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# Recurrent tonsillitis in children's rheumatic arthritides: a review

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Department of Rheumatology, Institute of Clinical and Experimental Medicine at Vilnius University, Lithuania **Introduction.** The chronization of reactive arthritis is frequently related to the persistence of arthritis triggering infection in the organism. Relapses of reactive arthritis can be induced by other bacteria than the triggers of this disease, for example, those persisting in the focus of chronic infection. The boundaries between reactive arthritis and juvenile idiopathic arthritis sometimes are blurred, and similar link between arthritis and focus of chronic infection exists in them. The aim of the current review is to discuss the features of recurrent tonsillitis in children with rheumatic arthritides and their impact on physician's decisions.

Material and methods. The literature data for the period of 1980–2008 concerning connection between children's rheumatic arthritides and foci of chronic infection were analysed.

**Results.** The essential part of children's rheumatic arthritides is associated with the upper respiratory tract infections. In pediatric patients, foci of chronic infection are the most frequent in the upper respiratory tract, and the main of them is recurrent tonsillitis. Despite the lower number of tonsillitis recurrences in patients with rheumatic arthritides and recurrent tonsillitis, their tonsils are more profoundly damaged than in patients suffering from recurrent tonsillitis only.

**Conclusions.** In children with rheumatic arthritides the number of recurrences of tonsillitis should not serve as the only indication for tonsillectomy, and its results should not be evaluated only by the number of throat infections as is recommended in the great majority of recent literature sources. The decision to perform tonsillectomy and evaluation of its results in arthritis patients should be made from both otorhinolaryngological and rheumatological positions.

Key words: recurrent tonsillitis; reactive arthritis; juvenile idiopathic arthritis

## INTRODUCTION

In adults, reactive arthritis (ReA) in the greatest number of cases is triggered by urogenital and gastrointestinal pathogens. In children, more than half of all the cases are assotiated with the upper respiratory tract infections, infections of other localizations being less frequent (1, 2). The chronization of ReA is frequently assotiated with the persistence of arthritis triggering infection (3). ReA relapses can be induced by other bacteria than the triggers of the disease, for example, those persisting in the focus of chronic infection (4). In pediatric patients, the foci of chronic infection are the most frequent in the upper respiratory tract, and the main of them is recurrent tonsillitis.

The elucidation of ReA triggers is most effective at the very beginning of the disease, but if it was unsuccessful and the disease became chronic, the clinical features correspond with those of the categories of juvenile idiopathic arthritis (JIA), and the patient can be considered as suffering from JIA (5). As the boundaries between ReA and JIA are sometimes blurred, the similar link between arthritis and focus of chronic infection exist in JIA as well. We have ascertained that the cure of recurrent tonsillitis by tonsillectomy can essentially improve even the aggressive course of JIA (6).

It was commonly accepted that septic arthritis, in which causative microorganism was usually cultured from the synovial fluid, was most frequently caused by *Staphylococcus aureus* and *Haemophilus influenzae*, which could be derived from the chronically inflammed tonsils (7, 8).

Several decades ago the importance of acute and chronic tonsillitis on the course of rheumatic fever, which is the form of ReA triggered by *Streptococcus pyogenes*, was thoroughly investigated, and this research has made an essential contribution to the situation that today the problem of rheumatic fever is not as actual in pediatrics as before. The significance of influence of foci of the chronic infection as well as of the chronic tonsillitis on the course of other rheumatic arthritides is underestimated today and deserves resurrection, all the more in the latter years, when research in the understanding of chronic tonsillitis presented some new interpretations. The term of recurrent tonsillitis was introduced, and the number of recurrences was accepted as the only criterium in making the decision to perform tonsillectomy or not (9–11).

The objective of the current review is to discuss the features of recurrent tonsillitis in children with rheumatic arthritides and their impact on physician's decisions.

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### Characteristics of bacteriological status of palatine tonsils

The palatine tonsils are the major components of the lymphoid tissue in Waldeyer's ring and function as the host's first line defense system against exogenous microorganisms.

