Head and Neck Pathology (2019) 13:125–130
https://doi.org/10.1007/s12105-018-0913-7

ORIGINAL PAPER

Primordial Odontogenic Tumor: Report of a New Case and Literature Review

Bianca Bravim Bomfim[1] · Roberto Prado[2] · Renato Kobler Sampaio[2,3,5] · Danielle Castex Conde[4] · Bruno Augusto Benevenuto de Andrade[5] · Michelle Agostini[5] · Mário José Romañach[5,6]

Received: 19 February 2018 / Accepted: 15 March 2018 / Published online: 19 March 2018

Abstract
Primordial odontogenic tumor (POT) was recently recognized in the 2017 World Health Organization (WHO) Classification as a distinct mixed odontogenic tumor most commonly observed in the posterior mandible of young patients. POT appears as an expansile radiolucency associated to an unerupted tooth. The aim of the present study was to perform a retrospective microscopic evaluation of pediatric odontogenic tumors diagnosed in an Oral Pathology Laboratory from Rio de Janeiro—Brazil, in order to reclassify potential cases as POT. From 150 cases of odontogenic tumors in children diagnosed in the last 50 years, one case filled the criteria for POT, being therefore better diagnosed as such. The patient was in the first decade of life and presented a well-defined expansile tumor in the posterior mandible, which had been initially diagnosed as immature complex odontoma. To the best of our knowledge, only 12 cases of POT have been reported in the English-language literature. We herein present an additional case of POT and review of its clinicopathological findings is offered.

Keywords Primordial odontogenic tumor · Children · Mandible

Introduction

Primordial odontogenic tumor (POT) is a recently recognized, distinct mixed odontogenic tumor characterized by the proliferation of primitive odontogenic ectomesenchyme surrounded by odontogenic epithelium [1, 2]. POT tends to occur in the posterior mandible of young patients as a well-defined radiolucency around the crown of an unerupted tooth [3, 4]. Displacement and root resorption of adjacent teeth, as well as significant bone cortical expansion are usually evident. Most cases are easily enucleated and recurrences have not been reported to date [1–5].

POT appears as a well-circumscribed solid mass of fibrous consistency and multilobulated configuration composed of cellular to loose fibromyxoid tissue resembling dental papilla or primitive odontogenic ectomesenchyme, which is typically surrounded by cuboidal to columnar epithelial cells resembling the inner epithelium of the enamel organ [1–6].

The aim of the present study was to perform a retrospective morphological evaluation of odontogenic tumors diagnosed in children from a Brazilian population, in order to reclassify potential cases as POT. An English-language literature review was conducted for comparison and better understanding of this rare entity.

✉ Mário José Romañach
marioromanach@ufrj.br

[1] Oral Surgery, Fluminense Federal University (UFF), Niterói, Brazil

[2] Oral Surgery, School of Dentistry, State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil

[3] Oral Pathology, School of Dentistry, Veiga de Almeida University (UVA), Rio de Janeiro, Brazil

[4] Oral Pathology, Fluminense Federal University (UFF), Niterói, Brazil

[5] Oral Pathology, School of Dentistry, Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil

[6] Department of Oral Diagnosis and Pathology, Federal University of Rio de Janeiro School of Dentistry (FO-UFRJ), Av. Carlos Chagas Filho 373, Prédio do CCS Bloco K, 2° andar Sala 56. Ilha da Cidade Universitária, Rio de Janeiro 21.941-902, Brazil

Materials and Methods

Odontogenic tumors with a descriptive diagnosis or diagnosed as ameloblastomas, odontogenic myxomas, odontogenic fibromas, ameloblastic fibromas and complex odontomas from 1967 to 2017 were retrieved from the files of Oral Pathology Laboratory of the School of Dentistry of Federal University of Rio de Janeiro—Brazil. Only cases affecting patients in the first two decades of life were included in the study and hematoxylin and eosin-stained sections of each case were reviewed following the criteria for POT established in the 2017 WHO Classification of Odontogenic Tumors [1]. One case was better diagnosed as POT, and clinical, radiographic, and follow-up data were obtained from the patient's records. A literature review was conducted using the PubMed medical database using the keyword search "primordial odontogenic tumor" to compare our case with those from the literature.

