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Original Contribution

SATB2 is frequently expressed in ossifying and non-ossifying peripheral oral fibroma of the gingival region but not in reactive fibromatous lesions from other intraoral sites

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ABSTRACT

Ossifying and non-ossifying peripheral oral fibromas (POF) of the gingival and alveolar mucosa are localized, cellular, small fibrous nodular lesions likely resulting from diverse external/ internal physical and chemical irritation or injuries. A central nidus of metaplastic woven bone characterizes and defines the ossifying variant. The inherent tendency of these lesions to ossify remains elusive. We herein analyze SATB2 expression as osteoblastic transcription and differentiation factor in 28 gingival POFs (10 of them ossifying) and compare them to 28 fibrous lesions from different non-gingival intraoral sites. Strong to moderate diffuse nuclear SATB2 immunoreactivity was detected in all ossifying (10/10; 100%) and in 8/18 (44%) non-ossifying gingival POFs, but in only 1/28 (3%) non-gingival oral reactive nodular fibrous lesions. This study illustrates for the first-time consistent expression of the osteoblastic marker SATB2 in ossifying and most of non-ossifying POFs of the gingival area but lack of this marker in reactive fibrous lesions from other oral cavity sites. This finding is in line with the proposed origin of gingival POFs from periodontal ligaments and may explain the frequent ossification observed in them. It is mandatory to consider this finding when assessing biopsies from SATB2-positive oral cavity neoplasms to avoid misinterpretation.

1. Introduction

Peripheral oral fibroma (POF) is a benign localized lesion that originates from the gingival and alveolar oral mucosa and presents clinically as a painless, slowly growing, pedunculated or sessile firm nodule, usually < 2 cm in size. Histologically, POF is characterized by fibrous tissue that entraps variable numbers of fibroblastic cells. Presence of a well-defined island of metaplastic woven bone defines the ossifying (versus non-ossifying) variant [1,2]. Several descriptive names have been used for ossifying POF: peripheral cementifying fibroma, peripheral fibroma with cementogenesis, peripheral fibroma with osteogenesis, peripheral fibroma with calcification, calcified or ossified fibrous epulis, and calcified fibroblastic granuloma [1]. Both variants are considered reactive [3,4].

Women in their 2nd decade of life are mainly affected. Recurrence rates approach 20%. comparable but almost never ossifying fibrous lesions (traumatic fibromas and fibroepithelial polyps) may occur at any oral site including the tongue, lips, mouth floor, palate, and others, likely resulting from traumatization or chronic irritation.

The special AT-rich sequence-binding protein 2 (SATB2) encodes a nuclear matrix DNA-binding multifunctional transcriptional regulator protein [5] involved in osteoblast lineage commitment [6-8], craniofacial skeleton, and bone and neuronal evolution [9,10]. *SATB2* gene inactivation caused by diverse molecular mechanisms results in so-called SATB2-associated syndrome [11], a condition characterized by neurodevelopmental and behavioral disabilities, palatal clefts, dental anomalies, skeletal anomalies and, rarely, involvement and impairment of other organ systems [7,12].

In surgical pathology practice, SATB2 has been increasingly used as a context-specific marker of osteoblastic differentiation and as a marker of colorectal cancer [13]. In the head and neck, SATB2 represents a valuable adjunct for intestinal-type sinonasal adenocarcinoma and in uncommon mesenchymal neoplasms including variants of craniofacial osteosarcomas and phosphaturic mesenchymal tumors [14,15]. Expression of SATB2 in POF has not been studied before. We herein analyzed 56 fibromatous lesions from the oral cavity for expression of

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SATB2 and correlated topographic and morphological findings with the immunohistochemical SATB2 expression.

2. Materials and methods

All cases have been identified in the routine surgical pathology files of the Institute of Pathology, University Hospital of Erlangen, Germany. Tissue samples have been fixed in formalin overnight and embedded routinely for histological evaluation. Immunohistochemistry (IHC) was performed on 3-μm sections cut from paraffin blocks using a fully automated system ("Benchmark XT System," Ventana Medical Systems Inc., 1910 Innovation Park Drive, Tucson, Arizona, USA). The Anti-SATB2 antibody was retrieved from Abcam (clone EPNCIR130A, dilution, 1:200).

