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REVIEW ARTICLE

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Local allergy in the atopic march: new insights into adenotonsillar hypertrophy

Raha Zamani[a]*, Nima Rezaei[b]

[a]*Research Center for Immunodeficiencies, Children's Medical Center, University of Medical Sciences, Tehran, Iran*
[b]*Universal Scientific Education and Research Network, Tehran, Iran*

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Abstract
Adenoid hypertrophy (AH) and combined adenotonsillar hypertrophy (ATH) are primary causes of childhood sleep-disordered breathing (SDB), and they are strongly correlated with atopic diseases affecting the respiratory mucosa. Allergen sensitization, class-switching of B cells, and IgE production in the adenotonsillar tissue, namely local atopy, are crucial steps in the pathogenesis of allergic rhinitis (AR) and asthma. The adenotonsillar tissue is also responsible for a considerable part in circulating specific IgE, potentially contributing to the pathogenesis of atopy in other organs. Atopic children experience fewer benefits from adenotonsillectomy compared to their nonatopic counterparts. However, this surgical intervention is effective in relieving both obstructive and allergic symptoms in children with concomitant ATH and AR or asthma. Adjunctive treatments such as allergen immunotherapy reduce the risk of recurrence in atopic children undergoing adenotonsillar surgery. This review focuses on the evidence linking local adenotonsillar IgE sensitization and the atopic march and its implications in the treatment and outcomes of both conditions.

Introduction

Obstructive sleep apnea (OSA), the severe form of sleep-disordered breathing (SDB), is increasingly found in children, with the most recent reports estimating a prevalence of 12-20%.[1] OSA is known to have several cardiovascular, respiratory, metabolic, and developmental sequelae in children, if left untreated.[2] Adenotonsillar hypertrophy (ATH) is the primary cause of childhood OSA, affecting approximately 34-70% of children and adolescents.[2,3] AH and ATH are highly correlated with pediatric atopic diseases, particularly asthma and allergic rhinitis (AR).[4] The underlying mechanisms linking AH and ATH to atopic conditions remain partially understood. It is hypothesized that a bidirectional causal relationship exists, involving mucosal inflammation and lymphatic proliferation.[5] Recent studies

***Corresponding author**: Raha Zamani, Research Center for Immunodeficiencies, Children's Medical Center, University of Medical Sciences, Tehran, Iran. *Email address*: rahazamani6@yahoo.com

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have demonstrated the role of local IgE sensitization and target organ atopy, rather than systemic IgE production, in the pathogenesis of atopic disorders.[6-8] The adenotonsillar tissue is one of the most important sites of IgE synthesis, being directly exposed to inhalant and food allergens.[9]

Atopic March refers to the sequential progression of atopic diseases throughout childhood, beginning with atopic dermatitis (AD) and food allergy (FA) in infancy, and later developing into AR and allergic asthma (AA). The mechanism of this natural pattern is not yet fully understood but is probably a combination of shared predispositions (genetic or environmental) and sequential exacerbation (skin barrier impairment in AD causing epicutaneous sensitization to allergens). Whether these disorders are different profiles of the same condition or a cascade of events, they are highly correlated in incidence and severity.[10,11] The spectrum of atopic diseases is not limited to these four entities; eosinophilic esophagitis and chronic rhinosinusitis are also among the conditions associated with atopic multimorbidity.[12,13]

ATH is epidemiologically associated with the atopic predisposition, questioning its part in the pathogenesis of airway allergic diseases such as AR and asthma. Whether the association between adenotonsillar disease and atopy is because of common genetic causes, or a direct causal relationship, is a matter of debate.[4] This distinction is of particular importance given the impact of atopic comorbidities on the severity and treatment outcomes of ATH. Children with concurrent ATH and AR or asthma are more likely to have persistent OSA after adenotonsillectomy (A&T), despite improvement in both allergic and obstructive symptoms.[14-16] Many researchers have suggested routine allergy testing in children undergoing A&T or a different treatment plan for atopic children with SDB.[17] This study aims to review the evidence linking ATH and atopic diseases of the airway, focusing on their potential implication in management strategies for atopic children with SDB.