Results

One hundred and fifty cases of odontogenic tumors in pediatric patients were diagnosed, corresponding to 0.8% of a total of 16,989 cases diagnosed in the last 50 years. There were 37 cases of ameloblastoma, 20 cases of complex odontoma, 13 cases of odontogenic lesions with descriptive diagnosis, four cases of ameloblastic fibroma, and three cases of odontogenic myxoma. One case fulfilled the criteria for POT and therefore was reclassified as such. This case was presented in the 2013 Congress of the Brazilian Society of Oral Medicine and Pathology [7] with an initial diagnosis of immature complex odontoma with areas of ameloblastic fibroma with induction. The clinical and radiographic data were available in the charts of the patient. The literature review included six articles of POT previously reported in the English-language literature [1, 8–12]. Thus, to the best of our knowledge, only 12 cases of POT have been reported to date, all of them affecting patients in the first two decades of life (Table 1). The clinicopathological features of the present case is described below.

In 2013, a second opinion was requested from a private oral pathology laboratory in Rio de Janeiro, Brazil. The slides were from a 4-year-old boy who had been referred to an oral surgeon for evaluation of a mandibular asymmetry over the last 8 months. The patient had an otherwise non-contributory past medical history. Intra-oral examination revealed exuberant cortical bone expansion in the left posterior alveolar ridge, covered by intact mucosa (Fig. 1). Cone beam computerized tomography revealed a well-defined unilocular hypodense lesion in the posterior mandible measuring 3 × 2 cm; adjacent deciduous molars showed root resorption and displacement. Exuberant expansion of

Table 1 Primordial odontogenic tumors reported in the English-language literature

Authors	N	Age	Gnd	Site	Size (cm)	Associated teeth	Root resorption	Expanded bone cortices	Recurrence, follow-up
Mosqueda-Taylor et al. [1]	1	18	M	Mand	4.5 × 4	3rd molar	2nd pM	Buccal, inferior and alveolar	No, 20 years
	2	16	M	Mand	5.5 × 5	3rd molar	NA	Buccal and inferior	LFU
	3	16	M	Mand	6.5 × 5	3rd molar	1st–2nd pM	Buccal, inferior and alveolar	No, 10 years
	4	3	F	Mand	9 × 7	2nd dM, 1st pM	1st dM	Buccal, lingual, inferior, and alveolar	No, 9 years
	5	13	F	Mand	8 × 5	3rd molar	1st–2nd pM	Buccal, lingual, inferior, and alveolar	No, 3 years
	6	3	F	Max	3.5 × 3	1st dM	2nd dM, 1st pM	Buccal, palatine and FMS	No, 6 months
Slater et al. [8]	7	19	M	Mand	2.5 × 1.9	3rd molar	2nd pM	Buccal and lingual	NA
Ando et al. [9]	8	8	F	Max	1.6 × 1.5	1st dM	NA	Buccal and FMS	No, 16 months
Mikami et al. [10]	9	5	M	Mand	0.9 × 0.8	2nd dM	1st dM	Buccal	No, 7 months
Pardhe and Bajpai [11]	10	17	M	Mand	3 × 2	PMs and pMs	2nd PM, 1st–2nd pM	Buccal, inferior and alveolar	No, 6 months
Almazyad et al. [12]	11	15	F	Mand	3.5 × 2	3rd molar	1st–2nd pM	Buccal and alveolar	No, 3 months
	12	18	M	Mand	1.2 × 0.7	3rd molar	No	No	No, 20 months
Present study	13	4	M	Mand	3 × 2	2nd dM	1st dM, 1st pM	Buccal, lingual, inferior and alveolar	LFU

Mand mandible, *Max* maxilla, *Gnd* gender, *dM* deciduous molar, *PM* premolar, *pM* permanent molar, *NA* not available, *FMS* floor of maxillary sinus, *LFU* lost of follow up

