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ORIGINAL ARTICLE

Comparison of the histopathological characteristics of diffuse sclerosing osteomyelitis of the mandible, chronic suppurative osteomyelitis, and craniofacial fibrous dysplasia

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Abstract

Background: There are relatively few reports on the histopathological characteristics of diffuse sclerosing osteomyelitis of the mandible (DSOM), which is difficult to distinguish from chronic suppurative osteomyelitis (CSO) and craniofacial fibrous dysplasia (CFD). This study aimed to summarize and compare the histopathological characteristics of DSOM, CFD, and CSO.

Materials and Methods: In this study, hematoxylin and eosin-stained sections of patients with DSOM, CSO, and CFD at the Peking University Hospital of Stomatology from 2015 to 2020 were retrieved. The histopathological characteristics were summarized, including new bone formation, inflammatory cell infiltration, bone trabecular morphology, osteoclasts, sequestrum, bacterial mass, and calcified spherules, similar to cementicles. The histopathological characteristics of DSOM, CSO, and CFD were compared, and the results were statistically analyzed.

Results: In total, 50, 13, and 10 patients with DSOM, CSO, and CFD were included in this study, respectively. In terms of new bone formation, both DSOM and CSO showed reactive bone formation ($p = 1$), whereas CFD mainly showed fiber osteogenesis ($p < 0.001$). The inflammatory cells of DSOM were mainly lymphocytes and plasma cells, whereas those of CSO were mainly lymphocytes and neutrophils ($p < 0.001$), and there was usually no inflammatory cell infiltration in the CFD specimens ($p < 0.001$). DSOM, CSO, and CFD showed irregular bone trabeculae ($p = 0.045$, $p = 0.703$) and active osteoclasts ($p1 = 0.189$, $p2 = 0.256$). DSOM showed a small amount of bacterial mass but no sequestrum; neither of which was found in CFD ($p = 1$, $p = 1$), but it was common in CSO ($p = 0.011$ and $p = 0.025$). DSOM and CSO showed smooth and regular basophilic lines ($p = 0.308$), whereas CFD showed a rough and irregular basophilic line ($p < 0.001$).

Kuankuan Jia and Jianyun Zhang contributed equally to this work.

Conclusions: The histopathological characteristics of the three diseases were partly similar, but there were evident differences. The main differences are the type of new bone formation, types and distribution of inflammatory cells, and presence of sequestrum and bacterial masses. These differences will help clinicians diagnose DSOM.

KEYWORDS
chronic suppurative osteomyelitis, craniofacial fibrous dysplasia, diffuse sclerosing osteomyelitis of the mandible, histopathological characteristics

1 | INTRODUCTION

Diffuse sclerosing osteomyelitis of the mandible (DSOM) is an autoinflammatory disease characterized by recurrent swelling, pain, and trismus of the mandible.[1,2] It is also referred to as primary chronic osteomyelitis, chronic nonbacterial osteomyelitis, or juvenile mandibular chronic osteomyelitis.[3,4] DSOM has no accepted diagnostic criteria; thus, its diagnosis can be established based on a combination of the patient's medical history and clinical, radiographic, and histological findings.[5,6] Clinically, DSOM is often confused with chronic suppurative osteomyelitis (CSO) and craniofacial fibrous dysplasia (CFD). CSO is a suppurative lesion usually caused by an odontogenic infection and often presents with abscess and fistula formation.[7,8] CFD is a benign lesion of bone tissue resulting from the gradual replacement of normal bone tissue with an abnormal proliferation of fibrous bone connective tissue.[9,10] The clinical characteristics of CFD generally present with bone distension and no pain, but pain may occur when the disease progresses rapidly.[11] Thus, it is necessary to establish a differential diagnosis of the three diseases in clinical settings.

The histopathological features of DSOM, CSO, and CFD are similar, and all three diseases present with abnormal osteosclerosis and osteolysis.[2,12–15] According to the World Health Organization (WHO) 2017 Classification of Head and Neck Tumors, the lesion of CFD consists of woven bone with variable amounts of fibrous tissue.[16] But now, there are few reports on the histopathological characteristics of DSOM. Thus, we aimed to determine whether DSOM can be distinguished from CSO and CFD by histopathology.

Moreover, this study aimed to summarize and compare the histopathological characteristics of DSOM, CSO, and CFD and to provide clinicians with more evidence to distinguish DSOM through histopathology.

