Prevalence of Tonsillar Actinomycosis in Tonsillectomy Specimens; Clinical Importance and Management

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ABSTRACT

Aim: We aimed to assess the prevalence of actinomycosis in tonsillectomy specimens and its clinical importance and management in our center.

Materials and Methods: In this retrospective matched case-control study, patients who underwent tonsillectomy during 2010-2015 in Shahid Mostafa Khomeini Hospital, Tehran, were studied. Data regarding age, sex, indication for surgery (such as recurrent tonsillitis or sleep-disordered breathing), tonsil size, and length of disease before surgery were collected in both histopathologically positive (case) and negative (control) patients for actinomycosis.

Results: From the 260 studied tonsillectomy specimens, actinomycosis was found in 20 (8.75%) and 60 Actinomycosis negative cases were chosen randomly for the control group. There was no statistically significant difference between the groups with respect to age, sex, length of disease before surgery, and incidence of actinomycosis in tonsillectomy due to recurrent tonsillitis or sleep-disordered breathing. However, the tonsil size was significantly greater in specimens positive for actinomycosis (8.65±1.5 mL versus 4.38±0.22 mL, p<0.001).

Conclusion: Actinomycosis in tonsillectomy specimens is an incidental histopathological finding and does not necessarily correlate with active disease; while it is associated with tonsillar hypertrophy and increased tonsil size.

Keywords: Actinomycosis, tonsillectomy, recurrent tonsillitis, tonsillar hypertrophy

Introduction

Tonsillar Actinomycosis is a rare pathological condition in tonsillectomy specimens and its clinical importance is still controversial (1). Tonsillectomy is the most frequent surgery in children (2). The most common indications for tonsillectomy are recurrent tonsillitis and obstructive diseases such as sleep apnea, snoring, and mouth breathing (3). The histopathological examination of tonsillectomy specimens is done routinely to rule out occult malignancy or granulomatous disease (2-4).

The prevalence of Actinomycetes in tonsil specimens varies from 1.3-37% (5-7). Actinomyces are a genus of gram-positive, pleomorphic, non-spore forming anaerobic, non-acid-fast branched filamentous bacteria (7). Six species of Actinomyces may cause disease in humans, but the most...
common isolated species are *Actinomyces israelii* and *Actinomyces naeslundii* (7).

The pathogenic *Actinomyces* species are commensals and saprophytic flora of the oropharynx, gastrointestinal tract and female genital tract and humans are a natural reservoir of pathogenic *Actinomyces* species (8).

*Actinomycosis* is a chronic disease which can form abscess, tissue fibrosis and secretory sinuses (9). The most common type for *Actinomycosis* is cervicofacial with a prevalence of 11-97% (10). The route of entry of the microorganism into the gastrointestinal tract from the mouth to rectum, is typically a break or trauma in the mucosa. Integrity of mucosal membrane is an important factor against infections. But this mechanical barrier is very thin and fragile in the gingival margin and tonsillar crypts and mucosal trauma in the tonsillar surface leads to a proliferation of these fastidious anaerobic bacteria in tonsillar crypts. *Actinomyces* species normally colonize tonsillar crypts and the oral cavity and many *Actinomyces* infections have odontogenic origins (9,10).

The prevalence of tonsillar *Actinomycosis* has been reported as higher in patients with sickle cell anemia, beta (β) thalassemia and β-hemolytic streptococcus (7). These conditions diminish the oxidation-reduction potential and cause a proliferation of *Actinomyces* in tonsillar tissue. This process may lead to tonsillar hypertrophy (7).

It has been suggested that tonsillar *Actinomycosis* may be an etiological factor in obstructive tonsillar hypertrophy and chronic tonsillitis (5,7,11-14). We aimed to assess the relationship between *Actinomycosis* in tonsillectomy specimens and the main causes of tonsillectomy as recurrent tonsillitis or sleep disordered breathing to calculate its prevalence in our center.

**Materials and Methods**

In this matched case-control study we gathered data from *Actinomycosis* histopathology samples of 20 patients who underwent tonsillectomy during 2010-2015 in Shahid Mostafa Khomeini Hospital, Tehran, Iran. To increase study power, we chose 60 *Actinomycosis* negative (An) tonsillectomy specimens for the control group. Power analysis shows that sample size was enough to assess associations.

Epidemiological data including age, sex, indication for tonsillectomy such as recurrent tonsillitis or sleep disordered breathing, tonsil size, and length of disease before surgery were recorded in both the *Actinomycosis* positive (Ap) and An groups.

Sleep disordered breathing was defined by snoring and mouth breathing during sleep or an irregular sleep pattern with clinically significant awakening from sleep with choking or gasping. Recurrent tonsillitis was diagnosed as greater than 6 acute tonsillitis attacks in 1 year or 3 in 2 consecutive years (2,3).