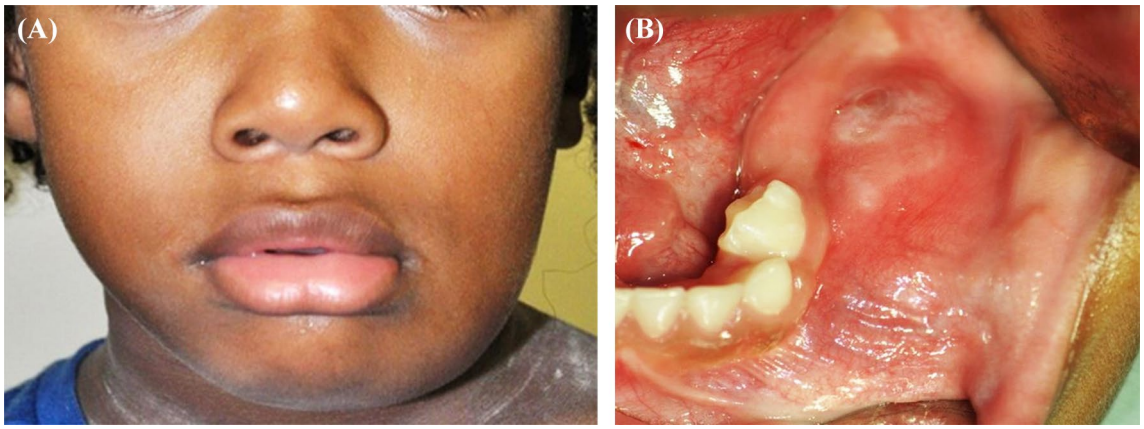

Fig. 1 Clinical features of primordial odontogenic tumor. **a** Asymptomatic swelling in the left posterior mandible of a 4-year-old boy, **b** causing displacement of the 1st deciduous molar and extensive buccal and lingual expansion of the posterior alveolar ridge with absence of the 2nd deciduous molar

cortical bone was evident, with perforation of the lingual cortical bone. The mandibular nerve canal was displaced inferiorly (Fig. 2). An excisional intraoral biopsy was performed under general anesthesia, in which a whitish lobulated tumor with fibrous consistency was easily enucleated from the adjacent bone (Fig. 3). The microscopic examination revealed a well-defined proliferation of a fibromyxoid mesenchymal tissue covered on the surface by columnar epithelial cells resembling ameloblasts containing stellate reticulum-like areas and small foci of calcification (Fig. 4). Five years ago, the initial interpretation of this case was of an immature complex odontoma containing areas of ameloblastic fibroma with induction. Currently, the histomorphological and radiographic findings supports a final diagnosis of primordial odontogenic tumor. Unfortunately, the patient was lost to follow-up.

Discussion

The term POT was first proposed by Mosqueda-Taylor et al. [1], who reported a series of six cases of a previously undescribed odontogenic tumor with features similar to primitive dental papilla and follicle, arising in areas of missing or unerupted teeth of patients before adult life. Since then, six additional cases have been identified in the English-language literature [8–12]. We present an additional case in order to contribute to a better classification and understanding of this rare odontogenic tumor.

POT affected seven boys and five girls. Eight patients (66.6%) were in the second decade and four patients (33.3%) were in the first decade, with median age of 12.1 years (varying from 3 to 19 years) [1, 8–12]. The mandible was affected in ten cases (83.3%) [1, 8, 10–12] and the maxilla in two cases (16.7%) [1, 9]. Radiographically, POT presented as a unilocular or bilocular radiolucent appearance associated with an unerupted third molar in eight cases (66.6%) [1, 8, 12] or a first or second deciduous molar in four cases (33.3%) [1, 9, 10]. The median size was 4 cm, with marked cortical bone expansion in all cases, mainly of the buccal and inferior cortices [1, 8–12]. Both maxillary cases showed involvement of the maxillary sinus [1, 9]. Indeed, most cases exhibited displacement and resorption of the adjacent teeth. Our patient was in the first decade of life, with similar radiographic features when compared to the literature.