2.1. Immunohistochemical scoring

Only nuclear staining was considered positive. The extent of SATB2 expression was scored as 0 = negative, 1+: 1–25% of cells, 2+: 26–50%, 3+: 51–75% and 4+ if > 75% of cells stained positive. The "intensity score" – was defined as negative (no staining), 1 + (weak positivity), 2 + (moderate positivity) and 3+ (strong positivity).

The results of the extent and intensity scores were then multiplied to obtain a final score of 0–12 for each lesion (Table 1).

3. Results

There were 56 lesions from 53 patients available for analysis. Three patients (case 10 and 11 in Table 1; and cases, 13 and 14, 16 and 17 in Table 2) underwent surgical excision of two lesions during same operation. The female to male ratio was 1.2: 1. Cases were distributed over a wide age range (15–82 years). The average age was 52 years (56 and 51 years for males and females, respectively). Twenty-eight lesions were gingival (14 in the maxilla, 13 in the mandible & one in unspecified gingival site). Ten (35%) of the gingival lesions were ossifying. The non-gingival reactive fibrous oral cavity lesions (28) were located in tongue [8], palate [8], mouth angle & lip [7], buccal mucosa [3] and unspecified non-gingival oral cavity [2].

3.1. Ossifying peripheral oral fibroma (n = 10)

Table 1 (Cases 1 to 10) shows the clinical and histological characteristics of the ten patients with ossifying POF. Affected were 6 women (60%) and 4 (40%) men; the average age was 51.1 years. 5 cases were localized in maxilla and 5 in the mandible. The lesion size ranged from 0.5–1.8 cm (mean, 0.9 cm).

Microscopically all were well-defined polypoid fibroepithelial growths (Fig. 1A). They showed low to moderate cellularity in the form of fibroblast-like spindled or fusiform cells without significant atypia (Fig. 1B, C). This fibroblastic component was admixed with a chronic inflammatory infiltrate composed of fibroblasts, histiocytes, lymphocytes and plasma cells, occasionally forming granuloma-like aggregates. A few neutrophils were seen. The background stroma of all lesions was fibroblastic with prominent collagenous material that varies from few collagen fibrils to large areas with hyalinization or sclerosis. Dense and mature collagen was seen predominantly in cases with a moderate inflammatory component. Variable stromal edema and prominent vascularization were seen in most cases as well as occasional myxoid changes (Fig. 1C). Bone formation was present in all cases and varied from a few psammomatous microcalcifications to well defined partially anastomosing trabeculae of lamellar and woven bone characteristically forming a well-defined central nidus-like bony island (Fig. 1D). The covering mucosa was frequently hyper-/parakeratotic. None of the lesions had evidence of intra-osseous component or features of peripheral odontogenic fibroma, peripheral giant cell granuloma or other specific entity.

SATB2 immunohistochemical staining showed very strong and diffuse nuclear positivity in all cases, both in the bony component and the fibrous tissue surrounding bone structures (Fig. 1E, F). The total SATB2 score was in the range of "6 to 12". All cases were marked as score "3" for SATB2 intensity.

Table 1
Clinicopathological features of ossifying and non-ossifying gingival peripheral oral fibromas (n = 28).

