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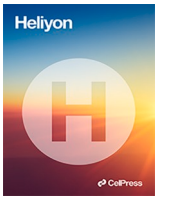

Case report

Florid cemento-osseous dysplasia: A case report and review of literature

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ABSTRACT

Florid cemento-osseous dysplasia (FCOD) is a benign slowly growing fibro-osseous disorder, usually diagnosed accidentally through routine radiographic examination. The lesions are generally asymptomatic, but, in the most severe cases, focal enlargement and pain may occur due to infection. Here, we report the rare case of a Caucasian middle-aged woman showing, at orthopantomography performed during routine dental check-up, the presence of multiple symmetrical, dense and lobulated radiopaque bone lesions in several areas of the jaws, surrounded by a radiolucent border. The lesions were asymptomatic. Histologically, the replacement of healthy bone by metaplastic bone and fibrous tissue, typical of FCOD, was observed. The lesion remained painless, clinically and radiologically stable over two years follow-up. In asymptomatic cases, no treatment is required, but active clinical and radiographic follow-up are recommended at long-term, to reduce the risk of dental infections and oral surgery involving the area of the lesion. The avascular nature of FCOD contributes to susceptibility to severe infection, bone sequestration and osteomyelitis, limiting the in-site penetration of the antibiotics. Therefore, a careful clinical and radiographic monitoring of the lesions is recommended together with periodical dental check-up.

1. Introduction

The term “fibro-osseous lesion” (FOL) is a generic name used for a group of jaw disorders in which bone is replaced by benign connective tissue matrix with different degrees of mineralization, from woven bone to cementum-like round acellular basophilic structures that are indistinguishable from cementicles [1]. In the maxillofacial region, the term FOL includes cemento-osseous dysplasia (COD), fibrous dysplasia (FD) and cemento-ossifying fibroma (COF), and their subtypes [1].

Lichtenstein described the first case of fibro-osseous lesions of the head and neck, in 1938. Since then, several classifications had been proposed because of the lack of consensus on diagnostic criteria. In 2017, WHO published the classification of head and neck tumors (further updated in 2024) [2,3], where the COD lesions are distinguished into the three subtypes: Periapical Cemento-Osseous Dysplasia (PCOD), when the lesions are limited to the anterior mandible and affect one or more teeth; Focal Cemento-Osseous Dysplasia (Focal COD) with a single lesion localized at the posterior jaws; Florid Cemento-Osseous Dysplasia (FOCD), a

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disseminated form of periapical osseous dysplasia, showing multifocal multiquadrant lesions that may, rarely, cause the deformation of the jaw bone [4]. Noffke further suggested a different nomenclature, omitting the word "cementum" to reflect the clinical and biological characteristics of these lesions, which, although localized at the periapical region of tooth, are not directly in contact with the dental root [5]. A further classification was proposed, according to the growth potential and distinguished the expansive lesion group, including the familial and non-familial types, and the non-expansive group, the latter including florid, focal and anterior mandibular variants [6].

Overall, COD lesions are a benign fibro-osseous conditions, mostly localized, as periapical and focal types, at the jaws near the periapical area of vital teeth [4,7]. A long asymptomatic course is often reported [4]. Middle-to-old aged African descent women are mostly affected [1,8,9].

FCOD, firstly described by Melrose, Abrams and Mills in 1976, has an unknown etiology, while the pathogenesis includes a reactive process of the alveolar bone of the jaws, where the normal bone tissue is replaced by connective matrix, consisting of a poorly cellularized cementum-like material and cellular fibrous connective tissue [1].