Atopic March or Atopic Multimorbidity

Atopy is known as the genetic predisposition to IgE-mediated hypersensitivity reactions, the core pathophysiology of many allergic diseases. AD, atopic rhinitis (AR), atopic asthma (AA), and FA are the most common atopic profiles, which are highly interconnected. AD is known as the first presentation of an atopic multimorbidity and a risk factor for other atopic diseases. Children with AD are more likely to develop IgE-mediated FA, AR, and AA later in life, and the risk is higher in early onset and severe forms of AD.[18-20] A Canadian birth cohort study of more than 2,000 children has shown that AD at 1 year of age increases the risk of AA and AR at 3 years of age, by almost 10-fold.11 The observation that multiple atopic profiles coexist in many individuals has led scientists to investigate the association between these disorders. The most known link between different atopic diseases may be the shared genetic, epigenetic, and environmental predispositions. Nonetheless, there is also some evidence suggesting a link beyond shared causality.[21,22]

The concept of atopic march relies on a trajectory profile of atopic disorders starting from AD in infancy and continuing to FA, RA, and AA in childhood. In this concept, these atopic profiles are linked via a causal relationship, in addition to the well-known shared predisposition. As such, it is proposed that the barrier disruption in AD facilitates penetration of food allergens and "epicutaneous sensitization," which later causes other forms of allergic reactions such as FA and AA. The dual allergen exposure hypothesis suggests that while allergen exposure through a defective skin barrier produces sensitization, oral exposure results in tolerance. It is demonstrated that children exposed to household peanut dust or even skin emollients containing peanut oil used to treat AD patches have an increased risk of developing peanut allergy. This risk could be prevented by early oral introduction of peanuts.[23,24] Another hypothesis behind the association between AD and FA is the role of intestinal dysbiosis caused by an inflammatory state in AD in inducing FA. While it is frequently observed that gut microbial diversity is attenuated in both AD and FA, the direction of the causal relationship is not yet fully established.[23]

The pathophysiology of AD primarily consists of barrier dysfunction and a dysregulated T-helper 2 (Th2) immune response. Interleukin-4 (IL-4), IL-31, IL-33, and IL-13 are the key cytokines that interact and downregulate epidermal barrier proteins such as Filaggrin and Keratin. Although AD is considered to be a multifactorial disease, a strong genetic predisposition is found to be present. Most known genetic variants associated with AD are either structural components of the skin or key molecules in the Th2 signaling pathways. Mutations in Filaggrin (responsible for the formation and maintenance of the stratum corneum), IL-4, IL-13, IL-31, IL-33, thymic stromal lymphopoietin (TSLP) and their receptors are among the most important genetic causes of AD.[18,23,25] Interestingly, mutations in barrier proteins are also associated with an increased risk of FA, although they do not directly influence the immune system. The duration and severity of AD are associated with the development of FA and aggressive treatments to shorten the disease duration and reduce the risk of future FA.[26,27] Furthermore, it is demonstrated that preservation of the skin barrier, using emollients and anti-histamines to suppress itching and scratching, can prevent the development of asthma in children with AD sensitized to grass pollen or house dust mite.[28] This finding further highlights an association beyond shared genetic predisposition and the key role of allergen sensitization. The dual allergen hypothesis is mainly focused on routes of sensitization or tolerance to food allergens. Inhalant allergens are also implicated in epicutaneous sensitization and future allergic reactions, but it is not yet fully known what are the routes of tolerance to inhalant allergens.

ATH and Atopy

Palatine, tubal, lingual, and pharyngeal (i.e. adenoid) tonsils, collectively known as the Waldeyer's ring, are lymphatic tissues of the upper aerodigestive tract (Figure 1).[34] They are suggested to be a part of mucosa-associated lymphoid tissue (MALT), named the nasopharynx-associated lymphoid tissue (NALT).[5,34] The tonsillar tissue primarily consists of lymphoid follicles within a stromal

