Tonsillectomy Can Essentially Improve the Aggressive Course of Juvenile Idiopathic Arthritis

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The objective of this work was to demonstrate the significance of a well-timed elucidation of chronic tonsillitis in juvenile idiopathic arthritis (JIA) by presenting some cases of aggressive JIA with essential improvement of patients after tonsillectomy.

164 children ranging in age from 1 to 16 years were referred to the children rheumatologist consultation and examined in a consultative outpatient clinic. In 82 of them the diagnosis of JIA was established according to the recent international criteria (Durban, 1997). In 62 patients with the disease duration of >2 years its progression was assessed. The aggressive course of the disease (without remissions and with multiple deformities of joints) was found in 15 patients. The possible causes of the aggressive course of the disease were analysed. Chronic purulent tonsillitis was evaluated as a possible cause of the aggressive course of disease in 5 patients. Their age ranged from 6 to 14 years, disease duration from 2 to 10 years. They all had been treated with nonsteroidal antiinflammatory drugs, corticosteroids *per os*, 4 with methotrexate and 1 with plaquenil unsuccessfully.

Tonsillectomy was performed with the cover of antibiotics selected by susceptibility of bacteria grown from the passages of tonsils before tonsillectomy. The status of the patients was evaluated 6 months following tonsillectomy. No clinical or laboratory signs of disease activity were found in 4 patients and in 1 patient the status was defined as "much better" (the number of active joints and erythrocyte sedimentation rate decreased considerably).

The causes why tonsillectomy was delayed were analysed. In 4 patients tonsillectomy was delayed because the status of tonsils was evaluated by some otorhinolaryngologists not sufficiently experienced in working with arthritis patients, and chronic tonsillitis was overlooked. In 1 patient the diagnosis of chronic tonsillitis was not clear enough and several times he was left for observation without diagnosis.

The conclusion is done that tonsillectomy can essentially improve even the aggressive course of JIA. Antirheumatic medicines (nonsteroidal antiinflammatory drugs, corticosteroids) due to their antiinflammatory activity can change the clinical presentation of chronic tonsillitis. So, children with JIA for timely exposure of chronic tonsillitis must be referred only to a highly skilled otorhinolaryngologist having an experience in detecting chronic tonsillitis in arthritis patients.

Key words: juvenile idiopathic arthritis, chronic tonsillitis, tonsillectomy

INTRODUCTION

Infection may be implicated in the onset and exacerbations of many different forms of rheumatic arthritides in children (1, 2). More and more facts have been found suggesting that juvenile chronic arthritis may represent a chronic form of reactive arthritis of various etiology (3). It becomes understandable in the light of the latest data on the pathogenesis of chronization of reactive arthritis. It is realized as result of persistence of the causative microorganism in joint tissues (4) or elsewhere in the

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organism (5), sometimes despite antibacterial treatment (6). This infection is thought to be alive and activation of such "slow infection" results in the exacerbations of arthritis (7, 8). Exacerbations can be caused by the same microorganism which triggered the onset of arthritis or by another occasional microorganism (9). A great variety of bacterial pathogens were presented in the literature as the possible triggers of juvenile chronic arthritis, but the most frequent triggers of arthritis in children or exacerbations of juvenile rheumatoid arthritis are the upper respiratory tract (tonsillitis, pharyngitis, maxillitis and otitis are also included into this term) pathogens (10, 1). Elucidation of chronic tonsillitis is a daily problem in children rheumatology. While analysing the causes of unsuccessful control of disease in juvenile idiopathic arthritis (JIA), we arrived to the conclusion that inaccurate estimation of chronic tonsillitis must underlie some of these cases. This work seeks to demonstrate the significance of timely exposure of chronic tonsillitis in JIA by presenting some cases of aggressive JIA with an essential improvement of patients after tonsillectomy.