Because FCOD is a benign, usually asymptomatic and slowly-growing condition it is usually diagnosed accidently during a routine dental radiographic examination [1,4,9,10]. The diagnosis of FCOD is based on both clinical and radiographic findings [9,11–13]; the histological assessment is useful for the differential diagnosis, in particular in presence of mixed multifaceted lesion rapidly growing, as in the case of osteoblastoma. No treatment is generally required, but active follow-up of the lesions is needed, since the avascular nature of the lesion contributes to susceptibility to severe infection and reduces the ability of antibiotics to reach the site [8]. In case of infective complications, symptoms and signs can occur, such as dull pain, purulent drainage, focal expansion and facial deformities [1].

The aim of this report is to describe the rare case of a Caucasian middle-aged women diagnosed with FCOD, as fortuitously observed during a routine dental visit, and to provide an updated overview of the current literature on this disorder.

2. Case report

A 44-year-old Caucasian woman was referred to the Oral Medicine Department (S.C. Odontostomatology II) of the St Paolo and Carlo Hospital in Milan because of a bone lesion in the left lower jaw, accidently detected by her general practitioner, a few weeks earlier during a routine radiographic examination. The patient was asymptomatic with no relevant co-morbidities and not under pharmacological therapies.

At extraoral examination, there were no swellings and asymmetries. Intraoral examination revealed the absence of evident or even palpable swellings or pathological mucosal signs. All teeth were normo-responsive at vitality test. Orthopantomography (Fig. 1) revealed the presence of a homogeneous radiopaque round area surrounded by a radiolucent border, with well-defined margins, at the radicular apex of tooth 3.3. Two distinct oval-shaped radiolucent lesions were detectable at the periapical area of teeth 3.5 and 3.6. A similar radiopaque round homogeneous lesion with well-defined margins, surrounded by a radiolucent border, was also present distally to tooth 3.7 and at the periapical area of tooth 4.7, also involving the periapical area of teeth 4.6, 4.5 and 4.4.

Cone-beam CT scan was further examined to evaluate the lesion at the periapical area of tooth 3.3, revealing the absence of continuity of the lesion with the dental root and a homogeneous radiographic aspect. The radiographic image of the lesion showed about 1.5 cm of major diameter and well-defined, but non-perfectly uniform, edges (Fig. 2).

In agreement with the patient, a multiple diagnostic incisional biopsy of the osseous lesion was performed at the radicular apex of tooth 3.3, under the clinical suspicion of FCOD in differential diagnosis with chronic diffuse sclerosing osteomyelitis, fibrous dysplasia, cemento-ossifying fibromas and osteomas. After signing informed consent, local anesthesia with mepivacaine 2 % with vasoconstrictor

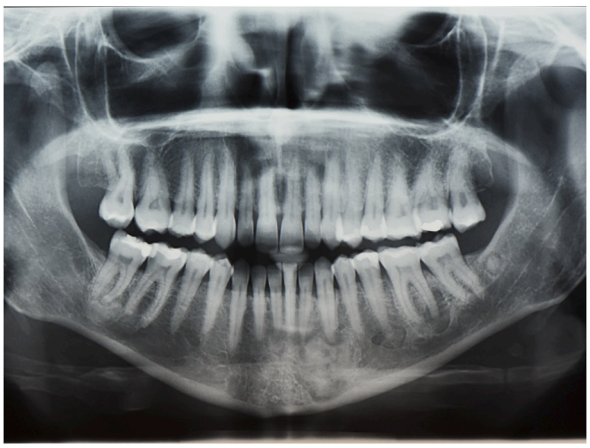

Fig. 1. Orthopantomography (November 2020) showing the presence of a radiolucent areas with well-defined contours, mimicking periapical endodontic lesions, in the apical region of teeth 3.5 and 3.6, mixed radiolucent-radiopaque lesion located on the periapex of tooth 3.3 and two radiopaque lesions with a radiolucent halo il periapical region of tooth 4.7 e in edentulous area corresponding to tooth 3.8.

