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Case Report

Clinical and pathological features of desmoplastic ameloblastoma: a literature review with three case reports

Peisheng Liang[1,2*], Guangsen Zheng[1,2*], Xingguang Liu[3], Wangyong Zhu[1,2], Qian Tao[1,2]

[1]Department of Oral and Maxillofacial Surgery, Guanghua School of Stomatology, Hospital of Stomatology, Sun Yat-sen University, China; [2]Guangdong Provincial Key Laboratory of Stomatology, Guangzhou, Guangdong, China; [3]Department of Oral and Maxillofacial Surgery, School and Hospital of Stomatology, Shandong University, Jinan, China. [*]Equal contributors.

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Abstract: Desmoplastic ameloblastoma is a rare variant of benign odontogenic tumors. Our objective was to describe the clinical and pathological features of desmoplastic ameloblastoma. Three cases of desmoplastic ameloblastoma that were treated in the authors' department were reviewed and analyzed along with radiological and histological data. The findings obtained from pathological examinations of two solid ameloblastomas served as controls. Moreover, 91 desmoplastic ameloblastoma cases in the literature were reviewed. Desmoplastic ameloblastoma is most commonly observed in the anterior and premolar regions of the mandible and maxilla, with a radiolucent and radiopaque appearance. After surgical resection, no recurrence was observed. On pathological examination, desmoplastic ameloblastoma was present in irregular and compressed epithelial islands scattered among massive stroma. In the epithelium, desmoplastic ameloblastoma expressed CK19 weakly to strongly and TGF-β_1 moderately to strongly, while vimentin was expressed strongly in the stroma. However, solid ameloblastoma tumors had strong CK19 expression, weak to strong TGF-β_1 expression, and negative to weak vimentin expression. The review of the literature was in agreement with our cases. Desmoplastic ameloblastoma has distinctive clinical and pathological features compared with solid ameloblastoma, and it might originate from an earlier odontogenic epithelium precursor or transition from ectomesenchyme.

Keywords: Desmoplastic ameloblastoma, cytokeratin 19, solid ameloblastoma, transforming growth factor β_1, vimentin

Introduction

Ameloblastoma is a benign odontogenic epithelium tumor with slowly growing, a high risk of recurrence and local invasive behavior [1]. It comprises about 1% of all tumors and cysts of the jaws [2]. According to the 2005 World Health Organization classification of odontogenic tumors, ameloblastomas can be classified into four different categories as follows: solid ameloblastoma (SA), peripheral ameloblastoma, unicystic ameloblastoma and desmoplastic ameloblastoma (DA) [3].

Desmoplastic ameloblastoma is a rare variant of ameloblastoma and was initially described by Eversolein [4] in 1984, presenting with clinical, imaging, and histological features that are distinct from those of more common types of ameloblastomas.

Clinically, DA usually occurs in the anterior or premolar regions in the mandible or maxilla, with localized swelling and teeth movement. This lesion most commonly occurs between the ages of 17 and 72 years with a male predilection. After suitable operation, the prognosis of DA is better than SA [1, 5, 6]. DA occasionally shows a "ground-glass" appearance, which presents as diffuse and mixed radiolucent and radiopaque lesion [7] in radiograph.

Histologically, DA is characterized by pronounced collagenous stroma and small nests of odontogenic epithelium. Several "hybrid lesion" cases have been reported with a combination

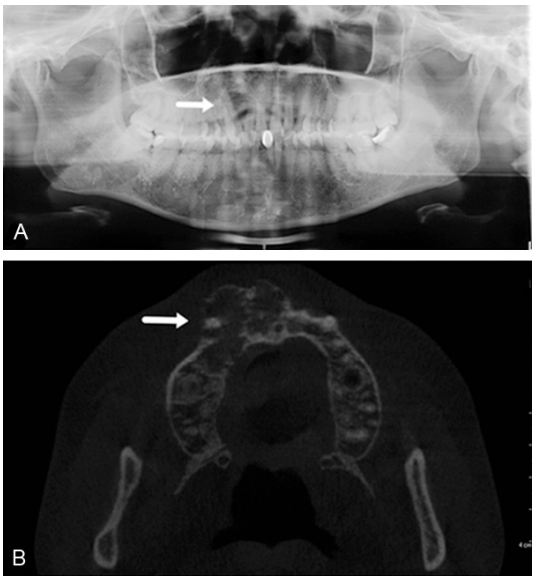

Figure 1. Radiological images of case 1. (A) Panoram ic film and (B) coronal view of the cone beam computed tomography (CBCT) scan. Buccal cortical expansion and honeycomb presentation are visible in the right premolar and canine regions of the maxilla.

of DA and common ameloblastoma histological appearances [8]. Furthermore, the epithelial and stromal markers expression of DA are various from those of SA in immunohistochemical staining [9, 10].

