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ORIGINAL ARTICLE

Periostin and fibronectin in nasal lesions: key players in polyps and inverted papillomas

Periostina y fibronectina en lesiones nasales: elementos clave en pólipos y papilomas invertidos

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Abstract

Background

Sinonasal lesions are common benign masses with overlapping clinical and histopathological features. Extracellular matrix proteins such as periostin, fibronectin, and tenascin-C play key roles in tissue remodeling and inflammation, yet their distinct expression profiles in these lesions remain poorly defined.

Aim

This study aimed to compare the immunohistochemical staining patterns of periostin, fibronectin, and tenascin-C in sinonasal lesions to elucidate their roles in pathogenesis and enhance differential diagnosis.

Methods

In this retrospective study, pathological specimens from 70 patients who underwent surgery for sinonasal polyps were analyzed. Immunohistochemical expression of periostin, fibronectin, and tenascin-C was assessed separately in epithelial and stromal compartments using a semi-quantitative scoring system. Associations between staining patterns and lesion types were evaluated using multinomial logistic regression.

Results

The cohort had a male-to-female ratio of 5:2 with a mean age of approximately 40 years. Nasal polyps demonstrated significantly higher stromal periostin staining compared to both antrochoanal polyps and inverted papillomas. Conversely, antrochoanal polyps exhibited significantly elevated epithelial periostin expression relative to inverted papillomas. Fibronectin expression was markedly increased in nasal polyps, especially in the stroma, supporting its role in inflammatory tissue remodeling. Tenascin-C expression did not differ significantly among the lesion types.

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Conclusions

Differential expression of periostin and fibronectin suggests distinct pathogenic mechanisms in sinonasal lesions. The compartment-specific staining patterns of periostin, along with the prominent fibronectin expression in nasal polyps, suggest these biomarkers could serve as valuable diagnostic tools and potential therapeutic targets. Further research is needed to explore these pathways in sinonasal disease management.

Resumen

Antecedentes

Las lesiones sinonasales son masas benignas comunes con características clínicas e histopatológicas superpuestas. Las proteínas de la matriz extracelular periostina, fibronectina y tenascina-C actuan en la remodelación de los tejidos y la inflamación, pero sus perfiles de expresión en estas lesiones siguen estando poco definidos.

Objetivo

Comparar los patrones inmunohistoquímicos de periostina, fibronectina y tenascina-C en lesiones sinonasales para dilucidar su papel en la patogénesis y mejorar el diagnóstico diferencial.

Métodos

En este estudio retrospectivo se analizaron muestras patológicas de 70 pacientes intervenidos quirúrgicamente de pólipos nasales. La expresión inmunohistoquímica de periostina, fibronectina y tenascina-C se evaluó por separado en los compartimentos epitelial y estromal mediante un sistema de puntuación semicuantitativo. Las asociaciones entre los patrones de tinción y los tipos de lesiones se evaluaron mediante regresión logística multinomial.

Resultados

La proporción hombre-mujer fue de 5:2 con edad media aproximadamente 40 años. Los pólipos nasales mostraron una tinción de periostina estromal significativamente mayor que los antrocoanales y los invertidos. Por el contrario, los antrocoanales mostraron una expresión de periostina epitelial más elevada que los papilomas invertidos. La expresión de fibronectina aumentó notablemente en los pólipos nasales, sobre todo en el estroma, lo que refuerza su papel en la remodelación del tejido inflamatorio. La tenascina-C no mostró diferencias significativas entre los tipos de lesión.

Conclusiones

La expresión diferencial de periostina y fibronectina sugiere distintos mecanismos patogénicos en las lesiones nasosinusales. Los patrones de tinción específicos del compartimento de la periostina, junto con la prominente expresión de fibronectina en los pólipos nasales, sugieren que estos biomarcadores podrían servir como herramientas de diagnóstico y posibles dianas terapéuticas. Se necesita más investigación para explorar estas vías en el tratamiento de la enfermedad nasosinal

Remark

1) Why was this study conducted?

This study was conducted to evaluate the expression patterns of periostin, fibronectin, and tenascin-C in sinonasal lesions. The goal was to better understand their roles in pathogenesis and improve differential diagnosis.

2) What were the most relevant results of the study?

Nasal polyps showed significantly higher stromal periostin and fibronectin expression compared to other lesion types. Tenascin-C expression did not show significant differences among the groups.

3) What do these results contribute?

These results highlight the potential of periostin and fibronectin as diagnostic biomarkers and therapeutic targets in differentiating sinonasal lesions.

