as methoxamine, whose role is supported by recent publications of Breslin and McBrien.[13] It is interesting to note that glucocorticoids and colloids, used in the treatment of anaphylaxis, have also been implicated as causative agents for anaphylaxis and should be avoided in sensitised patients. Nevertheless, as the manageability of methoxamine in childhood is still a topic of debate,[14] steroids, bronchodilators, and anti-histamine H1 and H2 blockers are to be considered as the first line to treat SMB atopic children in case of anaphylaxis.

The importance of this case report is the knowledge of the possibility of a SMB allergy also in childhood. The underlying mechanism remains unknown, because to our knowledge, our report is the first case ever described in literature in such early childhood. Nevertheless, it is useful to know its entity because the prevalence of allergic disease in childhood is deeply increasing and the access to Pediatric Acute and Emergency Units is equally raised, so that in case of urticaria and anaphylactic episodes it is important to perform a good allergic anamnesis, in order to start the correct treatment and to alert physicians on the cautious use of drugs.

Ethical disclosure

Protection of human subjects and animals in research. The authors declare that no experiments were performed on humans or animals for this investigation.

Confidentiality of data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

References

1. Madan V, Walker SL, Beck MH. Sodium metabisulfite allergy is common but is it relevant? Contact Dermatitis. 2007;57:173–6.
2. Boner AL, Guarise A, Vallone G, Fornari A, Piacentini F, Sette L. Metabisulfite oral challenge: incidence of adverse responses in chronic childhood asthma and its relationship with bronchial hyperreactivity. J Allergy Clin Immunol. 1990;85:479–83.
3. Towns SJ, Mellis CM. Role of acetyl salicylic acid and sodium metabisulfite in chronic childhood asthma. Pediatrics. 1984;73:631–7.
4. Jacobs MC, Rycroft RJ. Contact dermatitis and asthma from sodium metabisulfite in a photographic technician. Contact Dermatitis. 1995;33:65–6.
5. Merget, Korn M. Metabisulphite-induced occupational asthma in a radiographer. Eur Respir J. 2005;25:386–8.
6. Steiner M, Scaife A, Semple S, Hulks G, Ayres JG. Sodium metabisulphite induced airways disease in the fishing and fish-processing industry. Occup Med (Lond). 2008;58:545–50.
7. Sánchez-Pérez J, Abajo P, Córdoba S, García-Díez A. Allergic contact dermatitis from sodium metabisulfite in an antihemorrhoidal cream. Contact Dermatitis. 2000;42:176–7.
8. Heshmati S, Maibach HI. Active sensitization to sodium metabisulfite in hydrocortisone cream. Contact Dermatitis. 1999;41:166–7.
9. Campbell JR, Maestrello CL, Campbell RL. Allergic response to metabisulfite in lidocaine. Anesthetic Solution Anesth Prog. 2001;48:21–6.
10. Gall H, Boehncke WH, Gietzen K. Intolerance to sodium metabisulfite in beer. Allergy. 1996;51:516–7.
11. White JM, Goon ATJ, Jowsey IR, Basketter DA, Mak RK, Kimber I, et al. Oral tolerance to contact allergens; a common occurrence? Contact Dermatitis. 2007;56:247–54.
12. Dalton-Bunnow MF. Review of sulfite sensitivity. Am J Hosp Pharm. 1985;42:2220–6.
13. Breslin Drs, McBrien ME. Management of severe anaphylactic reactions should include administration of alpha adrenergic agonists. Anesth Analg. 2014;98:1499–505.
14. Zaritsky A. Advanced pediatric life support: state of the art. Circulation. 1986;74:IV124–8.

G. Vitaliti*, F. Guglielmo, L. Giunta, P. Pavone, R. Falsaperla

Pediatric Complex Operative Unit and Pediatric Acute and Emergency Unit, Policlinico-Vittorio-Emanuele Hospital, University of Catania, Italy

* Corresponding author.
E-mail address: giovitaliti@yahoo.it (G. Vitaliti).

http://dx.doi.org/10.1016/j.aller.2013.10.003

Effect of tonsillectomy on the efficacy of house dust mite sublingual immunotherapy

To the Editor,

Tonsils are part of Waldeyer's ring and play important immunological roles, including mucosal antigen capture and presentation to lymphocytes. A healthy immune response to allergens and successful allergen-specific immunotherapy both require the generation of allergen-specific cells for induction of peripheral T-cell tolerance.[1] Functional allergen-specific T-regulatory cells have been identified in lingual and palatine tonsils with percentages approximately three times higher than those in peripheral blood, indicating their role in controlling allergen-specific T-cell responses in human tonsils.[2] To date, nothing is known about the possible effect of tonsillectomy on the efficacy of sublingual immunotherapy (SLIT).