In this paper, we reported and investigated the clinical and pathological features of 3 DA cases. Moreover, a literature review of DA immunohistochemical features was performed by searching MEDLINE, yielding reports of 91 patients from 26 papers from 1993 through 2016. Because diagnosis is important for treatment of DA, this study assessed its clinical and pathological features in order to obtain a clearer understanding of this rare disease.

Material and methods

A retrospective review was performed of 3 patients diagnosed with DA who received treatment at the Hospital of Stomatology, Sun Yat-sen University from 2012 through 2015. Patients' clinical and pathological records were reviewed. The study has been reviewed by the Hospital of Stomatology, Sun Yat-sen University Ethics Committee. This study also complied with the principles of the Declaration of Helsinki for medical protocol and ethics.

Case reports

Case 1: A 49-year-old woman presented with a painless enlarged swelling in the right suborbital region that had persisted for 2 months. Panoramic film and cone beam computed tomography (CBCT) scans revealed a mixture of ill-defined radiolucency and radiopacity, 3.4 cm × 2.7 cm × 2.0 cm, involving the alveolar bone in the 15-21 region (**Figure 1**). Removal of the tumor and resection of the bone around the tumor were performed.

Case 2: A 35-year-old woman complained of a painless mass that had been present for several months. Radiography showed two lesions in the mandible. One was a tumor in the 35-44 region, with honeycomb-like bone expansion. The other lesion was completely radiolucent and located in the 37-38 region (**Figure 2**). Because of the extensive tumor invasion, the patient received a partial mandibulectomy and mandible reconstruction with a free fibula osseous flap.

Case 3: A 39-year-old manreporteda painless swelling in the left mandible that had been present for more than 10 years but showed significant recent enlargement. Panoramic film and CBCT examinations indicated mandible destruction from 36 to 42, with root absorption at 34, 35, and 36 (**Figure 3**). This patient received radical treatment and reconstruction similar to that performed in case 2.

Pathological examination

After formalin-fixation and paraffin-embedding, specimens from the three DA cases were cut into 4-μm-thick sections and stained with hematoxylin-eosin (H&E stain). Moreover, immunohistochemical staining was performed to evaluate CK19, vimentin, and transforming growth factor β_1 (TGF-β_1) expression levels. Briefly, sections were heat-treated in Tris-EDTA buffer (pH 9.0) at 120°C for 10 min. Endogenous peroxidases were blocked with 0.9% hydrogen peroxide, followed by incubation with 1% bovine serum. Monoclonal antibodies, including CK-19 (Cell Signaling Technology, USA), vimentin (Cell Signaling Technology, USA) and TGF-β_1 (Cell Signaling Technology, USA), were used for overnight incubation at 4°C. Biotinylated anti-mouse/anti-rabbit antibody and astreptavidin-per-

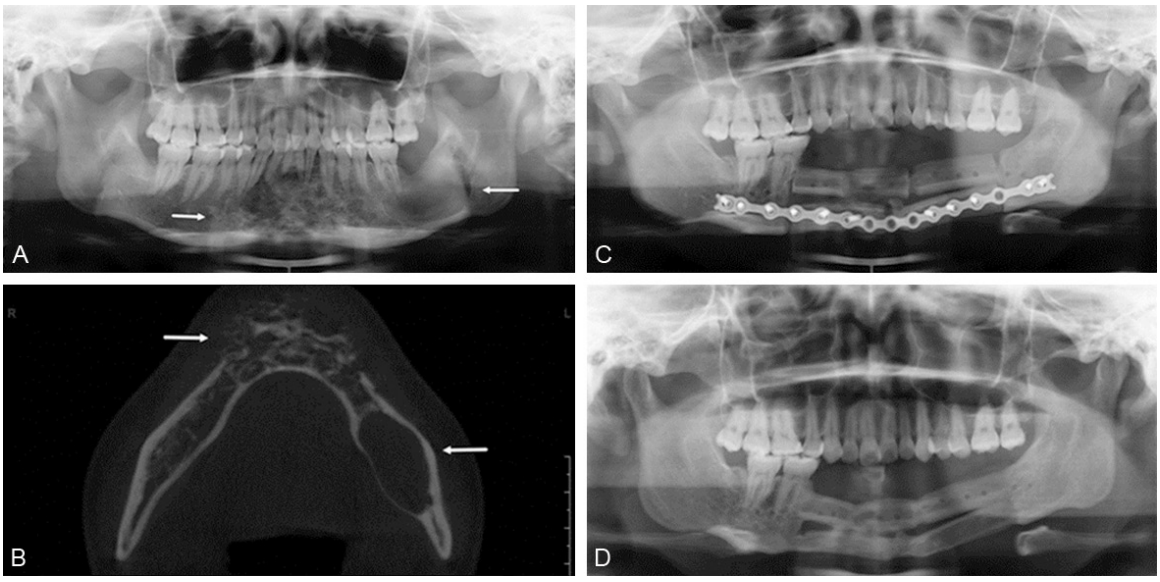

Figure 2. Radiological images of case 2. A, B. Panoramic film and coronal view of the CBCT scan before the operation. A dominant labial swell and "soap bubble" lesion in the anterior part of mandible are visible. A completely radiolucent lesion is located in the left mandibular molar region, which was diagnosed as a dentigerous cyst histologically. C, D. Panoramic films 3 and 30 months after operation, respectively.

