EDITORIAL

Classification and nomenclature of fibro-osseous lesions

The World Health Organization's (WHO) fourth edition of the *Classification of Head and Neck Tumours*, published in 2017, included not only tumors but also other lesions, such as cysts,[1] which had been excluded in the previous edition.[2] Furthermore, it introduced "fibro-osseous lesion" (FOL) as a lesion group for the first time in the WHO classification of odontogenic and maxillofacial bone tumors.[1] There are 3 recognized FOLs; fibrous dysplasia (FD), cemento-ossifying fibroma (COF), and cemento-osseous dysplasia (COD).[1] Because of their histologic similarity, they must be distinguished by clinical and radiologic criteria.[3] Over the last half century, progress has been made concerning their classification and nomenclature, with a better understanding of their character. The 3 earlier WHO editions in 1971,[4] 1992,[5] and 2005[2] served as milestones in this process. The 3 FOLs in the 2017 edition were described in chapter 8, titled "Odontogenic and Maxillofacial Bone Tumours." Although this chapter contributed invaluably to a recent publication on jaw malignancies,[6] the following issues should be revisited regarding FOLs.

BRIEF OVERVIEW OF THE 4 WHO EDITIONS RELATING TO FOLS

The highlights of the past 4 editions regarding FOLs are depicted in Figure 1. Lesions considered to be odontogenic are shown in blue boxes and those related to bone are shown in red boxes. Changes in terminology and/or appearance of new lesions that arose between these editions are depicted in white boxes; these and other once-common terms have been discussed elsewhere.[7,8] The 1992 edition[5] assigned unique International Classification of Disease for Oncology (ICD-O) codes to most FOLs, but these were withdrawn from all except ossifying fibroma (in the 2005 edition[2]) and COF (in the 2017 edition[1]). The first 3 editions did not use "neoplasm" and "tumour" as synonyms but used tumour in "its broadest sense"[9] as a swelling, including cysts and neoplasms. Nevertheless, the 2005 edition[2] excluded most odontogenic cysts. The word tumour in the 8th chapter of the 2017 edition was only applied to neoplasms (including the aneurysm bone cyst), all of which were awarded ICD-O codes.[1]

DEVELOPMENT OF THE CLASSIFICATION AND NOMENCLATURE OF FIBRO-OSSEOUS LESIONS

In the 1971 edition, FOLs were assigned both to "neoplasms and other tumours related to the odontogenic apparatus" and to "neoplasms and other tumours related to bone."[4] The former were so assigned because of the presence of cementum-like tissue. Over the course of 4 editions we have come almost full circle by reassigning putative odontogenic and osseous origins to broadly the same lesions as in the 1971 edition.

Brannon and Fowler suggested in 2001 that because the cementoid elements in FOLs were variants of bone and not of dental cementum, "ossifying fibroma" and "osseous dysplasia" were the appropriate terms.[10] Two of the authors of the chapter on odontogenic tumors in the 2005 edition first used ossifying fibroma in their 2004 textbook but not osseous dysplasia,[11] which first appeared in the 2005 edition.[2]

OSSIFYING FIBROMA TO CEMENTO-OSSIFYING FIBROMA?

The introduction to chapter 8 of the 2017 edition stated, "Regarding the bone lesions, within the group of ossifying fibromas, the prefix 'cemento-' has been added to the variant that is confined to the jaws and that, although strictly speaking, should be listed among the mesenchymal odontogenic tumours, nevertheless has been included among the fibro-osseous lesions in view of differential diagnostic considerations."[12] Furthermore, the re-introduction of the 'cemento-' prefix reflects that this lesion arising in the tooth-bearing area "is of odontogenic origin and arises within the periodontal ligament."[13] This was not new to the discussion of FOLs. Waldron and Giansanti[14] used the term "tumor of periodontal origin" to describe "benign fibro-osseous lesions of the jaws." Kawai et al. identified some CODs as being of periodontal origin.[15] The 2005 edition considered osseous dysplasias to have originated "from the periodontal ligament," while at the same time removing the 'cemento-' prefix.[2]