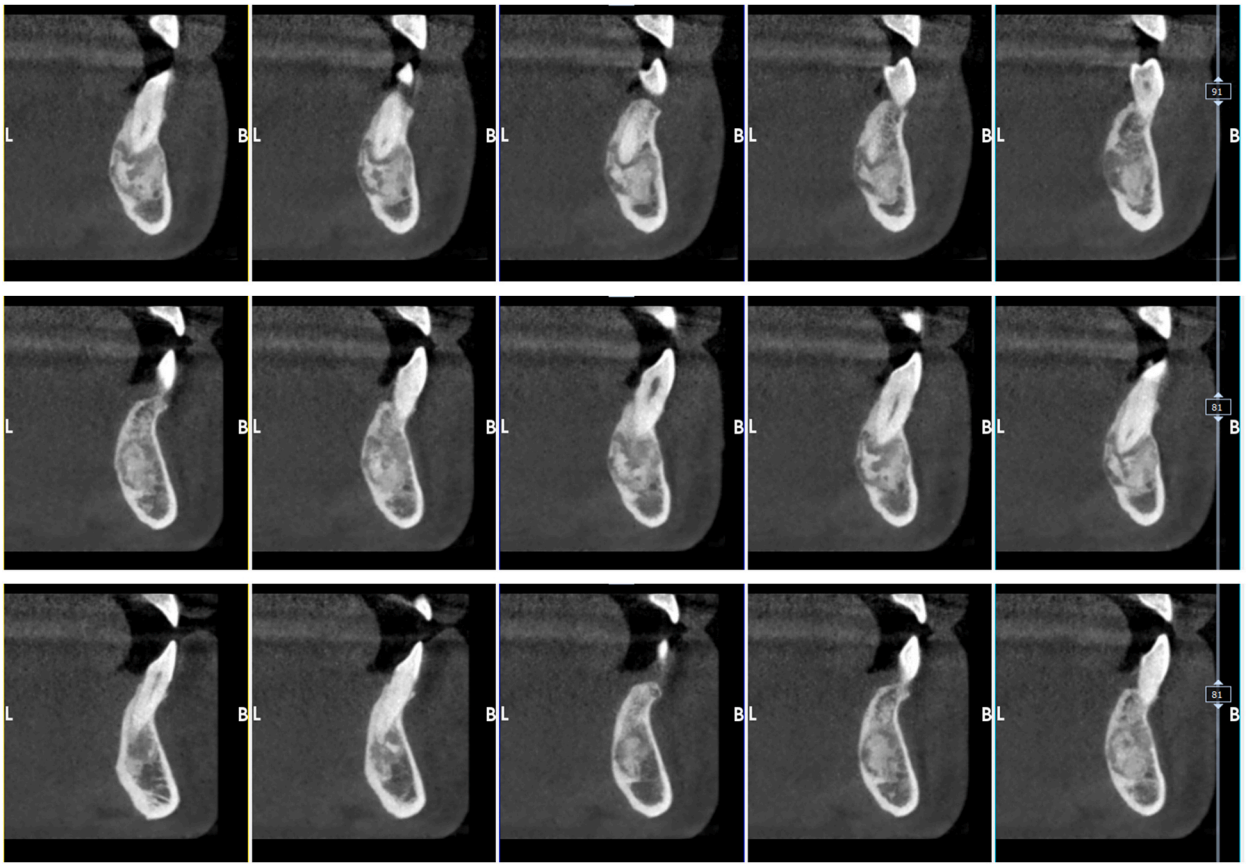

Fig. 2. CBCT (February 2021) section of the left mandibular canine revealed mixed radiolucent-radiopaque bone lesion with thinning of the mandibular lingual cortical bone and the absence of osseous expansion.