Acute tonsillitis may be caused by different bacteria and viruses, but Streptococcus pyogenes has been demonstrated to be the most frequent causative agent (12, 13). In subclinical phase of recurrent tonsillitis, superficial tonsillar swabs have shown the presence of Streptococcus pyogenes only in 6-17% of patients (14, 15). The pathogenic bacteria from tonsillar surface in recurrent tonsillitis were shown to differ significantly from those from the core tissue, and many authors question the value of a tonsillar surface swab (14, 16, 17). Highly hyperplastic tonsils probably harbour bacterial infection of a more or less chronic nature in the core, even in cases without a history of throat infection (15). Investigation of ultrastructure of the tonsils surgically removed due to recurrent tonsillitis has demonstrated the anatomical evidence of microbial biofilms in tonsillar tissue, which might serve as a possible explanation for the chronicity and recurrent nature of some forms of tonsillitis (18). Recently, bacterial biofilms have been defined as a structured community of bacterial cells enclosed in a selfproduced extracellular polymeric matrix, adherent to an inert or living surface (19). Capability of Streptococcus pyogenes cultured from children with symptoms of pharyngeal infection to form biofilms in vitro was demonstrated (20). These biofilms were considered to become multispecies as they develop incorporating other bacteria, such as Moraxella catarrhalis or non-typeable Haemophillus influenzae, inducing high antibacterial resistance and creating mutually beneficial relationship for survival of these microorganisms (20).

Tonsils are active immunologic organs. All the ten toll-like receptors, components of the innate immune system which recognize pathogenic microorganisms, are expressed in human adenoid and tonsil tissue and may play a vital role in the immunological outcomes of these tissues (21). Challenging tonsillar cells obtained from recurrent tonsillitis with Streptococcus pyogenes and Haemophilus influenzae induce TH1 type cytokine response in vitro (22). Immunoglobulin levels (IgA, IgM and IgG), complement fractions (C3, C4), cytotoxic T lymphocytes and activated B lymphocytes are increased in patients with chronic tonsillitis as a response to chronic bacterial stimulus, and tonsillectomy restores these parameters to the normal values by removal of bacterial stimulus (23). The mRNA of interleukin (IL)-1beta, IL-2, IL-4, Il-6, Il-8, interferon-gamma and tumour necrosis factor-alpha were expressed in the whole tonsillar tissue of all the tested subjects with recurrent tonsillitis (24). Upregulation of immunocompetent cells should occur continuously due to persistent antigen deposition even between exacerbations, and significantly higher incidence of Il-1beta, Il-2 and Il-6-producing cells were found in the recurrent tonsillitis in comparison with tonsil tissue from children with tonsillar hypertrophy (25). Tonsillectomy affects the general interleukin status of patients. In preoperative serum samples of children with recurrent tonsillitis, IL-1 beta and IL-6 levels were found to be elevated as compared with the levels of control patients and significantly diminished already one month after tonsillectomy (26).

### **Recurrent tonsillitis**

Inflammatory diseases of the tonsils constitute the most common cause of primary care visits to physicians, and tonsillectomy represents one of the most common operations in children (27). The lifetime prevalence of recurrent tonsillitis is 11.7% with a significant predominance of female cases, and there is evidence for substantial genetic predisposition towards this disease (28). In a recent randomized controlled trial by Alho and colleagues (29) the effectivenes and safety of tonsillectomy compared with watchfull waiting in adults with recurrent streptococcal pharyngotonsillitis (3 episodes of pharyngitis in 6 months or 4 in 12 months) was shown to have some benefits over watchful waiting, however, the net benefit is unclear, and research into longer term outcomes is needed (30). Although absolute indications for tonsillectomy such as adenotonsillar hyperplasia with obstructive sleep apnea, suspicion of malignant disease exist, 75% of tonsillectomies in children are performed because of recurrent tonsillitis (31). In a great proportion of studies the number of recurrences of tonsillitis is acknowledged as the only indication for tonsillectomy considering the efficacy of this procedure to be the number of sore throat episodes and upper respiratory tract infections after tonsillectomy (9-11, 32). The comprehensive reviews with evidence-based approach came to a conclusion that the most reviewed studies have important limitations, and no consensus has yet been reached, however, concerning the number of annual episodes that justify tonsillectomy (10, 33, 34).

