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Expression of Periostin in Benign Salivary Gland Tumors

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Parotid tumors present a wide range of histological features, from benign to malignant. Periostin, an extracellular matrix protein specifically expressed in the periosteum and periodontal ligament, is isolated from osteoblast cell lines. It regulates fibrosis and collagen deposition and plays an important role in myocardial repair after myocardial infarction. It is also known to be involved in otorhinolaryngological-diseases. This study included 36 patients [38 specimens; 16 men and 20 women, mean age 59.2 (range 26-82) years] who underwent parotid tumor resection at the Division of Otorhinolaryngology, Tohoku Medical and Pharmaceutical University, between April 2017 and March 2022 and were clinically and pathologically diagnosed as having benign parotid tumors. Formalin-fixed, paraffin-embedded sections from the surgical specimens were autoclaved and immunostained with anti-periostin antibodies to evaluate the expression and distribution of periostin. Histologically, the tumors were diagnosed as pleomorphic adenomas in 15 cases (15 specimens), Warthin's tumors in 13 cases (15 specimens), basal cell adenomas in 2 cases (2 specimens), oncocytomas in 4 cases (4 specimens), and myoepitheliomas in 2 cases (2 specimens). An increased expression of periostin was found in 32 of 38 samples (84.2%) in the stroma of benign parotid tumors. Four distinct patterns of periostin expression were observed in benign parotid gland tumors: negative, superficial, infiltrative, and diffuse. Statistically significant differences were found between periostin expression patterns and histological classification of the tumors. Our results suggest that periostin may be involved in the pathogenesis of benign parotid tumors and could serve as a new biomarker for these tumors.

Keywords: benign salivary gland tumors; biomarker; capsule; patterns of periostin expression; periostin
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Introduction

Infra-auricular masses can be attributed to salivary gland diseases as well as diseases originating from the surrounding soft tissues, such as lymph nodes. In addition, the inside of the parotid gland is in contact with the parapharyngeal space, and it is necessary to differentiate masses arising from this area. Salivary gland diseases encompass a wide variety of diseases, including inflammatory diseases and degenerative diseases in addition to neoplastic diseases. However, it is not always easy to differentiate between them as the main symptom is often just a mass.

Parotid gland tumors histologically range from benign to malignant and exhibit a variety of histological patterns. According to the WHO 2017 classification, there are 11 types of benign tumors and 23 types of malignant tumors. Treatment is tailored according to histological findings, indicating that no uniform treatment policy has been established. Approximately 85% of salivary gland tumors occur in the parotid gland, and the majority of parotid tumors are pleomorphic adenomas. Warthin's tumor is a benign tumor of the parotid gland and is the second most common tumor after pleomorphic adenoma. In the early 1900s, enucleation was the preferred surgery for benign parotid gland tumors.

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However, it has been reported that the recurrence rate for parotid pleomorphic adenomas was as high as 45% (Rawson et al. 1950). Because of the high recurrence rate, total parotidectomy (TP) and superficial parotidectomy (SP) were proposed in the 1940s, which significantly reduced the recurrence rate (Guntinas-Lichius et al. 2006; Zernial et al. 2007). However, TP and SP are associated with complications such as a high rate of postoperative facial nerve paralysis and Frey syndrome.

Subsequently, partial superficial parotidectomy (PSP) was proposed, which preserves a portion of the normal parotid gland tissue and minimizes the dissection of facial nerve branches. This method is associated with fewer complications compared to SP and does not lead to a high recurrence rate (O'Brien 2003; Witt 2005). In terms of surgical approach, enucleation is selected for Warthin's tumor, whereas PSP is often performed for pleomorphic adenoma.