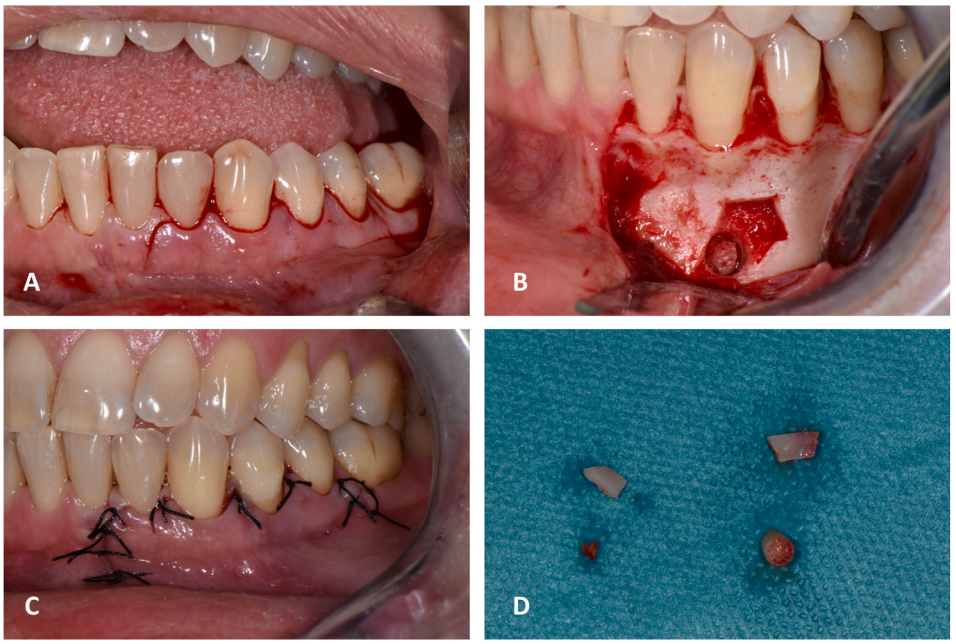

Fig. 3. Surgical procedure (a, b, c) and bone specimens (d).

(adrenaline 1:100.000), a full-thickness intrasulcular flap setup arrangement and soft tissue detachment were carried out. Three bone samples (of major axis from 2 to 5 mm) and a portion of pathological bone tissue (using a core drill of 4 mm in diameter) were taken; 4/0 non-absorbable silk stiches were placed and compressive hemostasis was obtained. Specimens were fixed in formalin and sent to the Pathological Anatomy Department (Fig. 3a-b-c-d). No intra-operative and post-operative complications occurred.

After 3 weeks, the follow-up visit showed the soft tissue healing at the surgical site and the absence of signs and symptoms of infection and inflammation. The histopathological report showed the presence of trabeculae irregular in thickness and shape without osteoblastic and osteoclastic activity. The intercellular tissue consisted of hypocellular fibrous tissue with cementolites and spindle cells without cytological atypia. (Fig. 4). Through the combination of the clinical, radiological and histopathological findings, the diagnosis of "florid cemento-osseous dysplasia (FCOD)" (according to the 2017 WHO classification) was made. The patient was informed about the benign nature of the condition and about the management of the condition, which included active, long-term follow-up with clinical and radiographic examinations, reinforcing the importance of accurate oral hygiene and the need of early diagnosis and treatment of dental diseases, in order to avoid infection at the lesion sites.

A recall was, then, scheduled after 6 months to assess the progression of the bone lesions, which appeared asymptomatic and stable at the radiological examination (Fig. 5). A further visit was planned one year later, and a clinical plus radiological follow-up after 2 years. Eighteen months after the incisional biopsy, the patient was still asymptomatic, only reporting dentinal hypersensitivity during cold drink intake in the left lower jaw due to mild gingival recessions in the area of the intrasulcular flap performed during the biopsy. One more year later, the clinical picture was still stable, and, radiographically, the orthopantomography (Fig. 6) showed the opacification of osseous lesions at teeth 3.3, 3.6 and 4.7, as expected consistently with FCOD. Hence, no changes were further applied to the active and regular follow-up plan, considering the stability of the lesions and the high compliance of the patient. No adverse or unanticipated events occurred. The patient currently continues with periodic dental visits, every six months, with radiological assessments every two years, or in case of symptoms and/or infections.