2 | MATERIALS AND METHODS

Patients with DSOM, CSO, and CFD hospitalized in the Department of Oral and Maxillofacial Surgery, Peking University Hospital of Stomatology from 2015 to 2020 were included. The inclusion criteria were as follows: (1) patients diagnosed with DSOM, CSO, and CFD based on medical history and clinical, radiographic, and histological characteristics; (2) those who had undergone curettage or biopsy in our hospital; and (3) those with surgical bone specimens taken from the mandible. Patients with incomplete data were excluded from the study.

Hematoxylin and eosin (H&E)-stained sections of the included patients were collected from the Department of Pathology of our hospital. Two observers from the Department of Oral Pathology of our institution jointly evaluated all microscopic findings for each patient, and they were blinded to the clinical information and diagnoses of the patients. If there was an inconsistent assessment, another senior pathologist reviewed and determined the final result.

The histopathological characteristics evaluated by the observers included new bone formation patterns (including reactive bone formation or fiber osteogenesis), inflammatory cell infiltration (including inflammatory cell types and distribution), trabecular bone (divided into irregular or regular), bone basophilic line (divided into irregular or regular), osteoclasts, sequestrum, bacterial mass, and calcified spherules, similar to cementicles.

Data were analyzed using the Statistical Package for the Social Sciences version 24.0 (IBM, Armonk, NY). The chi-squared and Fisher–Freeman–Halton tests were used to determine differences in the histopathological characteristics of CSO, DSOM, and CFD in 2×2 or 2×3 tables. $p < 0.05$ was considered significant.

3 | RESULTS

In this study, 50, 13, and 10 patients with DSOM, CSO, and CFD met the inclusion criteria, respectively. The patients' demographic information is shown in Table 1.

Comparison of the histopathological features of the patients is shown in Table 2. All three diseases resulted in new bone formation. DSOM and CSO showed reactive bone formation ($p1 = 1$), and osteoblasts were observed around the bone, whereas CFD mainly showed fiber osteogenesis ($p2 < 0.001$), and bundles of collagen fibers oriented perpendicular to the bone surface without osteoblasts (Figure 1).

DSOM and CSO showed inflammatory cell infiltration in the bone marrow and soft tissue ($p1 = 1$), but there were statistical differences in the inflammatory cell types ($p1 = 0.048$) and distributions ($p1 < 0.001$). The DSOM specimens were mainly infiltrated by scattered lymphocytes and plasma cells, whereas the CSO specimens were mainly infiltrated by concentrated neutrophils and lymphocytes. The CFD specimens were usually free of inflammatory cell infiltration ($p2 < 0.001$), and only 30% of the patients with CFD had a small

TABLE 1 The epidemiological characteristics of DSOM, CSO, and CFD

Epidemiological characteristics	DSOM ($n = 50$)	CSO ($n = 13$)	CFD ($n = 10$)
Sex			
Male	25	9	4
Female	25	4	6
Mean years (year)	22.6 ± 15.3	47.0 ± 23.7	30.5 ± 9.6
Age range (year)	5–68	7–74	17–40

TABLE 2 The comparison of histopathological characteristics of DSOM, CSO, and CFD

Histopathological characteristics	DSOM ($n = 50$)	CSO ($n = 13$)	CFD ($n = 10$)	$p1$	$p2$
Bone formation					
No	1 (2.0%)	4 (30.8%)	1 (10.0%)	0.001[a]	0.308[a]
Reactive bone formation	46 (92.0%)	9 (69.2%)	0 (0)	1.000	<0.001
Fiber osteogenesis	0 (0)	0 (0)	8 (80.0%)		
Both	3 (6.0%)	0 (0)	1 (10.0%)		
Inflammatory cell infiltration					
No	3 (6.0%)	0 (0)	7 (70.0%)	1.000[a]	<0.001[a]
Cell types					
Lymphocyte and plasma cell	37 (74.0%)	3 (23.1%)	3 (30.0%)	<0.001	1.000
Neutrophil	5 (10.0%)	2 (15.4%)	0 (0)		
Both	5 (10.0%)	8 (61.5%)	0 (0)		
Cell distribution					
Scattered	34 (68.0%)	5 (38.4%)	3 (30.0%)	0.048	0.592
Concentrated	12 (24.0%)	7 (53.8%)	0 (0)		
Both	1 (2.0%)	1 (7.7%)	0 (0)		
Trabecular bone					
No	2 (4.0%)	4 (30.8%)	1 (10.0%)	0.003[a]	1.000[a]
Irregular	33 (66.0%)	6 (46.2%)	8 (80.0%)	0.045	0.703
Regular	4 (8.0%)	3 (23.1%)	0 (0)		
Both	11 (22.0%)	0 (0)	1 (10.0%)		
Bone basophilic line					
No	1 (2.0%)	4 (30.8%)	1 (10.0%)	0.001[a]	0.308[a]
Irregular	12 (24.0%)	1 (7.7%)	8 (80.0%)	0.407	0.001
Regular	21 (42.0%)	6 (46.2%)	1 (10.0%)		
Both	16 (32.0%)	2 (15.4%)	0 (0)		
Osteoclast	33 (66.0%)	6 (46.2%)	9 (90.0%)	0.189	0.256
Sequestrum	0 (0)	6 (46.2%)	0 (0)	<0.001	1.000
Bacterial mass	2 (4.0%)	5 (38.4%)	0 (0)	0.003	1.000
Calcified spherules similar to cementicles	0 (0)	0 (0)	8 (80%)	1.000	<0.001