Periostin is an extracellular matrix protein that is specifically expressed in the periosteum and periodontal ligament and has been isolated from osteoblast cell lines. This protein regulates fibrosis and collagen deposition, and also plays an important role in myocardial repair after myocardial infarction. It is also known to be involved in various otorhinolaryngological diseases (Ohta et al. 2013, 2014; Tateda et al. 2022, 2023; Sato et al. 2023). According to recent studies, periostin expression is significantly higher in cardiac disease and tumor tissues in the majority of cancers compared to normal tissues (Hoersch and Andrade-Navarro 2010). Periostin is overexpressed in a variety of solid epithelial tumors, and its interaction with cell-surface receptor integrins, which modulates intracellular signaling pathways, has a direct effect on the hallmarks of cancer (Gonzalez-Gonzalez and Alonso 2018). It is upregulated in metastasis and can influence the size and number of metastatic lesions, underscoring its critical role in the formation and remodeling of cancer tissue microenvironments (Gonzalez-Gonzalez and Alonso 2018).

To the best of our knowledge, no studies focusing on the role of periostin in benign parotid tumors have been reported. Given the suggested involvement of periostin in tumorigenesis, our study investigated the expression sites of periostin in benign parotid gland tumors.

Materials and Methods

Subjects

The patient group consisted of 38 patients [mean age ± standard deviation (SD) 59.2 ± 14.1 (range 26-82) years] with benign salivary gland tumors. These were all new cases without any instances of recurrence or signs of infection. All patients underwent benign parotid tumor surgery at the Division of Otolaryngology, Tohoku Medical and Pharmaceutical University Hospital from April 2017 to March 2022. Out of these patients, 36 presented with single lesions and two had double lesions. Only patients with typical clinical and histological findings were included in the patient group. The benign parotid gland tumors included in this study were of five different histologic types. Tumors were histologically diagnosed as pleomorphic adenomas in 15 cases (15 specimens) (Fig. 1A), Warthin's tumors in 13 cases (15 specimens) (Fig. 1B), basal cell adenomas in 2 cases (2 specimens) (Fig. 1C), oncocytomas in 4 cases (4 specimens) (Fig. 1D), and myoepitheliomas in 2 cases (2 specimens) (Fig. 1E). As a control group, normal parotid tissue specimens were obtained from patients aged 31 to 78 (mean age ± SD; 54.1 ± 15.1) years who had undergone PSP for pleomorphic adenoma. Histopathological diagnoses of benign salivary gland tumors were conducted at the Division of Pathology, Tohoku Medical and Pharmaceutical University Hospital. The study was approved by the ethics review committee of Tohoku Medical University Hospital (approval no. 2021-2-115). The requirement for obtaining informed consent was waived because of the adoption of an opt-out policy in the study.

Immunohistochemistry analysis for detection of periostin

Exactly 4-μm sections were cut from paraffin-embedded tissue blocks, deparaffinized, and rehydrated in a graded series of alcohols. Endogenous peroxidase activity was blocked using 3% H_2O_2 in absolute methanol at room temperature for 10 minutes. All sections were preincubated in Protein Block Serum-Free (Dako Cat No. X0909, Agilent Technologies Inc., Santa Clara, CA, USA) at room temperature for 20 minutes to block nonspecific background staining. The sections were then incubated with a polyclonal antibody (diluted 1:2,730) against polyclonal anti-periostin antibody and kept at 4°C overnight, followed by incubation with a secondary antibody, EnVision+ Dual Link System-HRP (Dako Cat No. K4063), for 60 minutes at room temperature. Finally, the sections were incubated with liquid diaminobenzidine + Substrate Chromogen System (Cat No. K3468 Dako) and counterstained with hematoxylin.

Assessment of slides

The immunostained sections were assessed at × 40 and × 100 magnifications under a light microscope equipped with an eyepiece reticle. Cell counts were expressed as means per high-power field (0.202 mm^2). At least two sections were immunostained, and more than five fields per section were evaluated via the reticle.

Statistical analysis

Variables were compared using one-way analysis of variance, Chi-square test for independence, or Fisher's exact test, as appropriate. A *P*-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, EZR is a modified version of R Commander designed to add statistical functions frequently used in biostatistics (Kanda 2013).