3. Discussion

This case report describes the rare case of a middle-aged Caucasian woman affected by FCOD, representing an emblematic clinical picture for the dental general practitioner and the oral medicine specialist, although within the limitations of the study design (e.g., observational study on a single patient, lack of possibility to generalize). The diagnosis, both clinical and histopathological, and the management, including clinical and radiographic follow-up, were described analytically.

FCOD is a benign condition that can affect two or more quadrants of the jaws [2,4,6,8,14–16]. Lesions, often bilateral and symmetrical, as in our patient, are characterized by cellular-fibrotic tissue with calcified structures, irregular osseous trabeculae and cementoid mass and they are associated with vital teeth [6,17]. Despite the etiology is unknown, according to the WHO classification, some histological peculiarities suggest the pathogenesis could be associated with periodontal abnormalities [1,8]. FCOD could be associated with an abnormal cementum deposition, due to a disorder in the differentiation of periodontal ligament stem cells, which should normally differentiate into cementoblasts, fibroblasts and osteoblasts of the alveolar bone [18]. Other studies suggest that these lesions may represent a defect in extraligamentary bone remodeling, triggered by local factors or hormonal imbalances [19].

FCOD has a clear predominance for female patients, mainly African descents [8]. Around 90 % of cases are diagnosed between the third and fourth decade of life [15]. Although the majority of FCOD cases are sporadic and idiopathic, some very rare variants could be inherited in the form of autosomal dominant inheritance with a variable phenotypic expression [4,19].

Even though the lesions can affect both mandible and maxilla, the posterior mandible is preferentially involved, being affected most of cases, consistently with the clinical picture here reported [8]. A typical finding, suggestive of the diagnosis of FCOD, is the symmetry of the lesions, although unilateral cases can also occur and they may represent a transition stage towards the classical bilateral distribution of the more mature lesion [8].

Unless secondarily infected, FCOD remains asymptomatic, thus approximately 50 % of cases are casually discovered during a

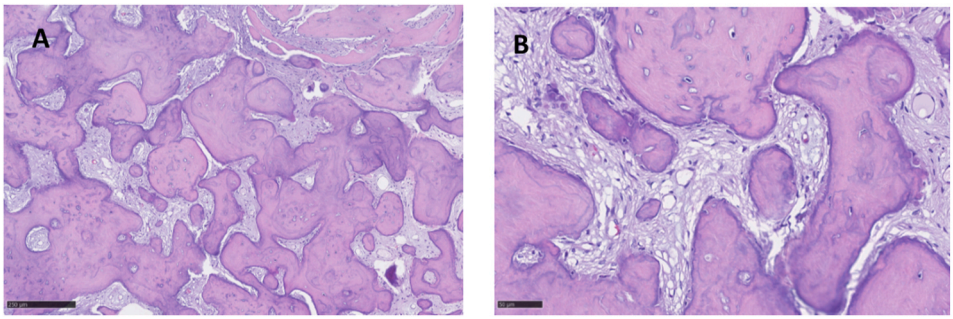

Fig. 4. Dysplastic bone tissue consisting of irregular trabeculae and hypocellular fibrous tissue can be observed; at the top right, there is the presence of normal bone, distinct from dysplastic bone, while below an isolated cementolite is visible (a, low magnification). The absence of osteoblastic and osteoclastic activity around the irregular trabeculae and the presence of rare spindle cells can be observed at higher magnification (b, high magnification).

