Article

Clinical and Radiological Features of Primary Chronic Osteomyelitis and Fibrous Dysplasia of the Mandible

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Abstract: Purpose of study: Differential diagnosis of chronic osteomyelitis and fibrous dysplasia of the mandible is a difficult task. The similarity of clinical, radiological and morphological manifestations of these diseases leads to errors and incorrect approaches to treatment.

Patients and methods: A retrospective comparative study of clinical and radiological features was conducted in patients with primary chronic osteomyelitis and fibrous dysplasia treated in the Department of Maxillofacial Surgery of the Russian Children's Clinical Hospital from 2015 to 2023. Clinical characteristics were assessed: pain, swelling and trismus, and radiological characteristics - sclerosis, lysis and formation of subperiosteal regenerate. Statistical methods were used to determine differences.

Results: The analysis of 36 patients with PCO and 12 patients with FD included in the study (average age 8.9 and 8.5 years, respectively); showed that girls and unilateral lesions predominated in both groups (PHO (83.3%) and FD (100%). Patients with PHO mainly complained of pain (94.4%), swelling of soft tissues (100.0%), and trismus (100%), while in patients with FD there was no pain and there was an increase in bones (83.3%) without trismus. Computed tomography of patients with PCO showed the formation of subperiosteal bone, lysis of the cortical layer, and expansion of the mandibular canal. on the affected side, whereas patients with FD generally had mo

derate to severe bone swelling, well-demarcated cortex, and displacement of the teeth and mandibular canal from the node.

Conclusions: These data highlight the importance of clinical and radiological features in various diseases. Pain, swelling, subperiosteal bone formation, unilateral expansion of the mandibular canal, clarity of the cortex-medullary boundary, and continuity of the cortical bone are key points in differentiating these conditions.

Keywords: fibrous dysplasia, chronic, productive osteomyelitis, lower jaw, children, computed tomography

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1. Introduction

Primary chronic osteomyelitis (PCO) of the mandible is a rare chronic non-purulent lesion of the mandible with an insufficiently studied pathogenesis [1]. Some scientists argue that PHO may be associated with infection, but the infectious agent cannot be identified, or opportunistic microflora is determined [2,3,4]. There is also a theory that the development of PHO is associated with muscle hyperactivity [5], or the first or mono manifestations of SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis) [6,7,8]. The classic manifestation of PCO is recurrent episodes of swelling and pain in the lower jaw. Some patients also experience trismus and progressive worsening of the mandibular deformity. Radiological characteristic changes include a combination of areas of osteosclerosis with osteolysis and subperiosteal formation of new bone [1]. This

radiological picture gave a second name for this condition - diffuse sclerosing osteomyelitis, widespread in the English-language literature.

The clinical and radiological features of fibrous dysplasia of the skull bones are similar to PHO, especially when only the lower jaw is affected, and upon morphological examination they are almost indistinguishable without additional immunohistochemical research [1,9,10,11]. FD is also characterized by a progressive increase in deformation of the affected bone, however, this disease is predominantly painless [12, 13], with the exception of the described cases of the development of neuralgia of the mandibular nerve due to its compression in the mandibular canal [14]. The X-ray picture of FD is often polymorphic and, based on the predominance of the fibrous and osteoid components, is divided into osteosclerotic, osteolytic or cystic and mixed type [15,16]. In most cases, FD manifests itself as a mixed type (osteosclerosis with osteolysis), similar to PHO.

For these reasons, the differential diagnosis of PCO and FD of the mandible can be challenging, since the clinical and radiographic characteristics of these two diseases are similar and morphologically practically indistinguishable [17,18,19,20]. Clinically, PCO is often misdiagnosed as FD or FD with infection; according to our data, this figure reaches 34.6% [22]. However, the underlying pathophysiological processes of these diseases, despite the commonality of changes, are different, which influences different strategies in the treatment of these diseases. Comparative studies of radiological and clinical manifestations have not been carried out to develop differential diagnostic principles, but this approach will reduce the time from the onset of the disease to making the correct diagnosis and choosing an adequate treatment method. The aim of this study was to explore the key features of differential diagnosis between these two diseases. The purpose of the study was to summarize data related to age and gender, clinical course, radiological characteristics of these diseases due to the high frequency of incorrect primary diagnoses and treatment provided at the place of residence.

2. Materials and Methods

A retrospective study was conducted, which included patients who were treated in a hospital setting for PHO or FD with damage to the lower jaw during the period from 2015 to 2023 in the Department of Maxillofacial Surgery of the Russian Children's Clinical Hospital in Moscow. In all cases, the diagnosis was based on clinical signs and symptoms, radiological results, as well as biopsy and bacteriological examination data.

Using data from hospital records, the age, gender and course of the disease of the patients were analyzed, and the clinical characteristics of the two diseases were assessed. Clinical parameters included assessment of pain, soft tissue swelling, bone deformity, trismus, lip numbness, and increased skin temperature in the lesions. Other variables included patient demographics (ie, age, gender, and disease course). When assessing radiology data, both panoramic radiographs and computed tomography (CT) were analyzed. Cone beam computed tomography was not used for analysis due to the narrow diagnostic window, which did not allow the construction of adequate three-dimensional models and evaluation of soft tissues. The following CT radiological parameters were analyzed: bone structure, condylar involvement, tooth displacement, displacement and width of the mandibular canal. Among the patients with FD there were patients with polyostotic and monostotic lesions of the mandible.

Data analyzed were processed using SPSS v24.0 (IBM, Armonk, NY).

3. Results

This study examined 48 inpatients. Among them, 36 were diagnosed with PCO, and 12 with FD. In 7 patients with PHO, FD was misdiagnosed at the place of residence, and in 2 patients, episodes of exacerbation were regarded as FD with infection.

When assessing demographic indicators, in PHO (1:2.6), in contrast to FD (1:1), the female gender predominated. The age of onset of both diseases was comparable (8.99 + 0.54 and 8.53 + 1.14 years, $p = 0.37$ $\alpha = 0.05$) and did not differ from other fibro-osseous lesions of the mandible (N = 76 , 8.6 + 0.41 years, $p=0.476$ $\alpha=0.05$).