Introduction

Sinonasal polyps, including antrochoanal polyps, nasal polyps, and inverted papillomas, represent the majority of benign masses affecting the nasal cavity [1]. Nasal polyps account for more than half of sinonasal masses. Their exact etiology remains multifactorial, often linked to chronic mucosal edema and typically present bilaterally [2]. Histopathologically, they present with epithelial injury, goblet cell metaplasia, a thickened basement membrane, and sometimes edematous fibro-inflammatory tissues [3]. Antrochoanal polyps are benign lesions that originate from the antrum of the maxillary sinus and extend to the choana, and are usually seen in children and young adults. Except for a minor part, they are mostly unilateral [4]. Histopathologically, they may include edema, inflammation, and squamous metaplasia [5]. Although inverted papilloma is a benign sinonasal lesion of ambiguous etiology, diagnosis and treatment are crucial because of its high recurrence rate and potential for carcinoma development [6].

Inverted papillomas and antrochoanal polyps are frequently unilateral, increasing the risk of misdiagnosis, particularly in endoscopic evaluations. Conversely, nasal polyps, typically bilateral, may mimic these lesions in endoscopic imaging, complicating accurate identification. Furthermore, differentiating nasal polyps from antrochoanal polyps can be challenging based on histopathological analysis alone. Clinical information, such as the laterality of the lesion-bilateral suggesting nasal polyps and unilateral favoring antrochoanal polyps-can be critical for guiding the pathologist in achieving an accurate diagnosis. Therefore, differentiating them is crucial for appropriate clinical management and prognostic assessment.

Emerging evidence suggests that extracellular matrix proteins, particularly periostin, fibronectin, and tenascin-C, play pivotal roles in tissue remodeling, fibrosis, and inflammation, all of which are central to the pathogenesis of sinonasal lesions. Periostin, a matricellular protein, involved in tissue growth and remodelling by interacting with integrins on the cell surface [7]. Fibronectin is a large dimer glycoprotein found in all tissues and required in many different cell-matrix interactions. Tenascin-C is an extracellular matrix protein, regulating cell migration and proliferation, especially in inflammatory conditions [8].

Despite their potential significance, comparative analyses of these markers across different sinonasal lesions are limited. This study aims to fill this gap by evaluating the immunohistochemical staining patterns of periostin, fibronectin, and tenascin-C in antrochoanal polyps, nasal polyps, and inverted papillomas. Understanding these molecular differences could enhance diagnostic precision and uncover novel therapeutic targets.

Materials and Methods

This retrospective study included 70 patients who underwent functional endoscopic sinus surgery for one of three diagnoses (antrochoanal polyp, inverted papilloma, or nasal polyp) between January 2015 and December 2018 at the Recep Tayyip Erdogan University Faculty of Medicine, Departmant of Otorhinolaryngology. Preoperatively, all patients were evaluated via endoscopic examination and paranasal sinus computed tomography. In cases where necessary, a biopsy was performed to confirm the diagnosis, while in others the diagnosis was made on the basis of clinical evaluation.

Tissue samples obtained from patients with antrochoanal polyp, nasal polyp and inverted papilloma, were fixed in 10% neutral-buffered formalin for 24 hours. Subsequently, tissues were embedded in paraffin blocks after tissue tracking with the Leica ASP300S automatic tissue tracking device. Finally, sections covered with Lysine at 4 µm thickness were taken with a Thermo Scientific sectioning machine. The immunohistochemical staining rates of fibronectin polyclonal antibodies (PAA037Hu01), periostin polyclonal antibodies (PAH339Hu01), and tenascin-C polyclonal antibodies (PAB975Hu01) were evaluated by an automated immunohistochemistry device (Ventana Medical System, SN:714592, Ref: 750- 700 Arizona, USA).

After the samples were available immunohistochemically with periostin, fibronectin, and tenascin-C dyes, they were evaluated by the same pathologist under an Olympus BX51 light microscope. In staining scoring, the rates of epithelial and stromal staining were separately assessed, and a semi-quantitative scoring system was used, ranging from 0 to 3 in the epithelium and 0 to 4 in the stroma. The expression of periostin, tenascin C, and fibronectin in the stromal tissue was analyzed using a 5-point scale, previously described method [9,10]. The scoring for stromal staining was as follows:

- 0: No detectable staining
- 1: Focal staining
- 2: Diffuse staining present in less than half of the stromal area
- 3: Expression in more than half but not in all parts of the tumor stroma
- 4: Expression extending throughout the stroma

Additionally, the intensity of epithelial staining was evaluated using a 4-point scale:

- 0: Negative
- 1: Weak
- 2: Moderate
- 3: Strong

The proportion of stained epithelial cells was also recorded in 10% intervals, ranging from 0% to 100%. This scoring system was used to quantify and characterize the expression patterns of the markers in both the tumor stroma and epithelial tissues, ensuring consistency and reproducibility in the evaluation of histopathological features.