The 2017 edition assigned ossifying fibroma to the fibro-osseous and osteochondromatous lesions (along with FD and COD)[16] and COF to the benign mesenchymal odontogenic tumors.[17] Furthermore, each was awarded its own ICD-O code, ICD-O-9262/0[16] and ICD-O-9274/0,[17] respectively, indicating that they might be different neoplasms. Nevertheless, the entry for each lesion confounded this. The entire entry for COF stated that it was "a distinct type of ossifying fibroma that occurs in the tooth-bearing areas of the jaws and is believed to be of odontogenic origin. It is a benign fibro-osseous lesion and is discussed in more detail in the 'Ossifying Fibroma' section."[17] The entry

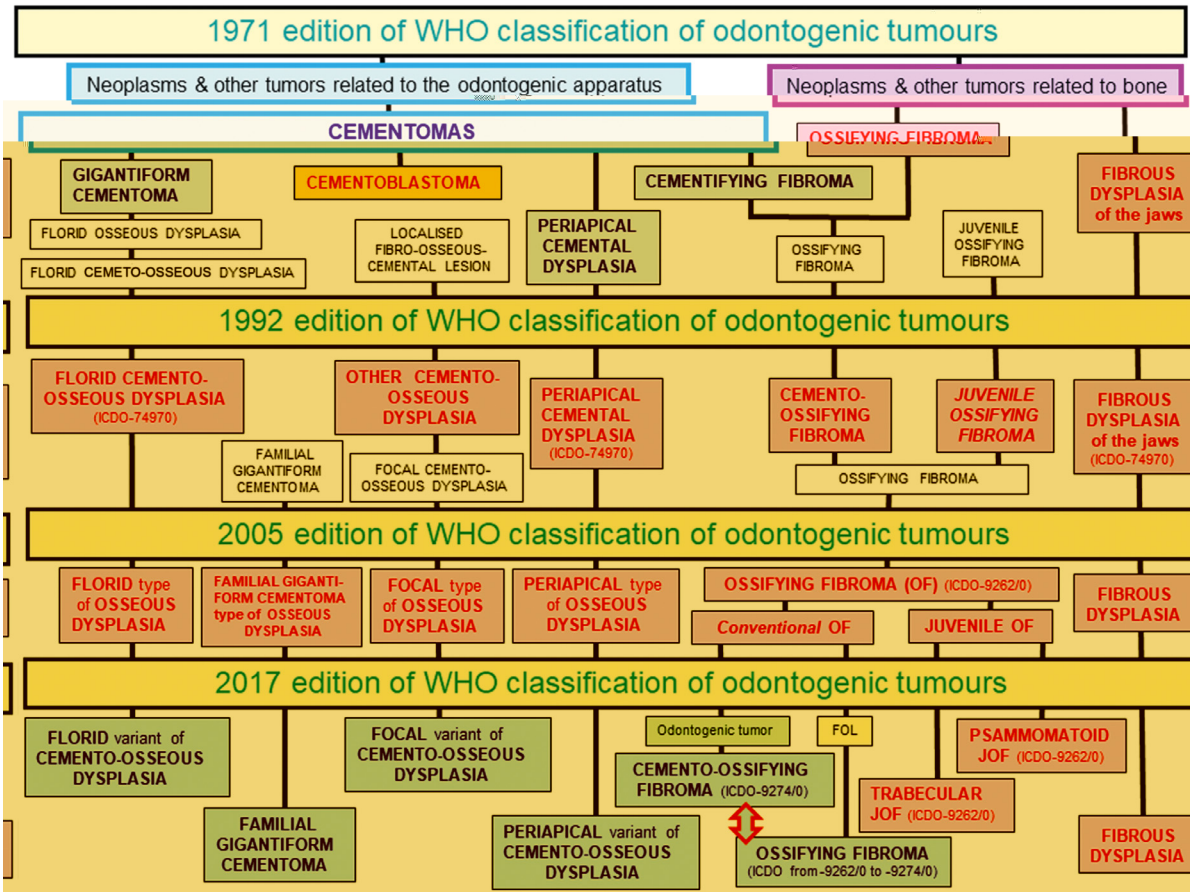

Fig. 1. Development of the nomenclature and classification of fibro-osseous lesions (FOL) of the jaws from the original 4 lesions called "cementoma" (before 1971), ossifying fibroma, and fibrous dysplasia. Cementoblastoma (in the yellow box with red text) is histologically not an FOL and therefore was excluded from further consideration. Lesions in red text and boxes arise in bone. Lesions in blue text and boxes arise from odontogenic tissues. Lesions that first appeared between the editions are in black text and white boxes; many are still in regular use. The awarding and withdrawal of the International Classification of Disease for Oncology (ICDO) code is inserted under the lesion's name. The 2-headed arrow illustrates the relationship between cemento-ossifying fibroma as an odontogenic tumor (light green box) and as an FOL (light yellow box). Key: c-osseous, cemento-osseous.

for ossifying fibroma in fibro-osseous and osteochondromatous lesions added that "ossifying fibroma of odontogenic origin—also called the cemento-ossifying fibroma (COF)—occurs exclusively in the tooth-bearing areas of the mandible and maxilla."[16] Furthermore, the acronym COF was used throughout the section on ossifying fibroma except for the juvenile ossifying fibroma (JOF) variants: juvenile trabecular ossifying fibroma (JTOF) and juvenile psammomatoid ossifying fibroma.[16]