Both PHO and FD were predominantly unilateral and affected the left side (1:1.31 and 1:1.4 for PHO and FD, respectively). In case of PCO, there were also bilateral unrelated lesions in 4 children and lesions of the submental region in 2 cases. PCO was localized mainly in the angle and ramus of the mandible, then in the condylar process and chin. FD most often affected the body, the lower jaw, and less often the branches without involving the condyle.

Among the clinical manifestations, pain, soft tissue swelling and trismus were observed only in patients with PCO. At the same time, 2 patients did not report significant pain, although there was swelling and trismus. Despite the clinical manifestations, the general blood test did not show an increase in the level of leukocytes, and the ESR was increased to 20-50 mm/h in 8 patients (CHECK). In FD, the leading complaint was the presence of deformation of the lower jaw (83.3%),

regardless of whether it was a monoosal or polyosal lesion. None of the patients with PHO and FD had fistulas, abscesses, increased skin temperature, or local numbness.

When assessing computed tomography data, patients with PCO had mixed sclerosis and ground glass symptoms, which did not differ significantly from patients with FD (in 8 of 12 patients). Cortical defects and decreased differentiation into cortical and medullary layers were more common in patients with PCO compared with patients with FD ($p = 0.014$ $\alpha = 0.05$). In patients with PCO, subperiosteal bone formation was observed, and the longer the duration of the disease, the less pronounced the boundary between the regenerate and the bone was, which was not observed in patients with FD, as well as deformation of the condylar process.

The characteristic increase in the inferior margin of FD was found in only five patients, and the pathognomonic "thumbprint" was found in only two (Figure 1).

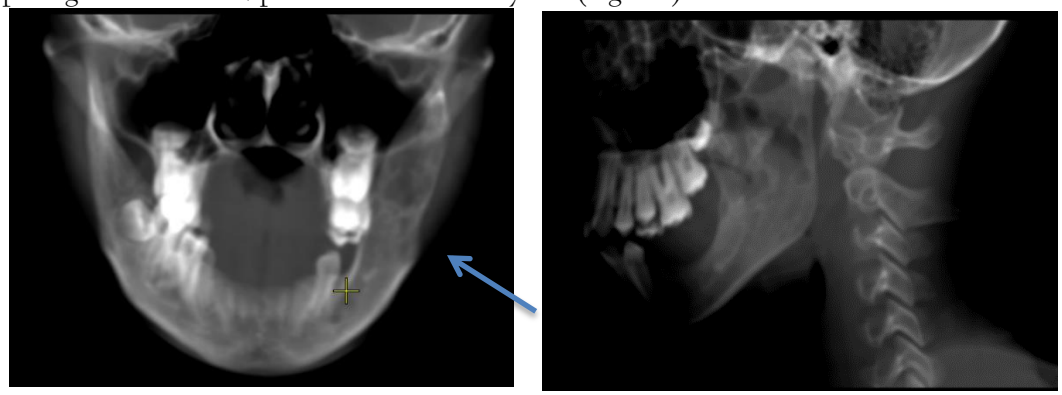

Figure 1. Digital indentation in the area of fibrous dysplasia and upward displacement of the mandibular canal according to teleradiography and computed tomography in boy X.

Analysis of the course and width of the mandibular canal during PHO and FD showed a number of differences. Thus, depending on the epicenter of the fibrous dysplasia node, displacement of the mandibular canal was noted both throughout its entire length (53.8%), and with preservation (38.5%) or elevation f. mentalis upward (7.7%) on the affected side while maintaining a downward displacement of the nerve canal due to compression by the FD lesion (Spearman correlation at 0.574) (Figure 1, Figure 2).