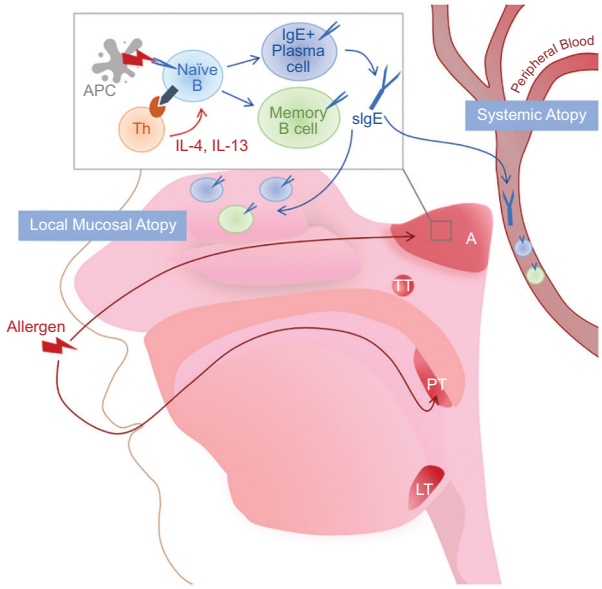

Figure 1 Adenoid and tonsils are proposed as one of the major IgE-producing sites, located at the forefront of allergen exposure. Upon first contact, a Th2-mediated immune response is initiated, resulting in class-switching and differentiation of B cells into IgE+ plasma cells and memory B cells. These cells then migrate to nasal, pharyngeal, and possibly bronchial mucosa, serving as primary immune actors in later allergen exposures. The adenotonsillar tissue houses memory B cells, memory T cells, and many other subtypes, acting as a reservoir for IgE-mediated immune pathways. The immune landscape of adenoids and tonsils varies between atopic and nonatopic children, emphasizing its important role in the pathogenesis of atopic phenotypes. Adenotonsillar IgE sensitization is found to have a strong correlation with upper and lower airway atopic diseases, even in the absence of systemic sensitization.[6-9,29-33] A=adenoid, TT=tubal tonsil, PT=palatine tonsil, LT=lingual tonsil, APC=antigen-presenting cell, Th=T helper lymphocyte.

extrafollicular region, surrounded by a specialized crypted reticular epithelium.[5] The germinal center of the lymphoid follicle is home to a distinct immune cell profile and is mainly responsible for T-cell-dependent B cell activation, which results in clonal expansion, class switching, memory formation, and J chain production.[34,35] The J chain plays an important role in the production and transportation of secretory immunoglobulins.[34] A recent large multi-omics study demonstrated that B cells are the most abundant immune cell subtypes in human palatine tonsils, followed by CD4+ T cells and myeloids.[33] The crypted surface of the tonsils and the presence of M cells ensures maximum antigen exposure and capture. Upon transportation of the antigen/allergen through the tonsillar epithelium, it is captured by the antigen-presenting cells (APCs) and introduced to the germinal center, where a primary or secondary immune response takes place.[5,35] Once activated by the Th cells, B cells undergo clonal expansion, somatic hypermutation, and class-switching, eventually differentiating into plasma cells and memory B cells. Antibodies produced by plasma cells are predominantly sIgA, which later nests in the nasopharyngeal mucosa.[5] Plasma cells and antibodies developed in the tonsils are found to migrate to the lung mucosa and salivary glands as well as the peripheral blood, suggesting an important role for the adenotonsillar tissue in the development of antigen memory, humoral immunity, and hypersensitivity.[34] The contribution of the adenotonsillar tissue to systemic and local immunity/atopy through antigen recognition and presentation, memory formation, and antibody production is summarized in Figure 1. Interestingly, a considerable proportion of plasma cells and APCs residing in the adenoids are found to be IgE+.[36,37] IgE sensitization in the adenotonsillar tissue is mediated by Th2 cells, releasing pro-inflammatory cytokines IL-4 and IL-13 and initiating B cell differentiation into IgE+ plasma cells and memory B cells. Allergen-specific IgE+ plasma cells are proposed to migrate to the nasopharyngeal mucosa and the peripheral blood.[31,36,37] A schematic summary of the local IgE sensitization in the adenotonsillar tissue is provided in Figure 1.

