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Relation of Actinomyces with Tonsillar Hypertrophy and Antibiotic Use

Original Investigation

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Abstract

Objective: This study aimed to investigate the incidence of Actinomyces in tonsillar tissues of patients undergoing tonsillectomy and to determine the association among tonsillar volume, preoperative antibiotic use, and presence of Actinomyces in tonsil tissues.

Methods: In this study, 142 patients who underwent tonsillectomy in last four years were included. Of the total patients, 97 (66.9%) were children and 47 (33.1%) were adults. The patients' age, sex, preoperative antibiotic use, tonsillar volume, and presence of actinomyces in tonsillar tissues were recorded.

Results: Actinomyces was identified in tonsillar tissues of 16 (16.4%) pediatric and 21 (44.6%) adult patients. Of all pediatric patients positive for Actinomyces, 13 were males and three were females whereas of all adult patients positive for actinomyces, 14 were males and seven were females. Tonsillar tissue volumes in both pediatric and adult patients positive for Actinomyces were statistically higher than the Actinomyces negative ones. Antibiotic use was higher and the incidence of Actinomyces was lower in pediatric patients than in adult patients positive for Actinomyces.

Conclusion: Our study results revealed that Actinomyces was prominent in adult patients with tonsillar hypertrophy. In addition, the frequent use of antibiotic decreased the incidence of Actinomyces in tonsillar tissues.

Keywords: Tonsillectomy, histopathological examination, actinomyces, antibiotic

Introduction

Actynomycetes are Gram-positive, spore-free, facultative anaerobic bacteria showing branching filaments with varying cellular morphology. They do not exist in the nature. Human is the only natural reservoir (1). They mostly cause actinomycotic infections involving cervicofacial, abdominopelvic, and pulmonothoracic regions (2, 3). *Actinomyces israelii* and *Actinomyces naeslundii* are the most prevalent species isolated in humans (4, 5). These bacteria are found in the gingival clefts and tonsillar crypts in normal structure of oral flora, especially in periodontal pockets, dental plaques, rotten teeth, and upper respiratory tracts (1, 6).

The role of Actynomycetes in the tonsillar tissue is not fully understood. Although Actynomycetes are parts of the normal flora of tonsil tissue, primary tonsillitis can cause infection if the mucosal barrier is impaired and spread to the surrounding tissues with the proteolytic enzymes they produce (3, 7).

In this study, it was aimed to investigate the incidence of Actinomycosis in the tonsillar tissue of patients who underwent tonsillectomy and to reveal the relationship between the presence of Actinomycosis and the age, gender, volume of tonsillar tissue, and the antibiotic use before the operation.

Methods

A total of 142 patients who underwent tonsillectomy with the diagnosis of recurrent acute tonsillitis or chronic tonsillitis between January 2012 and December 2015 at Başkent University Alanya Application and Research Center were included in this study. The study protocol was approved by the local ethics committee (Project no: KA12/27). Patients who had an attack of acute

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tonsillitis at least seven times in the last 1 year, at least five times in the last 2 years, and at least three times in the last 3 years or patients that were followed up with chronic tonsillitis infection for longer than 3 months were included in the study. Patients who underwent tonsillectomy due to malignancy were excluded from the study.

All patients underwent tonsillectomy under general anesthesia with a cold knife technique. Immediately after the operation, the tonsillar volume was calculated by measuring the three dimensions of the tonsillar tissue without placing the specimen in the formalin solution (8). All operations were performed by the same surgeon, and all the specimens were examined by the same pathologist. The information of age, gender, tonsillar tissue size, and presence of Actinomycosis in tonsillar tissue was recorded. Whether they used antibiotics within 15 days before the operation was also noted in the patient files, and if they did, for how long and which antibiotics they used was also recorded.

Once the tonsillar tissue was removed and its measurements were completed, it was placed in a 10% formalin solution (formaldehyde 37%-40%, Merck, Darmstadt, Germany) and sent for histopathological examination. Microscopic slices were taken after paraffin blocking. The slices were stained with hematoxylin and eosin and were examined under a light microscope (Axioskop 2; Carl Zeiss, Oberkochen, Germany). Actinomycosis was investigated in all tissue samples (Figure 1).