We aimed to assess the effect of tonsillectomy on clinical and immunological responses before and after three months of SLIT. The study was conducted at Ain Shams University Hospital, Cairo, Egypt, from January 2011 to August 2011, and included 26 adult patients with bronchial asthma

Table 1 Baseline serum levels of immunological markers in both groups.

	Tonsillectomy	Non-tonsillectomy	*p*
Total IgE (IU/mL)	600.0 (224.0, 692.0)	225.0 (115.5, 444.0)	0.033
Mite-specific IgE (kU/L)	0.82 ± 0.09	0.84 ± 0.07	0.508
Total IgG (IU/mL)	990.4 ± 245.1	954.7 ± 220.1	0.700
Total IgA (IU/mL)	102.2 ± 40.3	105.1 ± 32.6	0.845

All values are presented as mean ± SD except total IgE as median (interquartile range).

and/or allergic rhinitis, of whom 13 had undergone tonsillectomy during childhood. All patients had a positive skin prick test (SPT) reaction to house dust mite. An informed consent was obtained from all study participants, and the study was approved by the Research Ethics Committee of the Faculty of Medicine, Ain Shams University. Clinical and immunological assessments were performed at baseline and after three months of SLIT with a house dust mite extract. Clinical parameters included the presence of cough, wheezing, sneezing and itchy nose, rhinorrhea, and nasal obstruction. Immunological parameters included SPT reactivity, serum levels of total IgE, house dust mite-specific IgE, total IgA and total IgG.

Tonsillectomy and non-tonsillectomy groups were comparable at baseline in age (21 ± 11.5 years *vs.* 26.5 ± 8.1 years, respectively, $p = 0.172$), gender [4 males (30.8%) *vs.* 6 males (46.2%), respectively, $p = 0.420$], serum levels of mite-specific IgE, total IgA and total IgG, whereas total IgE levels were significantly higher in the tonsillectomy group (Table 1). After three months, SPT reactivity to house dust mite decreased significantly in both groups. The number of patients with a positive SPT to house dust mite was significantly reduced to four (30.8%), $p = 0.004$ in the tonsillectomy group, and three (23.1%), $p = 0.002$ in the non-tonsillectomy group. Furthermore, a highly significant reduction in serum levels of total and mite-specific IgE was observed in both groups after three months (Fig. 2). However, no significant differences were observed after three months of SLIT in the serum levels of total IgG (943.2 ± 204.7 IU/mL, $p = 0.133$ for the tonsillectomy group; 909.5 ± 253.1 IU/mL, $p = 0.133$ for the non-tonsillectomy group) or total IgA (101.2 ± 37.7 IU/mL, $p = 0.814$ for the tonsillectomy group; 107.7 ± 29.1 IU/mL, $p = 0.401$ for the non-tonsillectomy group). As regards the studied clinical parameters, a significant reduction in the frequency of wheezing, sneezing and itchy nose was observed in the non-tonsillectomy group but not in the tonsillectomy group (Fig. 1). However, the frequency of cough, rhinorrhea, and nasal obstruction did not change significantly in either group (data not shown).

Short-term reductions in serum levels of immunoglobulins have been observed following tonsillectomy, followed by a return of these levels to normal within a few months.[3,4] However, studies on the long-term immunological effects of tonsillectomy are scarce, and have been conducted mostly on children. Kaygusuz et al. recorded no difference in serum IgA, IgG or IgM levels among children 54 months after tonsillectomy, compared to that in non-tonsillectomised children.[5] On the other hand, long-term reductions have been reported for IgA levels in serum among the tonsillectomised compared to the non-tonsillectomised children, while other immunological parameters, including IgE, IgG and IgM, were preserved.[6] In the present study, serum levels of mite-specific IgE, total IgA and IgG were all comparable at baseline in both groups, which may be attributed to the long time since tonsillectomy. However, an interesting finding which warrants further investigation is the significantly higher total IgE levels in tonsillectomised adults at