Adenoids rapidly grow in size at 3–6 years of age and then start to involute around puberty, whereas the size of palatine tonsils peaks around 12 years of age and continues growing to the adult size.[5,35] A combination of genetic causes and immune dysregulation is known to be responsible for A(T)H in children. Increased levels of IL-32 and pro-inflammatory cytokines are proposed to be related to adenoid proliferation. Polymorphisms in several immune-related genes are found to be associated with an increased risk of AH, further supporting the role of immune dysregulation in its pathogenesis.[5] The high correlation between AH and ATH with atopic phenotypes, particularly asthma and AR, is well established.[38-42] ATH and asthma are found to be highly correlated both in incidence and severity.[43,44] ATH is also shown to be associated with systemic atopy, evidenced by skin prick test (SPT) results.[45,46] Increasing evidence suggests that the immune landscape of the adenotonsillar tissue differs in atopic and nonatopic children. As such, the immune landscape of adenoids in atopic children is shown to be Th2-dominant.[47] It is demonstrated that IgE class switching of B cells in response to local IL-4 takes place in the adenoids, and local IgE production correlates with atopic phenotypes.[31,36] In a study of 102 children with ATH, Cho et al. found a higher rate of adenotonsillar tissue allergen-specific IgE (sIgE) compared to serum sIgE.[29] Cumulatively, more than 70% of ATH cases were sensitized to more than one allergen in serum or the adenotonsillar tissue. Local adenotonsillar atopy was significantly associated with the lifetime prevalence of asthma and AR and the severity of nasal symptoms.[29] Furthermore, they demonstrated that while the adenoid tissue was predominantly sensitized to aeroallergens, tonsils commonly had systemic immunoglobulin E (sIgE) to food allergens.[29] Interestingly, while ATH and isolated AH correlate with an atopic profile, this is not the case in isolated TH, further supporting a difference in the immune landscape and function of adenoids and tonsils.[4] In another study, all children with ATH who were tested for sIgE had local sensitization to more than two allergens in the adenotonsillar tissue, while half had negative serum sIgE.[6] Notably, both studies found that more than one-third of cases with negative serum sIgE are positive in the adenotonsillar tissue.[6,29] The significance of local sIgE

production in the adenotonsillar tissue and other mucosal organs is also replicated in other studies.[6,7,45] Local IgE is proposed to play an important role in respiratory allergies, namely, rhinitis and asthma.[7,8] Durham et al. have suggested that class-switching and production of IgE occur locally in nasal and bronchial mucosa in AR and asthma patients, respectively.[7] It is suggested that only 0.2% of IgE released in response to allergens is produced in the peripheral blood and that target organ IgE production is more significant in the atopic response.[9,48] Nasal mucosa, adenoid and tonsils, lung, bone marrow and spleen are organs harboring the highest density of IgE-producing cells.[9] In addition, IgE+ memory cells are also most abundantly found in lymphatic organs such as adenoids and tonsils.[48] Studies on tissue and serum eosinophilia have similarly revealed that atopic children have higher eosinophilic infiltration in the adenotonsillar tissue, associated with a higher local IL-4 expression[49,50] Ekici et al. have shown that tissue eosinophilia is more sensitive than serum eosinophilia in predicting atopy, whereas no significant correlation was found between tissue eosinophilia and serum eosinophilia, suggesting that the adenotonsillar tissue serves as a reservoir for local atopy and sensitization.[45,50] A summary of the evidence behind local allergic sensitization in the adenotonsillar tissue of children with ATH is provided in Table 1. Shin et al. have demonstrated that atopic children have a higher rate of local IgE sensitization to Staphylococcus aureus enterotoxins, compared to nonatopic children.[30] Interestingly, IgE sensitization to Staphylococcus aureus enterotoxins is also proposed to play a role in the pathogenesis of AD and the onset of atopic march.[51] Hu et al.[52] have demonstrated that polysensitization to molds increases the risk of AH in children with AR, and aeroallergen sensitization alters the immune profile of the adenoid tissue.[52]

The association of ATH with atopic diseases and the role of the adenotonsillar tissue in allergen sensitization are rather complex. AH and SDB are highly associated with both asthma and AR in children, questioning a link beyond shared genetic predisposition and hypersensitivity.[4,53] The association of AR and OSA could primarily be explained by nasal congestion and airway collapsibility. Furthermore, cytokines released in AR, namely, IL-4, IL-10, and IL-1β are suggested to induce sleep cycle disruptions.[54,55] IL-6 is particularly implicated in regulating the circadian rhythm, and the level of its soluble receptor is found to be correlated with OSA severity.[56] A bidirectional association

Table 1 Summary of evidence on the significance of local adenotonsillar atopic reaction.