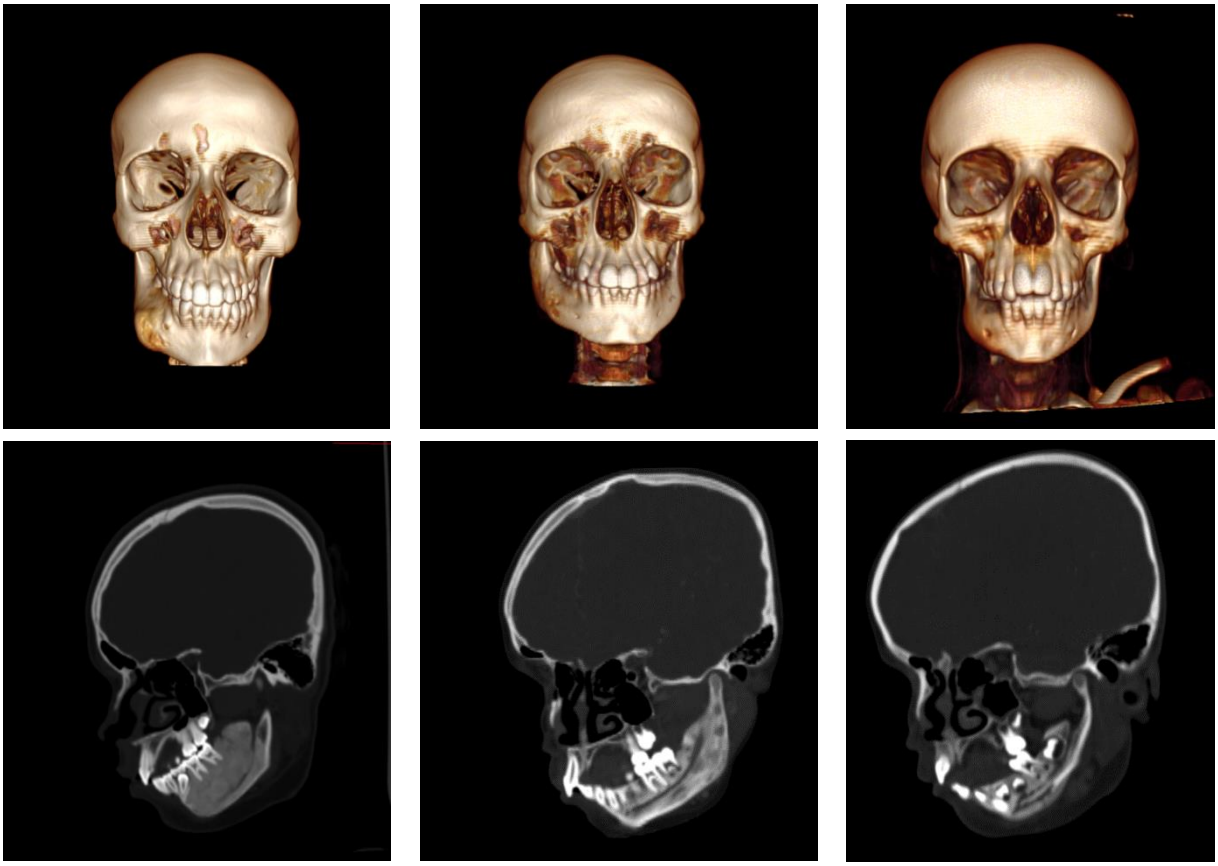

Figure 2. The relationship between the axial section of the course of the mandibular canal and the three-dimensional reconstruction of computed tomography data (3 patients) does not allow us to reliably judge the nature of the course depending on the exit location n. Mentalis

No such changes in the course of the nerve were noted during PCO, but there was an increase in the width of the mandibular canal by 1.5-2 times ($p<0.001$, $\alpha=0.05$). Moreover, these changes were pathognomonic only for PCO and were not found in other fibro-osseous lesions of the jaws (Figure 3, Table 1).

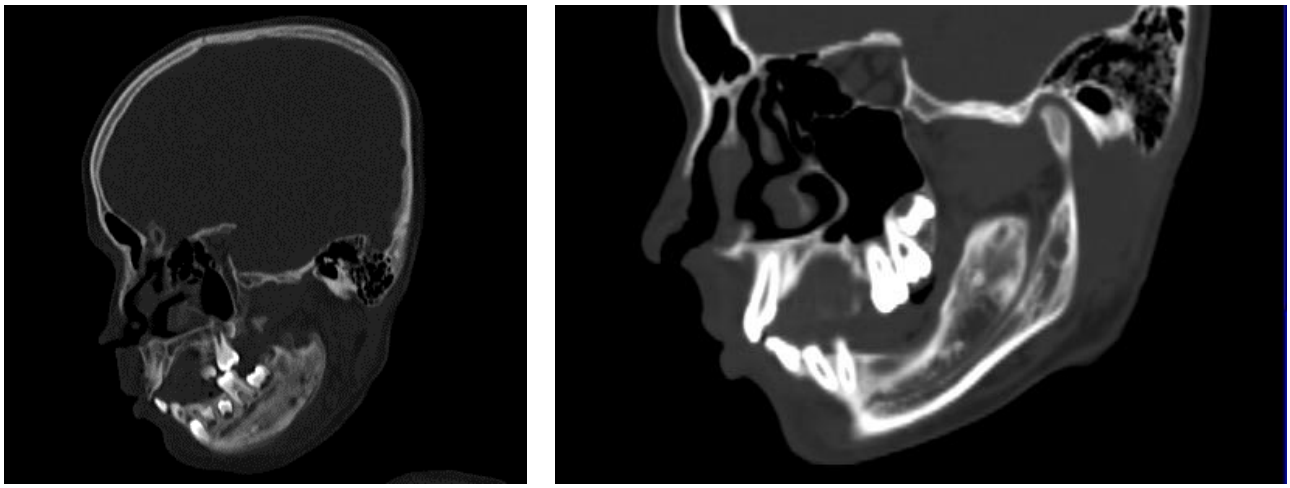

Figure 3 The nature of the position of the mandibular canal on the sagittal section of a native computed tomography study in 2 patients with fibrous dysplasia

Table 1. Width of the mandibular canal, mm for various formations of the lower jaw

Type of lesion	Width of the mandibular canal, mm
Inflammatory	3,1 ± 0,5
Dysplastic	2,3 ± 0,3B
Benign neoplastic	2,2 ± 0,3B
Malignant neoplastic	2,6 ± 0,4
Soft	2,0 ± 0,5B
Odontogenic	2,5 ± 0,4B
Reactive	2,3 ± 0,7B
P	<0,001

Note: B – statistically significant difference with the inflammatory type of lesion.

