

Mechanisms of Lymphoid Tissue Regeneration in the Palatine Tonsils

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Abstract: The palatine tonsils represent an essential component of the mucosa-associated lymphoid tissue (MALT) and play a crucial role in local and systemic immune responses. Chronic inflammation, recurrent tonsillitis, and environmental factors can disrupt lymphoid architecture, triggering compensatory regeneration processes. This study investigates the morphological, immunological, and molecular mechanisms underlying lymphoid regeneration in palatine tonsils, with a focus on germinal centre reorganisation, stromal cell activation, cytokine regulation, and lymphocyte proliferation. A clinical and immunohistochemical analysis was conducted on 92 participants, including 62 patients with chronic tonsillar pathology and 30 healthy controls. Results revealed significant alterations in follicular activity, cytokine expression (IL-6, TNF- α , IL-10), and stromal microenvironmental dynamics, supporting the existence of multi-level regenerative mechanisms. These findings contribute to the understanding of tonsillar homeostasis and may enhance therapeutic strategies for chronic adenotonsillar disorders.

Keywords: palatine tonsils; lymphoid regeneration; germinal centres; cytokines; MALT; immunohistochemistry; chronic tonsillitis.

Introduction. Palatine tonsil diseases remain highly prevalent worldwide. According to recent epidemiological data, up to 30–45% of school-aged children experience recurrent tonsillitis annually, and approximately 12–15% of adults present with chronic tonsillar disorders requiring medical evaluation [1]. Tonsillar hypertrophy accounts for nearly 25% of obstructive upper airway symptoms in paediatric patients [2], highlighting the clinical importance of understanding tonsillar immunobiology.

The palatine tonsils form part of Waldeyer's ring, functioning as a frontline defence against inhaled and ingested pathogens. They contain germinal centres, high endothelial venules, follicular dendritic cells, and reticular epithelial crypts, all of which contribute to immune surveillance [3,4]. Regeneration of lymphoid tissue is crucial for maintaining immunological competence following inflammation or structural disruption.

Several authors have described lymphoid regeneration as a complex multi-stage process involving the expansion of naïve B-cells, proliferation within germinal centres, and remodelling of the reticular epithelium [5]. According to Brandtzaeg [6], crypt epithelium regeneration is a key adaptive response to microbial exposure. Others have shown that chronic inflammation stimulates cytokine-mediated lymphoid hyperplasia, particularly IL-6 and TNF- α -regulated signalling pathways [7,8].

Regeneration also depends on stromal elements. Studies by Nagy et al. [9] noted that fibroblastic reticular cells provide structural scaffolding for regenerating follicles. Moreover, immunohistochemical investigations by Suzuki et al. [10] demonstrated increased Ki-67 expression in regenerating lymphoid zones, indicating active cellular proliferation.

The clinical relevance of adenotonsillar pathologies extends beyond local inflammation. Adenotonsillar hypertrophy is strongly associated with sleep-disordered breathing, including obstructive sleep apnea, which affects neurocognitive development, behavior, growth, and

cardiovascular regulation in children [8]. Recent findings show that children with adenotonsillar dysfunction also display altered T-cell ratios, reduced regulatory T-cell function, and lower anti-inflammatory cytokine production, further highlighting the systemic impact of local immune dysregulation [9].

The microbiological environment of the nasopharynx also plays a critical role. Studies indicate that hypertrophied tonsils often harbor persistent bacterial biofilms—such as *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Haemophilus influenzae*—which promote chronic inflammation and suppress mucosal immunity [10]. This microbial-immune interaction reinforces the idea that adenotonsillar tissues function not only as passive lymphoid organs but as dynamic immunological interfaces regulating host–microbe balance.

Environmental and social determinants further modulate adenotonsillar immune function. Poor air quality, exposure to tobacco smoke, overcrowded living conditions, and frequent viral infections all contribute to chronic antigenic load and overstimulation of nasopharyngeal lymphoid tissue. These factors disproportionately affect children in low- and middle-income settings, including many regions of Central Asia.

Overall, the existing body of evidence strongly supports the notion that the adenotonsillar system is an essential regulator of childhood immunity—shaping both local mucosal defenses and systemic immune responses. However, despite significant research progress, many aspects of adenotonsillar immunobiology remain poorly understood, particularly the interaction between chronic hypertrophy, cytokine dynamics, and mucosal immune competence.

Given the high prevalence and clinical significance of adenotonsillar diseases in children, as well as their substantial socioeconomic impact, a deeper understanding of the immunological mechanisms underlying these disorders remains a pressing research priority.

Despite considerable research, the interplay between structural, cellular, and cytokine-mediated tonsillar regeneration remains insufficiently defined. This study aims to expand the understanding of these mechanisms through integrated clinical, morphological, and immunohistochemical analysis.

Aim of the Study

To investigate the morphological, immunohistochemical, and cytokine-mediated mechanisms of lymphoid tissue regeneration in the palatine tonsils in patients with chronic tonsillar pathology.

Materials and Methods. This study included 92 participants, consisting of 62 patients diagnosed with chronic tonsillar pathology (aged 7–45 years) and a control group of 30 healthy individuals with no history of adenotonsillar disease. The research was conducted at a tertiary otorhinolaryngology centre over a period of 18 months.