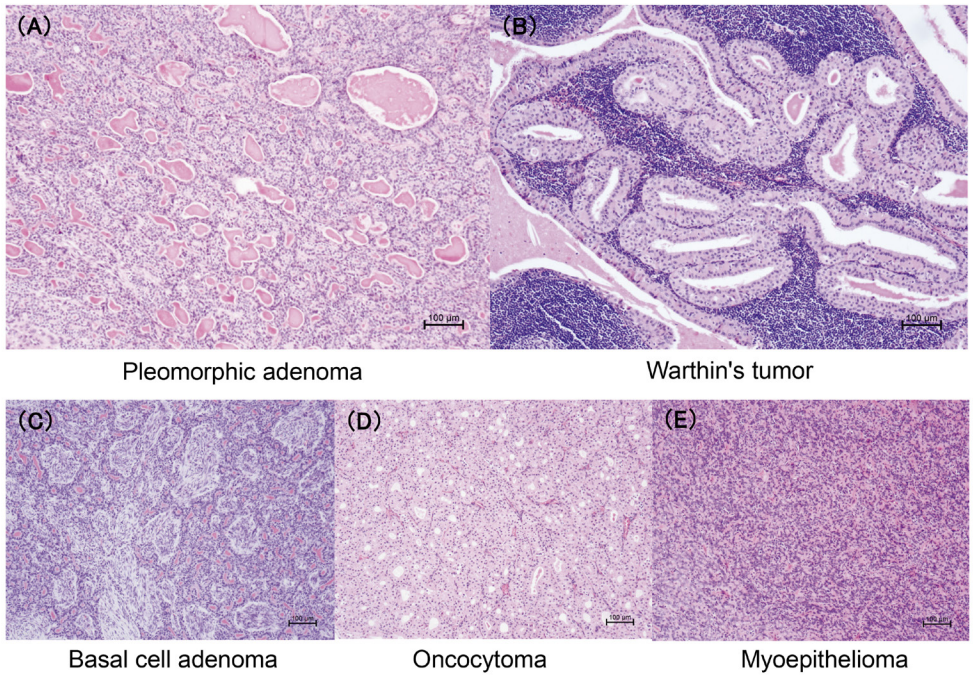

Fig. 1. Hematoxylin and eosin (HE) staining of benign parotid gland tumors.
(A) Pleomorphic adenomas showed a proliferation of the epithelial component in tubular, sheet-like, cord-like, or reticular arrangements. The mesenchymal component migrated from the epithelial component and was observed to be myxomatous, chondroid, fibrous, or vitreous. Osteogenesis was also observed (original magnification × 100). (B) Warthin's tumors demonstrated papillary, cystic, or tubular structures of the epithelium and a dense lymphocytic stromal component. The epithelial cells were organized in two layers of cylindrical, acidophilic cells (oncocytes) found on the luminal side of the ducts or cysts and small cuboidal or flattened basal-type cells located on the basement membrane side (original magnification × 100). (C) In basal cell adenomas, complex jigsaw-like nests of tumor cells were observed. The boundary between the foci and the stroma was distinct, and each foci was bordered by a basal lamina, which was sometimes thick and raised. A fenestrated array of tumor cells in a row was observed at the margins of the foci (original magnification × 100). (D) In oncocytomas, tumor cells grew in solid or cord-like nests, and conduit-like structures were observed in some areas (original magnification × 100). (E) In myoepitheliomas, tumor cells were mixed, and four morphologic types were observed: spindle cell, epithelioma, vitreous-like, and pale clear cell type (original magnification × 100).

Table 1. Periostin expression patterns and histopathological typing of benign salivary gland tumors.