The primary outcome is the differential expression patterns of periostin, fibronectin, and tenascin-C in antrochoanal polyps, nasal polyps, and inverted papillomas. Secondary outcome is the demographic distribution (age and gender) and their influence on polyp types.

Statistical analyzes were performed using IBM SPSS Statistics, Version 22.0 (SPSS Inc., Chicago, USA) and R version 4.4.0 (R Foundation for Statistical Computing, Vienna, Austria). Age was summarized as median and range and analyzed using One-way Kruskal-Wallis analysis with Bonferroni correction. Categorical variables (gender and staining scores) were expressed as frequencies and percentages, and analyzed using chi-square test. Bonferroni correction was applied to account for multiple comparisons.

A multinomial logistic regression model was constructed to evaluate the association between predictor variables and the diagnosis outcome (nnet version 7.3.19, multinom function). The reference category was set as antrochoanal polyp.

Initially, all variables with biological relevance were retained for the multivariate model. Parameters were eliminated stepwise according to multicollinearity check at each step (car version 3.1.2, vif function). Coefficients, standard errors, and z-values were extracted, and p-values were calculated. Model fit was assessed using the Akaike Information Criterion (AIC). The model's classification performance was evaluated using a confusion matrix to determine prediction accuracy. Odds Ratios (OR) with 95% Confidence Intervals (CI) were calculated by exponentiating the model coefficients. All statistical tests were two-tailed, and a p-value < 0.05 was considered statistically significant.

Ethical considerations

The study was conducted in accordance with the ethical standards stated in the 'Declaration of Helsinki', and was approved by the local ethics committee (protocol number: No: 2021/40. All included patients were provided with detailed information about the aims and methods of the study and signed informed consent forms

Results

Data from 70 patients were analyzed. Patient characteristics are given in Table 1.

The distribution of staining scores are given in Table 2. Although the stroma staining scores were graded from 0 to 4, no specimens received a score of 4 in this study. Thus, the observed scores ranged from 0 to 3 (Figures 1-8).

The regression model had low residual deviance (64.5) and an AIC of 100.5, which indicate an acceptable model fit, suggesting the model explains a substantial portion of the variability in diagnosis outcomes. The regression coefficients, p-values, and significance of each predictor variable for distinguishing between sinonasal diagnoses are given in Table 3.

In the comparison between inverted papilloma and antrochoanal polyp, age was a significant predictor. Each additional year of age increased the odds of having an inverted papilloma by 34% (OR= 1.34, p= 0.00064). Higher epithelial periostin levels were associated with significantly reduced odds of inverted papilloma (OR= 0.012, p= 0.0026), while higher stromal periostin levels significantly increased the odds (OR= 15.64, p= 0.0127). Although male gender was associated with higher odds, this relationship was marginally non-significant (p= 0.056). Fibronectin levels, both in the epithelium and stroma, showed positive trends but did not reach statistical significance (p >0.05).

For nasal polyp versus antrochoanal polyp, male gender was a significant predictor, increasing the odds by approximately 59-fold (OR= 59.47, p= 0.024). Age was also a significant factor,

Table 1. Patient characteristics. Results are given as Median (IQR) or n (%).

Parameter	Antrochoanal polyp (n= 26)	Inverted papilloma (n= 20)	Nasal polyp (n= 24)	p-value
Age, years	25 (19-30)	54 (40-57)	46 (33-56)	<0.001†
Gender, n (%)				0.4 ‡
Male	16 (62)	15 (75)	19 (79)	
Female	10 (38)	5 (25)	5 (21)	
Laterality, n (%)				<0.001‡
Left	13 (50)	10 (50)	-	
Right	13 (50)	10 (50)	-	
Bilateral	-	-	24 (100)	
Recurrence, n (%)	4 (15)	14 (70)	7 (29)	<0.001‡
Smoking	10 (38)	13 (65)	16 (67)	0.082‡

† Kruskal-Wallis rank sum test; ‡ Pearson's Chi-squared test

Table 2. Distribution of histopathological staining scores for periostin, fibronectin, and tenascin-C in sinonasal lesions

