of this outcome.

Conclusion

When COD diagnosis is established, patients should be periodically monitored with clinical and radiographic examination. Prophylaxis and reinforcement of adequate oral hygiene to control periodontal disease and to prevent tooth loss should be also encouraged. Trauma of any kind in the COD region, including trauma caused by complete dentures or surgical procedures should be avoided to prevent the exposure of the sclerotic masses to the oral cavity. In some cases, in which avoidance of invasive procedures is unfeasible, antibiotic prophylaxis is recommended. Presence of pain, suppuration and appearance of areas surrounded by

osteolysis with or without formation of bone sequestration are indications for intervention in infected COD. Despite the lack of standardization of the treatment regimen, the curettage/surgical removal of necrotic bone is the most recommended approach to such condition.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval The study was approved by the Human Research Ethics Committee of the study institution (No. 52652016.2.0000.5149).

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