Histopathological typing of benign salivary gland tumors	Periostin expression patterns				
	Negative type (n = 6)	Superficial type (n = 10)	Infiltrate type (n = 17)	Diffuse type (n = 5)	*P*-value
Pleomorphic adenoma (n = 15)	1	0	9	5	
Warthin's tumor (n = 15)	3	10	2	0	
Basal cell adenoma (n = 2)	0	0	2	0	< 0.001
Oncocytoma (n = 4)	0	0	4	0	
Myoepithelioma (n = 2)	2	0	0	0	

Chi-square test for independence test; $P < 0.001$

Results

Expression of periostin in benign parotid gland tumors

Periostin expression was investigated in 38 samples of benign parotid gland tumors from 36 patients (Table 1). It was present in 32 (84.2%) samples obtained from patients with benign parotid gland tumors. The following four patterns of periostin expression were observed: negative (Fig. 2; A-1, A-2), superficial (Fig. 2; B-1, B-2), infiltrative (Fig. 2; C-1, C-2), and diffuse (Fig. 2; D-1, D-2). In the superficial pattern, periostin was detected only in the subepithelial layers between the basal-type cell and the stromal tissue

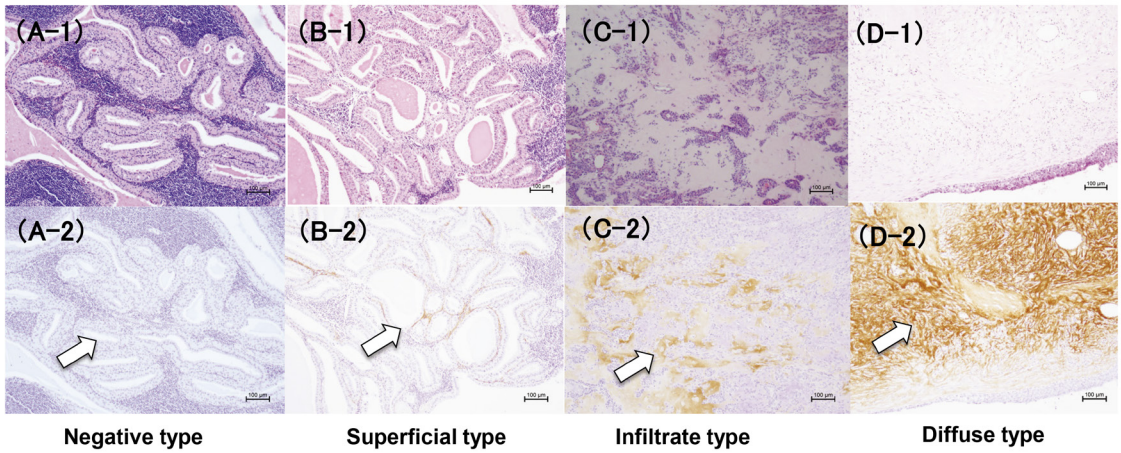

Fig. 2. Immunohistochemical staining for periostin in benign parotid gland tumors.
Immunohistochemical staining was categorized into the following four patterns: negative (n = 6), superficial (n = 10), infiltrative (n = 17), and diffuse (n = 5) (original magnification × 100) . (A-1) A Warthin's tumor was histologically identified by HE staining. (A-2) Immunohistochemical staining for periostin in a Warthin's tumor revealed no periostin, indicating a negative expression pattern (arrow). (B-1) A Warthin's tumor was histologically diagnosed by HE staining. (B-2) Immunohistochemical staining for periostin in a Warthin's tumor showed periostin only in the subepithelial layers between the basal-type cell and the stromal tissue, reflecting a superficial expression pattern (arrow). (C-1) A pleomorphic adenoma was histologically diagnosed by HE staining. (C-2) Immunohistochemical staining for periostin in pleomorphic adenoma showed variable expression in parts of the tumor stroma, indicating an infiltrative expression pattern (arrow). (D-1) A pleomorphic adenoma was histologically diagnosed by HE staining. (D-2) Immunohistochemical staining for periostin in pleomorphic adenoma showed widespread expression throughout the tumor stroma, indicating a diffuse expression pattern (arrow).

Table 2. Periostin expression patterns of the tumor capsules.

	Periostin expression patterns of the tumor capsules		
	Negative type (n = 18)	Positive type (n = 20)	*P*-value
Pleomorphic adenoma (n = 15)	0	15	
Warthin's tumor (n = 15)	12	3	
Basal cell adenoma (n = 2)	2	0	< 0.001
Oncocytoma (n = 4)	4	0	
Myoepithelioma (n = 2)	0	2	

Chi-square test for independence test; $P < 0.001$

(Fig. 2; B-2); in the infiltrative pattern, periostin was observed in parts of the tumor stroma to varying degrees (Fig. 2; C-2); and in the diffuse pattern, periostin was diffusely expressed in the tumor stroma (Fig. 2; D-2). No periostin expression was observed in the normal parotid tissue samples.