Microscopically, the combination of proliferating fibrous and covering epithelial odontogenic tissues resembling primitive (primordial) stages of normal odontogenesis is a key diagnostic feature [1, 2]. POT is usually circumscribed by a fibrous pseudocapsule and cuboidal to columnar odontogenic epithelium resembling the inner epithelium of the enamel organ, which covers entirely or partially the periphery of a mesenchymal proliferation of fusiform and stellate fibroblasts, randomly disposed in a variably myxoid to collagenous fibrous tissue [1–5]. The epithelial component may show ameloblastic differentiation, with occasional limited formation of calcified material [6], whereas the mesenchymal component may be predominantly myxoid [1]. The peripheral epithelium tends to invaginate into the mesenchymal component as a continuous double epithelial layer, which may occasionally show some expanded free ends with microcystic spaces and induction phenomenon [1, 2, 6]. Thus, epithelial nests may be present in the mesenchymal component close to the surface epithelium due to tangential sectioning [1, 6]. This microscopic feature of epithelial invagination leads to the typical multilobulated configuration of POT, which appears as a solid well-demarcated tumor easily enucleated from adjacent bone, as observed in the present case.

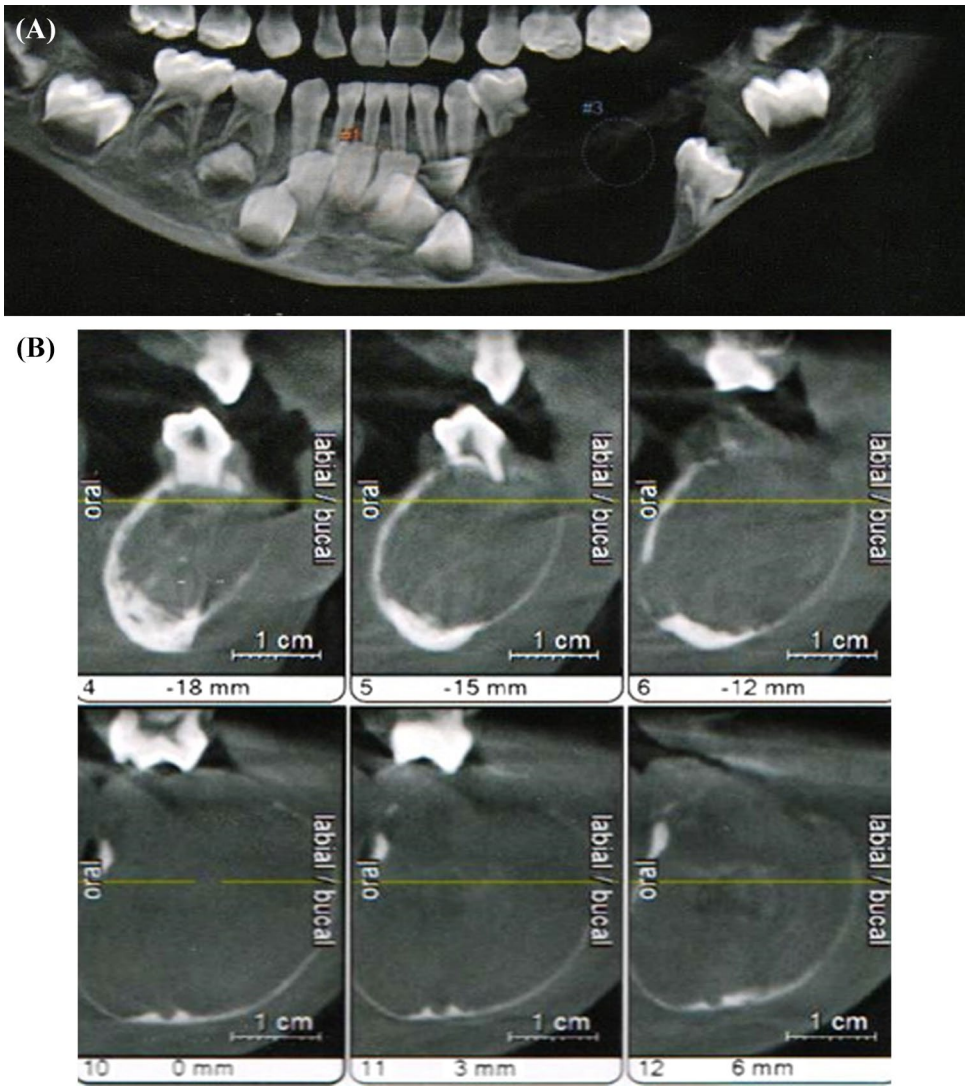