MATERIALS AND METHODS

One hundred sixty four children, age range 1 to 16 years, sent to the children rheumatologist consultation were examined in a consultative out-patient clinic. In 82 of them the diagnosis of JIA was established according to the recent international criteria (11). In 62 patients with the disease duration of >2 years the progression of disease was evaluated. Fifteen of them were found to have an aggressive course of the disease: without remissions and with multiple progressive deformities of joints. The possible causes of aggressive course were analysed from the patient cards, evaluating them from the very beginning of joint disease and from the parent's and patient's words. During this analysis belated prescription of antirheumatic treatment at the onset of disease, the order of nonadequate antirheumatic treatment, the incorrect usage of rightly prescribed medicines, the long-term persistence of the focis of chronic infection were evaluated.

RESULTS

Chronic purulent tonsillitis was evaluated as a possible cause of the aggressive course of JIA in 5 patients. Their demographic and baseline characteristics are presented in Table 1. The number of active joints before tonsillectomy ranged from 6 to 12, the number of joints with deformities from 5 to 10, and erythrocyte sedimentation rate from 23 mm/h to 35 mm/h by Panchenko. All patients had been on nonsteroidal antiinflammatory drugs permanently. Slow acting antirheumatic drugs had been used by these patients with no effect for 6–12 months. Patient № 5 used methotrexate twice. All patients had been prescribed corticosteroids *per os*, patients № 1 and № 5 for 3–4 courses. When chronic purulent tonsillitis was diagnosed, patients were directed for tonsillectomy and their status was evaluated after 6 months following operation (Table 1). In 4 patients no clinical or laboratory signs of disease activity we-

Table 1. **Baseline characteristics and influence of tonsillectomy in observed patients with the aggressive course of JIA**

Patient's №	Sex	Age (years)	Pattern of the disease	Disease duration (years)	Efficacy of slow acting antirheumatic drugs	Patient's status 6 months after tonsillectomy	Why tonsillectomy was delayed ?
1	B	13	Polyarthritis RF -	10	Methotrexate no effect	No clinical and laboratory signs of disease activity	The diagnosis of chronic tonsillitis was not clear enough, the patient was left for observation
2	B	6	Polyarthritis RF -	2	Plaquenil no effect	No clinical and laboratory signs of disease activity	
3	G	6	Polyarthritis RF -	3	Methotrexate no effect	No clinical and laboratory signs of disease activity	The status of tonsils was evaluated by some otorhinolaryngologists not sufficiently experienced in work with arthritis patients, and chronic tonsillitis was overlooked
4	B	14	Polyarthritis RF +	5	Methotrexate no effect	Much better than before tonsillectomy	
5	B	14	Polyarthritis RF -	8	Methotrexate no effect	No clinical and laboratory signs of disease activity	

re found, and in 1 patient the clinical status grew better: morning stiffness disappeared, the number of active joints decreased from 9 to 4 and erythrocyte sedimentation rate from 35 mm/h to 20 mm/h.

While analysing the reasons why tonsillectomy was delayed in the patients it turned out that in 4 of 5 cases chronic purulent tonsillitis had been overlooked because of insufficient experience of the otorhinolaryngologist (Table 1).

There are no distinct directions concerning the antibacterial therapy for conducting patients with JIA before and after tonsillectomy. In our earlier work we concluded that for the exposure of bacteria from tonsils in children with rheumatic arthritides passages from the detritus / secret pressed out from tonsils were more informative than passages from the surface of tonsils (12). Tonsillectomy in 5 patients presented in this work was performed with the coverage of antibiotics (2–3 days before tonsillectomy and 6–7 days after tonsillectomy) which were found to be optimal after evaluating both the superficial passages and passages from the detritus as is shown in Table 2. When we had such a possibility, 2–3 passages with the intervals of several weeks were evaluated. We had no exacerbations of arthritis after tonsillectomy in these patients and in other arthritis patients when we used antibacterial prophylaxis in such a manner. In the case presented in Table 2 a rarely occurring resistance of *Streptococcus pyogenes* to penicillin is demonstrated.

disease, and 3 died. In a prospective survey performed in Sweden, Gäre (14) concluded that 11.3% of patients with juvenile chronic arthritis were found to have severe disability. Continuing disease activity and presence of IgM rheumatoid factor (RF) were risk factors for disability. In our study the aggressive course of disease was stated in 18.3% of all patients with the diagnosis of JIA. We have shown that one third of cases with the aggressive course of JIA may be due to the persistence of chronic purulent tonsillitis. Antirheumatic medicines (nonsteroidal antiinflammatory drugs, corticosteroids) because of their antiinflammatory properties can reduce the clinical presentations of chronic tonsillitis, requiring from otorhinolaryngologist an experience in working with arthritis patients for correct evaluation of the status of tonsils. As is shown in this work, inaccurate evaluation of tonsils may have serious consequences in children with JIA.