Expression of periostin in the capsule of benign parotid gland tumors

The expression of periostin was investigated in the same 38 samples (Table 2), out of which 20 (52.6%) showed increased periostin expression in the tumor capsule. The breakdown of periostin-positive cases of tumor capsules was pleomorphic adenoma in all 15 cases (100%), myoepithelioma in 2 cases (100%), and Warthin's tumor in 3 out of 15 cases (20%). Two distinct patterns of periostin expression were observed in the tumor capsule: positive type (Fig. 3; A-1, A-2, A-3) and negative type (Fig. 3; B-1, B-2, B-3). A significant association was found between the pattern of periostin expression in the tumor capsule and the histology of benign parotid tumors (Table 2).

Expression of periostin, and clinical and histological factors

An association was observed between the periostin expression pattern and the histological types of the benign parotid gland tumors (Table 1). The Warthin's tumor was

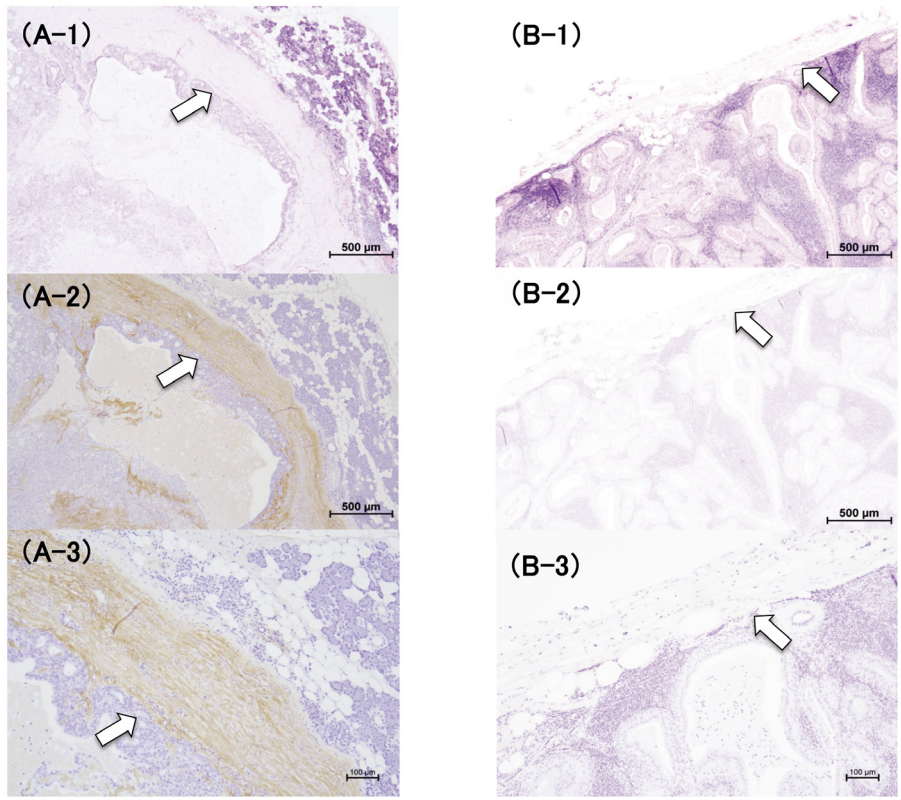

Fig. 3. Immunohistochemical staining patterns of periostin in the capsules of benign parotid gland tumors, categorized into two types: positive (n = 20) and negative (n = 18) (original magnification × 40 and × 100, respectively).
Case A. A 78-year-old Japanese woman presented with a parotid gland tumor. (A-1) Histological analysis identified a pleomorphic adenoma (HE staining). (A-2, A-3) Immunohistochemical staining revealed the presence of periostin in the capsule of the pleomorphic adenoma (arrow). Case B. A 77-year-old Japanese man was evaluated for a parotid gland tumor. (B-1) Histological examination revealed a Warthin's tumor (HE staining). (B-2, B-3) Immunohistochemical staining showed no periostin in the capsule of the tumor (arrow).