The patients were divided into two groups: (i) younger than 16 years "children" and (ii) older than 16 years "adults." In both the groups, the presence of Actinomycosis was compared with age, gender, and tonsillar tissue size.

The data obtained in the study were analyzed using the Statistical Package for Social Sciences (SPSS for Windows 22.00; IBM, NY, USA) program. The descriptive statistical data were calculated as number, percentage, mean, and standard deviation when the data were assessed. Before comparisons in age subgroups, the appropriateness of the data to the normal distribution was investigated in terms of age distribution and the tonsillar volume. Therefore, nonparametric Mann-Whitney *U* test was used for binary comparisons of age distribution and the tonsillar volumes among the groups. The data on gender distribution (male-female), presence of Actinomyces, and antibiotic use in groups were processed using the chi-square test which we use in the statistics of the data indicated by numbers. The findings were interpreted within a significance level of 0.05 and in a 95% confidence interval.

Informed consents were obtained from the adult patients themselves, and for children, they were obtained from their parents.

Results

In this study, 284 tonsillar tissues of 142 patients were examined histopathologically. There were 95 patients in the pediatric group. The mean age of the children was 6.3±2.4 years (3-15 years). Of the children, 55 were boys and 40 were girls. There were 47 patients in the adult group. The mean age was 28.8±9.4 years (16-56 years). Of these patients, 27 were male and 20 were female (Table 1).

The mean volume of the tonsils in the pediatric group was 7.6±3.3 cm^3 and 9.4±4.1 cm^3 in the adult group. In the pediatric group, while the mean volume of tonsils with Actinomyces in their tonsillar tissue was 9.6±3.9 cm^3, the mean volume of tonsils without Actinomyces was 7.2±3.0 cm^3 (p=0.030). In the adult group, the mean volume of tonsils with Actinomyces in tonsillar tissue was 9.7±4.1 cm^3, whereas the volume without Actinomyces was 8.0 ± 4.1 cm^3 (p=0.043). In both the pediatric and the adult groups, the volume of tonsils was higher in which Actinomyces was detected and this was statistically significant.

In the pediatric group, Actinomyces was detected in the tonsils of 16 patients (16.4%). Three of them were girls and 13 were boys. Actinomyces was detected in tonsillar tissues of 21 adult patients (44.6%). Of these, 14 were male and 7 were

Table 1. General descriptive demographic information

	Child (under 15 years)	Adult (16 years and over)
n, %	95 (66.9%)	47 (33.09%)
Median age, years	6.30±2.4	28.8±9.4
Range (min-max), y	3-15 y	16-56
Tonsillar volume, cm^3	7.6±3.3	9.4±4.1
Total	142 patients	

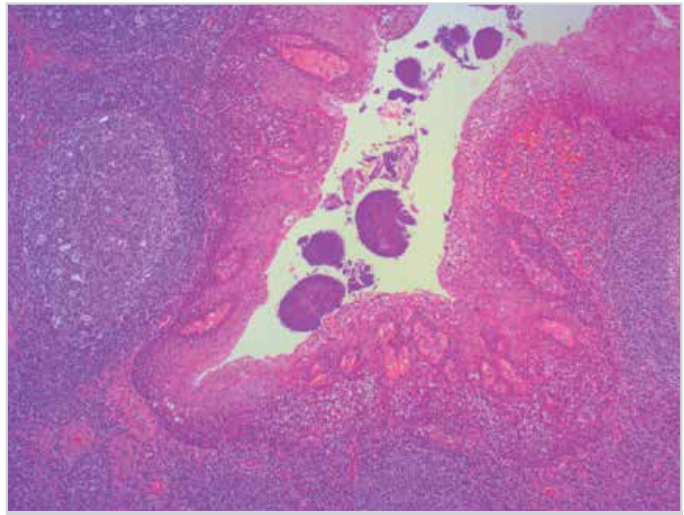

Figure 1. Actinomyces colonies in the tonsillar crypt lumen and leukocyte infiltration with polymorphic nucleus in the crypt epithelium. Hyperplasic lymphoid tissue with obvious germinal center is seen in subepithelial stromal area (hematoxylin and eosin, ×50).