The results of tonsillectomy in severe cases (7 or more episodes in the preceding year; 5 or more episodes in each of 2 preceding years; or 3 or more episodes in each of the 3 preceding years) reduced the number and severety of subsequent episodes of throat infection for at least 2 years (35) when the studies analyzing results of patients with mild symptoms (2-3 recurrent episodes a year) do not find differences vs watchful waiting without tonsillectomy (9, 11) and question the need of tonsillectomy in recurrent tonsillitis (11, 31). All these studies evaluate the results of tonsillectomy from the point of upper respiratory tract infections and do not pay attention to underlying systemic diseases. It was only in the continuous study of Bond and colleagues (32) that attention was paid to those diseases and under the inclusion criteria patients with renal diseases were excluded from the study. Rheumatic arthritides may also serve as the underlying disease in recurrent tonsillitis.

#### Recurrent tonsillitis and children's rheumatic arthritides

In our recent study (36) we compared clinical and bacteriological features of recurrent tonsillitis in children with JIA with those in children suffering from recurrent tonsillitis only and came to a conclusion that, despite the significantly lower rate of tonsillitis recurrences in children with JIA, their tonsils were more profoundly damaged (tonsillar crypt debris, paratonsillar scars) than in control patients without arthritis. When comparing bacteriological features of recurrent tonsillitis in patients with and without arthritis, no essential difference was found in the frequency of growing *Streptococcus pyogenes* or other bacteria on the surface of tonsils, however, in the tonsillar core tissue *Staphylococcus aureus* was cultured significantly more frequently in arthritis patients than in the patients without any underlying disease. Thus, persistence of *Staphylococcus aureus* in the tonsillar core seems to be assotiated with the course of JIA in patients with JIA and recurrent tonsillitis. Arthritis exacerbating effect of *Staphylococcus aureus* on *Streptococcus pyogenes*-induced ReA was also shown by experimental data. Superantigen produced by *Staphylococcus aureus* reactivates arthritis previously exposed to *Streptococcus pyogenes* cell wall polymers (4).

On the basis of the above data we consider that recurrent tonsillitis exerts its influence on the organism not only through the episodes of throat recurrent infection, but through the chronically persistent bacteria in the tonsillar tissue either. These bacteria could hardly be always elucidated and eliminated by the antibacterials with a conventional approach as they often enter a cell-wall deficient state, are organized into biofilms, and their influence on systemic diseases, such as rheumatic arthritides, should not be ignored between tonsillitis recurrences also (18, 37). The effectiveness of tonsillectomy from the point of underlying systemic disease is life-long as patient will never have another attack of systemic illness due to tonsillitis (38). In our practice we have had a lot of cases when even in aggressively progressing JIA tonsillectomy shifted the disease towards the benign course, sometimes till the recovery (6). These patients often had no complaints on sore throat but highly experienced otorhinolaryngologist evaluted their tonsils as purulent and directed for tonsillectomy. The clinical presentation of sore throat in arthritis patients could be decreased by the long-term use of nonsteroidal antiinflammatory drugs (NSAIDs) and corticosteroids. Thus, we share the opinion of the authors that the decision to perform tonsillectomy, especially in patients with underlying chronic systemic disease, should be made not only on the basis of the number of recurrences of tonsillitis, but also on the individual tactics for each patient, and then it may be a highly effective procedure (6, 39, 40). The decision to do tonsillectomy or not in arthritis patients should be made in collaboration of both otorhinolaryngologist and rheumatologist.