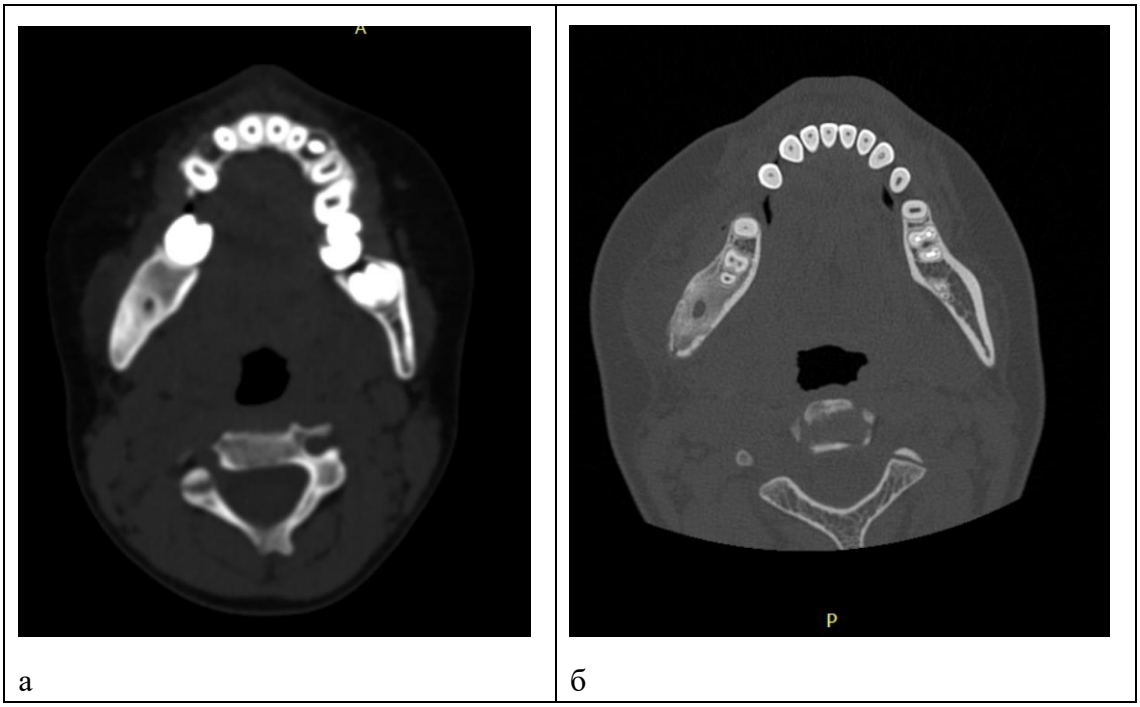

Figure 4 Multislice computed tomography data, axial sections, girls B., 7 years old (a) and girls K., 16 years old (b), with damage to the body of the mandible on the right and an increase in the width of the mandibular canal on this side.

4. Discussion

The analysis made it possible to confirm the importance of clinical and radiological features in the differential diagnosis of these two diseases. Among the clinical characteristics, the key points for chronic osteomyelitis were pain, soft tissue swelling and/or enlargement in the affected area, and trismus. As for the radiographic characteristics, both diseases had a mixed picture: a combination of the "ground glass" symptom with foci of sclerosis and lysis, blurred boundaries of the affected areas and unchanged bone. However, a number of differences were also found: lysis of the cortical layer, subperiosteal bone formation were more common in PCO, and unilateral widening of the mandibular nerve canal on the affected side was pathognomonic, while continuous cortical layer, bone widening, displacement of teeth and mandibular canals were more common in FD.

In addition, the changes detected on computed tomography: lysis of the medullary zone in the form of small cystic zones in patients with PCO, and in patients with FD as a large zone of cyst-like lesions with clear boundaries, corresponds to the data of other authors [24].

In the clinical picture, the presence of pain was a key factor in the differential diagnosis of both diseases. This is because PCO is an autoinflammatory disease [24], and FD is a disease that develops as a result of postzygotic activating mutations in GNAS at 1 of 2 positions: Arg201 (>95% of reported cases) or Gln227 (<5%) [25,26,27,28,29]. For this reason, pain is one of the main symptoms of PHO and is characterized by a recurrent course with exacerbations every few weeks or months. In case of FD with damage to the lower jaw, neither we nor other researchers encountered pain syndrome [21,22,23]. This fact and the fact that the GNAS1 gene mutation is not detected in PCO confirms the fact that osteomyelitis does not develop against the background of fibrous dysplasia [24]. In addition, bone swelling in FD is caused by slowly progressive expansion of the bone and not by soft tissue swelling. The edema observed with PCO is recurrent in nature and is a combination of soft tissue edema and moderate bone neocorticogenesis due to subperiosteal regeneration. In this case, edema can often prevail, which we observed when it was possible to achieve bone symmetry, but soft tissue symmetry was preserved. This is due to the fact that swelling of soft tissues during PCO is caused by inflammatory and hypertrophic changes in the masticatory muscles, which may be one of the causes of trismus [46].

When assessing age at onset, no statistical significance was found in our study. According to foreign researchers, FD usually manifests itself during the first and second decades of life, although cases of onset have been described as early as 3 years of age [68]. Primary chronic osteomyelitis is not age-related, but most published data are from adult patients, and the literature contains only case reports or small series of patients with early onset in childhood or adolescence. Heggie A et al. and Baltensperger M. et al. noted the high frequency and uniformity of disease features among

children and adolescents, respectively, which suggested that pediatric "variation" should be considered as a separate clinical entity and proposed the term "juvenile chronic osteomyelitis" to describe it [84,85,86].

The monoosseous form of FD rarely affects the lower jaw in isolation, more often on one side in the posterior regions, occurring equally in both boys and girls [69]. The affected bone gradually increases in size, maintaining its shape, but there is an unclear border with the surrounding bone tissue, and the affected area itself may have the appearance of "frosted glass" or a dense amorphous structure. Nodules of fibrous dysplasia usually begin to grow at a young age with a more radiolucent appearance and cease at the end of somatic growth with the appearance of cysts and/or radiodense areas as calcification progresses [22,70,71]. Although the boundaries of FD were generally poorly defined on MSCT, one of the factors for this could be the relatively wide slice thickness, as pointed out by other authors [72].

Unlike fibrous dysplasia, with PCO, a periosteal reaction can be detected during an exacerbation. According to Bisseret et al., the appearance of the underlying cortex during the periosteal reaction is an important criterion for assessing the aggressiveness of osteomyelitis and is more useful than the nature of the periosteal reaction [82]. Thus, the destruction of the cortical layer and the "moth-eaten" appearance indicate an aggressive course of the disease, and in our experience, it is a sign of exacerbation and a guideline for carrying out a sanitizing operation.

Fibrous dysplasia was always painless and was often an incidental finding. With PCO, during exacerbations there was always painful swelling and trismus, although a number of authors indicated that the frequency of these signs did not exceed 15%, which could be associated with the assessment both during the period of exacerbations and between [75,76,77]. Fever was much less common, as in other authors [74,]. The left side of the lower jaw is affected slightly more often (1.31:1) than the right side, which completely coincides with the data of the GREEN AUTHOR (1.3:1). Systemic signs such as body temperature, white blood cell count and erythrocyte sedimentation rate are either within normal limits or slightly elevated, which is similar to our case [73, 79]. Obtaining a positive culture for the responsible microorganisms from the lesion may be difficult or unrepresentative due to contamination by microflora of the skin or oral cavity, as indicated by most authors and confirmed by us, because the cultures were sterile or opportunistic microflora was sown, which could contaminate the samples during material collection [2,3,30,31,4].