Diagnosis	Molecule	Site	Score 0 (No)	Score 1 (+)	Score 2 (++)	Score 3 (+++)	p-value
Antrochoanal polyp	Fibronectin	Epithelial	24 (92%)	2 (8%)	-	-	0.107
		Stromal	6 (23%)	18 (69%)	2 (8%)	-	1
	Periostin	Epithelial	1 (3%)	2 (8%)	15 (58%)	8 (31%)	0.044
		Stromal	-	1 (3%)	3 (12%)	15 (58%)	0.097
	Tenascin-C	Epithelial	7 (27%)	16 (62%)	3 (11%)	-	0.066
		Stromal	-	14 (54%)	10 (38%)	2 (8%)	0.271
Inverted papilloma	Fibronectin	Epithelial	13 (62%)	8 (38%)	-	-	0.107
		Stromal	4 (19%)	15 (71%)	2 (10%)	-	1
	Periostin	Epithelial	2 (10%)	8 (38%)	8 (38%)	3 (16%)	0.097
		Stromal	-	1 (5%)	5 (24%)	7 (33%)	0.044
	Tenascin-C	Epithelial	4 (19%)	12 (57%)	5 (24%)	-	0.066
		Stromal	-	10 (48%)	10 (48%)	1 (4%)	0.271
Nasal polyp	Fibronectin	Epithelial	8 (35%)	14 (61%)	1 (4%)	-	1
		Stromal	-	16 (70%)	6 (26%)	1 (4%)	0.107
	Periostin	Epithelial	-	7 (30%)	13 (56%)	3 (13%)	0.096
		Stromal	-	-	-	8 (39%)	0.044
	Tenascin-C	Epithelial	-	20 (87%)	3 (13%)	-	0.066
		Stromal	-	6 (26%)	13 (56%)	4 (17%)	0.271

with each additional year increasing the odds by 26% (OR= 1.26, p= 0.0022). Higher epithelial periostin levels significantly reduced the odds (OR= 0.034, p= 0.014), while higher stromal periostin levels significantly increased the odds (OR= 41.28, p= 0.0018). Fibronectin levels in both compartments demonstrated significant positive associations (p <0.05). In contrast, tenascin-C levels (both epithelial and stromal) did not show any significant association with the diagnosis (p >0.05).

In summary, age was a consistent predictor, with older age being associated with increased odds of both inverted papilloma and nasal polyp. Additionally, male gender was significantly associated with nasal polyps.

The classification accuracy of the multinomial logistic regression model in predicting sinonasal diagnoses are given in Table 4. The confusion matrix compares predicted versus actual outcomes, providing insight into the model's ability to correctly classify each diagnosis type. An overall accuracy of 81.4% was achieved, with most misclassifications occurring between inverted papilloma and nasal polyp.

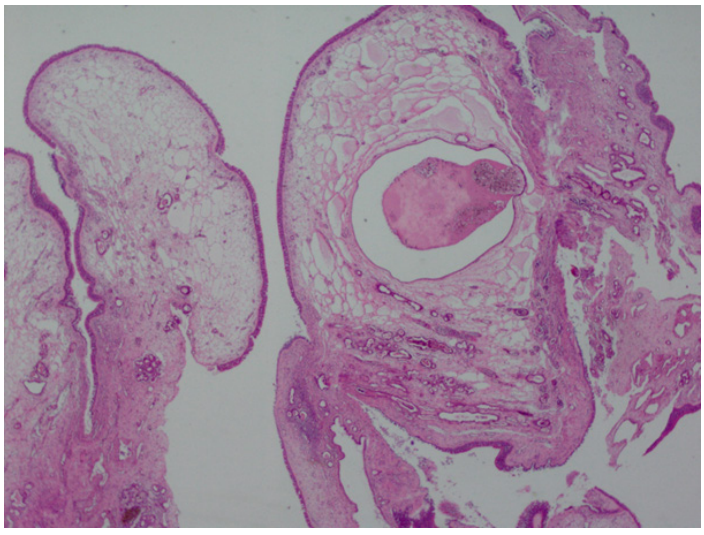

Figure 1. Representative histological image of a nasal polyp case stained with Hematoxylin & Eosin (H&E) at ×20 magnification, showing the characteristic epithelial and stromal features of the lesion

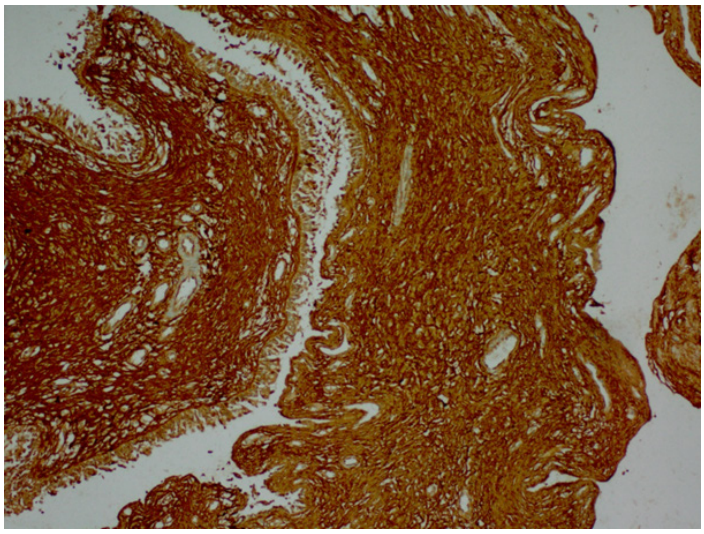

Figure 2. Immunohistochemical staining for periostin in a nasal polyp case at ×100 magnification. Stromal staining score: 4, indicating strong expression in the extracellular matrix. Epithelial staining score: 3, demonstrating moderate to strong periostin expression in the epithelium.