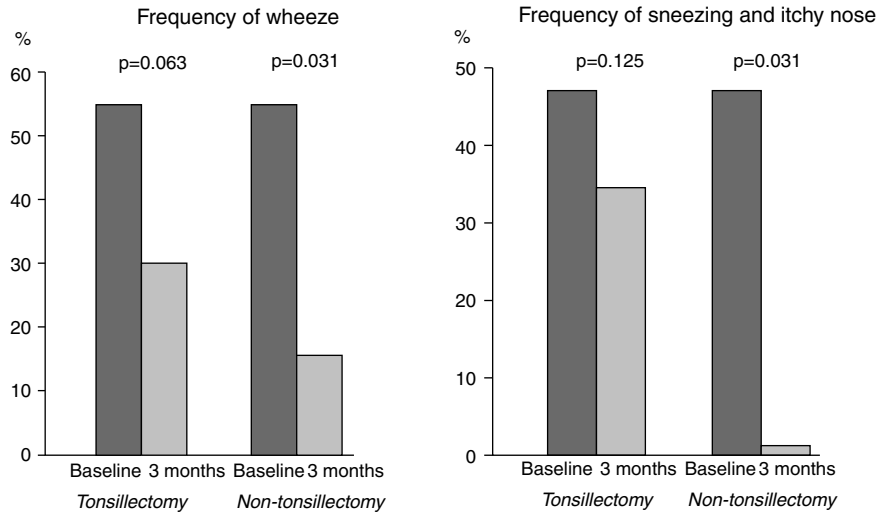

Figure 1 Symptoms at baseline and after three months of SLIT in both study groups.

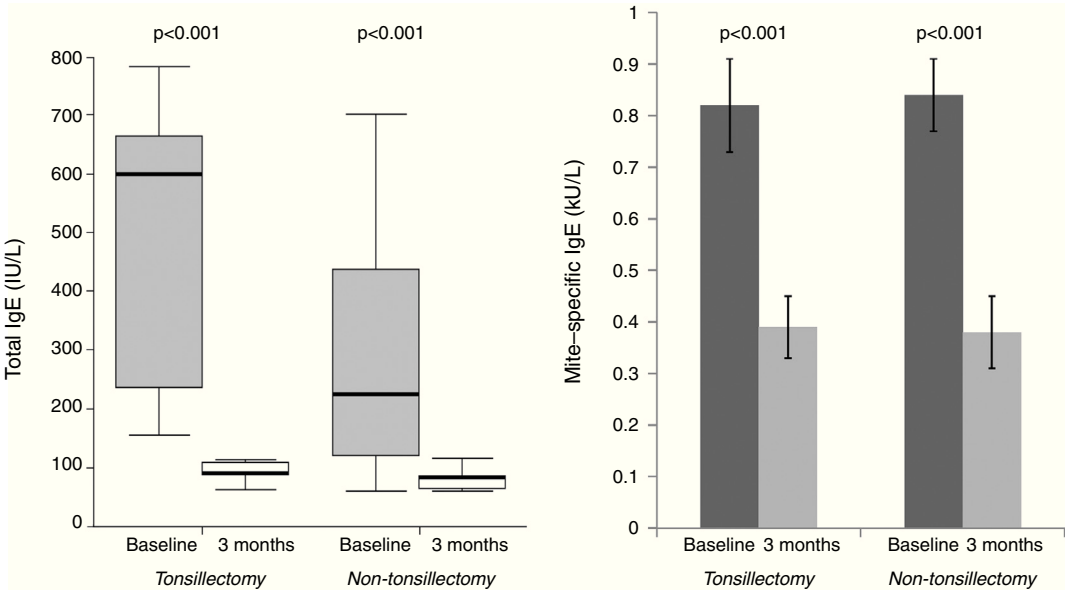

Figure 2 Total and mite-specific IgE levels in serum at baseline and after three months of SLIT in both study groups.

baseline, in comparison to levels in non-tonsillectomised adults.