Fig. 2 Imaging features of primordial odontogenic tumor. **a, b** Hypodense lesion of regular borders located in the left body of the mandible causing exuberant bone cortical expansion and displacement of adjacent teeth. The germ of the 2nd premolar was absent (cone beam computerized tomography scan; **a** panoramic section and **b** coronal section)

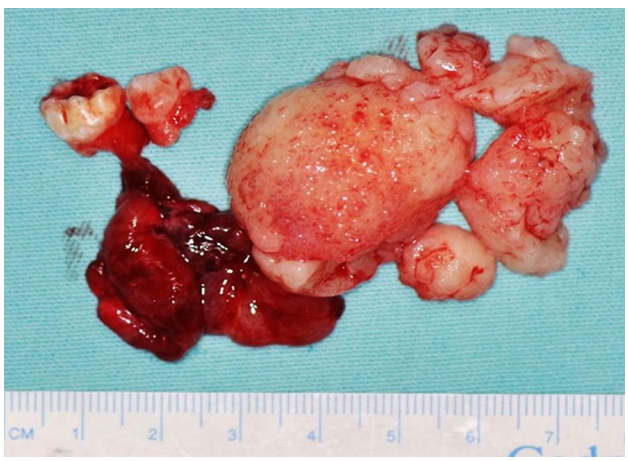

Fig. 3 Gross features of primordial odontogenic tumor. Multilobulated whitish solid mass of irregular surface, slippery to glossy appearance, measuring 4 × 3 cm, which was removed with a dark reddish dental follicular tissue and deciduous molars

Recurrences have not been reported in POT to date with follow-up varying from 6 months to 20 years [1, 8–12]. POT tends to expand into cortical bone, achieving a considerable size, particularly in pediatric patients. However, the peripheral columnar epithelium and fibrous pseudocapsule may contribute to the clear demarcation of the tumor, favoring its conservative surgical enucleation and outcome.

The exact origin of POT remains questionable, but is most likely related to mesenchymal proliferation similar to the dental papilla of a developing tooth [1, 2]. Recent immunohistochemical studies suggest the activity of both epithelial and mesenchymal components during the histogenesis of POT, justifying its inclusion within the group of mixed epithelial and mesenchymal odontogenic tumors in the current WHO classification [9, 13]. Epithelial cells are strongly positive for CK14, CK19, and Glut-1, whereas mesenchymal cells are strongly positive for vimentin and syndecan-1 (CD138) [9, 10, 13, 14]. Epithelial cells were