As stated in the introduction to chapter 8,[12] COF is both an odontogenic neoplasm and a FOL; a 2-headed arrow has been inserted between them in Figure 1. The ICD-O code for the COF-as-FOL has been changed to ICD-O-9274/0 to reflect the fact that it is the same as the COF-as-odontogenic-tumor. Furthermore, ICD-O-9262/0 is assigned only to the juvenile ossifying fibromas, which are not odontogenic. These are in red boxes. This is consistent with Waldron's contention that these differed from COF.[3,18]

JUVENILE OSSIFYING FIBROMA

The distinction between COF and the 2 types of JOF (JTOF and juvenile psammomatoid ossifying fibroma) was blurred later in the same ossifying fibroma section of the 2017 edition, which stated that JTOF arises within the jaws except in rare cases. Furthermore, an axial computed tomographic reconstruction of a JTOF (Figure 8.89[16]) was included that strongly suggested that it arose close to if not within the maxillary alveolus and was therefore possibly odontogenic.[16] The 2017 edition stated, "An important feature of a COF is that it is well

defined and can be shelled out relatively easily from the surrounding tissue."[16] A consecutive case series noted that nearly 60% of COFs have a radiolucent periphery suggestive of a capsule.[19] This feature, with or without a well-defined cortex, was also noted as characteristic of the lesion, particularly in younger patients, in a systematic review.[20] These radiologic features may therefore be central to distinguishing COF from JOF. Although only one COF recurred in the case series during follow-up after enucleation,[19] in the systematic review, 12% recurred.[20] In comparison, a systematic review of JOFs revealed that almost one-third recurred.[21]

SYNDROMIC CASES OF OSSIFYING FIBROMA

The 2017 edition reported that "multiple ossifying fibromas may be associated with hyperparathyroidism-jaw tumour syndrome, which is caused by CDC73 (also called HPRPT2) mutations. Lesions with similar histologic features have been reported in a familial setting as gigantiform cementoma."[16] Occasionally, a sole COF may be associated with this syndrome.[22,23]

IS CARTILAGE OBSERVED IN FIBROUS DYSPLASIA ARISING WITHIN THE JAWS?