The study of the morphological picture in both of these diseases had a typical trabecular pattern of chaotically located fibrous fibers. However, studies have shown that the histopathological picture of osteomyelitis may include replacement of normal bone marrow by fibrous connective tissue, sometimes accompanied by neutrophil infiltration and new bone formation. However, this infiltrate is difficult to detect, which makes it difficult to make a correct diagnosis, because the appearance is similar to that seen in FD or osteogenic sarcoma [79,80]. However, on CT scans, malignant tumors such as Ewing's sarcoma, chondrosarcoma, and osteosarcoma tend to have more aggressive appearances and soft tissue involvement. In these pathologies, the periosteal reaction radiographically resembles a "sunray" or "onion skin" pattern [34,82]. For this reason, in differential diagnosis it is always necessary to summarize all the data: the morphological picture, the data of radiological diagnostics and the clinical course of the disease.

Differential diagnosis of FD and PCO should also be carried out from systemic diseases that can cause secondary periostitis with an increase in bone volume in children, such as metabolic disorders, hematological malignancies (leukemia, lymphoma, Langerhans cell histiocytosis), sickle cell anemia and vasculitis [83].

The treatment of PCO and FD differs significantly. Surgery is the main treatment method for all forms of FD. In many cases, dysplastic bone can be contour resected to approximate facial symmetry without attempting a complete jaw resection after puberty [33, 35]. Unlike FD, surgical treatment involving curettage and decortication tends to recur after surgery. If left untreated, ongoing inflammation can lead to severe pain, bone destruction, pathological fractures, growth impairment, and functional limitations [45,56]. For this reason, treatment of PCO is combined or conservative, however, due to the low prevalence, large prospective randomized controlled trials have not been conducted to determine the best therapy and duration of treatment and all recommendations are based on small case series [45]. Nonsteroidal anti-inflammatory drugs are the most popular first-line treatment, with up to 80% of patients with PCO responding to treatment [12,14]. For those patients who do not respond to or become resistant to NSAIDs, corticosteroids, colchicine, antirheumatoid drugs, bisphosphonates, and tumor necrosis factor (TNF) inhibitors are used. Although corticosteroids can rapidly control inflammatory activity, they rarely lead to long-term remission [2,14]. Antirheumatoid drugs such as methotrexate and sulfasalazine are usually used only as adjunctive therapy as they are generally considered ineffective as monotherapy [8,15]. TNF inhibitors have shown promising results; however, the cost and wide profile of side effects prevent this approach from being recommended as routine [11]. Bisphosphonates, by inhibiting bone resorption, have also proven effective, leading to long-term remission in most patients [2, 11,

14[36,37]]. Pamidronate, the bisphosphonate most commonly used to treat PCO, is effective in resistance to naproxen therapy [14,16–18]. It has been suggested that bisphosphonate therapy is effective in patients because it promotes bone remodeling associated with sclerosis [14]. For these reasons, an effect was also observed on the administration of the drug denosumab, a monoclonal antibody to RANKL, directly blocking it, unlike bisphosphonates [4].

Success in treatment begins with an accurate diagnosis, so differentiating the two diseases is critical. Patients with PCO who are treated with bisphosphonates and/or denosumab tend to have longer periods of remission [22, 38]. Antiresorptive drugs act by binding the mineral component of the bone and inhibit the action of osteoclasts [42], so the activity of osteoclasts may play an important role in the development of pain syndrome [38], which is one of the main factors in reducing the quality of life of patients with PHO.

5. Conclusion

Jaw lesions, especially in children, should be detected as early as possible to prevent unfavorable treatment outcomes and improve prognosis. A limitation of this study was its retrospective nature, i.e. this limits the collection and analysis of information that can be obtained. Moreover, the number of isolated lesions of the mandible in FD is much lower, so to increase the reliability of the study, it is necessary to accumulate experience for adequate comparison. However, it should be noted that the results of this study highlight the importance of clinical and radiological features in the differential diagnosis of these two diseases. The key clinical feature is that PCO is accompanied by pain, swelling and trismus, while FD is only an increase in the volume of the affected bone. When performing a computed tomography analysis with PHO, focal lysis of the cortical layer with the presence of microcysts, expansion of the mandibular canal on the affected side and the formation of subperiosteal regenerate are noted, and with PD - moderate and pronounced expansion of the bone with a thin cortical layer and blurred boundaries, as well as displacement of the teeth and mandibular channels. However, these diseases are very rare and for the diagnosis of lesions of the oral cavity, especially lesions of the jaws, a multidisciplinary approach is necessary, and practitioners should seek expert advice from other specialists in the field of pathological anatomy and radiology, discussing each case together to increase the likelihood of correct diagnosis and adequate treatment.

Application of artificial intelligence:

The article is written without the use of artificial intelligence technologies.

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References

1. Jacobsson S: Diffuse sclerosing osteomyelitis of the mandible. International Journal of Oral and Maxillofacial Surgery. 1984;13(5):363-85. Jacobsson S, Dahlen G, Moller AJ: Bacteriologic and serologic investigation in diffuse sclerosing osteomyelitis (DSO) of the mandible. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics. 1982; 54:506
2. van Merkesteyn JP, Groot RH, Bras J, McCarroll RS, Bakker DJ. Diffuse sclerosing osteomyelitis of the mandible: A new concept of its etiology. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics. 1990; 70:414
3. Kugushev AYu. Combined treatment of diffuse sclerosing osteomyelitis of the lower jaw in children. Issues of hematology/oncology and immunopathology in pediatrics. 2019; 18(3):46-53.
4. van de Meent MM, Pichardo SEC, Rodrigues MF, Verbist BM, van Merkesteyn JPR. Radiographic characteristics of chronic diffuse sclerosing osteomyelitis/tendoperiostitis of the mandible: A comparison with chronic suppurative osteomyelitis and osteoradionecrosis. Journal of Cranio-Maxillofacial Surgery. 2018;46(9):1631-1636
5. Kahn MF, Hayem F, Hayem G, Grossin M: Is diffuse sclerosing osteomyelitis of the mandible part of the synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome? Analysis of seven cases. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics. 1994; 78:594
6. Marí A, Morla A, Melero M, Schiavone R, Rodríguez J. Diffuse sclerosing osteomyelitis (DSO) of the mandible in SAPHO syndrome: a novel approach with anti-TNF therapy. Systematic review Journal of Cranio-Maxillofacial Surgery. 2014;42(8):1990-6
7. Yanamoto S, Kawasaki G, Yoshitomi I, Mizuno A: Diffuse chronic sclerosing osteomyelitis of the mandible with synovitis, acne, pustulosis, hyperostosis, and osteitis: Report of a long-term follow-up case. Journal of Cranio-Maxillofacial Surgery. 68:212, 2010
8. Slootweg PJ: Maxillofacial fibro-osseous lesions: Classification and differential diagnosis. Seminars in Diagnostic Pathology. 1996; 13:104
9. Orpe E, Lee L, Pharoah M. A radiological analysis of chronic sclerosing osteomyelitis of the mandible. Dentomaxillofacial Radiology. 1996;25(3):125-129
10. Eversole R, Su L, ElMofty S: Benign fibro-osseous lesions of the craniofacial complex. A review. Head and Neck Pathology. 2008; 2:177
11. Ricalde P, Horswell BB: Craniofacial fibrous dysplasia of the fronto-orbital region: A case series and literature review. Journal of Cranio-Maxillofacial Surgery. 2001; 59:157