Table 3. Clinical characteristics and expression of periostin in 38 samples of benign salivary gland tumors.

		Negative type	Positive type	*P*-value	Superficial type	Infiltrate type	Diffuse type	*P*-value
Total	38	6	32		10	17	5	
Male, n (%)	17 (44.7%)	2 (5.3%)	15 (39.5%)	0.54	8 (21.1%)	6 (15.8%)	1 (8.5%)	0.0338
Female, n (%)	21 (55.3%)	4 (10.5%)	17 (44.7%)		2 (5.3%)	11 (29.0%)	4 (10.5%)	
Mean age ± SD (years)	59.2 ± 14.1	54.0 ± 7.9	60.1 ± 14.9	0.336	66.1 ± 8.4	55.9 ± 16.2	62.6 ± 18.3	0.222
Tumor site								
Superficial lobe, n (%)	27 (71.1%)	5 (13.2%)	22 (57.9%)	0.47	9 (23.7%)	9 (23.7%)	4 (10.5%)	0.165
Deep lobe, n (%)	11 (28.9%)	1 (2.6%)	10 (26.3%)		1 (2.6%)	8 (21.1%)	1 (2.6%)	
Pain, n (%)	1 (2.6%)	1 (2.6%)	0 (0%)	0.0192	0 (0%)	0 (0%)	0 (0%)	1
Mobility								
Good mobility, n (%)	36 (94.7%)	5 (13.2%)	31 (81.6%)	0.172	10 (26.3%)	16 (42.1%)	5 (13.2%)	0.492
No palpable tumor, n (%)	2 (5.3%)	1 (2.6%)	1 (2.6%)	0.173	0 (0%)	1 (2.6%)	0 (0%)	0.492

significantly dominant in the superficial periostin expression pattern (Table 1). Furthermore, a sex-related difference was found between the patterns of periostin expression in parotid gland tumors. Females were significantly more likely than males to exhibit the infiltrative and diffuse patterns of periostin expression (Table 3). Conversely, the superficial pattern was significantly more common in males than in females (Table 3). No association was found

Table 4. Tumor size and expression of periostin in 38 samples of benign salivary gland tumors.

		Negative type	Positive type	*P*-value	Superficial type	Infiltrate type	Diffuse type	*P*-value
Total	38	6	32		10	17	5	
Size (cm)								
Tumor ≦ 2	7 (18.4%)	1 (2.6%)	6 (15.8%)		2 (5.3%)	3 (7.9%)	1 (2.6%)	
2 < Tumor ≦ 4	24 (63.2%)	5 (13.2%)	19 (50%)	$P = 0.235$	5 (13.2%)	11 (28.9%)	3 (7.9%)	$P = 0.862$
Tumor > 4	7 (18.4%)	0 (0%)	7 (18.4%)		3 (7.9%)	3 (7.9%)	1 (2.6%)	

Table 5. Dynamic MRI pattern and expression of periostin in 18 samples of benign salivary gland tumors.

		Negative type	Positive type	*P*-value	Superficial type	Infiltrate type	Diffuse type	*P*-value
Total	18	3	15		4	9	2	
Dynamic MRI pattern								
Persistent pattern, n (%)	6 (33.3%)	1 (5.6%)	5 (27.8%)		1 (5.6%)	3 (16.7%)	1 (5.6%)	
Plateau pattern, n (%)	4 (22.2%)	0 (0%)	4 (22.2%)	0.549	0 (0%)	3 (16.7%)	1 (5.6%)	0.504
Washout pattern, n (%)	8 (44.4%)	2 (11.1%)	6 (33.3%)		3 (16.7%)	3 (16.7%)	0 (0%)	

Table 6. Clinical characteristics and histopathological typing of benign salivary gland tumors.