female. In both the pediatric and adult groups, the number of Actinomyces-positive male patients was higher, and it was found that this difference was statistically significant in terms of gender. The mean age of children with Actinomyces was 7.6±3.0 years, whereas the mean age of the adults with Actinomyces was 31.2±10.3 years (Table 2). While the relationship between the incidence of Actinomyces and the mean age was significant in children (p=0.043), it was not significant in adults (p=0.073). While the incidence of Actinomyces increases as the age increases in children, no such finding was found in adults.

Before the tonsillectomy operation, 42 children had a history of 1-week to 10-day antibiotic use (penicillin or clarithromycin) in the last 15 days. In adults, 10 patients had a history of antibiotic use (penicillin or clarithromycin) and two patients had a history of antibiotic use (ciprofloxacin). While six of the children with Actinomyces used antibiotics, three of the adults with Actinomyces used antibiotics. A statistically significant inverse relationship was found in terms of the use of antibiotics and the likelihood of Actinomyces in both the pediatric and adult groups (p=0.026 for children, p=0.020 for adults).

Table 2. Presence of actinomyces in child and adult groups

	Child			Adult		
	Actinomyces (+)	Actinomyces (-)	p	Actinomyces (+)	Actinomyces (-)	p
n (%)	16 (16.84%)	79 (83.15%)	0.000	21 (44.6%)	26 (55.3%)	0.000
Median age, y	7.62±3.00	6.11±2.25	0.043	31.28±10.32	26.88±8.90	0.073

Table 3. Rates of actinomyces detection in tonsillar tissue according to publications

Researchers	Number of patients			Presence of actinomyces
	Child	Adult	Total	
Kutluhan et al. (4)	90	-	90	30 (%33.3)
Riffat et al. (10)	1213	-	1213	221 (%18.2)
Bulut et al. (11)	38	60	98	24 (%24.4)
Ozgursoy et al. (5)	46	-	46	11 (%23.9)
van Lierop et al. (3)	172	-	172	20 (%11.6)
Aydın et al. (12)	1820	-	1820	12 (%6.7)
Papouliakos et al. (13)	753	-	753	6 (%8)
Ashraf et al. (7)	103	101	204	83 (%40.7)
Erkılıç et al. (14)	-	-	1220	101 (%8.2)
Toh et al. (15)	72	762	834	297 (%35.6)
Yasan et al. (6)	150	-	150	53 (%35.3)
Bhargava et al. (9)	170	132	302	86 (%28.5)
San et al. (16)	103	-	103	9 (%8.7)
Pransky et al. (17)	460	-	460	84 (%18.8)
Kansu	95	47	142	37 (%26)

Discussion

The presence of Actinomyces in the tonsillar tissue was first detected in 1896 (9). Since then, numerous studies were conducted on this subject, and various data were reported on the frequency of Actinomyces in tonsillar tissue in different publications (6.7%-40.7%) (Table 3). While Aydin et al. (12) examined 1820 tonsillectomy materials with the highest patient data and found Actinomyces in only 6.7% of them, Riffat and Walker (10) studied tonsillar tissues in 1213 patients and found Actinomyces in 18.2% of them. In our study, tonsillectomy materials of 142 patients were examined and Actinomyces was detected in 37 (26%) of them.

Considering the gender factor, there are many studies that show that Actinomyces is more common in men. However, there is no definite consensus on this issue. Although San et al. (16) published in their article that Actinomyces was more common in men, in some other studies, it was reported that there was no difference in terms of gender (3, 4, 9). Erkiliç et al. (14) found Actinomyces in 101 of the tonsillectomy materials of 1220 patients and found that there was a clear female predominance. Yasan et al. (6) also found more Actinomyces in women in the same way. However, in our study, significant male predominance was found in both the pediatric and adult groups.