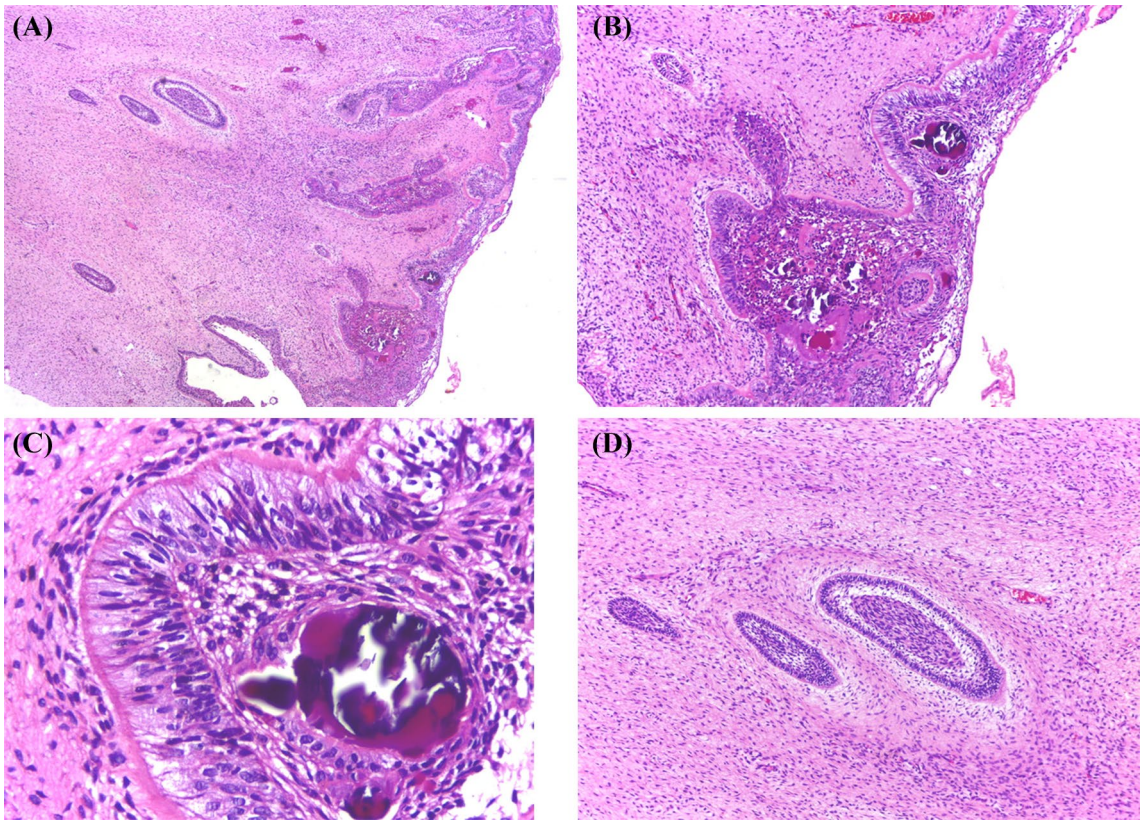

Fig. 4 Microscopic features of primordial odontogenic tumor. **a, b** Fibromyxoid mesenchymal tissue covered by columnar odontogenic epithelium with ameloblastic differentiation, which invaginates into the mesenchymal component showing **c** induction phenomenon and small foci of calcification. **d** Ameloblastic fibroma-like epithelial islands are observed in the fibromyxoid tissue (HE; **a** ×40; **b** ×100; **c** ×400; **d** ×100)

negative for BRAF and calretinin, whereas mesenchymal cells showed a low nuclear labeling index for Ki67 (< 5%), with some increased positivity in areas of mesenchymal condensation [10, 12–14]. These areas also showed activation of odontogenic transcription factors expressed during early tooth morphogenesis, indicating the initial induction of odontogenic signaling [10, 11, 14].

The strong preference for areas of missing teeth or developing unerupted teeth of children and young adolescents, and some microscopic resemblance to odontogenic tumors such as ameloblastic fibroma (AF), ameloblastic fibrodentinoma (AFD), ameloblastic fibro-odontoma (AFO) and immature odontoma [8, 15], may reinforce the argument that POT could possibly represent a hamartomatous rather than neoplastic lesion by nature. However, unlike developing odontomas, POT tend to show a higher potential for continuous growth, with considerable cortical bone expansion and limited production of hard dental tissue, indicating a neoplastic nature. The present case was formerly diagnosed as "immature complex odontoma with areas of ameloblastic fibroma with induction" [7], but the diagnosis of POT was achieved after retrospective identification of the criteria first proposed by Mosqueda-Taylor et al. [1] for this truly new odontogenic tumor. We have reviewed the features of 12 cases of POT previously reported in the literature and added this retrospectively discovered case of POT from 150 cases of odontogenic tumors in children diagnosed in a Brazilian Oral Pathology laboratory over the last 50 years.

Oral surgeons and pathologists should consider POT during the evaluation of a well-defined multilobulated tumor associated with an unerupted tooth in the posterior mandible of young patients. Microscopic evaluation including the periphery of solid odontogenic tumors is recommended to avoid diagnostic misinterpretation. Additional series of cases of POT may contribute to a better understanding of the clinical, histological and biological spectrum of this rare entity.