12. Wu H, Yang L, Li S, Jin X, Xu J, Lu J, Zhang C, Teng L. Clinical characteristics of craniomaxillofacial fibrous dysplasia Journal of Cranio-Maxillofacial Surgery. 2014;42:1450
13. Assaf AT, Benecke AW, Riecke B, Zustin J, Fuhrmann AW, Heiland M, Friedrich RE. Craniofacial fibrous dysplasia (CFD) of the maxilla in an 11-year old boy: a case report. Journal of Cranio-Maxillofacial Surgery. 2012 ;40(8):788-92
14. Unal Erzurumlu Z, Celenk P, Bulut E, Barıs YS: CT imaging of craniofacial fibrous dysplasia. Case Rep Dentistry 1:2015, 2015
15. Bousson V, Rey-Jouvin C, Laredo JD, Le Merrer M, Martin-Duverneuil N, Feydy A, Aubert S, Chapurlat R, Orcel P. Fibrous dysplasia and McCune-Albright syndrome: imaging for positive and differential diagnoses, prognosis, and follow-up guidelines. European Journal of Radiology. 2014;83(10):1828-42
16. Johannsen A: Chronic sclerosing osteomyelitis of the mandible. Radiographic differential diagnosis from fibrous dysplasia. Acta radiologica: Diagnosis (Stockh).1977; 18:360
17. Pereira TDSF, Gomes CC, Brennan PA, Fonseca FP, Gomez RS. Fibrous dysplasia of the jaws: Integrating molecular pathogenesis with clinical, radiological, and histopathological features. Journal of Oral Pathology and Medicine. 2019;48(1):3-9
18. Van Merkesteyn JP, Groot RH, Bras J, Bakker DJ: Diffuse sclerosing osteomyelitis of the mandible: Clinical radiographic and histologic findings in twenty-seven patients. Journal of Maxillofacial & Oral Surgery. 1988; 46:825
19. Montonen M, Li TF, Lukinmaa PL, Sakai E, Hukkanen M, Sukura A, Konttinen YT. RANKL and cathepsin K in diffuse sclerosing osteomyelitis of the mandible. Journal of Oral Pathology and Medicine. 2006;35(10):620-5
20. Burke AB, Collins MT, Boyce AM. Fibrous dysplasia of bone: craniofacial and dental implications. Oral Diseases. 2017;23(6):697-708.
21. Kugushev AYu. Fibrous-bone formations of the skull and mandible in children: clinic, diagnosis, treatment approaches, dissertation for the degree of Doctor of Medical Sciences.2023; 330
22. Mainville GN, Turgeon DP, Kauzman A: Diagnosis and management of benign fibro-osseous lesions of the jaws: A current review for the dental clinician. Oral Diseases. 2017;23:440
23. El-Shanti HI, Ferguson PJ: Chronic recurrent Multifocal osteomyelitis. Clinical Orthopaedics and Related Research. 2017; 462:11
24. de Noronha Santos Netto J, Machado Cerri J, Miranda AMMA, Pires FR: Benign fibro-osseous lesions: Clinicopathologic features from 143 cases diagnosed in an oral diagnosis setting. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics. 2013; 115:56
25. Godse AS, Shrotriya SP, Vaid NS: Fibrous dysplasia of the maxilla. Journal of Pediatric Surgery. 2009; 44:849
26. Weinstein LS, Liu J, Sakamoto A, Xie T, Chen M. Minireview: GNAS: normal and abnormal functions. Endocrinology. 2004; 145(12):5459-64
27. Lumbroso S, Paris F, Sultan C; European Collaborative Study. Activating Gsalpha mutations: analysis of 113 patients with signs of McCune-Albright syndrome--a European Collaborative Study. The Journal of Clinical Endocrinology and Metabolism. 2004;89(5):2107-13
28. Idowu BD, Al-Adnani M, O'Donnell P, Yu L, Odell E, Diss T, Gale RE, Flanagan AM. A sensitive mutation-specific screening technique for GNAS1 mutations in cases of fibrous dysplasia: the first report of a codon 227 mutation in bone. Histopathology. 2007;50(6):691-704.
29. Grime PD, Bowerman JE, Weller PJ: Gentamicin impregnated polymethylmethacrylate (PMMA) beads in the treatment of primary chronic osteomyelitis of the mandible. British Journal of Oral and Maxillofacial Surgery. 1990; 28:367
30. Groot RH, van Merkesteyn JP, van Soest JJ, Bras J: Diffuse sclerosing osteomyelitis (chronic tendoperiostitis) of the mandible. An 11- year follow-up report. Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology. 1992; 74:557