Study	Subjects	Main findings
29	Atopic and nonatopic children with ATH (n=102)	Higher rates of AT sIgE compared to serum sIgE AT sIgE is associated with lifetime prevalence of asthma and AR, and symptoms of AR.
6	Children with ATH (n=83), healthy controls (n=59)	Higher rates of AT sIgE compared to serum sIgE. Fifty percent of serum sIgE-positive cases and 36% of serum sIgE-negative cases had positive sIgE in adenoid tissue. Forty-three percent of serum sIgE-positive cases and 44% of serum sIgE-negative cases had positive sIgE in tonsils. Half of the cases with local AT sensitization to more than two allergens were not sensitized in their serum.
45	Atopic and nonatopic children with ATH (n=44)	AT sIgE and eosinophilia was significantly higher in atopic children.
50	Atopic (n=57) and nonatopic (n=68) children with ATH	Adenoid tissue eosinophilia is more sensitive and specific in predicting local (AR) and systemic (SPT) atopy.
49	Children with AH and OME (n=45)	Atopic children had higher levels of IL-4 and eosinophils in the adenoid tissue and the middle ear.
47	Atopic (n=11) and nonatopic (n=5) children with AH	Adenoids of children with house dust mite and grass pollen–induced allergic rhinitis had a Th2-dominant immune pattern, compared to a Th1-dominant pattern in nonallergic children. Sublingual allergen immunotherapy downregulated Th2-related genes.
36	Children with ATH or OME (n=12)	More than 10% of plasma cells and 16% of macrophages in the adenoid tissue of atopic children were stained positive for IgE, compared to very few or no IgE positivity in nonatopic children. IgE+ cells were clustered and predominantly located in the extrafollicular region of the adenoids.
37	Atopic (n=14) and nonatopic (n=16) children with AH or OME	Allergen sensitization was associated with an increase in IgE+ cells in all three regions of the adenoid tissue and an increased expression of the high-affinity receptor for IgE in the extrafollicular region.
31	Atopic (n=19) and nonatopic (n=18) children with OME or AH	AT Epsilon germline transcripts are correlated with IL-4 transcripts, suggesting an IL-4-mediated IgE class switch in the adenotonsillar tissue.

AT=Adenotonsillar, ATH=Adenotonsillar hypertrophy, sIgE=Systemic immunoglobulin E, AR=Allergic rhinitis, SPT=Skin prick test, OME=Otitis media with effusion.

is also consistently reported between SDB and asthma. Asthma is shown to be a risk factor and an exacerbating factor in SDB. On the other hand, SDB may also cause or complicate asthma in children (Figure 2). Comorbid AR is shown to be a risk factor for SDB in children with asthma.[53] It is suggested that the dysregulated immune response and inflammatory markers released in asthma may contribute to the proliferation of upper airway lymphoid tissue (i.e., tonsils and adenoid) and thus airway obstruction and SDB. Furthermore, SDB is associated with a more severe form of asthma and poor asthma control.[53] Several mechanisms are proposed for this observation. First, SDB because of upper airway obstruction can cause bronchoconstriction through neuromuscular alterations of the oropharynx and the thoracic cavity.[43,57] Second, intermittent hypoxia during sleep predisposes to inflammation of both the upper and lower airway.[58] And lastly, risk factors and genetic causes common to both conditions may result in an association between asthma severity and SDB. The release of proinflammatory leukotrienes, a result of airway inflammation, is known to be associated with both upper airway collapsibility and lower airway resistance. Increased leukotrienes in the adenotonsillar tissue and even the urine of children with OSA support their important role in the pathogenesis of this disease.[59,60] High expression of leukotriene receptors is found in the tonsils of children with OSA and is shown to increase adenotonsillar proliferation.[43,61] Administration of montelukast, a cysteinyl leukotriene receptor antagonist, combined with intranasal steroids is shown to improve residual SDB in children after A&T for OSA.[62,63] Understanding the mechanisms of this association may have clinical implications in timing and indications of A&T in atopic children, that is, more than half of the children with ATH. Indeed, A&T may suppress the hypersensitivity cascade or conversely break the tolerance to allergens.