No	Age/sex	Site	Size (cm)	Type	Cellularity	SATB2%	SATB2 intensity	Total score
1	52/F	Maxilla right (Region 13)	0,8 × 0,4	Ossifying	High	4+	3	12
2	71/F	Maxilla	1,8 × 1,0	Ossifying	High	4+	3	12
3	60/F	Maxilla left (Region 24)	0,5 × 0,4	Ossifying	High	4+	3	12
4	35/F	Maxilla left (Region 25)	0,6 × 0,6	Ossifying	High	4+	3	12
5	20/M	Mandible right (Region 44)	0,8 × 0,5	Ossifying	High	4+	3	12
6	63/F	Maxilla left (Region 23/24)	0,8 × 0,5	Ossifying	Moderate	3+	3	9
7	29/F	Mandible (Region 31)	0,6 × 0,6	Ossifying	High	3+	3	9
8	40/M	Mandible middle (Regions 31–41)	1,2 × 0,6	Ossifying	High	2+	3	6
9	74/M	Mandible left	1,0 × 0,3	Ossifying	Moderate	2+	3	6
10*	67/M	Mandible right (Region 45)	1,0 × 0,5	Ossifying	Moderate	2+	3	6
11*	67/M	Maxilla right (Region 13)	0,5 × 0,4	Non-ossifying	Moderate	1+	1	1
12	25/F	Maxilla left (Regions 23/24)	0,9 × 0,6	Non-ossifying	High	3+	3	9
13	15/F	Mandible right (Regions 41,42)	0,6 × 0,5	Non-ossifying	High	2+	3	6
14	53/F	Gingiva not specified	0,6 × 0,4	Non-ossifying	High	2+	2	4
15	68/F	Mandible left (Regions 32/33)	0,6 × 0,5	Non-ossifying	Moderate	2+	2	4
16	72/F	Mandible right (Region 46)	1,5 × 0,5	Non-ossifying	High	2+	2	4
17	20/F	Mandible right (Regions 41,42)	0,8 × 0,4	Non-ossifying	High	2+	2	4
18	42/F	Mandible left (Region 36)	0,8 × 0,4	Non-ossifying	High	1+	3	3
19	65/M	Palate/maxilla left (Region 26)	0,5 × 0,5	Non-ossifying	Moderate	1+	1	1
20	69/M	Maxilla and Mandible (Regions 48, 37, 17–18)	1,0 × 0,5	Non-ossifying	Moderate	1+	1	1
21	65/F	Maxilla middle (Regions 11/21)	0,7 × 0,4	Non-ossifying	Low	1+	1	1
22	32/F	Palate/Maxilla right (Regions 14/15)	1,1 × 07	Non-ossifying	Low	1+	1	1
23	56/F	Maxilla	0,8 × 0,6	Non-ossifying	Low	1+	2	2
24	73/M	Maxilla	0,9 × 0,5	Non-ossifying	Moderate	0	0	0
25	55/M	Maxilla	2,5 × 2,2	Non-ossifying	Low	0	0	0
26	30/M	Mandible right (Region 48)	0,9 × 0,5	Non-ossifying	Low	0	0	0
27	43/F	Mandible left (Region 38)	0,4 × 0,4	Non-ossifying	Low	0	0	0
28	40/M	Maxilla right (Region 12)	0,5 × 0,3	Non-ossifying	Low	0	0	0

* This patient had two separate lesions removed at same time.

Table 2
Clinicopathological features of non-gingival fibrous oral lesions (n = 28).

No	Age/sex	Site	Size (cm)	Type	Cellularity	SATB2%	SATB2 intensity	Total score
1	82/F	Palate	0,3 × 0,3	Non-ossifying	Moderate	1+	1	1
2	77 M	Top of the tongue	0,5 × 0,4	Non-ossifying	Moderate	1+	1	1
3	36/M	Left tongue margin	1,0 × 0,5	Non-ossifying	Moderate	1+	1	1
4	48/M	Oral cavity unspecified	0,4 × 0,4	Non-ossifying	Moderate	1+	1	1
5	61/M	Tongue	0,3 × 0,3	Non-ossifying	Moderate	1+	1	1
6	76/M	Left tongue	0,9 × 0,4	Non-ossifying	Moderate	1+	1	1
7	72/F	Hard palate	1,2 × 0,7	Non-ossifying	Low	1+	1	1
8	55/M	Top of the tongue	0,4 × 0,3	Non-ossifying	Low	1+	1	1
9	66/M	Left 1/3 of the tongue	1,2 × 0,7	Non-ossifying	Low	1+	1	1
10	25/F	Tongue	0,4 × 0,3	Non-ossifying	Low	1+	1	1
11	48/M	Tongue	0,3 × 0,3	Non-ossifying	Low	1+	2	2
12	39/F	Oral cavity unspecified	1,4 × 1,5	Non-ossifying	Moderate	0	0	0
13*	44/F	Right mouth angle	0,6 × 0,5	Non-ossifying	Moderate	0	0	0
14*	44/F	Left mouth angle	0,7 × 0,5	Non-ossifying	Moderate	0	0	0
15	60/F	Right buccal mucosa	0,7 × 0,7	Non-ossifying	Moderate	0	0	0
16**	55/M	Right palate	0,8 × 0,3	Non-ossifying	Low	0	0	0
17**	55/M	Right palate	1,0 × 0,3	Non-ossifying	Low	0	0	0
18	65/M	Lower lip	0,6 × 0,5	Non-ossifying	Low	0	0	0
19	77/F	Right mouth angle	0,5 × 0,4	Non-ossifying	Low	0	0	0
20	70/F	Palate	2,0 × 1,5	Non-ossifying	Low	0	0	0
21	47/M	Lower lip	0,7 × 0,6	Non-ossifying	Moderate	0	0	0
22	44/M	Right buccal mucosa	0,6 × 0,5	Non-ossifying	Low	0	0	0
23	65/M	Soft palate	0,5 × 0,3	Non-ossifying	Low	0	0	0
24	51/F	Palate	0,4 × 0,3	Non-ossifying	Moderate	0	0	0
25	50/M	Mouth angle	1,1 × 0,7	Non-ossifying	Low	0	0	0
26	44/F	Right palate	0,3 × 0,2	Non-ossifying	Low	0	0	0
27	48/F	Right mouth angle	0,5 × 0,3	Non-ossifying	Low	0	0	0
28	59/F	Right buccal mucosa	1,1 × 0,6	Non-ossifying	Low	0	0	0