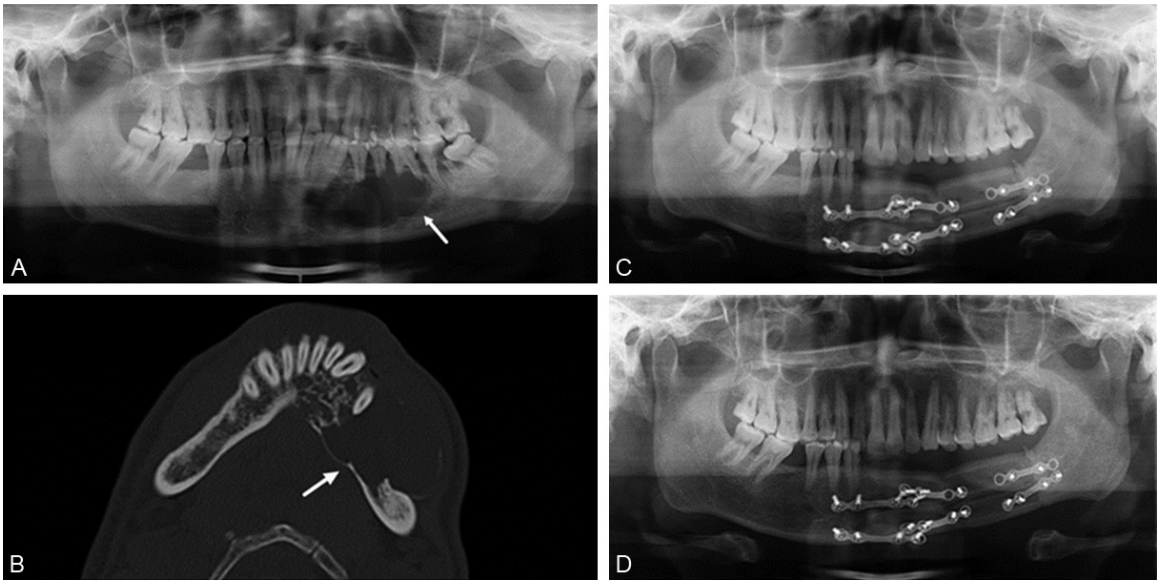

Figure 3. Radiological images of case 3. A, B. Panoramic film and coronal views of the CBCT scan before the operation. A giant lesion invading the mandible from 36-42, with root absorption and a combination of radiolucent and honeycomb presentation is visible. C, D. Panoramic films 3 and 10 months after operation, respectively.

oxidase complex were used as the secondary antibody. Staining was finished with a 3,3'-diaminobenzidine substrate. Immunohistochemical staining was observed and classified using a 4-grade scale as follows: negative (no positively stained cells), weakly positive (positively stained cells ≤ 25%), moderately positive (25% < positively stained cells ≤ 50%); strongly positive (positively stained cells > 50%).

Two SA specimens were analyzed using the same procedure as controls. The three DA cases and two SA cases were labeled as DA1, DA2, and DA3 and SA1 and SA2, respectively.