Although the 2017 edition[24] remarked that cartilage is rarely observed in association with FD, it did not clarify that this remark was based on an 8-case series of FD affecting the lower limb.[25] Therefore, this inference of a relationship between FD arising in the jaws, originating from fibrous membrane, and FD arising within the lower limbs, originating from cartilage, unnecessarily confuses the reader.

CEMENTO-OSSEOUS DYSPLASIA

The 2017 edition changed the osseous dysplasias of the 2005 edition to cemento-osseous dysplasia.[26] Although the need to add the 'cemento-' prefix was not mentioned in the introduction to chapter 8,[12] later commentary clarified that it was for the same reason as that for COF: origin in the periodontal ligament.[13] CODs are the most frequently occurring FOLs.[26] Both focal and florid subtypes are most commonly found in middle-to-old-aged females of sub-Saharan African and East Asian origins.[7,27] Due to the risk of infection following biopsy, a clinico-radiologic follow-up may be sufficient for

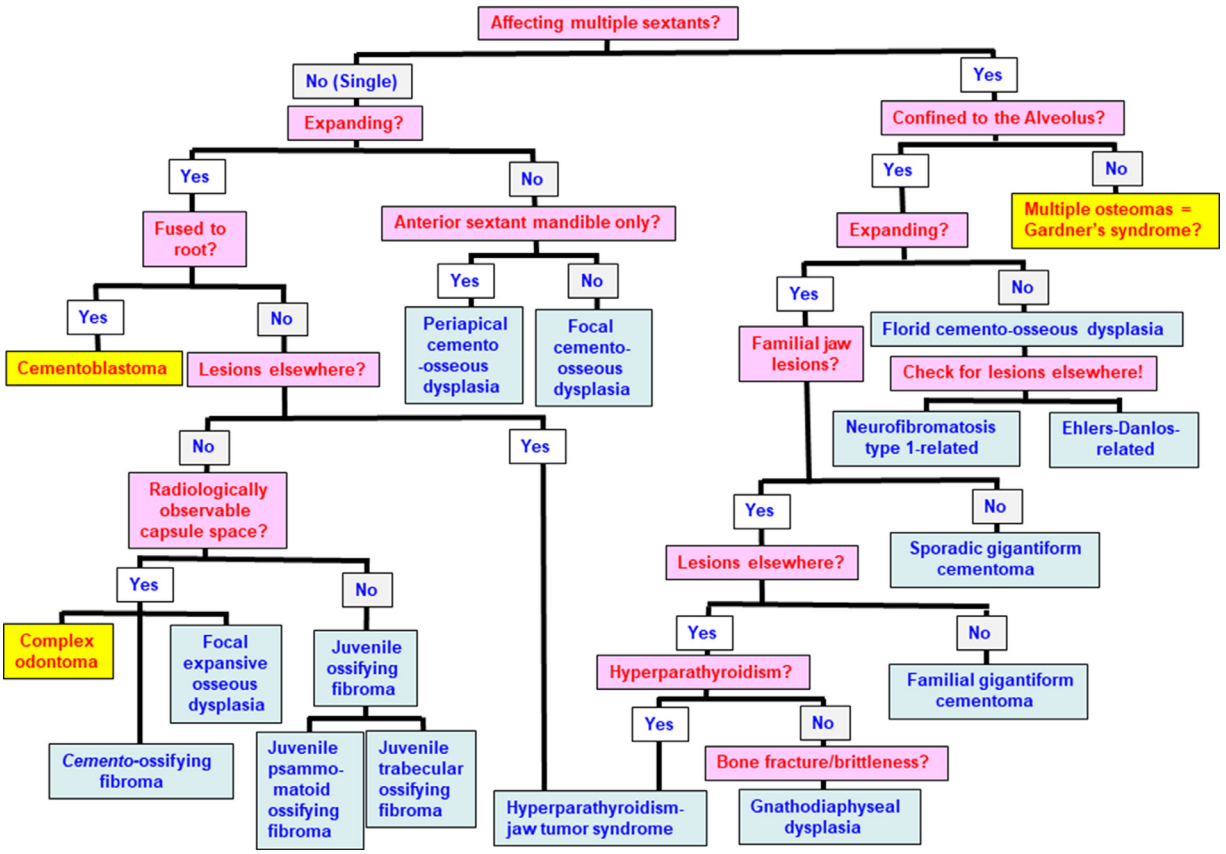

Fig. 2. Diagnostic flowchart of "well-defined fibro-osseous lesions arising within the bones of the jaws."[33] The fibro-osseous lesions are in blue boxes and non-fibro-osseous lesions necessary to the differential diagnoses are in yellow boxes. The red boxes with red type such as "Affecting multiple sextants?" represent decision points that direct the terminology to specific directions and destinations (the specific lesions in the blue or yellow boxes) based on the answers.

definitive diagnosis.[26] The 1971 edition reported an unusual type of COD that affected the anterior mandibular sextant of women of non-specified origin.[4] This was termed "periapical cemental dysplasia,"[4] but Raubenheimer and Noffke suggested a more appropriate term, "anterior mandibular osseous dysplasia."[28]

Although conventional CODs are generally innocuous, they occasionally become infected and produce symptoms.[7,29] A comparison of 2 case series in the same community, one from a radiology file and the other from a pathology file, found that the former was generally symptom-free, whereas the latter presented symptoms suggestive of an inflammatory dental cause.[7]

FAMILIAL GIGANTIFORM CEMENTOMA