* & ** these two patients had two separate lesions removed at the same time.

3.2. Non-ossifying gingival peripheral oral fibroma (n = 18)

Affected were 11 women (61%) and 7 (39%) men; the average age was 49.4 years (range, 15–73 years). Ten cases were localized in maxilla, 7 in the mandible and one case in gingiva not specified. The lesion size ranged from 0.4–2.5 cm (mean, 0.9 cm).

Histologically, non-ossifying gingival POFs were identical to their ossifying counterparts, but they lacked a bony component. SATB2 immunohistochemistry showed very strong to moderate nuclear positivity in 8 (44%) cases (Fig. 1F). Five cases revealed weak SATB2 expression and another 5 were negative. The total SATB2 score was in the range of "0 to 9".

3.3. Fibrous lesions from other non-gingival oral sites (traumatic fibromas & fibroepithelial polyps; n = 28)

Table 2 shows the clinical and histological features of the non-gingival oral fibrous lesions (traumatic fibromas/ fibroepithelial polyps). Affected were 13 women (46%) and 15 (54%) men; the average age was 55.8 years (range 25–82 years). Eight cases were localized in the tongue, 7 cases in palate, 7 cases in the lip and mouth angle and 5 cases in the buccal mucosa and oral cavity not specified. The lesion size ranged from 0.3–2.0 cm (mean, 0.7 cm).

Histologically, these lesions showed polypoid localized fibrous nodules composed of coarse collagen fibers entrapping interspersed fibroblastic stromal cells and small vessels (Fig. 2A, B). The covering mucosa was frequently hyper-/parakeratotic (Fig. 2A). No bone formation or psammomatous calcified bodies were seen. SATB2 immunohistochemical staining showed moderate nuclear positivity in one case from the tongue (3%); 10 cases showed weak SATB2 expression and 17 cases were negative. The total SATB2 score was in the range of "0 to 2" (Fig. 2 C, D).

3.4. Correlation of SATB2 expression in POF with site and histological type

Overall, strong to moderate diffuse SATB2 immunoreactivity was detected in 10/10 (100%) ossifying, 8/18 (44%) non-ossifying gingival POF, and 1/28 (3%) non-gingival oral fibromas.