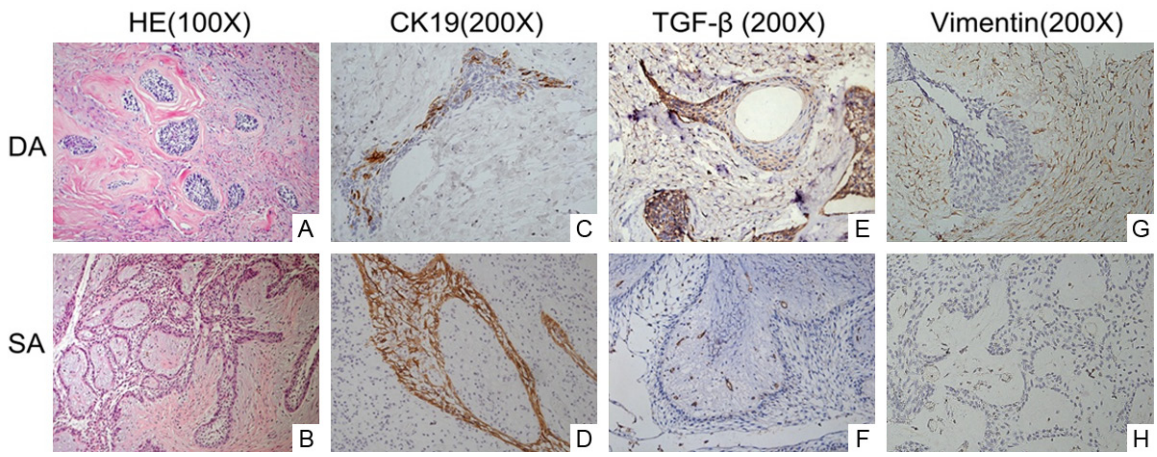

Figure 4. Pathological images of DA and SA. A. The odontogenic epithelium is surrounded by extensive stroma in DA1. B. The epithelium of SA2 is arranged in a follicular pattern. C. Only a few CK19-positive cells are present in DA1. D. CK19 stains strongly positive in SA2. E. TGF-β_1 stains strongly positive in the peripheral cells of DA1's epithelial nests. F. Several TGF-β_1-positive cells are scattered in SA1 stellate-like structures. G. Vimentin is significantly expressed in DA2 stroma. H. There is negative vimentin staining in SA1 stroma. DA: desmoplastic ameloblastoma; SA: solid ameloblastoma.

Table 1. Immunohistochemical expression of CK19, vimentin, and TGF-β_1

Tumor Type	CK19	TGF-β_1		Vimentin
		Peripheral cells	Stellate cells	
DA	±(DA1); ++(DA2&3)	++(DA1); +(DA2&3)	-(DA1~3)	++(DA1~3)
SA	++(SA1&2)	-(SA1&2)	±(SA1); +(SA2)	-(SA1); ±(SA2)

Negative (-): no positively stained cells; Weakly positive (±): positively stained cells ≤ 25%; Moderately positive (+): 25% < positively stained cells ≤ 50%; Strongly positive (++): positively stained cells > 50%. DA: desmoplastic ameloblastoma; SA: solid ameloblastoma. The case number is indicated in brackets.

Review of the literature

The authors performed a search on MEDLINE and reviewed a total of 91 cases of DA and data on immunohistochemical features reported in 26 papers that were reported in the literature from 1993 through 2016.

Results

General results of 3 cases in the authors' institution

Clinically, the three cases showed DAs in the anterior and premolar regions of the mandible and maxilla, with radiolucent and radiopaque appearances. After surgical resection, cases 2 and 3 have been disease-free for 24 months and 7 months, respectively. Unfortunately, we lost touch with the patient from case 1 after only 2 months of follow-up.

Microscopically, the three DA tumor specimens contained typical histologic DA features. The tumors contained variant desmoplasticstroma and narrow epithelial nests that were scattered and compressed by extensive collagenous fibers (**Figure 4A**). Interestingly, we found a dentigerous cyst, which was separated from the tumor, in the 37-38 regionin case 2. A conventional SA appearance was seen in the control group.

The immunohistochemical expression data of CK19, vimentin, and TGF-β_1 in DA and SA are listed in **Table 1**. Both DA and SA epithelium strongly expressed CK19, except for one DA tumor with only slightly positive staining (**Figure 4C**, **4D**). TGF-β_1 was differentially expressed in both locations and showed different intensity levels of staining in DA and SA specimens. DA and SA specimens. In peripheral epithelium nest cells, DA specimens were positively stained and SA specimens were negative for TGF-β_1, while reciprocal staining was observed in stellate cells (**Figure 4E**, **4F**). Vimentin was intensely expressed in DA stroma, but its expression was weak or absent in SA stroma (**Figure 4G**, **4H**).

Table 2. Review of the immunohistochemical features of 91 desmoplastic ameloblastoma patients in the literature: 1993 through 2006