Author Contributions BBS and RP contributed with clinical and surgical information, final data analyses of the case, and manuscript editing. RKS and DCC contributed with the microscopic analyses of the case, final data analyses, and manuscript editing. BABdA, MA and MJR contributed to the clinical and microscopic analyses of the case, performed the study design, reviewed the laboratory archives and the literature, and contributed to the manuscript writing and editing. All authors gave final approval and agreed to all aspects of the work.

Compliance with Ethical Standards

Conflict of interest All of authors have indicated they have no potential conflicts of interest and no financial relationships relevant to this article to disclose.

Ethical Approval This study was carried out following the Helsinki Declaration for study involving human subjects.

Informed Consent This was a descriptive, retrospective study using stock material that does not correspond to a biobank or a bio repository and was collected for assistance purposes.

References

1. Mosqueda-Taylor A, Neville BW. Primordial odontogenic tumour. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, editors. World Health Organization Classification of Head and Neck Tumours. IARC: Lyon; 2017. pp. 223–4.
2. Mosqueda-Taylor A, Pires FR, Aguirre-Urízar JM, et al. Primordial odontogenic tumour: clinicopathological analysis of six cases of a previously undescribed entity. Histopathology. 2014;65:606–12.
3. Wright JM, Vered M. Update from the 4th edition of the World Health Organization Classification of Head and Neck tumours: odontogenic and maxillofacial bone tumors. Head Neck Pathol. 2017;11:68–77.
4. 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. 2017. https://doi.org/10.1007/s00428-017-2182-3.
5. Bilodeau EA, Collins BM. Odontogenic cysts and neoplasms. Surg Pathol Clin. 2017;10:177–222.
6. Woo SB. Primordial odontogenic tumor. In: Woo SB, editor. Oral pathology: a comprehensive atlas and text. 2nd ed. Elsevier; 2017. p. 416.
7. Bomfim BB, Prado R, Conde DC, Sampaio RK, Romañach MJ. Immature complex odontoma: report of a case with features of ameloblastic fibroma with induction. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;117:e164.
8. Slater LJ, Eftimie LF, Herford AS. Primordial odontogenic tumor: report of a case. J Oral Maxillofac Surg. 2016;74:547–51.
9. Ando T, Shrestha M, Nakamoto T, Uchisako K, Yamasaki S, Koizumi K, Ogawa I, Miyauchi M, Takata T. A case of primordial odontogenic tumor: a new entity in the latest WHO classification (2017). Pathol Int. 2017;67:365–9.
10. Mikami T, Ohashi Y, Bologna-Molina R, Mosqueda-Taylor A, Fujiwara N, Tsunoda N, Yamada H, Takeda Y. Primordial odontogenic tumor: a case report with histopathological analyses. Pathol Int. 2017;12:638–43.
11. Pardhe N, Bajpai M. Primordial odontogenic tumor of mandible: a case with proposed diagnostic criteria. Iran J Med Sci. 2018;43:97–9.
12. Almazyad A, Li CC, Tapia ROC, Robertson JP, Collette D, Woo SB. Primordial odontogenic tumour: report of two cases. Histopathology. 2018. https://doi.org/10.1111/his.13488.
13. Bologna-Molina R, Mikami T, Pereira-Prado V, Pires FR, Carlos-Bregni R, Mosqueda-Taylor A. Primordial odontogenic tumor: an immunohistochemical profile. Med Oral Patol Oral Cir Bucal. 2017;22:e314–23.
14. Bologna-Molina R, Mikami T, Pereira-Prado V, Tapia-Repetto G, Pires FR, Carlos R, Mosqueda-Taylor A. Primordial odontogenic tumor: subepithelial expression of Syndecan-1 and Ki-67 suggests origin during early odontogenesis. Oral Dis. 2018;24:72–7.
15. Ide F, Kikuchi K, Kusama K, Muramatsu T. Primordial odontogenic tumour: is it truly novel? Histopathology. 2015;66:603–4.