4. Discussion

Ossifying and non-ossifying POF of the gingival and alveolar mucosa are very similar lesions except for the presence of a mature metaplastic bony island/ component in the ossifying variant [1,2,16,17]. On the other hand, the non-ossifying variant is essentially comparable to other nodular fibrous oral lesions in the spectrum of traumatic fibroma and fibroepithelial polyps, both being composed of paucicellular to moderately cellular fibrous connective tissue covered by squamous mucosa with frequently variable hyper-/parakeratotic changes. Clinical appearance/site is the major distinguishing feature of the gingival (fibrous epulis-like) POF versus similar nodular fibrous lesions from other oral cavity sites. It is generally accepted that these lesions, irrespective of their name and location, are induced by persistent mechanical injury and other type of irritation [3,4,18,19]. The main questions, why some gingival lesions ossify while others do not, and why the non-gingival fibrous counterparts never ossify, remain a subject of controversy. Elanagai et al. studied the expression of osteopontin in the normal gingival tissue and in different types of focal reactive lesions of the gingiva including ossifying POF to explore its potential role in the development of the bony component [20]. They found osteopontin expression in all cases of ossifying POF and suggested, that POF arises from osteopontin expressing stromal cells – osteoblasts derived from the periodontal ligament. However, the exact nature of the ossifying POF and its relationship to the non-ossifying variant remained speculative, some authors adopted the notion that these two lesions possibly represent different entities due to their different histological features including the presence of a bony component in the ossifying type [20].

In the present study, we analyzed for the first time the two types of gingival POF for expression of the osteoblastic differentiation marker SATB2 in a trial to explain their inherent tendency to ossify and form a mature bone and to address histogenesis and relationship between the ossifying and the non-ossifying variant. Our study included as a control