Our results show that previous tonsillectomy does not affect the efficacy of SLIT in reducing SPT reactivity or in changing serum immunoglobulin levels. Both total and mite-specific IgE levels in serum were successfully reduced in both groups after SLIT. However, there was no change in serum levels of IgG in either group after treatment. Concerning this point, it may be more useful to measure the blocking activity of allergen-specific IgG or IgG subsets, including IgG1 and IgG4, instead of total IgG levels in sera.[7] Similarly, IgA levels in our study did not change significantly in either group after three months. Data on serum IgA levels after SLIT are still conflicting, and it appears that in contrast to subcutaneous immunotherapy, SLIT elicits mucosal IgA responses, and shows IgA subclass selectivity.[8] In line with our findings, an absence of early systemic immunological changes has been demonstrated for allergen-specific IgG1, IgG4, and IgA levels in plasma during the first eight weeks of SLIT in respiratory allergic children.[9] A possible explanation for the similar trends in all measured immunological parameters in both of our study groups after three months of SLIT is that maybe during tonsillectomy, only palatine tonsils and occasionally adenoids are removed; the lingual and tubal tonsils are preserved and continue their lifelong role in the induction of immunological responses[2]; thus the effect of tonsillectomy might be limited and is of short duration.

Despite the similar changes in immunological parameters between the tonsillectomy and the non-tonsillectomy groups, the reduction in the frequency of wheezing, sneezing and itchy nose after SLIT was not statistically significant in the tonsillectomy group. This suggests that tonsillectomy might affect the efficacy of SLIT in improving local allergic symptoms. Since this finding depends on patient-reported outcomes, it could have been affected by the patients' and the researchers' knowledge of the study objective – namely, checking whether tonsillectomy negatively affects the efficacy of SLIT. To minimise this potential bias, triple-blinding should be performed for future studies (patients should be blinded to this specific objective of the study, and researchers and statisticians should be blinded to the tonsillectomy status of the subjects). In addition, large-scale randomised controlled studies may confirm these findings.

To our knowledge, this is the first study to report the effect of previous tonsillectomy on the clinical and immunological efficacy of SLIT. Further large-scale investigations should focus on the effect of tonsillectomy on local immunological changes following SLIT, and on similar findings for other allergens.

Ethical disclosures

Patients' data protection. Confidentiality of data. The authors declare that no patient data appears in this article.

Right to privacy and informed consent. The authors declare that no patient data appears in this article. An informed consent was obtained from all study participants, and the study was approved by the Research Ethics Committee of the Faculty of Medicine, Ain Shams University.

Protection of human subjects and animals in research. The authors declare that no experiments were performed on humans or animals for this investigation.

Conflict of interest

The authors declare that no funding or grant was received for the study, and that they have no conflict of interest, financial or personal relationship related to the study.

Acknowledgments

The authors wish to thank Professor Al-Saied M. Abou-Gamrah, Professor Emeritus of Allergy and Clinical

Immunology, Ain Shams University, Egypt, for his role in conceiving the study, and also Professor Cezmi A. Akdis, Director of the Swiss Institute of Allergy and Asthma Research, University of Zurich, Switzerland, for his valuable contribution in scientific revision of the article.

References

1. Kücüksezer UC, Palomares O, Rückert B, Jartti T, Puhakka T, Nandy A, et al. Triggering of specific toll-like receptors and proinflammatory cytokines breaks allergen-specific T-cell tolerance in human tonsils and peripheral blood. J Allergy Clin Immunol. 2013;131:875–85.
2. Palomares O, Rückert B, Jartti T, Kücüksezer UC, Puhakka T, Gomez E, et al. Induction and maintenance of allergen-specific FOXP3+ Treg cells in human tonsils as potential first-line organs of oral tolerance. J Allergy Clin Immunol. 2012;129:510–20, 520.e1-9.
3. Ikincioğullari A, Doğu F, ikincioğullari A, Eğin Y, Babacan E. Is immune system influenced by adenotonsillectomy in children? Int J Pediatr Otorhinolaryngol. 2002;66:251–7.
4. Amorós Sebastiá LI, Ferrer Ramírez MJ, López Mollá C, Carrasco Llatas M, Plá Mochilí A, Díaz Ruiz M, et al. Changes in immunoglobulin levels following adenoidectomy and tonsillectomy. Acta Otorrinolaringol Esp. 2004;55:404–8.
5. Kaygusuz I, Alpay HC, Gödekmerdan A, Karlidag T, Keles E, Yalcin S, et al. Evaluation of long-term impacts of tonsillectomy on immune functions of children: a follow-up study. Int J Pediatr Otorhinolaryngol. 2009;73:445–9.
6. van den Akker EH, Sanders EA, van Staaij BK, Rijkers GT, Rovers MM, Hoes AW, et al. Long-term effects of pediatric adenotonsillectomy on serum immunoglobulin levels: results of a randomized controlled trial. Ann Allergy Asthma Immunol. 2006;97:251–6.
7. Akdis CA, Akdis M. Mechanisms of allergen-specific immunotherapy. J Allergy Clin Immunol. 2011;127:18–27.
8. Calderón MA, Simons FE, Malling HJ, Lockey RF, Moingeon P, Demoly P. Sublingual allergen immunotherapy: mode of action and its relationship with the safety profile. Allergy. 2012;67:302–11.
9. Dehlink E, Eiwegger T, Gerstmayr M, Kampl E, Bohle B, Chen KW, et al. Absence of systemic immunologic changes during dose build-up phase and early maintenance period in effective specific sublingual immunotherapy in children. Clin Exp Allergy. 2006;36:32–9.