Study and year of publication	Case (n)	Age (yr)	Sex		Position		Immunohistochemical staining
			M	F	Mand	Max	
Siar et al. [32] 2016	3	NA	NA		NA		F-actin (-)-(±), Cortactin (±)-(+), N-WASP (-)-(+), WIP (±)-(+)
Bologna-Molina et al. [33] 2015	2	NA	NA		NA		Glypican-1 (++)
Siar et al. [34] 2015	3	NA	NA		NA		Podoplanin (-)-(+), E-cadherin (+), β-catenin (+), CD44v6 (-)-(+), Jagged1 (-)-(+), Jagged2 (-), Deltal (-)-(+)
Khalil et al. [35] 2015	1	NA	NA		NA		Twist (+)
Siar et al. [36] 2014	4	NA	NA		NA		Snail (++), Slug (-)-(++), SIP1 (-)-(++), Twist (-)-(++)
Oteri et al. [11] 2014	1	17	M		Max		CK19 (±), Bcl-2 (±), Ber-EP4 (-), EMA (-)
Ramesh et al. [12] 2014	1	45	F		Max		Vimentin (+), CK19 (+), CD68 (+)
Pal et al. [13] 2013	4	NA	NA		NA		CK10 (-), CK13 (+), CK14 (++), CK15 (+), CK16 (++), CK17 (+), CK18 (+), CK19 (+), CK20 (±)
Bologna-Molina et al. [37] 2013	5	NA	NA		NA		PCNA 80.94% ± 10.4, Ki-67 1.9% ± 1.24
Siar et al. [38] 2012	8	NA	NA		NA		Wnt1 (±)-(++), Wnt2 (-), Wnt3 (±)-(+), Wnt4 (-), Wnt5 (-), Wnt6 (-), Wnt7 (-), Wnt8a (-)-(±), Wnt8b (±)-(+), Wnt10a (±)-(+), Wnt10b (-)
Krishna et al. [39] 2012	3	NA	NA		NA		MDM2 (+)
Siar et al. [40] 2010	10	NA	NA		NA		Notch1 (-)-(+), Notch2 (-), Notch3 (-)-(+), Notch4 (++)
Bologna-Molina et al. [14] 2010	1	66	1		1		CK1 (-), CK5 (+), CK6 (-), CK10 (-), CK13 (+), CK14 (+), CK16 (-), CK18 (-), CK19 (-), CK20 (-), laminin V (++), type IV collagen (++), S-100 (+), SMA (-), Bcl-2 (-), p21 (-)
de Medeiros et al. [23] 2010	4	NA	NA		NA		Fibronectin (-)-(+), tenascin (+)-(++)
Bologna-Molina et al. [41] 2009	4	NA	NA		NA		CD138 (+), Ki-67 1.5%
Kumamoto et al. [42] 2008	3	NA	NA		NA		Bid (++), Bim (++), Bad (++), Noxa (++), Puma (++), Fas (++)
Kumamoto et al. [43] 2007	4	NA	NA		NA		IGF1 (++), IGF2 (++), IGF receptor (++)
Dos et al. [8] 2006	1	36	1		1		Fibronectin (++), tenascin (-)
Kumamoto et al. [44] 2005	4	NA	NA		NA		p63 (+)-(++), p73 (±)-(+)
Kumamoto et al. [45] 2004	4	NA	NA		NA		Surviving (±)-(++), XIAP (+)-(++)
Kumamoto et al. [10] 2002	4	NA	NA		NA		HGF (±), c-Met (±), TGF-β (+)-(++), TGF-β receptors (+)-(++)
Nagatsuka et al. [46] 2002	3	NA	NA		NA		Type IV collagen α1&α2 (++)
Fukumashi K et al. [15] 2002	3	NA	NA		NA		CK8 (-)-(+), CK13 (+), CK19 (-)-(+)
Kumamoto et al. [9, 47] 2001	4	NA	NA		NA		anti-FasL (±), caspase-3 (++), ssRNA (-)-(±), amelogenin (±), CK19 (+)
Takata et al. [16] 1999	7	17-48	6	1	4	3	type IV collagen (-)-(+), TGF-β (-)-(++)

Negative (-): no positively stained cells; Weakly positive (±): positively stained cells ≤ 25%; Moderately positive (+): 25% < positively stained cells ≤ 50%; Strongly positive (++): positively stained cells > 50%. CK, cytokeratin; EMA, epithelial membrane antigen; F, female; HGF, hepatocyte growth factor; IGF, insulin-like growth factor; M, male; Mand, mandibule; Max, maxilla; MDM2, mouse double minute 2 homolog; NA: not available; PCNA, proliferating cell nuclear antigen; SMA, smooth muscle autoantibody; XIAP, X chromosome-linked inhibitor of apoptosis protein; TGF, transforming growth factor.

General results of cases in literature

Immunohistochemical characteristics of 91 cases with DA collected from 26 reports are presented in **Table 2**. CK19 in DA was mildly or moderately expressed and only a few cases were negative [11-15]. Vimentin [12] and TGF-β_1 [10, 16] usually showed moderate or strongly positive staining. The review of literature was consistent with our results above.

Discussion

DA is rare, accounting for only approximately 0.9%-13% of ameloblastoma patients [17]. Sun [5] summarized 115 DA cases, showing that DA prefers the anterior or premolar regions in the mandible or maxilla (91.7%), and it is rarely found in the mandibular molar region (8.3%). The mandible is slightly more susceptible than the maxilla (54.9% vs. 45.1%). Furthermore, Philipsen [18] reported that DA occurs in patients at an average age of 42.9 years. The three cases we described are consistent with these epidemiological characteristics.

Li [17] classified DA radiographs into three subtypes. The osteofibrosis type, which comprises almost half of DA tumors, is radiolucent and radiopaquein appearance, with the so-called “honeycomb” or “soap bubble” features. The radiolucent type, which has a completely radiolucent appearance, is somewhat analogous to odontogenic cysts. The compound type is a rare subtype with both radiolucent and radiopaque features combined with a large radiolucent change. Analyzing CBCT coronal figures, Luo [19] discovered that DA has a characteristic buccal bony expansion, which is distinct from the observed buccal-lingual expansion in SA. Cases 1 and 2 were both typical osteofibrosis type DAs, while case 3 was compound type DA. All three cases expanded in the buccal area.

Curettage and resection are both major treatments for DA [6]. However, because of limited DA case reports and a lack of understanding of DA biological behavior and prognosis, there are no defined strategies for DA treatment. Sun [5] examined 69 cases and found an overall recurrence rate of 15.9% and a time-to-recurrence of 36.9 months on average. Furthermore, their results suggested that curettage results in a higher potential of recurrence than resection, which may be because of the lesions’ ill-defined boundaries. In our study, patients underwent resection to prevent residual tumor. The patients from cases 2 and 3 have remained disease-free so far.