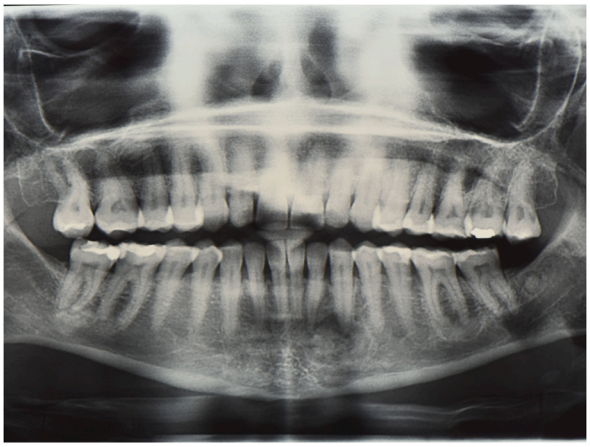

Fig. 5. Orthopantomography (November 2021) showing no significant changes in radiological images.

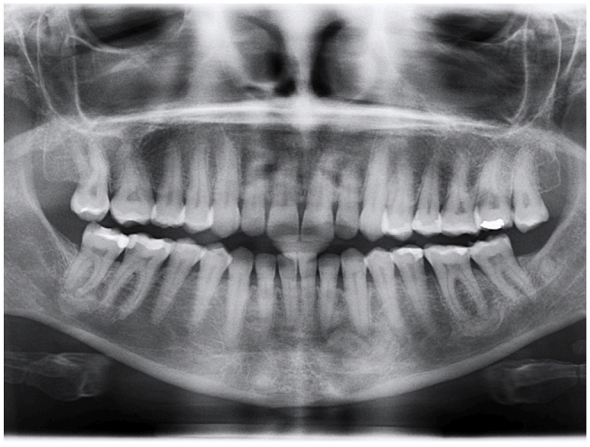

Fig. 6. Orthopantomography (November 2023) showing opacification of bone lesions on the periapical areas of teeth 3.3, 3.6 and 4.6.

radiographic investigation carried out for other reasons, as also occurred in our patient [6,8]. In case of infection, there may be signs and symptoms, including pain, swelling, pus draining fistula, paresthesia, bone expansion and facial deformity [6,8,17]. The access of oral bacteria to the lesions can occur due to chronic inflammatory periodontal disease, dental caries leading to pulp necrosis, tooth surgical extraction (representing the main risk factor for infection) as well as and minor irritation caused by dentures in edentulous areas [20].

The diagnosis of FCOD follows clinical and radiographic investigations [8]. Pulp necrosis should be always assessed by dental sensitivity/vitality tests [17]. Radiographically, FCOD is characterized by the presence of multiple slowly growing lobular radiopacities, at the root apices of vital teeth, with a circumferential radiolucent area, also known as "cotton wool appearance" lesions (similarly to Paget's disease radiographic findings) [1,9]. Of note, different radiographic aspects can be observed depending on the stage at which they are found: during the early stage (osteolytic stage), there is a round or oval apical radiolucent area with a well-defined radiopaque border; in the mixed stage (cementoblastic phase), the radiolucent lesion may include radiopacities, while, in the mature stage (osteogenic stage), the area becomes completely radiopaque with a radiolucent border [1]. Regardless of the stage, the lesions are usually located in tooth-bearing areas of the jaws and they are often confined within the alveolar bone [1,8,9]. CBCT is a relevant diagnostic tool, useful to differentiate FCOD from other lesions that exhibit a similar sclerotic appearance on conventional radiographs (such as panoramic radiograph) [21].

The further histopathological assessment of one the multiple FCOD lesions, which we performed to achieve the final diagnosis, is important for differential diagnostic pathway [4]. Several bone lesions may have radiographic appearances similar to FCOD and should be excluded (Table 1). Moreover, FCOD is not associated with serum biochemical alterations or systemic manifestations [19]. Incisional biopsy, however, may increase the risk of bone infection or fracture, and some authors suggest that histological investigation is not always required [9,14]. Histopathologically, FCOD is a benign fibro-osseous lesion [9], similar to cemento-ossifying fibroma and fibrous dysplasia, characterized by replacement of bone by a benign connective tissue matrix with various degrees of mineralization in the form of woven bone or cementum-like round basophilic acellular intensely basophilic structures. These lesions are not surrounded

Table 1
Differential diagnosis of FCOD.