Atopic Multimorbidity after Childhood A&T

A&T is the first-line treatment for ATH in otherwise healthy children. The decision for surgery is made based on the severity of sleep apnea, size of the adenoids and tonsils, obesity, and comorbid conditions.[64,65] Less commonly, A&T is performed with or without endoscopic sinus surgery as a treatment for childhood chronic rhinosinusitis.[66] A&T has a success rate of more than 70% in the resolution of OSA in healthy children.[67,68] Nonetheless, sleep apnea may persist or recur after A&T in a subset of patients. Various studies investigated the factors associated with the failure of surgery in childhood OSA. Comorbid allergic disease, particularly asthma and AR, and markers of systemic atopy, such as the serum IgE level, are among the predictors of persistent OSA because of adenotonsillar regrowth after A&T in children.[69,70] It could be hypothesized that ongoing allergic reactions and cytokine release cause the re-proliferation of the lymphatic adenotonsillar tissue, and that AR itself is partly responsible for OSA symptoms.[71] Nonetheless, several studies have shown that A&T or adenoidectomy not only helps with upper airway disease but may also alleviate the symptoms and severity of lower airway disease (e.g., AA). Kohli et al. and Skarzynski et al. have shown in their systematic reviews that A&T results in better asthma control scores, less frequent exacerbations, reduced medication need, emergency room visits, and hospitalizations in asthmatic children.[15,16] Interestingly, A&T also reduced the level of molecular markers of asthma severity.[15,16,72] Similarly, improvements in AR symptoms are reported after A&T, although this should be interpreted cautiously concerning the high overlap between AR and ATH symptoms.[14,73,74] Nonetheless, children with concomitant AR and ATH experience less improvement in both obstructive and allergic symptoms compared to children without AR.[71,73] Despite the positive impact of A&T on allergic diseases of the airway, systemic allergy remains unchanged after A&T.[75,76] This further highlights the role of local sensitization and atopy in AR and asthma.

Management of OSA in the Atopic Child

As mentioned above, comorbid atopy, particularly AR and asthma, is a risk factor of persistent OSA after A&T.[77] Furthermore, children with atopic diseases have worse quality-of-life (QOL) both pre- and post-A&T.[17,78] Higher

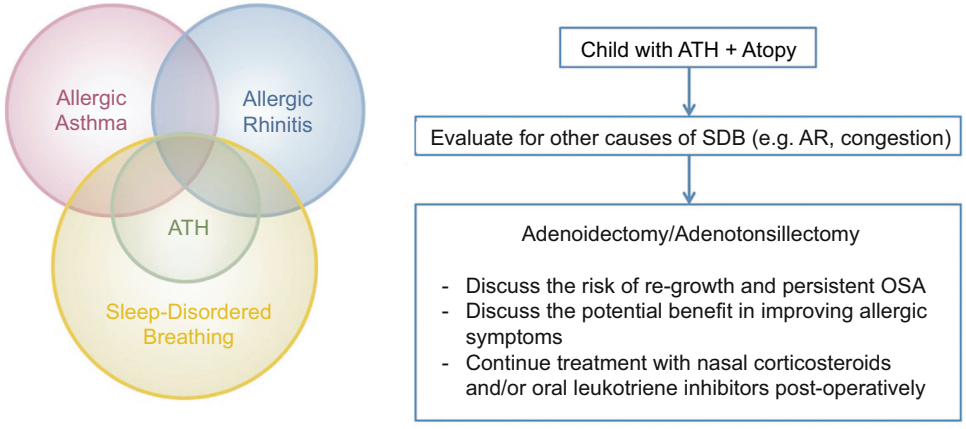

Figure 2 Graphical summary of the link between sleep-disordered breathing, ATH, allergic diseases of the airway, and the recent evidence in clinical management of children with concomitant ATH and asthma/allergic rhinitis. ATH=Adenotonsillar hypertrophy; SDB=sleep-disordered breathing; AR=allergic rhinitis; OSA=obstructive sleep apnea.