Compared with children, it is stated that adults had more Actinomyces in the tonsillar tissue (7, 12, 15). Moreover, it was reported that tonsils in children younger than 3 years had no Actinomyces (16). In our study, the incidence of Actinomyces was significantly higher in the adult group than the pediatric group.

The role of Actinomyces found in the tonsillar tissue was not fully understood. Özgürsoy et al. (5) made histological examination of the tonsillar specimens and found that there was a significant increase in lymphoepithelial squamous cell metaplasia and secondary follicles in the Actinomycosis-positive tonsillar tissue. Takasaki et al. (18) published a 75-year-old case with unilateral excessive tonsillar hypertrophy that could be confused with malignancy and emphasized that Actinomyces causes lymphoid hypertrophy in the tonsils.

There are a number of studies investigating Actinomyces in tonsillectomy materials obtained for both recurrent tonsillitis and obstructive sleep apnea. In the majority of these publications, patients with obstructive sleep apnea had a higher incidence of Actinomyces in the tonsillectomy specimens than in those with recurrent attacks of tonsillitis (9, 17). As a result, it is thought that Actinomyces settled in the tonsillar tissue can play a role in tonsillar hypertrophy. It is thought that the microorganisms settled in the tonsil produce some toxins, resulting in tonsil hypertrophy (3, 10). On the other hand, Toh et al. (15) found no significant relationship between the size of the tonsil and the presence of Actinomyces. Likewise, Yasan et al. (6) reported that Actinomyces did not cause tonsillar hypertrophy. However,

no tonsil size was measured in any study except one (4). In our study, the size of the tonsils was compared and it was found that tonsils with Actinomyces in both the pediatric and the adult groups were significantly larger than those without Actinomyces.

One of the most important complications of Actinomyces settled in the tonsillar tissue, except the tonsil hypertrophy is bleeding in the late postoperative period. Schrock et al. (19) examined 1522 patients who underwent tonsillectomy and found a significant relationship between postoperative bleeding and Actinomycosis. In this study, 15 of the 113 patients with Actinomycosis were found to have bleeding in the late postoperative period. Although we experienced bleeding in three patients in the late period after tonsillectomy, they were not related to Actinomyces.

Considering that the patients with recurrent attacks of tonsillitis and that less Actinomyces was found in the tonsils of patients using antibiotics, Pransky et al. (17) suggested that administering penicillin therapy to the patients with obstructive sleep apnea for 12 weeks would reduce the size of tonsils and eventually eliminate the obstructive symptoms. But there is no study conducted on this subject. On the other hand, Bhargava et al. (9) found that patients with sickle cell anemia had a high rate of Actinomyces in their tonsils despite receiving long-term antibiotic treatment. Riffat and Walker (10) examined 1213 children who had tonsillectomy and found that children who underwent surgery for obstructive sleep apnea had a higher rate of Actinomyces colonization in the tonsillar tissues than children who underwent surgery for recurrent tonsillitis. They also interpreted the result that the frequent use of antibiotics reduced the prevalence of Actinomyces in tonsillar crypts. It was found that our patients who used antibiotics in the last 2 weeks before surgery had less Actinomyces and that there was a significant negative correlation between antibiotic use and the presence of Actinomyces in tonsillar specimens.

Some systemic diseases increase the incidence of Actinomyces. Bhargava et al. (9) found that Actinomyces in the tonsillar tissues of people with sickle cell anemia, thalassemia, and bronchial asthma was at higher rate and the probability of disease formation was also higher. It was thought that poor dental hygiene caused this situation.

Conclusion

Actinomyces are microorganisms that can be found in the tonsillar tissues opportunistically. Their presence in tonsillectomy material does not always indicate active infection. There is a higher incidence in adult tonsillar tissue than in children. Similarly, there is a higher rate in men than in women. It is thought that they cause lymphoid hypertrophy with the enzymes they produce. Frequent use of antibiotics reduces the frequency of Actinomyces in tonsillar tissue.

Ethics Committee Approval: Ethics committee approval was received for this study from the local ethics committee (Project no: KA12/27).

Informed Consent: Written informed consent was obtained from patients and patients' parents who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the author.

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