		Pleomorphic adenoma	Warthin's tumor	Basal cell adenoma	Oncocy toma	Myoepithe lioma	*P*-value
Total	38	15	15	2	4	2	
Male	17 (44.7%)	4 (10.5%)	10 (26.3%)	0 (0%)	2 (5.3%)	1 (2.6%)	0.159
Female	21 (55.3%)	11 (29.0%)	5 (13.2%)	2 (5.3%)	2 (5.3%)	1 (2.6%)	
Mean age ± SD (years)	59.2 ± 14.1	54.1 ± 15.3	65.8 ± 8.68	62.0 ± 9.9	55.5 ± 22.9	51.5 ± 12.0	

between the periostin expression pattern and other clinical characteristics, including the involvement of the superficial and deep lobes (Table 3). Furthermore, no association was found between periostin expression pattern and tumor size (Table 4), or between periostin expression pattern and dynamic MRI pattern (Table 5). Finally, no association was found between clinical characteristics and the histopathological typing of benign salivary gland tumors (Table 6).

Discussion

Periostin was cloned by Takeshita et al. as osf-2, a gene specifically expressed in osteoblasts and similar to midline fasciclin-1, an intercellular adhesion factor of Drosophila melanogaster, and subsequently localized specifically to the outer bone membrane and periodontal ligament. It was later renamed periostin because of its specific localization in the epiphyseal and periodontal ligaments and its involvement in cell adhesion (Takeshita et al. 1993; Horiuchi et al. 1999). Recent studies have reported the expression of periostin not only in the epiphyseal and periodontal ligaments but also in embryogenesis; various pathological conditions such as myocardial infarction, cancer, myelofibrosis, and muscular dystrophy; and in the healing and regeneration-related processes including wound healing and skeletal muscle regeneration (Urasawa et al. 1996; Stanton et al. 2000; Kruzynska-Frejtag et al. 2001; Goetsch et al. 2003; Wang et al. 2003; Katsuragi et al. 2004; Norris et al. 2007; Hamilton 2008; Oku et al. 2008). In otorhinolaryngology, periostin expression has been reported in chronic sinusitis, vocal folds polyps, IgG4-related diseases, organized hematoma, and eosinophilic otitis media (Ohta et al. 2013, 2014; Tateda et al. 2022, 2023; Sato et al. 2023). Studies on tumors and periostin have reported periostin overexpression in thymoma and non-small-cell lung cancer (Sasaki et al. 2001a, b). Subsequently, it has been reported in ovarian cancer, neuroblastoma, breast cancer, colorectal cancer, bladder cancer, squamous cell carcinoma of the head and neck, pancreatic cancer, thyroid cancer, and other cancer types, highlighting a close relationship between periostin expression and malignant transformation and progression of cancer, including invasion, metastasis, and prognosis (Sasaki et al. 2001a, b, 2002, 2003; Gillan et al. 2002; Bao et al. 2004; Kudo et al. 2006; Fukushima et al. 2008; Puppin et al. 2008; Kim et al. 2011; Li et al. 2015; Ratajczak-Wielgomas et al. 2017; Kujawa et al. 2020; Yue et al. 2021). To the best of our knowledge, no studies have

reported on the role of periostin in parotid tumors.

Benign parotid tumors are classified into 11 types according to the 2017 WHO classification. The current study included five types of benign parotid tumors: pleomorphic adenoma, Warthin's tumor, basal cell adenoma, oncocytoma, and myoepithelioma. In the four histological types (pleomorphic adenoma, Warthin's tumor, basal cell adenoma, and oncocytoma) analyzed in the present study, various levels and patterns of periostin expression were observed in the stroma of the tumors. In a previous study, Tateda et al. (2022, 2023) reported that periostin was overexpressed in vocal fold polyps, which are non-neoplastic lesions of the larynx. In these polyps, periostin expression was found in the interstitial spaces, and the pattern of expression was classified into four types: negative, superficial, infiltrate, and diffuse (Tateda et al. 2022, 2023).