Note: $p1$: Statistical parameters between DSOM and CSO. $p2$: Statistical parameters between DSOM and CFD.
[a]p-value between histopathological characteristics with and without presentation.

amount of scattered lymphocyte infiltration in the bone marrow (Figure 1).

Bone trabeculae were mainly irregular in the three disease specimens. There was no statistical difference between DSOM and CFD in the bone trabeculae ($p2 = 0.703$). However, there was a statistical difference between DSOM and CSO in the bone trabeculae ($p1 = 0.045$), which may be due to the coexistence of irregular and regular bone trabeculae in 22% of the DSOM specimens, but there was no coexistence of irregular and regular bone trabeculae in the CSO specimens (Figure 2).

A large number of basophilic lines were observed in the bone tissues of the three diseases. The basophilic lines of DSOM and CSO were regular ($p1 = 0.407$), whereas those of CFD were irregular ($p2 < 0.001$), as shown in Figure 2.

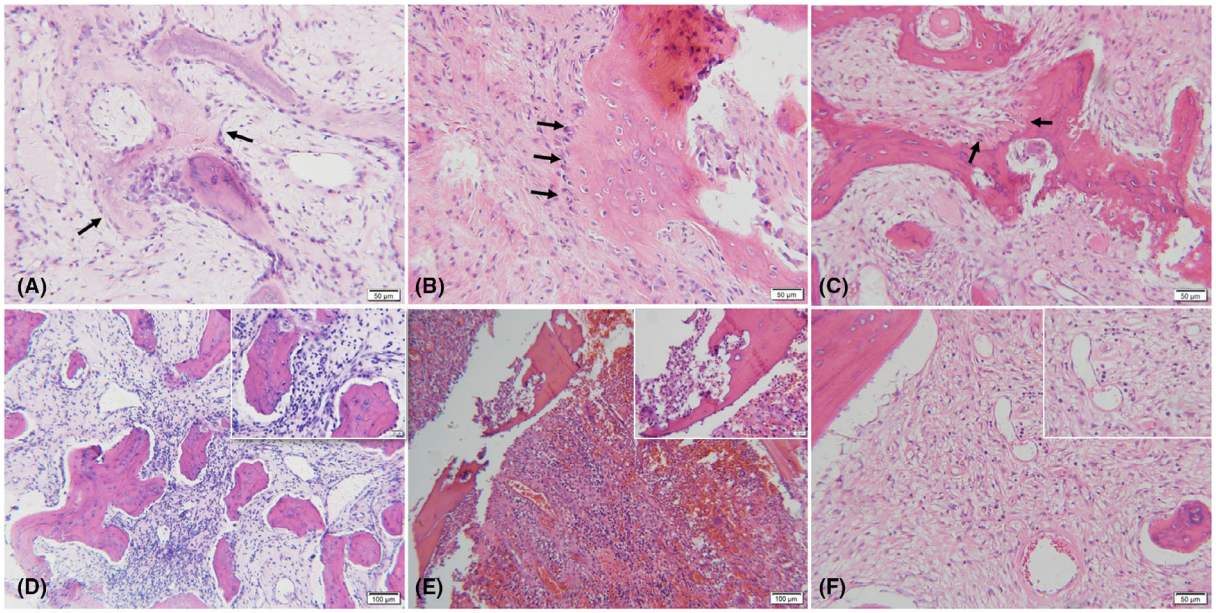

FIGURE 1 Histopathological sections (hematoxylin and eosin staining) showed new bone formation patterns (A–C) and the characteristics of inflammatory cell infiltration (D–F) in the diffuse sclerosing osteomyelitis of the mandible (DSOM), chronic suppurative osteomyelitis (CSO), and craniofacial fibrous dysplasia (CFD) specimens. (A) DSOM, osteoblasts surrounding the new bone trabeculae (arrow). (B) CSO, osteoblasts surrounding the new bone trabeculae (arrow). (C) CFD, fiber osteogenesis (arrow), and bundles of collagen fibers oriented perpendicular to the bone surface without osteoblasts around. (D) DSOM, a large number of scattered lymphocytes and plasma cells infiltrated in the bone marrow. (E) CSO, numerous concentrated neutrophils and lymphocytes infiltrated in the bone marrow and soft tissue. (F) CFD, few scattered lymphocytes infiltrated in the bone marrow.

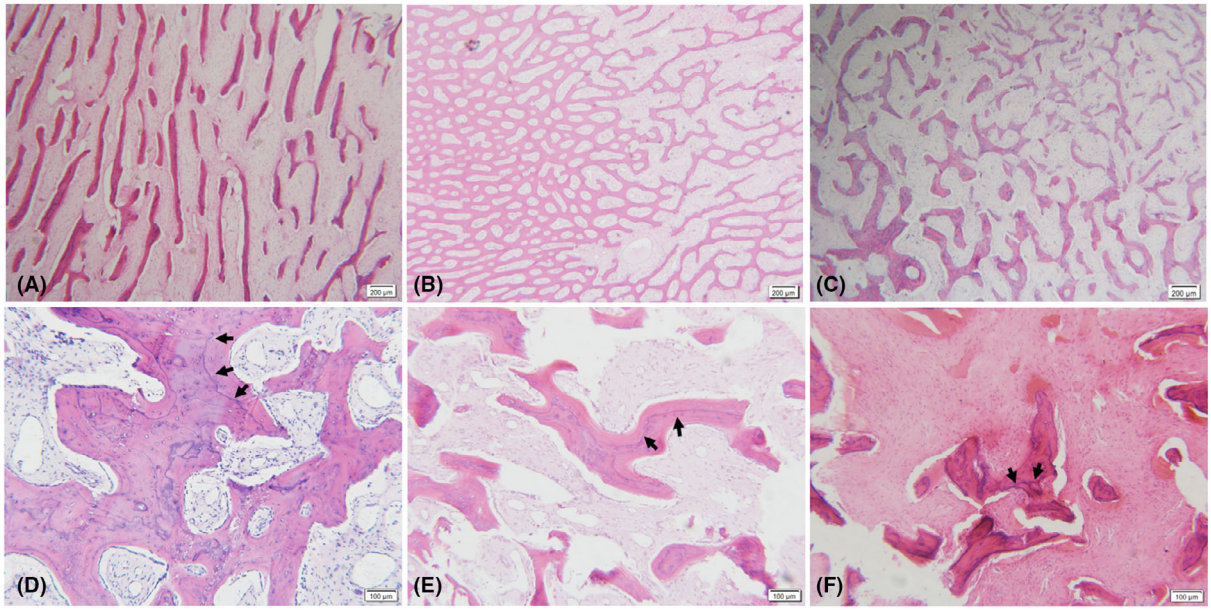

FIGURE 2 Histopathological sections (hematoxylin and eosin staining) showed bone trabecular morphology (A–C) and basophilic line (D–F) in the diffuse sclerosing osteomyelitis of the mandible (DSOM), chronic suppurative osteomyelitis (CSO), and craniofacial fibrous dysplasia (CFD) specimens. (A) DSOM, regular trabeculae of the reactive bone and is stream-like. (B) DSOM, a large number of basophilic lines, with most of them being smooth and regular (arrows) and a few being rough and irregular. (C) CSO, regular trabeculae of the reactive bone with a mesh shape. (D) CSO, a large number of smooth and regular basophilic lines. (E) CFD, immature and irregular bone trabeculae. (F) CFD, a large number of rough and irregular basophilic lines (arrows).