For cases showing severe and extensive bone destruction, reconstruction with free composite tissue flaps after osteotomy can contribute to quality of life and appearance. Cervelli [20] and Mijiti [21] reported two DA cases with free fibula osseous flaps used for immediate reconstruction. The patients from cases 2 and 3 in our study, who underwent reconstruction with free fibula osseous flaps, had a satisfactory recovery and appearance after surgery.

Histologically, DA exhibits irregular and compressed epithelial islands scattered among massive desmoplastic stroma, which consists of a large number of fibroblasts and extensive type I collagen [22, 23]. The distinct DA appearance suggests that it might have a different origin from common ameloblastoma [24]. To investigate differentiation and the relationship between the tumor epithelium and stroma, we examined the epithelial marker CK19, the stromal marker vimentin, and the extracellular matrix formation-related marker TGF-β_1 by immunohistochemical staining.

The expression of cytokeratins, including CK19, correlates with the differentiation of tumor epithelium in ameloblastoma [25]. CK19, a typical cytokeratin marker, has also been used to estimate the degree of epithelial differentiation in ameloblastoma. Fukumashi [15] and Pal [13] suggested that DA may form in early stages of tooth development because CK19 expression is lower in DA than that for other ameloblastoma types. Case 1 exhibited poor CK19 expression, indicating that the tumor was probably derived from immature odontogenic epithelium.

TGF-β has various biological functions, including epithelial-mesenchymal transition induction and extracellular matrix formation enhancement by stimulating fibroblasts, among other roles [26, 27]. TGF-β and its major isoform TGF-β_1 are differentially expressed in different types of ameloblastoma [27, 28]. Takata [27] found that DA tumor cells produced a lot of TGF-β, which induced desmoplastic stroma synthesis. TGF-β_1 immunohistochemical expression in our

cases was consistent with the previous reports. Furthermore, we found TGF-β_1-positive cells on the outer layer of the epithelial islands, which contacted stroma directly. The peripheral cells likely secreted TGF-β_1 and stimulated fibroblasts to synthesize large quantities of collagen.

Vimentin, a type of intermediate filament, is found in mesenchymal cells. Ramesh [12] and Sherlin [29] reported that DA have high vimentin expression with mass collagen formation. We found the same results in our immunohistochemical experiments and hypothesized that fibroblasts were possibly active during proliferation and collagen synthesis. Moreover, DA exhibited no stromal cellular atypia, distinct from odontogenic epithelial tumors with ectomesenchymal tissue, such as that found in ameloblastic fibroma [30].

The desmoplastic mechanism underlying DA has still not been elucidated. In contrast with normal ameloblastoma, DA is hypothesized to derive from ectomesenchyme because of its poorly differentiated epithelium, its extensive desmoplastic stroma, and the observation of mesenchymal-epithelial transitions in long bone ameloblastoma, also called adamantinoma [7, 31].

Based on our literature review and analysis, we can conclude that DA has prominent clinical and pathological features, which are distinct from conventional ameloblastoma.

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Disclosure of conflict of interest

None.

Address correspondence to: Qian Tao, Department of Oral and Maxillofacial Surgery, Guanghua School of Stomatology, Hospital of Stomatology, Sun Yat-sen University, 56 Lingyuanxi Road, Guangzhou 510055, Guangdong, China. Tel: +862083846030; Fax: +862083846030; E-mail: taoqian@mail.sysu.edu.cn

References

[1] Almeida Rde A, Andrade ES, Barbalho JC, Vajgel A and Vasconcelos BC. Recurrence rate following treatment for primary multicystic ameloblastoma: systematic review and meta-analysis. Int J Oral Maxillofac Surg 2016; 45: 359-367.

[2] Iakovou M, Chrysomali E, Piperi E, Fanourakis G, Sklavounou A, Vlachodimitropoulos D and Tseleni-Balafouta S. A comparative study of bone remodeling molecules expression in different types of jaw ameloblastoma. J Oral Pathol Med 2015; 44: 543-551.

[3] Barnes L. Pathology and genetics of head and neck tumours. IARC 2005.

[4] Eversole LR, Leider AS and Hansen LS. Ameloblastomas with pronounced desmoplasia. J Oral Maxillofac Surg 1984; 42: 735-740.

[5] Sun ZJ, Wu YR, Cheng N, Zwahlen RA and Zhao YF. Desmoplastic ameloblastoma-A review. Oral Oncol 2009; 45: 752-759.

[6] Majumdar S, Uppala D, Kotina S, Veera SK and Boddepalli R. Desmoplastic ameloblastoma. Int J Appl Basic Med Res 2014; 4: S53-55.

[7] Kahn LB. Adamantinoma, osteofibrous dysplasia and differentiated adamantinoma. Skeletal Radiol 2003; 32: 245-258.