31. Matharu J, Taylor H, Sproat C, Kwok J, Brown J, Patel V: Diffuse sclerosing osteomyelitis: A case series and literature review. Oral Surg Oral Med Oral Pathol). Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology. 2020; 129:437
32. Boyce AM, Florenzano P, de Castro LF, Collins MT: Fibrous Dysplasia/McCune-Albright Syndrome; Seattle: University of Washington 1993
33. Belli E, Matteini C, Andreano T: Sclerosing osteomyelitis of Garre periostitis ossificans. Journal of Craniofacial Surgery. 2002; 13:765
34. Ricalde P, Magliocca KR, Lee JS: Craniofacial fibrous dysplasia. Oral and maxillofacial surgery clinics of North America. 2012; 24:427
35. Montonen M, Iizuka T, Hallikainen D, Lindqvist C: Decortication in the treatment of diffuse sclerosing osteomyelitis of the mandible. Retrospective analysis of 41 cases between 1969 and 1990. Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology. 1993; 75:5
36. Jacobsson S, Hollender L: Treatment and prognosis of diffuse sclerosing osteomyelitis (DSO) of the mandible. Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology. 1980; 49:7
37. Otto S, Troeltzsch M, Burian E, Mahaini S, Probst F, Pautke C, Ehrenfeld M, Smolka W. Ibandronate treatment of diffuse sclerosing osteomyelitis of the mandible: Pain relief and insight into pathogenesis. Journal of Cranio-Maxillo-Facial Surgery. 2015;43(9):1837-42
38. Urade M, Noguchi K, Takaoka K, Moridera K, Kishimoto H. Diffuse sclerosing osteomyelitis of the mandible successfully treated with pamidronate: A long-term follow-up report. Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology. 2012; 114:9
39. Otto S, Burian E, Troeltzsch M, Kaeppler G, Ehrenfeld M. Denosumab as a potential treatment alternative for patients suffering from diffuse sclerosing osteomyelitis of the mandible-A rapid communication. Journal of Cranio-Maxillo-Facial Surgery. 2018 ;46(4):534-537.
40. Hallmer F, Korduner M, Moystad A, Bjornland T: Treatment of diffuse sclerosing osteomyelitis of the jaw with denosumab shows remarkable results-A report of two cases. Clinical Case Reports International. 2018; 6:2434
41. Baron R, Ferrari S, Russell RG: Denosumab and bisphosphonates: Different mechanisms of action and effects. Bone 2011; 48:677
42. Jia K, Li X, An J, Zhang Y. Comparing Clinical and Radiographic Characteristics of Chronic Diffuse Sclerosing Osteomyelitis and Craniofacial Fibrous Dysplasia in the Mandible. Journal of Maxillofacial & Oral Surgery. 2021;79(5):1053-1061
43. Giedion A, Holthusen W, Masel LF, Vischer D. Subacute and chronic "symmetrical" osteomyelitis. Annales de radiologie.1972;15(3):329–332.
44. Hofmann SR, Kapplusch F, Girschick HJ, Morbach H, Pablik J, Ferguson PJ, Hedrich CM. Chronic recurrent multifocal osteomyelitis (CRMO): presentation, pathogenesis, and treatment. Current Osteoporosis Reports. 2017;15(6):542–554.
45. Rukavina I. SAPHO syndrome: a review. Journal of Children Orthopaedics. 2015;9(1):19–27.
46. Buch K, Thuesen ACB, Brøns C, Schwarz P. Chronic nonbacterial osteomyelitis: a review. Calcified Tissue International. 2019;104(5):544–553.
47. Greenwood S, Leone A, Cassar-Pullicino VN. SAPHO and recurrent multifocal osteomyelitis. Radiologic clinics of North America. 2017;55(5):1035–1053.
48. Borzutzky A, Stern S, Reiff A, Zurakowski D, Steinberg EA, Dedeoglu F, Sundel RP. Pediatric chronic nonbacterial osteomyelitis. Pediatrics. 2012;130(5): 1190–1197.
49. Kołodziejczyk B, Gazda A, Hernik E, Szczygielska I, Gietka P, Witkowska I, Płaza M. Diagnostic and therapeutic difficulties in a patient with chronic recurrent multifocal osteomyelitis coexisting with ulcerative colitis. Reumatologia. 2019;57(2):109–116.