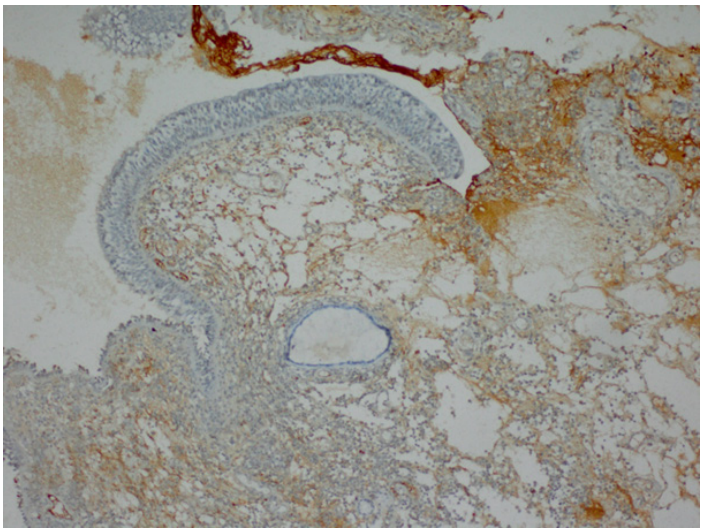

Figure 3. Immunohistochemical staining for fibronectin in a nasal polyp case at ×100 magnification. Stromal staining score: 2, showing mild to moderate expression in the stromal component. Epithelial staining score: 0, indicating an absence of fibronectin expression in the epithelial layer.

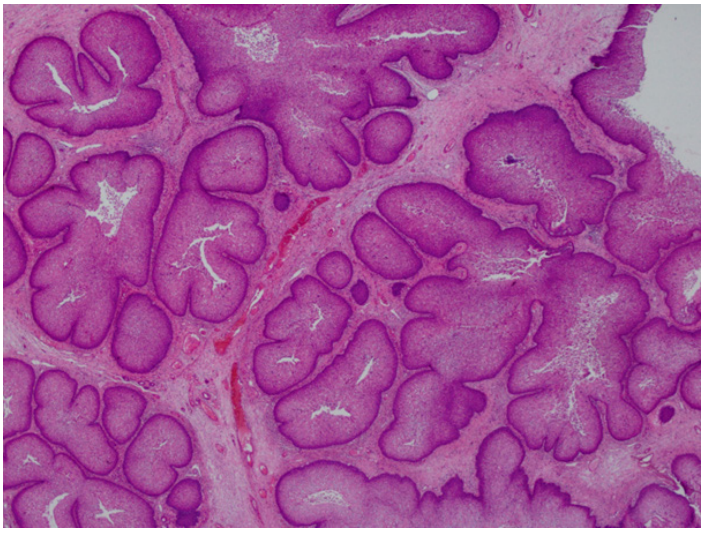

Figure 4. Representative histological image of an inverted papilloma case stained with Hematoxylin & Eosin (H&E) at ×20 magnification, demonstrating the characteristic endophytic growth pattern.

Discussion

This study provides novel insights into the immunohistochemical staining patterns of periostin, fibronectin, and tenascin-C across antrochoanal polyps, nasal polyps, and inverted papillomas. The findings contribute to a better understanding of their differential diagnosis, addressing a key gap in the current literature. Notably, antrochoanal polyps have been described as closely resembling maxillary sinus cysts, with some researchers proposing they are nasal extensions of these cysts. While protein ratios in aspiration samples have shown no differences between these entities [11], the hypothesis that obstruction of acinar mucous glands contributes to antrochoanal polyp formation remains inconclusive [12,13]. Understanding such nuances adds depth to the etiological framework of these lesions.

Periostin emerged as the most diagnostically significant marker. Stromal periostin staining was significantly higher in nasal polyps, consistent with previous studies linking periostin to tissue remodeling in chronic inflammation. Wang et al. revealed that tissue periostin is remarkably overexpressed in patients with nasal polyps than in chronic rhinosinusitis without nasal polyps and normal nasal mucosa, with tissue periostin level correlating with IL-5, a cytokine central to eosinophillic inflammation. Additionally, serum periostin levels have been found to be significantly higher in patients with rhinosinusitis with nasal polyps compared to both healthy volunteers and patients with rhinosinusitis without polyps [7], further supporting periostin's association with inflammatory polyp formation. However, Wang et al found no correlation between serum periostin levels and nasal polyps, emphasizing the importance of tissue-level evaluation-a methodological approach adopted in our study to ensure precise histopathological insights [14].