Tonsillectomy was performed with the cold dissection and suture ligation method and tonsils were sent in formalin to the pathology department. Histopathological analysis of the specimens was performed by two pathologists in the pathology ward of the hospital using direct microscopy and hematoxylin-eosin staining which is highly effective in showing *Actinomyces* colonies. Mean tonsillar size was recorded as the multiplication of length by height by width of tonsils measured and recorded in the pathologic results. The assessment of each tissue sample included an evaluation of mucosal surface, crypts and associated lymphoid tissue. The pathological feature of *Actinomycosis* was explained as aggregates of filamentous basophilic microorganisms arranged in radial spoke-like fusions. The diagnosis of *Actinomycosis* is established by two of the following conditions: positive culture, sulfur granules, and biopsy specimens showing the organisms (15).

Sulfur granules in infections other than *Actinomycosis* are very rare; therefore, their presence strongly supports the diagnosis (Figure 1). Although the ideal route for diagnosis is culture, its failure rate is very high because of the overgrowth of other microorganisms, lack of growth due to previous antibiotic therapy and inadequate anaerobic conditions or short-term incubation (16). Therefore, histopathological features from surgical specimens is the most preferred tool for diagnosis (Figures 2 and 3). Because our research was retrograde and on the pathologic specimens, and all the datas were without any information about patients, research was done completely secret and there was no need to ethics committee approval and informed consent.

**Statistical Analysis**

Logistic regression analysis was used to assess the relationship between tonsil size and *Actinomycosis*, after controlling confounding variables. Data were analyzed using SPSS software, version 16.

*Figure 1. Sulfur granule*
The categorical variables were analyzed with chi-square test and non-parametric data with Mann-Whitney U test.

**Independent Variables**: Data regarding age, sex, indication for surgery (such as recurrent tonsillitis or sleep-disordered breathing), tonsil size, and length of disease before surgery were collected.

**Dependent Variables**: Histopathologically positive (case) and negative (control) patients for actinomycosis.

**Confounding Variables**: Sex, indication for surgery (such as recurrent tonsillitis or sleep-disordered breathing)

**Main Variable**: Tonsil size.

**Results**

Twenty (8.75%) specimens (out of 260) were positive for Actinomycosis. Sixty (An) patients were chosen for the control group. The patients’ demographic data are summarized in Table I.

The mean ± standard deviation (SD) ages of patients in the Ap and An groups were 16.24±4.73 (range: 4-24 years) and 12.02±2.07 (range: 3-20) years, respectively (p=0.124). There were 9 (42.9%) women and 11 (57.1%) men in the Ap group and 26 (43.3%) women and 34 (56.7%) in the An group (p=0.927).

All the patients in the case group had recurrent tonsillitis and 14 (66.7%) had sleep disordered breathing as the indication for surgery. In the An group, 58 (98.3%) patients had recurrent tonsillitis and 31 (51.7%) had sleep disordered breathing. There was no statistically significant difference between the two groups in recurrent tonsillitis (p=1) or sleep disordered breathing (p=0.234).

Mean ± SD length of disease before surgery was 6.2±1 year in the Ap group and 5.8±1 year in the An group (p>0.05). The mean ± SD tonsil size in the Ap group was 8.65±1.54 mL and in the An group was 4.38±0.22 mL (p<0.001). Logistic regression analysis showed that Actinomycosis increased the tonsil size by 1.8 times (OR: 1.8, CI: 95%, 1.2-4.3).

**Discussion**

**Prevalence**: In our study the prevalence of tonsillar actinomycosis was 8.75%. The prevalence of Actinomycosis in the tonsils varies from 1.3% to 37% (5-7) and it has been identified in 6.7% (17), 18.3% (5), 29.5% (20), 28.5% (7), and 11.5% (18) of all tonsil specimens in different studies. The wide range of variation in reported frequencies have been attributed to different staining techniques by different laboratories and a difference in patients and working groups as well as indications for tonsillectomy (17,18).

**Age and Sex**: Some studies reported a relationship between Actinomyces colonization and age (17-19). Ashraf and colleagues reported a mean age of 23.34 years for patients with actinomycosis and 15.91 years for those without actinomycosis indicating a positive correlation with older age.
Several studies have aimed to identify the relationship between tonsillar Actinomycosis and clinical tonsillar disease including recurrent tonsillitis or sleep-disordered breathing (5,7,17,20,21). This theory was suggested in 1910 by Lord stating that isolation of Actinomyces from tonsillar crypts may correlate with tonsillar hypertrophy due to the production of toxin by the microorganism (22). However, this has never been proven.

A higher prevalence of Actinomycosis was reported in specimens from tonsillectomy for obstructive symptoms compared with recurrent tonsillitis (5-7,14,23). They suggested that tissue colonization with Actinomyces may have an etiological role in lymphoid hyperplasia and tonsillar hypertrophy (5,7,14). Therefore, administration of a 12-week course of oral penicillin to all patients with obstructive symptoms has been suggested (5). However, it has not been proven by other studies (4,7,20,21). Toh et al. (6) demonstrated that Actinomycosis does not have any effect on tonsillar size while another study (23) reported larger sizes of tonsils with Actinomycosis. In our study, tonsillar size was significantly greater in the case group. Therefore, colonization of microorganisms may have an important role in size.