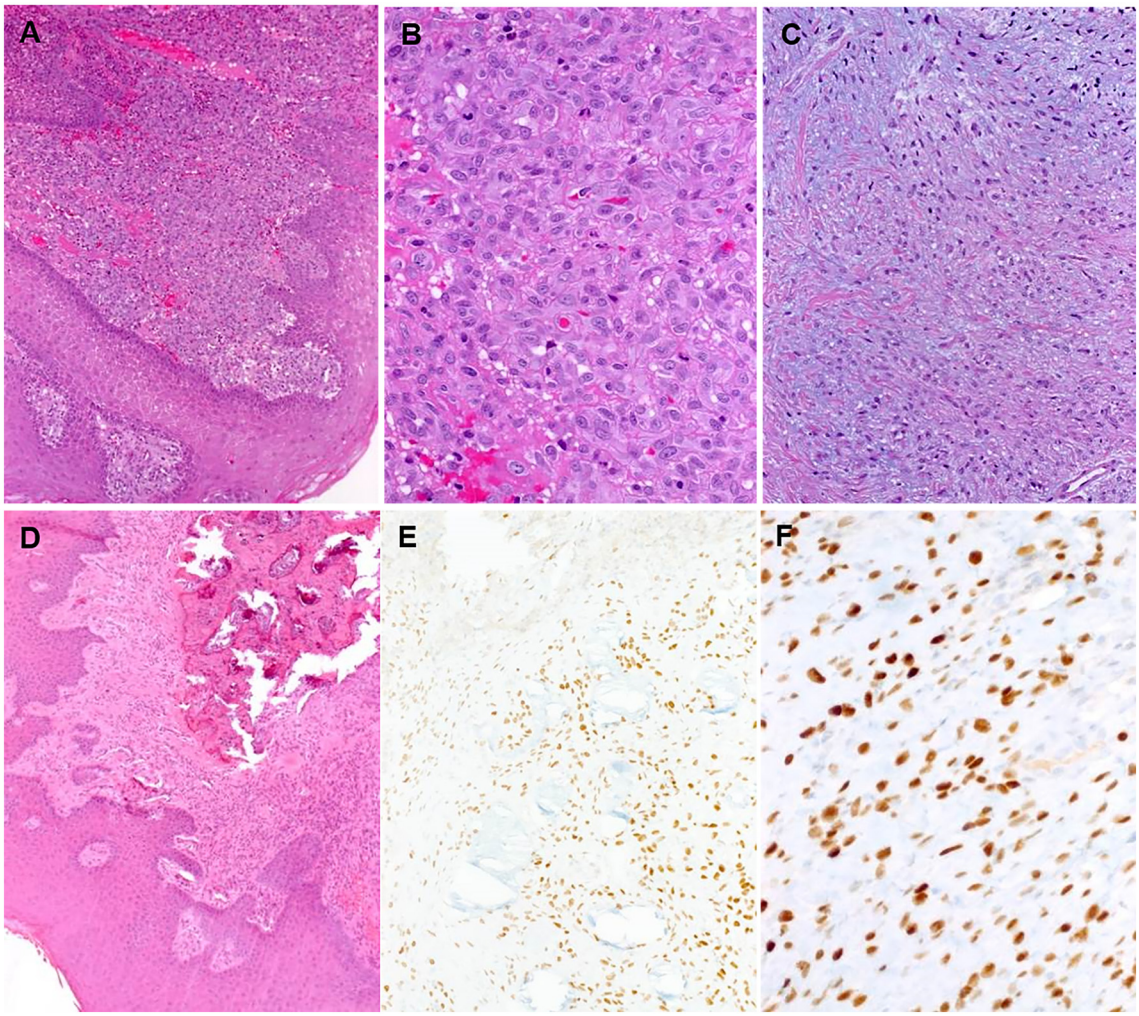

Fig. 1. Ossifying and non-ossifying gingival peripheral oral fibroma presents as a small polypoid lesion covered by hyperplastic mucosa (A) and composed of an admixture of stromal and inflammatory cells (B: higher magnification of cellular stromal area). The stroma varies from sparsely fibrous (B) to fibromyxoid (C). The bony component is frequently represented by a well-defined nidus-like bone island (D). Strong and diffuse SATB2 expression is seen in the peri- and intertrabecular fibroblastic cells in ossifying lesions (E) and diffusely in stromal cells in non-ossifying POF (F).

group histologically comparable localized reactive nodular fibrous lesions from different sites of the oral cavity and the lips in the spectrum of fibroepithelial polyps and traumatic fibromas.

All of ossifying and almost half of the non-ossifying gingival lesions were strongly to moderately SATB2 positive. SATB2 is a transcription regulator that directly binds osteoblast-associated genes to promote or repress their expression. On the other side; SATB2 influences the activity of transcriptional complexes and indirectly manages the expression of genes that are important in osteoblast maturation and differentiation [3-12]. Frequent SATB2 expression in POF reported in this study has not been described before. It indicates osteoblastic differentiation of stromal component that is similar to and in line with the reported osteopontin expression in reactive lesions of the gingiva [21,22].

The etiology of gingival POF is still enigmatic. Iatrogenic and traumatic factors such as tartar and chewing forces have been implicated. Moreover, POF has been suggested to develop as a consequence of periodontal ligament hyperplasia. Considering the etiology of these lesions, another possible factor of POF development suggests the irritation of the tissues surrounding the tooth and bone, which might stimulate osteoblastic proliferation as a result of *SATB2* gene expression in the stromal cells of the periodontal ligaments. Lack of (no more than weak or focal) expression of SATB2 in non-gingival fibrous oral lesions contrasts with that in gingival counterparts and is in line with the hypothesis that gingival lesions do originate from the periodontal fibrous ligament which likely is composed of mesenchymal cells primed to differentiate along the osteoblastic lineage. On the other hand, other fibrous oral lesions represent localized increase in fibrous tissue of the subepithelial stroma which is not related to the periodontal ligaments or associated with underlying bone tissue. The lower frequency of SATB2 expression in non-ossifying gingival POF (44%) is in contrast with the uniform reactivity of SATB2 in all of the gingival ossifying lesions. This suggests that ossifying lesions are likely more advanced or are associated with higher osteoblastic activation sufficient to produce mature bone.

SATB2 is positive in numerous malignant and benign head and neck lesions such as osteosarcoma, osteoblastoma, giant cell tumor, fibrous dysplasia and in epithelial neoplasms such as sinonasal intestinal-type adenocarcinoma [8,23]. More recently, SATB2 expression was reported to be consistently present in phosphaturic mesenchymal tumors including head and neck cases, some of them may closely resemble central giant cell granuloma [15]. Our current study adds to the list of SATB2 expressing orofacial lesions and should be included in the differential diagnosis, especially when expecting any osteogenic process or osteoblastic neoplasm on biopsy. As it is sometimes tricky and challenging to identify and reliably assess crushed resection margins of fibroblastic osteosarcoma and giant cell granuloma of maxillofacial bones, SATB2 expression in any polypoid intraoral lesions or biopsies