Conditions	Different features
Paget's disease	- Involvement of other bones - Biochemical serum changes (e.g. elevate alkaline phosphatase levels)
Chronic diffuse sclerosing osteomyelitis (CDSO)	- Inflammatory signs - Changes are not confined to tooth-bearing areas - Patients usually report chronic dull cyclic pain - Soft tissue swelling
Idiopathic osteosclerosis (IOS)	- A radiopaque lesion without radiolucent periphery - Not exhibit a symmetrical localization
Fibrous dysplasia	- Significant face asymmetry - Malocclusion - Unilateral involvement
Osteoblastoma and osteoid osteoma	- Single lesion - Can cause dull and nocturnal pain
Cementoblastoma	- A solitary lesion - Generally, fused to the root of posterior mandibular teeth - Often teeth have decreased sensitivity or are not vital
Ameloblastoma	- A solitary lesion - Normally localized in the posterior area of the mandible and in the ascending ramus - Painless slow-growing swelling and root resorption
Cemento-ossifying fibroma	- The lesion is encapsulated and clearly separated from the surrounding healthy bone tissue - Greater bucco-lingual/palatal expansion
Osteoma	- Often associated with facial asymmetry, pain and surface ulceration, but, in some cases, it can be asymptomatic - Prevalent at younger age, maximum seen in the sixth decade - Often associated with Gardner syndrome
Odontoma	- Generally associated with retention of deciduous teeth, non-eruption of permanent teeth, and tooth displacement. - May be associated with pain and expansion of the cortical bone. - Pathognomonic radiological features (compound odontoma)
Odontogenic cysts	- Rounded radiolucent lesions surrounded by a sclerotic rim - Generally solitary lesion - May cause resorption or displacement of adjacent teeth
Odontogenic keratocyst	- Often solitary lesion - Swelling is the most common clinical manifestation - More frequency in the posterior mandible
Hypercementosis	- Radiographically there are increased thickness of roots due to an excessive deposition of cementum and a mild interdental bone loss
Genetic disorders	
Hyperparathyroidism-jaw tumor syndrome (HPT-JT)	- Hyperparathyroidism - Multiple parathyroid adenomas - Proliferative disorders in other tissues (endocrine or not)
Gnathodiaphyseal dysplasia (GDD)	- Involvement of other bones - Bone fragility - Frequent bone fractures at the young age - Generalized osteopenia
Familial gigantiform cementoma	- Severe maxillofacial deformities - Progressively rapid growth - Typically presents in the first 2 decades of life
Gardner syndrome	- Familial adenomatous polyposis - Multiple osteomas - Sebaceous cysts - Dental anomalies - Involvement of other bones
Malignant disorders	
Osseous metastases	- Generally, occurring in older age - The majority involves a single site - Often associated with swelling - Patients may report other symptoms, as pain and paresthesia - Other signs can be observed, as increased tooth mobility, facial asymmetry, mucosal ulceration, jaw deviation, and trismus
Osteosarcoma	- The most common symptom is swelling; less frequently, pain, paresthesia and ulcerations - Radiological features may vary from purely osteogenic (sun-ray appearance) to pure osteolytic or a mix of both

by a capsule and, in the first osteolytic stage, there is fibrotic tissue rich in cells and vessels without cement-like deposits, but, with the maturation of the lesions, cement-like formations and irregular trabeculae occur; in the final osteoclastic stage, there is the interconnections of these structures with few cellular elements [6].