According to the directions, a focus of chronic infection is a contraindication for prescription of methotrexate in patients with rheumatic arthritides. Data of this study show that these instructions must be followed very precisely. In diagnosing chronic tonsillitis in children with arthritis we also adhered strongly to the direction not to consider the diagnosis of chronic tonsillitis earlier than 1 month from an acute inflammatory process in the upper respiratory tract or after antibacterial therapy as it may lead to an incorrect conclusion.

Table 2. **Passages from tonsils of patient № 4 before tonsillectomy**

6 weeks before tonsillectomy		1 week before tonsillectomy	
Superficial	From detritus	Superficial	From detritus
Negative	*Staphylococcus aureus* Penicillin-resistant Oxacillin-resistant Erythromycin-resistant Lincomycin-susceptible Streptomycin-resistant Doxycycline-resistant Gentamicin-susceptible Cephalexin-susceptible	Negative	*Streptococcus pyogenes* Penicillin-resistant Oxacillin-susceptible Erythromycin-resistant Lincomycin partly susceptible Streptomycin-resistant Doxycycline-resistant Gentamicin-susceptible Cephalexin-susceptible

Note. Tonsillectomy to this patient was performed with the cover of cephalexin.

DISCUSSION

Prognosis of JIA is better than the prognosis of rheumatoid arthritis in adults. As Calabro et al. (13) have reported on 100 patients with juvenile rheumatoid arthritis observed prospectively for 15 years, 64 were in remission, 33 continued to have active

Streptococcus pyogenes is the predominant bacterial pathogen in pharyngitis and tonsillitis (15). An apparent increase in the number of serious invasive streptococcal infections, sometimes their course being dramatically rapid, has been reported in the last decade (16, 17). Genetic analysis disclosed a new M type 1 group A streptococcus clone contemporarily

with the increase in the invasive disease, the same genetic profile being found in isolates from patients of invasive disease (especially with the clinical presentation of necrotising fasciitis) and uncomplicated pharyngitis (18). Holm et al. (19) reported that low antibody titers against M1 were common in patients with the invasive disease, indicating that host immunity plays a role in the outcome of infection (19). With reports on invasive streptococcal infections, an apparent increase in descriptions of arthritides associated with group A streptococci is observed. Recurrent severe prolonged arthritis in adults (20), multifocal septic arthritis (21) and reactive arthritis other than rheumatic fever (22, 23) in children have been referred.

The evaluation of *Staphylococcus aureus* cultured from tonsils is discrepant in the literature. In our opinion, it deserves serious attention. We have grown *Staphylococcus aureus* from passages from tonsils in 48.0% of children with juvenile chronic arthritis and only in 7.8% of healthy controls (24). This pathogen tends to a long persistence in the tonsils or pharynx and exhibits the other phagotypic characteristics and a higher resistance to antibiotics as compared to the strains cultured from healthy control children (25). Experimental data showed that the superantigen produced by *Staphylococcus aureus* can reactivate arthritis in the joints that have been previously exposed to the group A streptococcal cell wall polymers (26). Staphylococcal superantigens may compromise the ability of the host's immune system to clear bacterial antigens, allowing them to persist and thus to perpetuate inflammatory and immune responses (27). *Staphylococcus aureus* itself may trigger reactive arthritis (28). So, the arthritis-promoting, exacerbating action of staphylococcal infection persisting in tonsils can be expected in JIA.