During tonsillectomy, we observed significantly increased bleeding in patients with arthritis (36). The most persuasive explanation for the more abundant haemorrhage during tonsillectomy in our arthritis patients seems to be more significantly pronounced paratonsillar scarring process as in our study NSAIDs were stopped 2-3 days before tonsillectomy and restored 2-3 days after it. Such tactics is sufficient to protect patient from increase of bleeding by NSAIDs even in operations of greater extent than tonsillectomy (41). Authors suggest that to avoid the antiplatelet effect during surgery, NSAIDs other than aspirin should be withheld for duration of 4 to 5 times the drug half-life. COX-2 inhibitors have less impact on haemostasis compared with traditional NSAIDs with predominant COX-1 inhibition and may be considered safer with regard to perioperative blood loss (42). As aspirin irreversibly blocks COX-1 and the normal platelet life span is approximately 10 days, in rare cases when aspirin is given as an anti-inflammatory drug, its withholding 7 to 10 days before surgery is necessary to avoid inhibition of platelet function, which may increase intraoperative blood loss, haemorrhagic complications, and transfusion requirement (43). When NSAIDs are used for pain relief following paediatric tonsillectomy, it was concluded in Cochrane Database Systemic Review that they did not cause any increase in bleeding requiring a return to operating-room (44). Patients with chronic glucocorticoid therapy and suppressed hypothalamic-pituitary-adrenal axis need perioperative supplementation (41).

## CONCLUSIONS

The essential part of children's rheumatic arthritides is assotiated with the upper respiratory tract infections. The most frequent focus of chronic infection, recurrent tonsillitis, in children with rheumatic arthritides has bacteriological and clinical differences comparing with children suffering from recurrent tonsillitis only. In children with rheumatic arthritides the number of recurrences of tonsillitis should not serve as the only indication for tonsillectomy as despite the lower number of tonsillitis recurrences in these patients, their tonsils are more profoundly damaged than in patients suffering from recurrent tonsillitis only. The decision to do tonsillectomy and evaluating its efficacy should be made in collaboration of both otorhinolaryngologist and rheumatologist.

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#### Danutė Astrauskienė

# REUMATINIU ARTRITU SERGANČIŲ VAIKŲ PASIKARTOJANČIO TONZILITO YPATUMAI (apžvalga)

## Santrauka

Įvadas. Reaktyvaus artrito chroniškumas dažnai priklauso nuo jį inicijuojančios infekcijos persistencijos organizme. Artrito recidyvus gali sukelti ne tik ligą inicijavusios bakterijos, bet ir tos, kurios persistuoja lėtinės infekcijos židiniuose. Ribos tarp reaktyvaus ir jaunatvinio idiopatinio artrito neretai yra neryškios, o šių artritų ryšiai su lėtine infekcija labai panašūs. Šios apžvalgos tikslas – aptarti reumatiniu artritu sergančių vaikų pasikartojančio tonzilito ypatumus ir jų reikšmę gydytojo sprendimams.

Metodai. Išanalizuota 1980–2008 m. literatūra, nagrinėjanti vaikų reumatinių artritų ryšį su lėtinės infekcijos židiniais.

Rezultatai. Didžioji dalis vaikų reumatinių artritų atvejų yra susijusi su viršutinių kvėpavimo takų infekcijomis. Vaikų lėtinės infekcijos židiniai dažniausiai randami viršutiniuose kvėpavimo takuose, o dažniausias iš jų – pasikartojantis tonzilitas. Nors reumatiniu artritu ir pasikartojančiu tonzilitu sergantiems vaikams būdingas mažesnis tonzilito recidyvų skaičius, jų tonzilės yra labiau pažeistos nei vien tik pasikartojančiu tonzilitu sergančiųjų.

**Išvados.** Reumatiniu artritu sergančių vaikų tonzilito recidyvų skaičius negali būti vienintelis kriterijus, lemiantis paciento nukreipimą tonzilektomijai, o tonzilektomijos rezultatai neturėtų būti vertinami tik pagal nosiaryklės infekcijų skaičių po operacijos, nors tai rekomenduojama daugelyje pastarųjų metų literatūros šaltinių. Apsisprendimas atlikti tonzilektomiją reumatiniais artritais sergantiems vaikams ir jos rezultatų įvertinimas turėtų būti atliekami tiek iš otorinolaringologinių, tiek iš reumatologinių pozicijų.

Raktažodžiai: pasikartojantis tonzilitas, reaktyvus artritas, jaunatvinis idiopatinis artritas