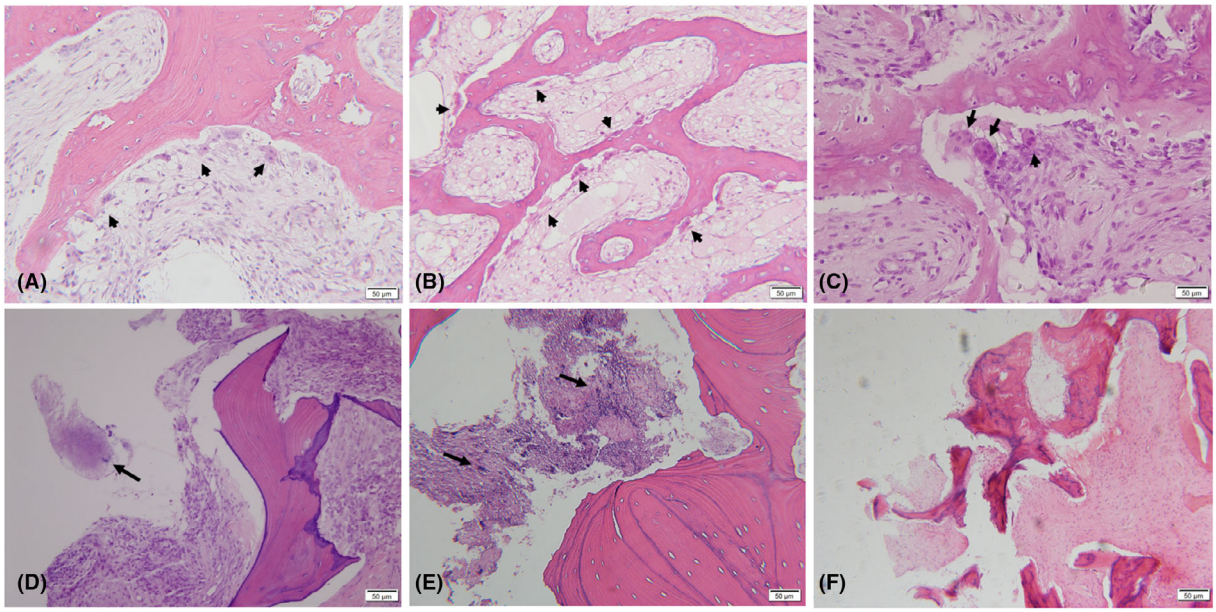

FIGURE 3 Histopathological sections (hematoxylin and eosin staining) showed the characteristics of osteoclast (A–C), sequestrum, and bacterial mass (D–F) in the diffuse sclerosing osteomyelitis of the mandible (DSOM), chronic suppurative osteomyelitis (CSO), and craniofacial fibrous dysplasia (CFD) specimens. (A, C, and E) DSOM, CSO, and CFD sections, respectively, showed a large number of active osteoclasts and absorption lacunae on the surface of the bone trabeculae (arrow). (B) DSOM, a small amount of bacterial mass at the boundary of the bone tissue, with a small amount of bacterial masses (arrow). (D) CSO, large pieces of sequestrum, surrounded by numerous bacterial masses (arrow). (F) CFD, no evidence of bacterial mass and sequestrum.

Active osteoclasts were observed around the bone trabeculae in all three disease specimens, and there was no statistical difference. No sequestrum was observed in the DSOM and CFD specimens ($p2 = 1$), but sequestrum was observed in the CSO specimens ($p1 < 0.001$). Only 4% of DSOM had a small bacterial mass, no bacterial mass was observed in the CFD specimens ($p2 = 1$), and there was no sequestrum in either disease. However, a bacterial mass was common in CSO ($p1 = 0.003$) and was present in large numbers around the sequestrum ($p1 < 0.001$). The results are shown in Figure 3.

Calcified spherules similar to cementicles were common in the fibrotic bone marrow of CFD specimens ($p2 < 0.001$), but they were not observed in the DSOM and CSO specimens.

4 | DISCUSSION

DSOM is a rare chronic nonsuppurative osteomyelitis of the mandible. Its clinical manifestations include recurrent swelling, pain, and trismus, but no abscess, internal or external fistula, or sequestrum. Radiographic findings of DSOM include intermingled sclerosis and lysis in the mandible bone, subperiosteal bone formation, cortical discontinuity due to osteolysis, and blurred boundary between the cortical and medulla due to osteosclerosis.[5,6] The clinical and radiographic manifestations of DSOM are similar to those of CSO and CFD; therefore, it is easily misdiagnosed as CSO or CFD, and patients with DSOM are provided inappropriate treatment in clinical practice.