levels of serum total IgE were found to be associated with a deterioration in QOL measures after A&T in a cohort of 70 children with SDB.[17] Recurrence of SDB and decreased QOL in atopic children could be attributed to the impacts of AR and asthma on sleep or the higher rates of adenotonsillar regrowth after surgery.[69] Based on this evidence, authors have suggested that routine testing for systemic allergy should be performed preoperatively in children with ATH, as it is a major determinant of A&T outcomes.[17] This is not supported by the study of Hofmann et al., showing no significant differences in symptoms 1 year after surgery in aeroallergen-sensitized versus nonsensitized children.[79] Nonetheless, they have only tested for sIgE in cases with elevated intraoperative serum total IgE, which may be normal in many cases in the absence of acute allergen exposure.[32] In addition, they have only examined allergy-related symptoms but not the overall QOL or sleep parameters.[79] As mentioned above, more than one-third of children with negative serum sIgE to aeroallergens have positive sIgE in the adenotonsillar tissue.[4,6,29] It is crucial to investigate whether tissue or serum sensitization is a better predictor of A&T outcomes, and if early surgery can alleviate future atopic reactions by reducing the source of aeroallergen sensitization and IgE production. It is consistently reported that AR and asthma severity are decreased in children undergoing A&T.[15,16] On the other hand, it is also evident that children with these atopic profiles will not benefit from A&T as much as nonatopic children.[17,78] Whether the decision for surgical management of SDB should be made differently or at least more cautiously in atopic children is still a matter of debate. Many studies have shown the beneficial impact of adjunctive treatments for atopic children undergoing A&T to prevent or treat persistent symptoms. Intranasal steroids and oral leukotriene receptor inhibitors are suggested to improve persistent OSA after adenotonsillar surgery by suppressing adenotonsillar regrowth and mucosal inflammation.[80,81] Concomitant obstruction in other levels of the airway, such as sleep-dependent laryngomalacia and lingual tonsil hypertrophy could also contribute to the failure of A&T.[82,83] Drug-induced sleep endoscopy (DISE) can identify and occasionally treat multilevel obstructions and is found to improve OSA symptoms in children with persistent disease after A&T.[83] Allergen immunotherapy is a novel approach in the treatment of atopic diseases. They are shown to reduce the Th2-related pathways in the adenoid tissue of children with concomitant AR and ATH, as well as decrease markers of systemic atopy in the peripheral blood.[47,84] A recent groundbreaking study has shown that subcutaneous immunotherapy with a dual mite allergen can reduce the risk of recurrence in children with concurrent AH and AR, as well as improve postoperative OSA symptoms.[85] While this is the first study to investigate the role of immunotherapy in persistent OSA after A&T, it is in line with previous studies on the effectiveness of allergen immunotherapy for AR and asthma.[47,86] The most evidence-based clinical points in the management of concurrent ATH and asthma/AR are summarized in Figure 2.

Future Perspective

The direction of causality between adenotonsillar disease and systemic atopy is yet to be fully unraveled and could have potential implications in the management of ATH. Future studies should focus on determining the impact of A&T on atopic disease outcomes, particularly asthma and AR, preferably through a randomized process. To the best of our current knowledge, atopic children are at a greater risk of adenotonsillar regrowth and persistence of AR symptoms. Future research should determine the cost-effectiveness of pre-operative allergy testing and polysomnography in these children, as well as the effectiveness and timing of adjunctive systemic treatments such as allergen immunotherapy. With the considerable prevalence of atopy and its correlation with ATH, it is crucial to develop specific guidelines and recommendations for the management of OSA in atopic children with or without evident ATH.

Conclusion

Allergen sensitization, B cell activation, class switching, and differentiation into IgE+ plasma cells take place in the adenotonsillar tissue, among a few other major IgE-producing sites. Children with AH or ATH are found to have local IgE sensitization to inhalant and food allergens in their adenotonsillar tissue, which was more significantly associated with airway atopic diseases than systemic IgE sensitization. Medical and surgical treatments of ATH are shown to improve atopic diseases, although atopic children generally benefit less from A&T compared to nonatopic children. Both asthma and AR symptoms and severity are improved after A&T. Future studies are needed to determine if the age of surgery, sensitization profile, or adjunctive treatments, namely, allergen immunotherapy, influence the outcomes of A&T in atopic children.

Author's Contribution

All authors contributed equally.

Conflicts of Interest

The authors declare no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

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