In contrast, epithelial periostin levels were notably elevated in antrochoanal polyps but significantly lower in inverted papillomas. This differential staining pattern suggests distinct roles for periostin in polyp formation and progression. Notably, the lower periostin levels in inverted papillomas may reflect downregulation in tumorigenesis, raising questions about its potential role in malignant transformation. Moreover, inverted papillomas are known to present with inflammatory processes that can complicate diagnosis, sometimes leading to false-negative histopathological results (6). In such cases, periostin staining features-especially when considering both epithelial and stromal patterns-may offer critical diagnostic clarity. These findings align with studies highlighting periostin's association with inflammation and fibrosis but extend current knowledge by distinguishing stromal versus epithelial expression-a methodological detail often overlooked in previous research.

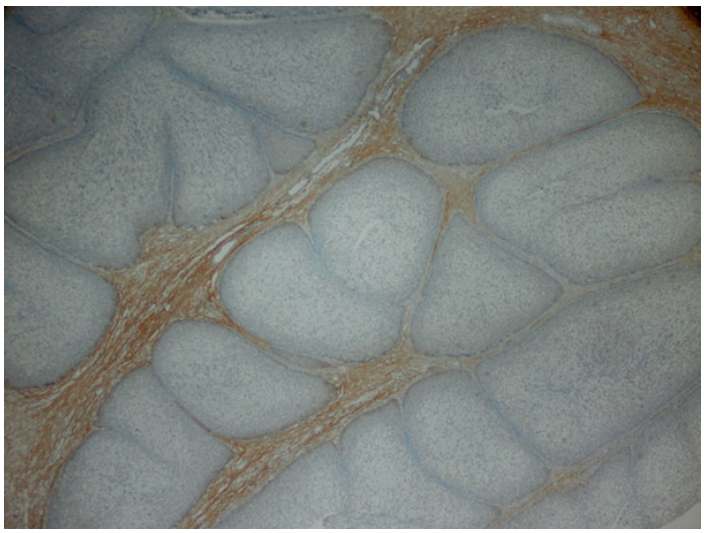

Figure 5. Immunohistochemical staining for tenascin in an inverted papilloma case at ×40 magnification. Stromal staining score: 3, indicating moderate expression in the stroma. Epithelial staining score: 0, suggesting no detectable tenascin expression in the epithelial component.

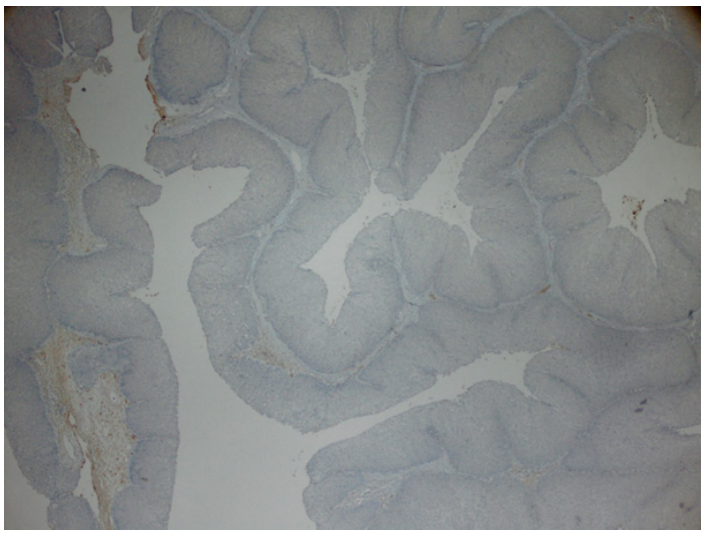

Figure 6. Immunohistochemical staining for fibronectin in an inverted papilloma case at ×40 magnification. Stromal staining score: 1, reflecting weak expression in the stroma. Epithelial staining score: 0, demonstrating no fibronectin expression in the epithelial component.