We summarized and compared the differences in the clinical, radiographic and histopathological manifestations of DSOM, CSO, and CFD based on previous studies, as shown in Table 3.[5,6] However, the diagnosis of DSOM cannot be confirmed by clinical and radiographic manifestations. In this study, we observed and summarized the histopathological characteristics of DSOM and compared them with those of CSO and CFD, hoping to provide information for the diagnosis of DSOM based on histopathological characteristics.

This study found that DSOM and CSO showed inflammatory cell infiltration and reactive bone formation, and a number of studies have found that abnormal secretion of inflammatory cytokines may be the etiology of DSOM,[17–21] and that inflammatory cells and cytokines may lead to abnormal bone metabolism in the lesion bone tissues. Similarly, CSO is also an inflammatory response but caused by microbial infection that leads to abnormal bone metabolism in the lesion bone tissue. Therefore, both diseases show reactive new bone formation and a large number of osteoclasts and basophilic lines, confirming that bone remodeling is active in both diseases. Montonen et al.[13] found elevated expressions of receptor activator of nuclear factor κB ligand and cathepsin K in the specimens of patients with DSOM through immunohistochemistry, which also indicated that osteoclasts in DSOM were more active. Therefore, immunohistochemical staining for inflammatory factors may improve the accuracy of the diagnosis of DSOM; however, this needs to be verified by further studies.

In contrast to the inflammatory response caused by microbial infection in CSO, the abnormal expression of inflammatory cytokines in DSOM may be related to gene mutation. Previous studies have

TABLE 3 The clinical, radiographic, and histopathological characteristics of DSOM, CSO, and CFD

	DSOM	CSO	CFD
Clinical symptoms	Recurrent pain and swelling of the mandible	Mild or severe pain and swelling of the mandible	Progressive enlargement of the mandible bone
	Trismus	Trismus	No trismus
	Progressive mandibular deformity	Fistula formation	Most are painless
		Episodes of suppuration	
Medical history	History of intermittent pain and swelling of the mandible	History of dentoalveolar infection, trauma, or dentoalveolar surgical procedures	History of swollen and gradually asymmetricalmandible
Radiographic characteristics	Intermingled osteosclerosis and osteolysis	Intermingled osteosclerosis and osteolysis	Swelling, thin, and continuous cortex bone
	Blurred boundary between the cortex and medulla	Sequestrum formation	Clearly demarcated between the cortex and medulla
	Cortical discontinuity	Pathological fractures	Cyst-like pattern of the medulla
	Subperiosteal bone formation	Subperiosteal bone formation	Mandibular canal displacement
	Edema of masticatory muscles		
Histopathological characteristics	Scattered lymphocyte and plasma cell infiltration	Concentrated lymphocyte, plasma cell and neutrophil infiltration	usually no inflammatory cell infiltration
	Reactive bone formation	Reactive bone formation	Fiber osteogenesis
		Sequestrum and bacterial mass	Calcified spherules similar to cementicles

found that a significant proportion of autoinflammatory diseases, such as tumor necrosis factor receptor-associated cycle syndrome and Mediterranean fever, are often caused by single gene mutations.[22,23] DSOM is considered to be an autoinflammatory disease and may be associated with the PSTPIP2 gene.[17,24,25] With continuous studies on the pathogenesis of DSOM, gene mutational analysis may become a new means of diagnosing DSOM in the future.

The results of this study showed that the new bone formation pattern of CFD was mainly fiber osteogenesis, which was significantly different from the reactive bone formation pattern of DSOM. CFD is a benign dysplastic disease caused by mutations in GNAS gene that encodes the α-subunit of the stimulatory G-protein.[26–28] The abnormal proliferation of fibroblasts in CFD bone tissue resulted in normal bone tissue being gradually replaced by fibrous tissue. Subsequently, the fibrous tissue calcified to form elongated trabeculae of woven or lamellar bone and calcified spherules, similar to cementicles.[14,15] Therefore, in the CFD specimens, there are bundles of collagen fibers on the surface of bone tissue. However, there are no osteoblasts around them, and the formation of calcified spherules similar to cementicles in the bone marrow cavity is not observed. Fiber osteogenesis also leads to rough and irregular basophilic lines in the trabecular bone of CFD.

Abnormal bone metabolism in all three diseases leads to irregular bone trabeculae. However, the new bone tissues generated by periosteal reaction in DSOM and CSO did not show repeated abnormal bone remodeling; therefore, regular bone trabeculae showing mesh or stream-like shapes could be observed in some specimens.