Markowitz with colleagues (29) summarized data of literature for the period 1953–1993 on the efficacy of orally administered penicillin for eradication of *Streptococcus pyogenes* in pharyngotonsillitis and concluded that bacteriological treatment fails is about 10%. It has been suggested that a wide variety of the normal pharyngeal flora may play a role in penicillin treatment failures (30). *Staphylococcus aureus* seems to be a very serious candidate in this respect. A strain of *Streptococcus pyogenes* resistant to penicillin, which was concomitant with *Staphylococcus aureus,* was also demonstrated in this work. So, it seems that our practice to presribe antibacterial prophylaxis before and after tonsillectomy according to the susceptibility of bacteria grown from the passages of tonsils is acceptable as long as more grounded directions are prepared.

The above presented literature about the significance of tonsillar bacteria in the pathogenesis of arthritis taken together with the data that persistence of the causative microorganism elsewhere in the body can predispose to the chronization of arthritis (5) arises the question of a very careful exposure of chronic purulent tonsillitis and its eradication.

Such a position is in accordance with our data showing that tonsillectomy can essentially improve even than aggressive course of JIA and that for a timely exposure of chronic tonsillitis children with JIA must be referred only to a highly skilled otorhinolaryngologist having experience in exposing chronic tonsillitis in arthritis patients.

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ŽENKLUS TEIGIAMAS TONZILEKTOMIJOS POVEIKIS JAUNATVINIO IDIOPATINIO ARTRITO AGRESYVIAI EIGAI

S a n t r a u k a

Šio darbo tikslas yra pagrįsti laiku nustatyto lėtinio tonzilito reikšmę sergantiems jaunatviniu idiopatiniu artritu (JIA) pateikiant duomenis apie agresyvios eigos JIA sergančių vaikų ženklų būklės pagerėjimą po tonzilektomijos. Ištyrėme 164 ligonius nuo 1 iki 16 metų amžiaus, kurie buvo atsiųsti vaikų reumatologo konsultacijai. Iš jų 82 vaikams, remiantis tarptautiniais kriterijais (Durbanas, 1997), diagnozavome JIA. Įvertinome ligos progresavimą 62 ligoniams, kurie sirgo ilgiau nei dvejus metus. Iš jų 15 vaikų sirgo agresyvios eigos JIA (be remisijų ir su daugybinėmis sąnarių deformacijomis). Išanalizavome galimas agresyvios ligos eigos priežastis. Penkiems ligoniams labiausiai tikėtina priežastis galėjo būti lėtinis pūlingas tonzilitas. Šių ligonių amžius nuo 6 iki 14 metų, ligos trukmė 2–10 metų. Visi jie buvo gydyti nesteroidiniais priešuždegiminiais vaistais, kortikosteroidais *per os*, keturi – metotreksatu ir vienas – plakveniliu.

Tonzilektomija buvo atlikta kartu taikant antibiotikų terapiją, parinkus juos pagal pasėliuose iš tonzilių išaugintų bakterijų jautrumą. Praėjus 6 mėn. po tonzilektomijos, 4 ligoniams visai nebebuvo klinikinių bei laboratorinių ligos aktyvumo rodiklių, vieno ligonio būklė labai pagerėjo (ženkliai sumažėjo aktyvių sąnarių skaičius bei eritrocitų nusėdimo greitis).

Išnagrinėjus tonzilektomijos vėlavimo priežastis, paaiškėjo, kad 4 ligoniams lėtinis tonzilitas nebuvo laiku diagnozuotas dėl nepakankamos otorinolaringologų darbo su artritu sergančiais ligoniais patirties. Vienam ligoniui lėtinio tonzilito diagnozė nebuvo pakankamai aiški, jis buvo paliktas stebėjimui be išvados.

Pateikti ligonių duomenys rodo, kad tonzilektomija gali ženkliai pagerinti net agresyvią JIA eigą. Šia liga sergantieji lėtinio tonzilito išaiškinimui turėtų būti siunčiami tik pas aukštos kvalifikacijos otorinolaringologus, turinčius darbo su artritu sergančiais vaikais patirtį, nes priešreumatiniai vaistai (nesteroidiniai priešuždegiminiai preparatai, kortikosteroidai), turėdami priešuždegiminį poveikį, mažina tonzilito klinikines apraiškas.

Raktažodžiai: jaunatvinis idiopatinis artritas, lėtinis tonzilitas, tonzilektomija