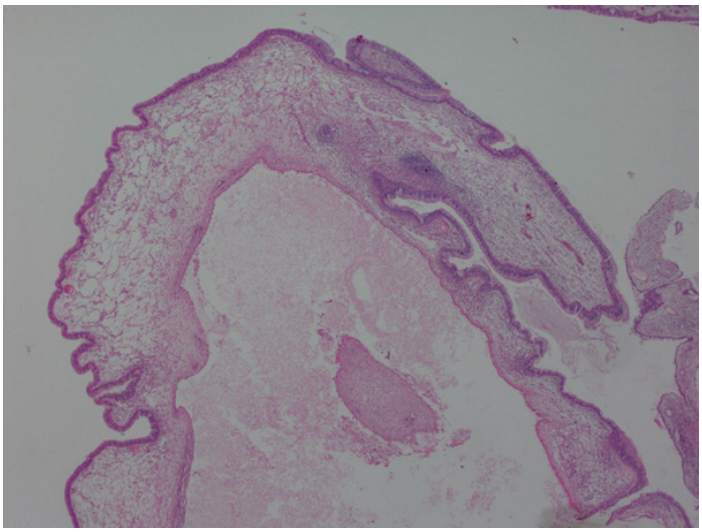

Figure 7. Representative histological image of an antrochoanal polyp case stained with Hematoxylin & Eosin (H&E) at ×20 magnification, displaying polypoid architecture with inflammatory infiltration.

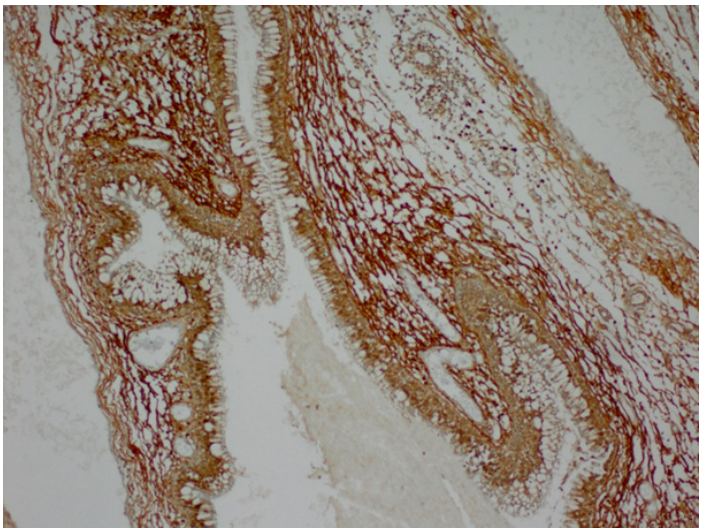

Figure 8. Immunohistochemical staining for periostin in an antrochoanal polyp case at ×100 magnification. Stromal staining score: 3, indicating moderate expression in the stromal compartment. Epithelial staining score: 2, showing mild to moderate periostin expression in the epithelial layer.

While earlier research, such as that by Stankovic et al., demonstrated upregulated periostin in nasal polyp tissues [15], these studies did not differentiate between stromal and epithelial compartments. Our findings emphasize this novel compartmental analysis, suggesting that periostin's distinct expression profiles could serve as a more precise diagnostic marker. Moreover, although earlier studies often focused on serum periostin levels, we prioritized tissue-level analysis to minimize confounding factors and provide more direct histopathological insights. This approach enhances the accuracy of differentiating between sinonasal lesions, particularly in distinguishing inverted papillomas, where histological ambiguity can lead to diagnostic challenges.

Our findings are further supported by Danielides et al., who evaluated periostin levels in various unilateral benign lesions. They reported no significant differences in tissue POSTN mRNA, protein, or serum levels in inverted papillomas compared to controls, while choanal

Table 3. Regression Coefficients and Significance (Reference Group: Antrochoanal Polyp)

	Inverted Papilloma		Nasal Polyp	
Predictor	**Coefficient**	**p-value**	**Coefficient**	**p-value**
Intercept	-15.49	0.0047	-23.44	0.00027
Male gender	3.58	0.0560	4.08	0.0240
Age	0.29	0.00064	0.23	0.0022
Periostin (Epitel)	-4.46	0.0026	-3.36	0.0140
Periostin (Stroma)	2.75	0.0127	3.72	0.0018
Fibronectin (Epitel)	2.84	0.0820	3.64	0.0170
Fibronectin (Stroma)	2.78	0.0830	4.89	0.0052
Tenascin-C (Epitel)	-0.10	0.9310	-0.19	0.8860
Tenascin-C (Stroma)	-1.63	0.0680	-0.089	0.9020

Table 4. Model Performance (Confusion Matrix)

Predicted	**Antrochoanal Polyp**	**Inverted Papilloma**	**Nasal Polyp**
Antrochoanal Polyp	24	2	2
Inverted Papilloma	1	15	3
Nasal Polyp	1	3	19

polyps exhibited increased tissue POSTN protein expression [16]. These results align with our observation of distinct epithelial and stromal periostin patterns among inverted papillomas, antrochoanal polyps, and nasal polyps, underscoring the heterogeneous nature of these lesions and the need for further focused research on periostin in these contexts.