The introduction to chapter 8 of the 2017 edition stated that "familial gigantiform cementoma remains an enigmatic condition evading precise characterization but has nevertheless been mentioned in the hope of more clarity in the near future."[12] This commendable plea deserves a response based on the existing evidence. This is illustrated in Figure 2. The term "familial gigantiform cementoma" (FGC) was first used by Young et al.[30] The 2017 edition included it among the fibro-osseous and osteochondromatous lesions and described FGC as a rare autosomal disease presenting as multiple focal/quadrant lesions at an early age that displays a "remarkable facial deformation."[31] The 2017 edition states that "(n)o other bones are affected,"[31] which disagrees with other kindreds with FGC and multiple long bone fractures.[32] A subsequent commentary introduced the jaw lesions of gnathodiaphyseal dysplasia, which are unlike COD because they rapidly expand and "grow in a tumor-like fashion with rapid recurrence following corrective surgery."[33] Gnathodiaphyseal dysplasia is also inherited in an autosomal dominant fashion. Its gene is anoctamin 5 (ANO5).[33] Although Noffke et al. recommended the replacement of FGC with the more descriptive "expansive osseous dysplasia,"[34] the majority of their cases are single lesions occurring in the anterior mandibular sextant of black South Africans, which, like the similarly expansive lesions COF and JOF, require complete ablation.[35] Other lesions that may be associated with conventional (nonexpansive) COD are neurofibromatosis type 1[36] and Ehlers-Danlos syndrome.[37]

CONCLUDING REMARKS

The oral and maxillofacial radiologist (OMR) serves oral and maxillofacial healthcare professionals, including dentists, by clarifying the diagnostic pathway. This role is exemplified by determining the lesion's character (expansion, marginal definition, etc.) and extent (solitary or multiple). The OMR expertly interprets conventional radiographs and cross-sectional imaging from cone beam computed tomography[32,38] to computed tomography and magnetic resonance imaging.[32,39]

When the 2017 edition is reviewed in preparation for the WHO's next edition, representation should be sought from clinicians directly responsible for the definitive diagnosis and management of patients with FOLs.[40] An OMR should be among them.[40]