Based on these findings, we investigated the expression pattern of periostin in benign parotid tumors in this study. None of the parotid tumors included in this study showed periostin expression in the epithelium.

The four histological types and the expression patterns of periostin were examined in this study. In cases of pleomorphic adenoma, periostin exhibited the following expression patterns: negative in one case, infiltrate in nine cases, and diffuse in five cases. High expression of periostin was noted in spindle-shaped cells and areas of fibrosis in the stroma. In Warthin's tumor, periostin expression was categorized as follows: negative in three cases, superficial in ten cases, and infiltrative in two cases. In the superficial type, the most common periostin phenotype in Warthin's tumors, periostin was detected only in the subepithelial layer between basal-type cells and the stromal tissue. The superficial pattern was consistently observed in all 10 cases within Warthin's tumors, marking it as a characteristic finding. The rates of recurrence and malignant transformation for this tumor are low. In all cases of basal cell adenoma, periostin expression was of the infiltrative type, with high expression observed in spindle-shaped cells and the fibrotic stroma. In all four cases of oncocytoma, periostin expression was of the infiltrative type, with high expression observed in spindle-shaped cells and stromal fibrosis. In myoepithelioma cases, periostin expression was negative. Previous studies have reported the expression of periostin in the fibrous stroma of invasive carcinomas and the fibrous capsules found in tumors (Shimazaki and Kudo 2008).

Among benign parotid tumors, pleomorphic adenomas are clinically characterized by the possibility of recurrence; hence, enucleation is not the surgical technique of choice. Instead, partial lobectomy is preferred, which involves excision of the tumor along with the normal parotid gland. Most tumors have a low risk of recurrence if surgical margins are negative, with postoperative recurrence rates of approximately 7%. However, this is not the case for tumors that extend histologically outside the capsule in a finger-like or pseudopodial pattern. In addition, about 6% of polymorphous adenomas develop into cancer. In our study, out of the 15 cases of pleomorphic adenoma, 14 exhibited periostin expression of infiltrative or diffuse type. Conversely, in Warthin's tumors, which do not recur frequently, 13 of the 15 cases were of the negative or superficial type in terms of periostin expression. The only significant factor was the sex (Table 3). We think that it simply means the difference in material number of pleomorphic adenoma and Warthin's tumor.

In terms of parotid tumor capsules, pathological examinations revealed that pleomorphic adenoma, Warthin's tumor, basal cell adenoma, oncocytoma, and myoepithelioma showed capsules. Among these, pleomorphic adenoma was found to be carcinomatous in about 6% of cases, and myoepithelioma was reported to be malignant in a few cases. The capsules of pleomorphic adenoma and myoepithelioma, which have been reported to be potentially carcinomatous, were positive for periostin expression in all cases. Significant differences were observed between the histological types of benign parotid tumors and the expression pattern of periostin. For the tumor capsule, significant differences were observed between the histological type of benign parotid tumor and the presence or absence of periostin expression in the tumor capsule. This suggests a possible association between pleomorphic adenoma, and increased expression and localization of periostin and the possibility of recurrence. Our study has several limitations. First, the number of patients with salivary gland tumors recruited in this study was relatively small because the samples were collected from only a single center. Second, we should investigate the relationship between benign salivary gland tumors and malignant salivary gland tumors to ascertain differences in periostin expression between benign salivary gland tumors and malignant salivary gland tumors, which were not investigated in this study. Further research with many more samples is required to reveal the mechanism of expression of periostin in salivary gland tumors. Third, the relationship between periostin expression and benign salivary gland tumors growth was not investigated in this study. In conclusion, our results indicate that overexpression of periostin is likely involved in the pathogenesis of benign parotid tumors. We propose that periostin could serve as a novel biomarker for these tumors and might offer a new avenue for therapeutic intervention.

In conclusion, our results indicate that overexpression of periostin is likely involved in the pathogenesis of benign salivary gland tumors. Based on these findings, periostin emerges as a potential novel biomarker and therapeutic target for these tumors.

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Conflict of Interest

The authors declare no conflict of interest.

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