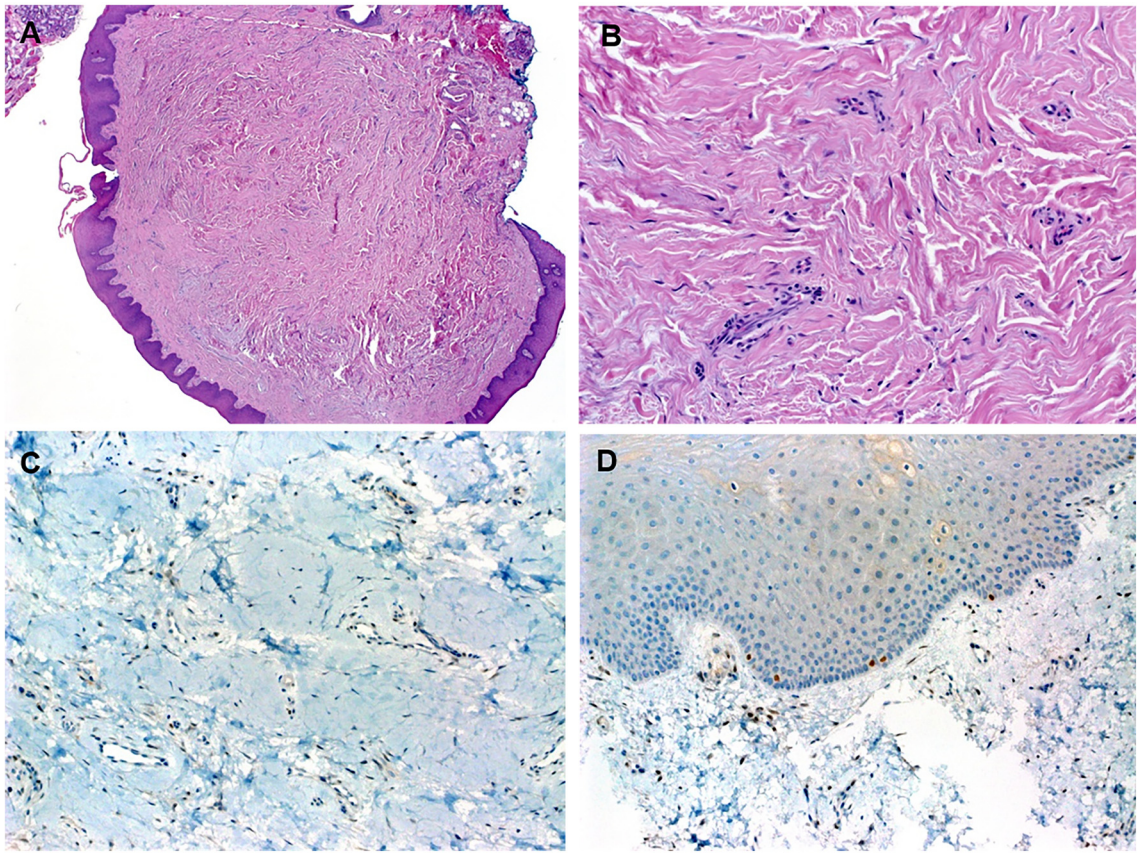

Fig. 2. A: Non-gingival reactive fibrous nodular lesions from different sites of the oral cavity present as polypoid collagenized paucicellular fibrous tissue covered by hyperplastic squamous mucosa. **B**: coarse collagen fibers admixed with a few cells and vessels. **C**: SATB2 is either negative (**C**) or only weakly and focally expressed (**D**) in the non-gingival fibrous oral lesions. Single SATB2-positive cells are seen in the basal mucosa.

should be approached with caution to avoid over-interpretation as meaningful neoplasm or positive margins.

In summary, this study highlights consistent expression of SATB2 in ossifying and most of non-ossifying peripheral oral fibroma of the gingival region of the maxilla and mandible in line with an origin from periodontal ligament/fibrous tissue and explaining the inherent tendency of these lesions to form bone. The question, why a subset of these lesions does not ossify despite SATB2 expression remains enigmatic.