Acute inflammation is characterized by intense inflammation, polymorphonuclear neutrophil infiltration with microabscess formation, whereas chronic inflammation is characterized by lymphocytic infiltration and bone remodeling with myelofibrosis.[7,8,29] DSOM is considered an autoinflammatory disease,[17,24] often presenting as a chronic inflammatory disease; therefore, the DSOM specimens are mainly characterized by lymphocyte and plasma cells infiltration. However, CSO is a suppurative osteomyelitis of the jaw, which is often caused by maxillofacial space infection or odontogenic infection. The cortex and periosteum of the mandible are destroyed and hyperplastic under the stimulation of bacteria and pus, often presenting as acute inflammation.[8] Therefore, a large number of neutrophils can be observed in the CSO specimens.

In this study, a small part of the DSOM specimens had a bacterial mass, which was consistent with the hypothesis that DSOM may be caused by the low toxicity bacterial infection proposed by Jacobsson et al.[30,31] However, only a few microbial culture tests successfully cultured microorganisms consistent with the resident bacteria of the skin and oral mucosa, and the test lacked a control group. Thus, the possibility of sample contamination cannot be ruled out. In addition, in this study, the bacterial mass in the DSOM specimens was not only small in quantity but also small in volume; therefore, the possibility of sample contamination during biopsy and section staining cannot be excluded.

In conclusion, this study found that the histopathological characteristics of the three diseases were similar to some extent, but there were also evident differences, which were mainly reflected in the type of new bone formation, types and distribution of inflammatory cells, and presence of sequestrum and bacterial mass (Table 3). Combining with clinical and radiographic information, pathologists can establish a more accurate diagnosis by these differentiation between three diseases. With further studies on the etiology and pathogenesis of

DSOM, immunohistochemistry and gene mutational analysis may become new methods for establishing the diagnosis of DSOM.

AUTHOR CONTRIBUTIONS

Jingang An and Jianyun Zhang performed study concept and design; Kuankuan Jia and Jianyun Zhang performed development of methodology and writing, review and revision of the paper; Kuankuan Jia provided acquisition, analysis, and interpretation of data; Jingang An, Tiejun Li, and Yi Zhang provided technical and material support.

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None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/jop.13384.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The regional Ethical Review Board of Peking University School and Hospital of Stomatology approved this study (PKUSSIRB-202056096), and the study was performed in accordance with the Declaration of Helsinki.

PATIENT CONSENT STATEMENT

All persons gave their informed consent prior to their inclusion in the study.