[8] dos Santos JN, De Souza VF, Azevedo RA, Sarmento VA and Souza LB. "Hybrid" lesion of desmoplastic and conventional ameloblastoma: immunohistochemical aspects. Braz J Otorhinolaryngol 2006; 72: 709-713.

[9] Kumamoto H, Yoshida M and Ooya K. Immunohistochemical detection of amelogenin and cytokeratin 19 in epithelial odontogenic tumors. Oral Dis 2001; 7: 171-176.

[10] Kumamoto H, Yoshida M and Ooya K. Immunohistochemical detection of hepatocyte growth factor, transforming growth factor-beta and their receptors in epithelial odontogenic tumors. J Oral Pathol Med 2002; 31: 539-548.

[11] Oteri G, Lentini M, Pisano M and Cicciu M. Peripheral desmoplastic ameloblastoma in adolescent age: clinico-pathological and immunohistochemical analisys of a case. Open Dent J 2014; 8: 159-163.

[12] Ramesh V, Singh S, Bailwad S, Kiran K, Agarwal R and Singh A. The complexity of stromal changes in desmoplastic ameloblastoma. Ann Med Health Sci Res 2014; 4: S14-17.

[13] Pal SK, Sakamoto K, Aragaki T, Akashi T and Yamaguchi A. The expression profiles of acidic epithelial keratins in ameloblastoma. Oral Surg Oral Med Oral Pathol Oral Radiol 2013; 115: 523-531.

[14] Bologna-Molina R, Mosqueda-Taylor A, de Almeida-Oslei P, Toral-Rizo V and Martinez-Mata G. Peripheral desmoplastic ameloblastoma: histopathological and immunohistochemical profile of a case. Med Oral Patol Oral Cir Bucal 2010; 15: e846-849.
[15] Fukumashi K, Enokiya Y and Inoue T. Cytokeratins expression of constituting cells in ameloblastoma. Bull Tokyo Dent Coll 2002; 43: 13-21.
[16] Takata T, Miyauchi M, Ogawa I, Zhao M, Kudo Y, Sato S, Takekoshi T, Nikai H and Tanimoto K. So-called 'hybrid' lesion of desmoplastic and conventional ameloblastoma: report of a case and review of the literature. Pathol Int 1999; 49: 1014-1018.
[17] Li B, Long X, Wang S, Cheng Y and Chen X. Clinical and radiologic features of desmoplastic ameloblastoma. J Oral Maxillofac Surg 2011; 69: 2173-2185.
[18] Philipsen HP, Reichart PA and Takata T. Desmoplastic ameloblastoma (including "hybrid" lesion of ameloblastoma). Biological profile based on 100 cases from the literature and own files. Oral Oncol 2001; 37: 455-460.
[19] Luo J, You M, Zheng G and Xu L. Cone beam computed tomography signs of desmoplastic ameloblastoma: review of 7 cases. Oral Surg Oral Med Oral Pathol Oral Radiol 2014; 118: e126-133.
[20] Cervelli D, Marianetti TM, Boniello R, Grussu F, Gasparini G, Azzuni C and Pelo S. Giant neglected desmoplastic ameloblastoma: reconstruction with free fibula flap. J Craniofac Surg 2012; 23: e171-174.
[21] Mijiti A, Ling W, Maimaiti A and Moming A. Single-stage management of huge desmoplastic ameloblastoma of the anterior mandible. J Plast Reconstr Aesthet Surg 2013; 66: 1440-1441.
[22] Savithri V, Janardhanan M, Suresh R and Kumar RV. Desmoplastic ameloblastoma with osteoplasia: review of literature with a case report. J Oral Maxillofac Pathol 2013; 17: 298-301.
[23] de Medeiros AM, Nonaka CF, Galvao HC, de Souza LB and Freitas Rde A. Expression of extracellular matrix proteins in ameloblastomas and adenomatoid odontogenic tumors. Eur Arch Otorhinolaryngol 2010; 267: 303-310.
[24] Masthan KM, Anitha N, Krupaa J and Manikkam S. Ameloblastoma. J Pharm Bioallied Sci 2015; 7: S167-170.
[25] Matsuo A and Ueno S. Immunohistochemical demonstration of keratin in ameloblastoma as an indication of tumor differentiation. J Oral Maxillofac Surg 1991; 49: 282-288; discussion 288-289.
[26] Mia MM and Bank RA. The pro-fibrotic properties of transforming growth factor on human fibroblasts are counteracted by caffeic acid by inhibiting myofibroblast formation and collagen synthesis. Cell Tissue Res 2016; 363: 775-789.
[27] Takata T, Miyauchi M, Ogawa I, Kudo Y, Takekoshi T, Zhao M, Sato S, Nikai H and Komiyama K. Immunoexpression of transforming growth factor beta in desmoplastic ameloblastoma. Virchows Arch 2000; 436: 319-323.
[28] Iezzi G, Piattelli A, Rubini C, Artese L, Goteri G, Perrotti V and Carinci F. Expression of transforming growth factor beta1 in ameloblastomas. J Craniofac Surg 2008; 19: 1618-1621.
[29] Sherlin HJ, Natesan A, Ram P, Ramani P and Thiruvenkadam C. Immunohistochemical profiling of Ameloblastomas using cytokeratin, vimentin, smooth muscle actin, CD34 and S100. Ann Maxillofac Surg 2013; 3: 51-57.
[30] Saran RK, Nijhawan R, Vasishta RK and Rattan V. Desmoplastic ameloblastoma: a case report with fine-needle aspiration cytologic findings. Diagn Cytopathol 2000; 23: 114-117.
[31] Hazelbag HM, Laforga JB, Roels HJ and Hogendoorn PC. Dedifferentiated adamantinoma with revertant mesenchymal phenotype. Am J Surg Pathol 2003; 27: 1530-1537.
[32] Siar CH, Rahman ZA, Tsujigiwa H, Mohamed Om Alblazi K, Nagatsuka H and Ng KH. Invadopodia proteins, cortactin, N-WASP and WIP differentially promote local invasiveness in ameloblastoma. J Oral Pathol Med 2016; 45: 591-598.
[33] Bologna-Molina R, Mosqueda-Taylor A and Molina-Frechero N. Differential expression of glypican-1 in ameloblastoma variants. Appl Immunohistochem Mol Morphol 2015; 23: 153-160.
[34] Siar CH, Ishak I and Ng KH. Podoplanin, E-cadherin, beta-catenin, and CD44v6 in recurrent ameloblastoma: their distribution patterns and relevance. J Oral Pathol Med 2015; 44: 51-58.
[35] Khalil E, Rehman A and Ahmed F. Immunoexpression of twist in different morphological variants of ameloblastomas. J Ayub Med Coll Abbottabad 2015; 27: 296-303.
[36] Siar CH and Ng KH. Differential expression of transcription factors Snail, Slug, SIP1, and Twist in ameloblastoma. J Oral Pathol Med 2014; 43: 45-52.
[37] Bologna-Molina R, Mosqueda-Taylor A, Molina-Frechero N, Mori-Estevez AD and Sanchez-Acuna G. Comparison of the value of PCNA and Ki-67 as markers of cell proliferation in ameloblastic tumors. Medicina Oral Patologia Oral Y Cirugia Bucal 2013; 18: E174-E179.
[38] Siar CH, Nagatsuka H, Han PP, Buery RR, Tsujigiwa H, Nakano K, Ng KH and Kawakami T. Differential expression of canonical and non-canonical Wnt ligands in ameloblastoma. J Oral Pathol Med 2012; 41: 332-339.