References

[1] Buchner A, Hansen LS. The histomorphologic spectrum of peripheral ossifying fibroma. Oral Surg Oral Med Oral Pathol 1987;63(4):452–61.
[2] Bhaskar SN, Jacoway JR. Peripheral fibroma and peripheral fibroma with calcification: report of 376 cases. J Am Dent Assoc 1966;73(6):1312–20.
[3] Buchner A, Shnaiderman A, et al. Relative frequency of localized reactive hyperplastic lesions of the gingiva: a retrospective study of 1675 cases from Israel. J Oral Pathol Med 2010;39(8):631–8. Sep.
[4] Maturana-Ramírez A, Adorno-Farías D. A retrospective analysis of reactive hyperplastic lesions of the oral cavity: study of 1149 cases diagnosed between 2000 and 2011, Chile. Acta Odontol Latinoam 2015;28(2):103–7.
[5] FitzPatrick DR, Carr IM. Identification of SATB2 as the cleft palate gene on 2q32-q33. Hum Mol Genet 2003 Oct 1;12(19):2491–501.
[6] Sheehan-Rooney K, Palinkasova B, et al. A cross-species analysis of Satb2 expression suggests deep conservation across vertebrate lineages. Developmental dynamics: an official publication of the American Association of Anatomists 2010;239(12):3481–91.
[7] Zhao Xiaoying, Qu Zhihu, et al. The role of SATB2 in skeletogenesis and human disease. Cytokine Growth Factor Rev 2014;25(1):35–44. Feb.
[8] Conner JR, Hornick JL. SATB2 is a novel marker of osteoblastic differentiation in bone and soft tissue tumours. Histopathology 2013;63(1):36–49. Jul.
[9] Magnusson K, de Wit M, Brennan DJ, et al. Satb2 in combination with cytokeratin 20 identifies over 95% of all colorectal carcinomas. Am J Surg Pathol 2011;35:937–48.
[10] Eberhard J, Gaber A, Wangefjord S, et al. A cohort study of the prognostic and treatment predictive value of SATB2 expression in colorectal cancer. Br J Cancer 2012;106:931–8.
[11] Zarate YA, Fish JL. SATB2-associated syndrome: mechanisms, phenotype, and practical recommendations. Am J Med Genet A 2017 Feb;173(2):327–37.
[12] Zarate YA, Kalsner L. Genotype and phenotype in 12 additional individuals with SATB2-associated syndrome. Clin Genet 2017;92(4):423–9. Oct.
[13] Ordóñez NG. SATB2 is a novel marker of osteoblastic differentiation and colorectal adenocarcinoma. Adv Anat Pathol 2014 Jan;21(1):63–7.
[14] Skalova A, Sar A, Laco J, et al. The role of SATB2 as a diagnostic marker of sinonasal intestinal-type adenocarcinoma. Appl Immunohistochem Mol Morphol 2018 Feb;26(2):140–6.
[15] Agaimy A, Michal M, Chiosea S, et al. Phosphaturic mesenchymal tumors: clinicopathologic, immunohistochemical and molecular analysis of 22 cases expanding their morphologic and immunophenotypic spectrum. Am J Surg Pathol 2017;41(10):1371–80. Oct.
[16] García de Marcos JA, García de Marcos MJ, et al. Peripheral ossifying fibroma: a clinical and immunohistochemical study of four cases. J Oral Sci 2010;52:95–9.
[17] Childers ELB, Morton I, et al. Giant peripheral ossifying fibroma: a case report and clinicopathologic review of 10 cases from the literature. Head Neck Pathol 2013;7(4):356–60.
[18] Chang JY, Kessler HP, et al. Localized juvenile spongiotic gingival hyperplasia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106(3):411–8.
[19] Damasceno LS, da Silva Gonçalves F, et al. Stromal myofibroblasts in focal reactive overgrowths of the gingiva. Braz Oral Res 2012;26(4):373–7. Jul-Aug.
[20] Elanagai R, Veeravarmal V, Nirmal RM. Osteopontin expression in reactive lesions of gingiva. J Appl Oral Sci 2015;23(1):26–32. Jan-Feb.
[21] Cantor H. The role of Eta-1/osteopontin in the pathogenesis of immunological disorders. Ann N Y Acad Sci 1995;760:143–50.
[22] Elanagai R, Veeravarmal V, et al. Osteopontin expression in reactive lesions of gingiva. J Appl Oral Sci 2015;23(1):26–32.
[23] Skalova A, Sar A. The role of SATB2 as a diagnostic marker of sinonasal intestinal-type adenocarcinoma. Appl Immunohistochem Mol Morphol 2018 Feb;26(2):140–6.