Fibronectin staining also revealed valuable diagnostic insights. Its expression was significantly higher in nasal polyps, supporting its established role in inflammatory remodeling processes. Notably, angiogenesis has been reported to play a critical role in the development of both nasal polyps and antrochoanal polyps, with higher levels observed in nasal polyps [17]. This angiogenic activity could explain the elevated fibronectin expression in nasal polyps, as fibronectin is integral to angiogenesis and tissue remodeling. In a study by Feng et al., fibronectin expression was observed to be higher in non-eosinophilic nasal polyps compared to eosinophilic polyps, leading the authors to propose an inverse relationship between eosinophil counts and fibronectin levels [18]. Although our study did not stratify nasal polyps based on eosinophilic versus non-eosinophilic inflammation, our findings of significant differences in epithelial and stromal staining between nasal polyps and antrochoanal polyps are consistent with the general association between fibronectin expression and inflammatory phenotypes in nasal polyps. However, due to differences in study design and subgroup classification, direct comparisons remain limited, underscoring the need for further research in this area.

However, fibronectin did not significantly differentiate inverted papillomas, indicating that while it may serve as a marker for inflammatory lesions like nasal polyps, its role in distinguishing complex lesions like inverted papillomas may be limited. Interestingly, earlier studies have demonstrated increased fibronectin levels in inverted papilloma-associated carcinomas but not in benign lesions, indicating that fibronectin's diagnostic utility may be stage-dependent [19].

Interestingly, tenascin-C expression did not differ significantly across the three lesion types. Although some studies reported elevated tenascin-C in nasal polyps, our results suggest that tenascin-C may play a baseline role in extracellular matrix stability rather than serving as a differential marker. Its consistent expression across lesion types highlights its limited diagnostic value but suggests it may contribute to maintaining structural integrity in sinonasal tissues.

The interplay between periostin, fibronectin, and tenascin-C also warrants attention. Previous studies indicate that these molecules interact directly through specific binding domains. Periostin's emilin-like and fasciclin 1 regions serve as binding sites for fibronectin and tenascin-C, respectively, suggesting a coordinated role in tissue remodeling and inflammatory responses. Interestingly, both fibronectin and tenascin-c levels were found to be significantly elevated in nasal polyps compared to healthy nasal mucosa [8]. Understanding these molecular interactions, particularly periostin's binding with fibronectin and tenascin-C through its

emilin-like and fasciclin 1 domains, could open avenues for developing novel therapeutic strategies targeting extracellular matrix dynamics in sinonasal lesions [20,21]. Similarly, in another study, tenascin-c expression was notably higher in nasal polyps but was either absent or minimal in conchal control tissues, urther supporting their involvement in inflammatory tissue remodeling [19]. This simultaneous elevation of fibronectin and tenascin-C in nasal polyps underscores the biological plausibility of their interaction with periostin in driving disease pathology. Understanding these molecular interactions could open avenues for developing novel therapeutic strategies targeting extracellular matrix dynamics in sinonasal lesions.

Collectively, our findings support periostin as the most promising marker for distinguishing between sinonasal lesions, particularly given its distinct epithelial and stromal staining patterns. Fibronectin also shows potential for identifying nasal polyps but appears less informative for inverted papillomas. Tenascin-C, by contrast, does not offer significant differentiation.

Morphologically, submucosal fibrosis, few mucous glands, mucosal epithelial hyperplasia, inflammatory cell infiltration particularly composed of eosinophils, neovascularization, and prominent edema are observed in nasal polyps [22].

Our findings suggest that periostin, particularly when evaluated in both epithelial and stromal compartments, holds the most promise for distinguishing between these sinonasal lesions. Fibronectin may also aid in identifying nasal polyps, while tenascin-C appears less useful for differentiation.

This study has several limitations. First, the relatively small sample size may limit the generalizability of the findings. Second, the absence of a control group with normal nasal mucosa restricts direct comparisons with healthy tissue. Third, the study did not assess correlations between staining patterns and clinical outcomes, such as polyp recurrence or malignant transformation. Additionally, nasal polyps and inverted papillomas were not categorized based on severity or staging, factors that may influence biomarker expression. Lastly, cases of squamous cell carcinoma arising from inverted papillomas were not included, which could have provided further insights into periostin and fibronectin alterations during malignant progression.

Conclusion

Our findings suggest that periostin and fibronectin may play distinct roles in the pathogenesis of antrochoanal polyps, nasal polyps, and inverted papillomas. The differential staining patterns of periostin, particularly between stromal and epithelial compartments, highlight its potential utility in distinguishing these pathologies. Notably, the significantly lower periostin levels in inverted papillomas raise important questions regarding its role in tumor biology and malignant transformation. Understanding these molecular differences could enhance diagnostic precision and potentially uncover novel therapeutic targets. Future research should focus on elucidating periostin-related signaling pathways and its interactions with other extracellular matrix proteins to contribute to the development of targeted strategies for sinonasal diseases.

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