One study showed that the prevalence of Actinomycosis colonization was higher in patients with recurrent tonsillitis than sleep-disordered breathing, but no statistically significant correlation was found between the presence of Actinomycosis and tonsillar hypertrophy or recurrent tonsillitis (19).

Another study found no relationship between clinical tonsillar disease and the presence of Actinomyces, in spite of finding a higher rate of cryptitis in tonsils with Actinomycosis, histopathologically (17).

A strong correlation was found between Actinomycosis and chronic tonsillitis showing positive tissue reaction to Actinomyces colonization in tonsil crypts suggesting its probable role in chronic and antibiotic resistant tonsillar symptoms (1).

In two other studies, no tissue reaction was found due to Actinomyces colonization in tonsils, therefore they reported no correlation between tonsillar Actinomycosis and recurrent tonsillitis (6,18). We also found no statistically significant difference in the indication for surgery such as recurrent tonsillitis or sleep disordered breathing between the two groups.

According to different studies it seems that Actinomycosis colonization in tonsillar tissue does not indicate any active disease and there seems to be no correlation between its colonization and clinical tonsillar disease.

**Histopathology:** Tonsillar actinomycosis in the present study was diagnosed via the presence of sulfur granules in histopathological sectioning and confirmed by histopathologic analysis of specimens, but there was no specific tissue reaction such as cryptitis or micro-abscess formation or fibrosis in the specimens. The diagnosis of Actinomycosis was accurately done by the isolation of Actinomyces species from specimen culture or immunofluorescence staining, but less than 50% of cases were positive because of previous treatment with antibiotics, unsuitable culture media, or growth of other bacteria species (24,25). The presence of Actinomycotic sulfur granules in histological sections is highly supportive for diagnosis because these granules are very rare in other infections, however it is not diagnostic (26).

In one study, microorganisms were situated deeply in tonsilar crypts in histological examination but there was no specific tissue reaction to Actinomyces colonization (18). Gaffney et al. (20) found no relationship between the presence of Actinomycosis and tonsillar fibrosis or micro-abscess in reviewing the histology results of tonsil specimens with Actinomycosis. Aydin et al. (17) found cryptitis in tonsillar tissue and suggested that cryptitis can be used as a histological indicator of tonsillar Actinomycosis.

Riffat and Walker (27) used histopathological analysis with hematoxylin-eosin staining plus microbiological culture for Actinomycosis and suggested that Actinomyces colonization in tonsillar tissue cannot be neglected as passive saprophytes and its correlation with clinical diseases must be further studied.

**Management:** Actinomyces species are susceptible to several antibiotics such as penicillin G, erythromycin, and tetracyclines (8). Penicillin G is the drug of choice for all clinical forms of Actinomycosis and tetracycline is the drug of choice for patients who are allergic to penicillin (24,28).

The treatment of choice for Actinomycosis in chronic fibrosing conditions is long-term high doses of antibiotics to penetrate into the suppurated fibrosis, in conjunction with drainage of the abscess and surgical excision of fistula and sinus tracts (24).

In some trials, oral penicillin for 12 weeks was suggested as a medical management of tonsillar Actinomycosis (5,29,30). However, in another study, this method appeared to be ineffective because, in some patients with sickle cell anemia who had received penicillin for a long period, there was Actinomycosis in their tonsils. Therefore, surgical excision has been recommended as the definitive treatment for head and neck Actinomycosis and tonsillectomy is the definite therapy for tonsillar Actinomycosis (7).
We hypothesize that the presence of *Actinomyces* in tonsillar specimens may have an etiological role in tonsillar hypertrophy and long-term tonsillar problems and chronic tonsillitis refractory to antibiotics. However, there was no specific evidence of tissue reaction to *Actinomyces* in tonsillar specimens and their presence was found to be due to superficial colonization of the tonsillar crypts. Therefore, it seems to be an incidental finding.

**Study Limitations**

This study was based on data gathered from patient medical records. We were not able to investigate the relation between sleep disorders and nasal obstruction. It is probable that some patients with history of mouth breathing suffered from a very common disease such as allergic rhinitis, which was not identified in patients with sleep-disorder breathing. This nasal obstruction may also affect our data analysis and influence some associations between sleep-disorder breathing and tonsil size.

**Conclusion**

In this study, we found no relationship between tonsillar Actinomycosis and tonsillectomy indications such as recurrent tonsillitis and sleep disordered breathing. However, tonsil size in Ap specimens were found to be significantly larger than An ones. Therefore, the presence of *Actinomyces* colonization in tonsillar specimens may have an etiological role in tonsillar hypertrophy and long-term tonsillar lesions and chronic tonsillitis refractory to antibiotics with no correlation or questionable relation with tonsillectomy indications such as recurrent tonsillitis and sleep-disordered breathing. However, this needs further study with a larger number of specimens or long-term prospective studies with meticulous methods for identifying the microorganism.

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**Ethics**

**Ethics Committee Approval**: Because our research was retrograde and on the pathologic specimens, and all the datas were without any information about patients, research was done completely secret and there was no need to ethics committee approval.

**Informed Consent**: Because our research was retrograde and on the pathologic specimens, and all the datas were without any information about patients, research was done completely secret and there was no need to informed consent.

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