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REFERENCES

1. El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. *WHO Classification of Head and Neck Tumours*, Lyon, France: International Agency for Research on Cancer; 2017.
2. Barnes L, Eveson J, Reichert P, Sidransky D, eds. *WHO Classification of Tumours, Pathology and Genetics of Tumours of the Head and Neck*, Lyon, France: International Agency for Research on Cancer; 2005.
3. Waldron CA. Fibro-osseous lesions of the jaws. *J Oral Maxillofac Surg*. 1985;43:249-292.
4. Pindborg JJ, Kramer IRH, Torloni H. *Histological Typing of Odontogenic Tumours, Jaw Cysts and Allied Lesions*. Geneva, Switzerland: World Health Organization; 1971 WHO International Histological Classifications of Tumours No. 5.
5. Kramer IJH, Pindborg JJ, Shear M. *Histological Typing of Odontogenic Tumours*. 2nd ed. New York, NY: Springer-Verlag; 1992.
6. MacDonald D, Martin M, Nguyen C. Malignant lesions in the anterior maxilla. *Clin Radiol*. 2020;75:497-506.
7. MacDonald-Jankowski DS. Florid cemento-osseous dysplasia: a systematic review. *Dentomaxillofac Radiol*. 2003;32:141-149.
8. MacDonald-Jankowski DS. Fibro-osseous lesions of the face and jaws. *Clin Radiol*. 2004;59:11-25.
9. Philipsen HP, Reichart PA. Classification of odontogenic tumours. A historical review. *J Oral Pathol Med*. 2006;35:525-529.
10. Brannon RB, Fowler CB. Benign fibro-osseous lesions: a review of current concepts. *Adv Anat Pathol*. 2001;8:126-143.
11. Reichart PA, Philipsen HP. *Odontogenic Tumours and Allied Lesions*. Berlin, Germany: Quintessence Publishing Co Ltd.; 2004.
12. Tanaka T, Speight PJ. Introduction. WHO classification of odontogenic and maxillofacial bone tumours. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. *WHO Classification of Head and Neck Tumours*, Lyon, France: International Agency for Research on Cancer; 2017. p. 205.
13. Speight PM, Takata T. New tumour entities in the 4th edition of the World Health Organization Classification of Head and Neck tumours: odontogenic and maxillofacial bone tumours. *Virchows Arch*. 2018;472:331-339.
14. Waldron CA, Giansanti JS. Benign fibro-osseous lesions of the jaws: a clinical-radiologic-histologic review of sixty-five cases. *Oral Surg Oral Med Oral Pathol*. 1973;35:190-201.
15. Kawai T, Hiranuma H, Kishino M, Jikko A, Sakuda M. Cemento-osseous dysplasia of the jaws in 54 Japanese patients: a radiographic study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999;87:107-114.