50. Jansson A, Renner ED, Ramser J, Mayer A, Haban M, Meindl A, Grote V, Diebold J, Jansson V, Schneider K, Belohradsky BH. Classification of non-bacterial osteitis: retrospective study of clinical, immunological and genetic aspects in 89 patients. Rheumatology. 2007;46(1):154–160.
51. Roderick MR, Shah R, Rogers V, Finn A, Ramanan AV. Chronic recurrent multifocal osteomyelitis (CRMO) – advancing the diagnosis. Pediatric Rheumatology. 2016;4:47.
52. Zemann W, Pau M, Feichtinger M, Ferra-Matschy B, Kaercher H. SAPHO syndrome with affection of the mandible: diagnosis, treatment, and review of literature. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2011;111(2): 190–195.
53. Gorecki P, Stockmann P, Distler JHW. Implication of bisphosphonate use in the treatment of SAPHO syndrome: case report and discussion of current literature. Journal of Medical Hypotheses and Ideas. 2015; 9(2):72–78.
54. Skrabl-Baumgartner A, Singer P, Greimel T, Gorkiewicz G, Hermann J. Chronic non-bacterial osteomyelitis: a comparative study between children and adults. Pediatric Rheumatology. 2019;17(1):49.
55. Oliver M, Lee TC, Halpern-Felsher B, Murray E, Schwartz R, Zhao Y; CARRA SVARD CRMO/CNO workgroup. Disease burden and social impact of pediatric chronic nonbacterial osteomyelitis from the patient and family perspective. Pediatric Rheumatology. 2018;16(1):78.
56. Chen Z, Chen L, Feng G. Bone inflammation and chronic recurrent multifocal osteomyelitis. European Review for Medical and Pharmacological Sciences. 2018;22(5):1380–1386.
57. Roderick MR, Sen ES, Ramanan AV. Chronic recurrent multifocal osteomyelitis in children and adults: current understanding and areas for development. Rheumatology. 2018;57(1):41–48.
58. Miettunen PM, Wei X, Kaura D, Reslan WA, Aguirre AN, Kellner JD. Dramatic pain relief and resolution of bone inflammation following pamidronate in 9 pediatric patients with persistent chronic recurrent multifocal osteomyelitis (CRMO). Pediatric Rheumatology. 2009;7(1):2.
59. Simm PJ, Allen RC, Zacharin MR. Bisphosphonate treatment in chronic recurrent multifocal osteomyelitis. The Journal of Pediatrics. 2008;152(4):571–575.
60. Gleeson H, Wiltshire E, Briody J, Hall J, Chaitow J, Sillence D, Cowell C, Munns C. Childhood chronic recurrent multifocal osteomyelitis: pamidronate therapy decreases pain and improves vertebral shape. The Journal of Rheumatology. 2008;35(4):707–712.
61. Assiri KI. Monostotic fibrous dysplasia involving the mandible: a case report. SAGE Open Medical Case Reports. 2020; 8:2050313X20936954.
62. Mohan RPS, Verma S, Gupta N, Ghanta S, Agarwal N, Gupta S. The radiological versatility of fibrous dysplasia: an 8-year retrospective radiographic analysis in a north Indian population. Indian Journal of Dental Research. 2014;5(3):139-145.
63. Punyani SR, Srivastava S, Jasuja VR. Craniofacial fibrous dysplasia report of a case with diverse radiological spectrum. Clinical Cases in Mineral and Bone Metabolism. 2016;13(3):249-252.
64. Gupta D. Osteomyelitis of the mandible mimicking fibrous dysplasia: a radiographic controversy. Clinical Dental. (0974-3979). 2013;7(3).
65. Schulze D, Blessmann M, Pohlenz P, Wagner K, Heiland M. Diagnostic criteria for the detection of mandibular osteomyelitis using cone-beam computed tomography. Dentomaxillofacial Radiology. 2006;35(4):232-235.
66. Chen Wongworawat Y, Jack D, Inman JC, Abdelhalim F, Cobb C, Zuppan CW, Raza A. Regional lymph node enlargement in clinically severe cherubism. Clinical Pathology. 2019; 12:2632010X19861107.
67. De Melo WM, Sonoda CK, Hochuli-Vieira E. Monostotic fibrous dysplasia of the mandible. Journal of Craniofacial Surgery. 2012;23(5):452-454.
68. Davidova LA, Bhattacharyya I, Islam MN, Cohen DM, Fitzpatrick SG. An analysis of clinical and histopathologic features of fibrous dysplasia of the jaws: a series of 40 cases and review of literature. Head & Neck Pathology. 2020;14(2):353-361.
69. Soluk-Tekkesin M, Sinanoglu A, Selvi F, Cakir Karabas H, Aksakalli N. The importance of clinical and radiological findings for the definitive histopathologic diagnosis of benign fibro-osseous lesions of the jaws: study of 276 cases. Journal of stomatology, oral and maxillofacial surgery. 2021;123(3):364-371.
70. MacDonald-Jankowski DS, Yeung R, Li TK, Lee KM. Computed tomography of fibrous dysplasia. Dentomaxillofacial Radiology. 2004;33(2):114-118.
71. Worth HM. Principles and Practice of Oral Radiologic Interpretation. Year Book Medical Publishers; 1963.
72. Taihi I, Radoi L. Chronic non-suppurative mandibular osteomyelitis with proliferative periostitis: a review. Quintessence International. 2018;49(3):219-226.
73. Gonçalves M, Gonçalves A. Garre's osteomyelitis associated with a fistula: a case report. International Journal of Clinical Pediatric Dentistry. 2002;26(3):311-313.
74. Kannan S, Sandhya G, Selvarani R. Periostitis ossificans (Garrè's osteomyelitis) radiographic study of two cases. International Journal of Paediatric Dentistry. 2006;16(1):59-64.
75. Lincoln TA, Webber SJ. An extremely unusual case of Garrè's osteomyelitis of the mandibular condyle after surgical removal of third molars. Journal of Maxillofacial & Oral Surgery. 2012;70(12):2748-2751.
76. Seok H, Kim S-G, Song J-Y. Proliferative periostitis of the mandibular ramus and condyle: a case report. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2015;41(4):198-202.
77. Chang Y-C, Shieh Y-S, Lee S-P. Chronic osteomyelitis with proliferative periostitis in the lower jaw. Journal of Dental Sciences. 2015;10(4):450-455.
78. Kawai T, Hiranuma H, Kishino M, Murakami S, Sakuda M, Fuchihata H. Gross periostitis ossificans in mandibular osteomyelitis: review of the English literature and radiographic variation. Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology. 1998;86(3):376-382.
79. Bisseret D, Kaci R, Lafage-Proust MH, Alison M, Parlier-Cuau C, Laredo JD, Bousson V. Periosteum: characteristic imaging findings with emphasis on radiologic-pathologic comparisons. Skeletal Radiology. 2015;44(3):321-338.
80. Cheon J-E, Kim I-O, Kim WS, Yeon KM. Isolated periostitis as a manifestation of systemic vasculitis in a child: imaging features. Pediatric Radiology. 2010;40(1):116-119.
81. Heggie A, Shand J, Aldred M, Talacko A. Juvenile mandibular chronic osteomyelitis: a distinct clinical entity. International Journal of Oral and Maxillofacial Surgery. 2003;32(5):459-468.
82. Baltensperger M, Grätz K, Bruder E, Lebeda R, Makek M, Eyrich G. Is primary chronic osteomyelitis a uniform disease? Proposal of a classification based on a retrospective analysis of patients treated in the past 30 years. Journal of Cranio-Maxillo-Facial Surgery. 2004;32(1):43-50.
83. Theologie-Lygidakis N, Schoinohoriti O, Iatrou I. Surgical management of primary chronic osteomyelitis of the jaws in children: a prospective analysis of five cases and review of the literature. Oral and maxillofacial surgery. 2011;15(1):41-50.

84. Zain-Alabdeen EH, Al-Sadhan RI, AlSuhaim FS, AlMutairi KM. Delayed diagnosis in the maxillofacial region: two case reports. Journal of Taibah University Medical Sciences. 2017;12(6):548-554.
85. Zain-Alabdeen E, Abdelfattah A, Kordi O, Al-Sadhan R. The dilemma of juvenile fibrous dysplasia versus chronic osteomyelitis of the posterior mandible: A case report. Clinical Case Reports International. 2022;10(10):6379.