REFERENCES

1. Marzola C. Chronic diffuse sclerosing osteomyelitis of the maxilla and the mandible. *Rev Bras Odontol*. 1970;27(165):238-241.
2. Jacobsson S. Diffuse sclerosing osteomyelitis of the mandible. *Int J Oral Surg*. 1984;13(5):363-385.
3. Renapurkar S, Pasternack MS, Nielsen GP, Kaban LB. Juvenile mandibular chronic osteomyelitis: role of surgical debridement and antibiotics. *J Oral Maxillofac Surg*. 2016;74(7):1368-1382.
4. Obel G, Krogdahl A, Thygesen T, Godballe C. Juvenile mandibular chronic osteomyelitis: 3 cases and a literature review. *J Oral Maxillofac Surg*. 2013;71(2):305-309.
5. 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. *J Craniomaxillofac Surg*. 2018;46(9):1631-1636.
6. 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. *J Oral Maxillofac Surg*. 2021;79(5):1053-1061.
7. Mallikarjun K, Kohli A, Kumar A, Tanwar A. Chronic suppurative osteomyelitis of the mandible. *J Indian Soc Pedod Prev Dent*. 2011;29(2):176-179.
8. Horst SA, Hoerr V, Beineke A, et al. A novel mouse model of Staphylococcus aureus chronic osteomyelitis that closely mimics the human infection: an integrated view of disease pathogenesis. *Am J Pathol*. 2012;181(4):1206-1214.
9. Yang L, Wu H, Lu J, Teng L. Prevalence of different forms and involved bones of craniofacial fibrous dysplasia. *J Craniofac Surg*. 2017;28(1):21-25.
10. Burke AB, Collins MT, Boyce AM. Fibrous dysplasia of bone: craniofacial and dental implications. *Oral Dis*. 2017;23(6):697-708.
11. Assaf AT, Benecke AW, Riecke B, et al. Craniofacial fibrous dysplasia (CFD) of the maxilla in an 11-year old boy: a case report. *J Craniomaxillofac Surg*. 2012;40(8):788-792.
12. Van Merkesteyn JP, Groot RH, Bras J, Bakker DJ. Diffuse sclerosing osteomyelitis of the mandible: clinical radiographic and histologic findings in twenty-seven patients. *J Oral Maxillofac Surg*. 1988;46(10):825-829.
13. Montonen M, Li TF, Lukinmaa PL, et al. RANKL and cathepsin K in diffuse sclerosing osteomyelitis of the mandible. *J Oral Pathol Med*. 2006;35(10):620-625.
14. Jeyaraj P. Histological diversity, diagnostic challenges, and surgical treatment strategies of fibrous dysplasia of upper and mid-thirds of the craniomaxillofacial complex. *Ann Maxillofac Surg*. 2019;9(2):289-314.
15. Pereira T, Gomes CC, Brennan PA, Fonseca FP, Gomez RS. Fibrous dysplasia of the jaws: integrating molecular pathogenesis with clinical, radiological, and histopathological features. *J Oral Pathol Med*. 2019;48(1):3-9.
16. El-Mofty SK, Nelson B, Toyosawa S. Fibrous dysplasia. *WHO Classification of Head and Neck Tumors*. 4th ed. IARC; 2017:253-254.
17. Hofmann SR, Schwarz T, Moller JC, et al. Chronic non-bacterial osteomyelitis is associated with impaired Sp1 signaling, reduced IL10 promoter phosphorylation, and reduced myeloid IL-10 expression. *Clin Immunol*. 2011;141(3):317-327.
18. Wagner AD, Andresen J, Jendro MC, Hulsemann JL, Zeidler H. Sustained response to tumor necrosis factor alpha-blocking agents in two patients with SAPHO syndrome. *Arthritis Rheum*. 2002;46(7):1965-1968.
19. Jansson A, Renner ED, Ramser J, et al. Classification of non-bacterial osteitis: retrospective study of clinical, immunological and genetic aspects in 89 patients. *Rheumatology*. 2007;46(1):154-160.
20. Hofmann SR, Morbach H, Schwarz T, Rösen-Wolff A, Girschick HJ, Hedrich CM. Attenuated TLR4/MAPK signaling in monocytes from patients with CRMO results in impaired IL-10 expression. *Clin Immunol*. 2012;145(1):69-76.
21. Hofmann SR, Kubasch AS, Ioannidis C, et al. Altered expression of IL-10 family cytokines in monocytes from CRMO patients result in enhanced IL-1beta expression and release. *Clin Immunol*. 2015;161(2):300-307.
22. McDermott MF, Aksentijevich I, Galon J, et al. Germline mutations in the extracellular domains of the 55 kDa TNF receptor, TNFR1, define a family of dominantly inherited autoinflammatory syndromes. *Cell*. 1999;97(1):133-144.
23. McDermott MF. A common pathway in periodic fever syndromes. *Trends Immunol*. 2004;25(9):457-460.
24. Malmstrom M, Fyhrquist F, Kosunen TU, Tasanen A. Immunological features of patients with chronic sclerosing osteomyelitis of the mandible. *Int J Oral Surg*. 1983;12(1):6-13.
25. Chitu V, Ferguson PJ, de Bruijn R, et al. Primed innate immunity leads to autoinflammatory disease in PSTPIP2-deficient cmo mice. *Blood*. 2009;114(12):2497-2505.
26. Idowu BD, Al-Adnani M, O'Donnell P, et al. 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.
27. Weinstein LS, Liu J, Sakamoto A, Xie T, Chen M. Minireview: GNAS: normal and abnormal functions. *Endocrinology*. 2004;145(12):5459-5464.
28. Godse AS, Shrotriya SP, Vaid NS. Fibrous dysplasia of the maxilla. *J Pediatr Surg*. 2009;44(4):849-851.

29. Sybenga AB, Jupiter DC, Speights VO, Rao A. Diagnosing osteomyelitis: a histology guide for pathologists. *J Foot Ankle Surg*. 2020;59(1):75-85.
30. Jacobsson S, Dahlen G, Moller AJ. Bacteriologic and serologic investigation in diffuse sclerosing osteomyelitis (DSO) of the mandible. *Oral Surg Oral Med Oral Pathol*. 1982;54(5):506-512.
31. Jacobsson S, Hallen O, Hollender L, Hansson CG, Lindstrom J. Fibro-osseous lesion of the mandible mimicking chronic osteomyelitis. *Oral Surg Oral Med Oral Pathol*. 1975;40(4):433-444.

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