16. El-Mofty SK, Nelson B, Toysawa S. Ossifying fibroma. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. *WHO Classification of Head and Neck Tumours*, Lyon, France: International Agency for Research on Cancer; 2017:251-252.
17. Odell EW. Cemento-ossifying fibroma. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. *WHO Classification of Head and Neck Tumours*, Lyon, France: International Agency for Research on Cancer; 2017. p. 231.
18. Waldron CA. Fibro-osseous lesions of the jaws. *J Oral Maxillofac Surg*. 1993;51:828-835.
19. MacDonald-Jankowski DS, Li TK. Ossifying fibroma in a Hong Kong community: the clinical and radiological features and outcomes of treatment. *Dentomaxillofac Radiol*. 2009;38:514-523.
20. MacDonald-Jankowski DS. Ossifying fibroma: a systematic review. *Dentomaxillofac Radiol*. 2009;38:495-513.
21. Chrcanovic BR, Gomez RS. Juvenile ossifying fibroma of the jaws and paranasal sinuses: a systematic review of the cases reported in the literature. *Int J Oral Maxillofac Surg*. 2020;49:28-37.
22. Yamashita Y, Akiyama T, Mizusawa N, Yoshimoto K, Goto M. A case of hyperparathyroidism-jaw tumour syndrome found in the treatment of an ossifying fibroma in the maxillary bone. *Int J Oral Maxillofac Surg*. 2007;36:365-369.
23. du Preez H, Adams A, Richards P, Whitley S. Hyperparathyroidism jaw tumour syndrome: a pictoral review. *Insights Imaging*. 2016;7:793-800.
24. El-Mofty SK, Nelson B, Toysawa S. Fibrous dysplasia. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. *WHO Classification of Head and Neck Tumours*, Lyon, France: International Agency for Research on Cancer; 2017:253-254.
25. Ishida T, Dorfman HD. Massive chondroid differentiation in fibrous dysplasia. (fibrocartilaginous dysplasia). *Am J Surg Pathol*. 1993;17:924-930.
26. El-Mofty SK, Nelson B, Toysawa S, Wright JM. Cemento-osseous dysplasia. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. *WHO Classification of Head and Neck Tumours*, Lyon, France: International Agency for Research on Cancer; 2017:254-255.
27. MacDonald-Jankowski DS. Focal cemento-osseous dysplasia: a systematic review. *Dentomaxillofac Radiol*. 2008;37:350-360.
28. Raubenheimer E, Noffke C. Regarding the use of the term "cementum" in pathologic proliferations. *Head Neck Pathol*. 2018;12:629-630.
29. Martinez CJH, Villafuerte KRV, Felix Silva PH, et al. Periodontal and dental considerations in florid cemento-osseous dysplasia: clinical and radiographic analysis of 11 cases. *Oral Health Prev Dent*. 2019;17:425-431.
30. Young SK, Markowitz NR, Sullivan S, Seale TW, Hirschi R. Familial gigantiform cementoma: classification and presentation of a large pedigree. *Oral Surg Oral Med Oral Pathol*. 1989;68:740-747.
31. El Mofty SK. Familial gigantiform cementoma. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. *WHO Classification of Head and Neck Tumours*, Lyon, France: International Agency for Research on Cancer; 2017. p. 253.
32. MacDonald D, ed. *Oral and Maxillofacial Radiology: A Diagnostic Approach*, 2nd ed., Hoboken, NJ: Wiley-Blackwell; 2020.
33. El-Mofty S. Regarding the use of the term "cementum" in fibro-osseous lesions of the craniofacial skeleton. *Head Neck Pathol*. 2018;12:631-632.
34. Noffke CE, Raubenheimer EJ, MacDonald D. Fibro-osseous disease: harmonizing terminology with biology. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;114:388-392.
35. Raubenheimer EJ, Noffke CE, Boy SC. Osseous dysplasia with gross jaw expansion: a review of 18 lesions. *Head Neck Pathol*. 2016;10:437-443.
36. Visnapuu V, Peltonen S, Alivuotila L, Happonen RP, Peltonen J. Craniofacial and oral alterations in patients with neurofibromatosis 1. *Orphanet J Rare Dis*. 2018;13:131.
37. Şakar O, Aren G, Mumcu Z, Ünalan F, Aksakallı N, Tolgay CG. Familial gigantiform cementoma with Ehlers-Danlos syndrome: a report of 2 cases. *J Adv Prosthodont*. 2015;7:178-182.
38. MacDonald D, Scarfe W, Angelopoulos C. Cone beam computed tomography and maxillofacial diagnosis. In: Scarfe W, Angelopoulos C, eds. *Maxillofacial Cone Beam Computed Tomography*, Cham, Switzerland: Springer; 2018:469-551.
39. Kim D, Heetfeld A, Steffen IG, Hermann KGA, Hamm B, Elgeti T. Magnetic resonance imaging features of craniofacial fibrous dysplasia. *Pol J Radiol*. 2018;84:e16-e24.
40. Reichart P, Sciubba JJ, Philipsen HP. Splitters or lumpers: The 2017 WHO Classification of Head and Neck Tumours. *J Am Dent Assoc*. 2018;149:567-571.