The management of FCOD is mainly related to regular long-term follow-up, with periodical dental recall, prophylaxis and reinforcement of oral care, to maximize oral health, by preventing or stabilizing periodontal disease and by preventing dental caries, thus

reducing the risk of tooth loss [4,9]. In this case report, we consistenly perfomed a regular, clinical and radiographic, long-term follow-up, in agreement with the patient, who showed high compliance at dental visits and high standards of home oral hygiene. High standards of home oral hygiene and dental check-ups are decisive in order to reduce the risk of oral infections, even in patients with removable prostheses that, if poorly fitting, could cause the resorption of alveolar bone and contribute to the risk of bone exposure [22]. Accordingly, in asymptomatic non-infected lesions, surgical intervention is not required, but the long-term clinical and radiographic (panoramic, intraoral RXs, or CBCT) follow-up is highly indicated [1,17]. Dentoalveolar surgery, involving the area affected by FCOD, correlates with the risk of bone infection due to the scarce tissue vascularization, which, in worst cases, can result in bone sequestration and osteomyelitis, or even bone fracture [4,9,14]. The surgical treatment of FCOD, under antibiotic coverage, depends on the presence of symptoms, deformations or functional alterations [23]. Although a consensus on the gold standard therapy is still missing, bone remodeling rather than wide resection is preferable in case of not infected deformities or functional alterations [4]. The management of infected painful lesions is more difficult because chronic inflammation and infection develop within the densely mineralized hypovascularized tissue, less prone of being reached by antibiotics [1]. In the most severe infected cases, the radical surgery treatment (removal and curettage of necrotic bone), under antiobiotic regimen, appears appropriate with a favorable prognosis and a complete healing [20,24–28]. Periapical surgery also showed satisfying results, even if some authors supported the combined endo-surgical treatment [4].

Should implant rehabilitation considered in FCOD patients, accurate, sectional radiographic images are mandatory to plan the implant placement in proximity of FCOD lesions without their involvement; if the lesion's involment could not be avoided, a tooth-supported prosthesis is the therapy of choice. Regular recall and accurate oral hygiene to prevent peri-*peri*-implantitis and implant loss are always highly recommended [14]. Finally, orthodontic treatment is not indicated in these patients in case the tooth movement involves the areas affected by FCOD: the high bone density and bone disorganization can be of impediment for bone remodeling. Furthermore, placement of mini-implants and mini-plaques, surgical maneuvers to apply traction to unerupted teeth and dental extractions should be avoided in the affected areas, in order to prevent bacterial contamination of lesions [18].

4. Conclusions

The presence of radiological findings related to multiple, symmetrical and round radiopaque areas with radiolucent borders, affecting the jaws and involving the apices of vital teeth of asymptomatic middle-aged women, has led, in this case report, to the clinical suspicion of FCOD. The final diagnosis is based on a combination of clinical and radiographic findings, supported by laboratory and histological assessments to exclude other diseases. When exposed to oral pathogens, the hypovascular, densely sclerotic bone tissue related to FCOD is prone to secondary infection, which can be difficult to manage with antibiotics. Surgical and orthodontic therapies, involving the sites of the lesions, should be avoided. Uncomplicated FCOD may remain asymptomatic for an indefinite period and it requires no invasive therapy, but only periodic clinical and radiographic long-term follow-up, together with professional oral hygiene sessions. High standards of home oral hygiene are also pivotal in order to reduce the risk of oral infection, to avoid the need of future tooth extractions and dento-alveolar surgery. Surgical treatment is performed only in selected symptomatic cases, under antibiotics coverage.

Ethical compliance statement

The authors confirmed that the patient provided written informed consent.

Data availability statement

This is a case-report; clinical data are available from the corresponding author on reasonable request, with no need of a publicly available data repository.

CRediT authorship contribution statement

Sem Decani: Writing – original draft, Investigation, Conceptualization. **Martina Quatrale:** Writing – original draft, Investigation. **Davide Costa:** Writing – review & editing, Investigation. **Laura Moneghini:** Writing – review & editing, Investigation. **Elena Maria Varoni:** Writing – review & editing, Investigation, Conceptualization.

Declaration of competing interest

The authors declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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