M. Refaat, Z.A. Ashour, M.N. Farres*, A.M. Eissa, M.M. Elsayed

Department of Allergy and Clinical Immunology, Faculty of Medicine, Ain Shams University, Cairo, Egypt

*Corresponding author.
E-mail address: mnfarris@yahoo.co.uk (M.N. Farres).

http://dx.doi.org/10.1016/j.aller.2013.09.007

Adolescent form of sporadic lymphangioleiomyomatosis (S-LAM)

To the Editor,

Lymphangioleiomyomatosis (LAM) is a rare progressive disease that has gone largely unrecognised by paediatricians, even by paediatric pulmonologists. We report a paediatric case of sporadic LAM (S-LAM) that first manifested as recurrent spontaneous pneumothorax.

We report the case of a 17-year-old girl who was brought to the emergency department because of a 12-h history of acute onset of chest pain on the left side and shortness of breath of sudden onset, with a two-hour history of transient episodes of loss of consciousness, squinting of the eyes, and stiffening of the hands for two minutes, followed by a 10-min period of postictal state. She had no history of trauma, fever or previous respiratory symptoms. She had started her latest menstrual period two days before. There was no family history of any respiratory disease, neurologic or other medical conditions. Her past medical history, including any intellectual disability, was negative, except for a previous episode of spontaneous pneumothorax one year previously that had not been studied after treatment with chest tube thoracostomy.

On physical examination, pulse rate was 104 beats per minute, respiratory rate was 24 breaths per minute, and pulse oximetry measurement was 94% O_2 saturation in ambient air at rest, and she had decreased breath sounds on the left hemithorax. The remainder of her examination, including a thorough neurological exam, was unremarkable. Echocardiogram, ophthalmologic examination, and skin examination under ultraviolet light did not show abnormalities. A chest radiograph revealed right upper lobe cystic parenchymal lesions and a pneumothorax greater than 50% on the left side, requiring thoracostomy tube placement (Fig. 1). High-resolution computed tomography of the chest revealed multiple, well-circumscribed, round, and thin-walled cysts that were scattered in a bilateral, roughly symmetric pattern (Fig. 2). Open lung biopsy showed multiple cysts that distorted the lung parenchyma and contained proliferating bundles of ''modified'' smooth muscle cells in their walls, involving alveolar septa, airways, lymphatics, and blood vessels. The smooth muscle component was positive for antibodies to vimentin, actin and desmin, but it also reacted with antibodies to human melanin black 45 (HMB 45) (Fig. 3). Having established a diagnosis of LAM, the patient underwent abdominal computed tomography, which showed a rounded lesion in the upper pole of the right kidney. Three months later, she underwent nephrectomy. The piece weighed 207 grams and had a rubbery, oval mass that measured 7.5 cm × 6.2 cm × 4.5 cm, well defined but unencapsulated, with yellow, ochre, and brown colours. Microscopic study showed a tripartite composition of fat, blood vessels, and smooth muscle cells in variable proportions, which reacted to the same antibodies as did the lung cysts. A diagnosis of angiomyolipoma was made. Cerebral magnetic resonance imaging with a gadolinium contrast agent revealed no abnormalities.

At the present time, the patient is scheduled for the performance of a surgical pleurodesis and for administration of inhibitors of mTOR (Sirolimus).