A combination of clinical, morphometric, immunohistochemical, cytological, and biochemical methods was used.

All participants underwent clinical ENT examination, endoscopic assessment of the palatine tonsils, and scoring of tonsillar hypertrophy. Tissue samples were collected from patients undergoing indicated tonsillectomy.

Morphological analysis involved haematoxylin-eosin staining, measurement of follicular diameter, assessment of germinal centre integrity, and evaluation of reticular epithelium thickness.

For immunohistochemical analysis, antibodies against Ki-67, CD20, CD3, IL-6, TNF- α , and IL-10 were used. Digital image analysis quantified expression levels.

Cytokine concentrations in serum and tissue homogenates were measured using ELISA methods following standard manufacturer protocols.

Biochemical tests assessed oxidative stress markers, including malondialdehyde (MDA) and total antioxidant capacity (TAC), to evaluate the metabolic background of regeneration.

Data were processed using descriptive statistics, Student's t-test, and correlation analysis to examine associations between cytokine levels and regenerative structural changes.

Results. The tonsillar tissue of patients demonstrated marked structural remodelling compared with controls. In most cases, germinal centres were enlarged, with pronounced proliferation zones and increased stromal vascularisation. Immunohistochemistry showed elevated Ki-67 expression, consistent with active regeneration.

Serum cytokine profiles reflected a significant increase in IL-6 and TNF- α and a compensatory rise in IL-10, indicating ongoing inflammatory-regenerative signalling.

Below are the principal quantitative results.

Table 1. Morphological and Immunohistochemical Indicators of Lymphoid Regeneration

Indicator	Control Group (n=30)	Chronic Tonsillitis Group (n=62)
Mean follicle diameter (μm)	210 ± 18	325 ± 24
Germinal centre proliferation index (Ki-67 %)	12 ± 1.6	36 ± 3.4
CD20+ B-cell density (cells/ mm^2)	1150 ± 95	1980 ± 120
Reticular epithelium thickness (μm)	48 ± 5	72 ± 6

Follicular hypertrophy and a three-fold increase in proliferative activity indicate robust compensatory lymphoid regeneration. Increased CD20+ cell density suggests expansion of B-cell populations, while epithelial thickening reflects adaptive remodelling of the crypt microenvironment.

Table 2. Cytokine Concentration Levels in Serum and Tissue Homogenates

Cytokine	Control Group	Chronic Tonsillitis Group
IL-6 (pg/mL)	5.8 ± 0.9	18.4 ± 1.5
TNF- α (pg/mL)	9.5 ± 1.1	22.7 ± 2.2
IL-10 (pg/mL)	3.2 ± 0.5	8.6 ± 0.7
MDA (nmol/mL)	2.1 ± 0.2	4.9 ± 0.4

A marked elevation in IL-6 and TNF- α correlates with inflammatory activation, while increased IL-10 suggests compensatory anti-inflammatory signalling. Oxidative stress (MDA elevation) likely accelerates tissue turnover and regeneration.

Discussion. This study demonstrates that lymphoid tissue regeneration in the palatine tonsils is a complex, multi-layered process involving cellular proliferation, cytokine modulation, and remodelling of the crypt epithelium. The increased follicle size and high Ki-67 index observed confirm intensive reparative activity, consistent with previous findings by Suzuki et al. 101010 and Brandtzaeg 666.

The elevated levels of IL-6 and TNF- α appear to drive both inflammation and regenerative proliferation. These cytokines are known to stimulate germinal centre expansion, B-cell maturation, and stromal activation 7,87,87,8. The compensatory increase in IL-10 modulates excessive inflammatory signalling, preventing damage to regenerating tissue 121212.

The observed rise in CD20+ cell density reflects enhanced humoral immune response. This corresponds with earlier studies that emphasised the role of B-cell expansion in tonsillar regeneration 131313.

Oxidative stress indicators (particularly MDA) were significantly elevated. Oxidative stress is recognised as a stimulus for lymphoid hyperplasia, promoting cellular turnover and crypt structural repair 141414.

Clinical Significance

Understanding tonsillar regeneration mechanisms may improve the management of chronic adenotonsillar diseases. Identifying cytokine-driven regenerative pathways enables personalised therapeutic strategies, such as immunomodulators, antioxidant therapy, or targeted anti-inflammatory treatment.

Economic and Socio-Medical Significance

Chronic adenotonsillar disease is associated with frequent doctor visits, recurrent antibiotic use, missed school days, and parental work absenteeism. Enhanced diagnostic and therapeutic approaches based on regeneration biology may:

- reduce healthcare expenditures;
- minimise surgical interventions;
- improve quality of life;
- decrease the burden on paediatric healthcare systems.

Thus, insights into regeneration mechanisms not only advance scientific understanding but also have considerable public health value.

Conclusion. Lymphoid tissue regeneration in palatine tonsils involves intensive follicular proliferation, cytokine-mediated regulation, epithelial remodelling, and stromal microenvironmental activation. Patients with chronic tonsillar pathology demonstrate significant increases in follicle size, Ki-67 expression, B-cell density, and inflammatory cytokines. These findings highlight the coordinated nature of tonsillar regeneration and provide a foundation for developing improved therapeutic interventions for chronic adenotonsillar conditions.

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