[39] Krishna A, Kaveri H, Kumar RN, Kumaraswamy K, Shylaja S and Murthy S. Overexpression of MDM2 protein in ameloblastomas as compared to adenomatoid odontogenic tumor. J Cancer Res Ther 2012; 8: 232.
[40] Siar CH, Nakano K, Han PP, Nagatsuka H, Ng KH and Kawakami T. Differential expression of Notch receptors and their ligands in desmoplastic ameloblastoma. J Oral Pathol Med 2010; 39: 552-558.
[41] Bologna-Molina R, Mosqueda-Taylor A, Lopez-Corella E, de Almeida OP, Carrasco-Daza D, Farfan-Morales JE, Molina-Frechero N and Damian-Matsumura P. Comparative expression of syndecan-1 and Ki-67 in peripheral and desmoplastic ameloblastomas and ameloblastic carcinoma. Pathol Int 2009; 59: 229-233.
[42] Kumamoto H and Ooya K. Immunohistochemical detection of BH3-only proteins in ameloblastic tumors. Oral Dis 2008; 14: 550-555.
[43] Kumamoto H and Ooya K. Immunohistochemical detection of insulin-like growth factors, platelet-derived growth factor, and their receptors in ameloblastic tumors. J Oral Pathol Med 2007; 36: 198-206.
[44] Kumamoto H, Ohki K and Ooya K. Expression of p63 and p73 in ameloblastomas. J Oral Pathol Med 2005; 34: 220-226.
[45] Kumamoto H and Ooya K. Expression of survivin and X chromosome-linked inhibitor of apoptosis protein in ameloblastomas. Virchows Arch 2004; 444: 164-170.
[46] Nagatsuka H, Siar CH, Nakano K, Tsujigiwa H, Gunduz M, Choufuku H, Lee YJ, Naito I, Sado Y and Nagai N. Differential expression of collagen IV alpha1 to alpha6 chains in basement membranes of benign and malignant odontogenic tumors. Virchows Arch 2002; 441: 392-399.
[47] Kumamoto H, Kimi K and Ooya K. Immunohistochemical analysis of apoptosis-related factors (Fas, Fas ligand, caspase-3 and single-stranded DNA) in ameloblastomas. J Oral Pathol Med 2001; 30: 596-602.