

## Implication of *Fusobacterium necrophorum* in Recurrence of Peritonsillar Abscess

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**Objective:** Peritonsillar abscess (PTA) is a common infectious complication of pharyngeal infection managed by otolaryngologists and emergency room physicians. *Streptococcus* and *Fusobacterium* (e.g., *Fusobacterium necrophorum*, *FN*) species are commonly isolated pathogens. The aim of this study was to determine the implication of culture results on abscess recurrence following drainage.

**Methods:** Single-institution retrospective review of patients treated at the University of Michigan between 2000 and 2017. Demographic and clinical outcome data were analyzed, including treatment details, culture data, and recurrence.

**Results:** One hundred fifty-six of the 990 patients in our study developed recurrence of their abscess (16%). The age ranges most susceptible to recurrence included adolescent (22.9%) and young adult groups (17.1%). Recurrent patients were more likely to have experienced acute progression of symptoms (79% vs. 71%,  $P = 0.03$ ), trismus (67% vs. 55%,  $P = 0.006$ ), voice changes (65% vs. 57%,  $P = 0.04$ ), and dysphagia (72% vs. 61%,  $P = 0.01$ ) compared to nonrecurrent patients. They were also more likely to have clinical lymphadenopathy noted on initial examination (67% vs. 56%,  $P = 0.009$ ). Culture data was sent for 852 patients (86%). The presence of *FN* was significantly more prevalent in the recurrent group ( $P < 0.0001$ ).

**Conclusion:** There is a high observed prevalence of *FN* species within PTA aspirates in the recurrent PTA population. PTA aspirate should be sent for anaerobic growth to screen for *Fusobacterium* species. In addition, follow-up and lower threshold for subsequent tonsillectomy should be considered in this at-risk group.

**Key Words:** Peritonsillar abscess, intratonsillar abscess, otolaryngology, *Fusobacterium necrophorum*, *Streptococcus anginosus*.

**Level of Evidence:** 3

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### INTRODUCTION

Peritonsillar abscess (PTA) is the most commonly occurring abscess in the head and neck region. There is an annual incidence of 30 cases per 100 thousand inhabitants in the United States, or a total of approximately 45 thousand cases per year.<sup>1</sup> The typical management of PTAs includes needle aspiration and drainage and is occasionally followed by formal incision and dissection of the peritonsillar space.<sup>2</sup> Adjunctive measures can include intravenous fluids, steroids, analgesic medications, and antibiotics. Although less common in contemporary times, surgical drainage or performance of *quinsy* tonsillectomy is occasionally performed for urgent evacuation of purulence in select patients.<sup>3–5</sup> Persistent disease or development of a

recurrent abscess can be common, with studies describing recurrence rates ranging from 9.6% to 40%.<sup>6–8</sup>

Factors that have been implicated in recurrent peritonsillar abscesses included younger age (16–30 years), prior history of recurrent tonsillitis, history of prior PTA, longer hospital stay, prior hospitalization for antibiotics, and extraperitonsillar spread on computed tomography (CT) imaging.<sup>6,7,9</sup> The consequence of these risk factors may include greater need for follow-up or stronger consideration for tonsillectomy.

The microbiological characterization of the peritonsillar abscess has also been well studied, albeit not in the context of recurrent disease. In a retrospective review on bacterial cultures from abscess aspirates, Mazur et al. found that the most frequently isolated pathogenic monoculture was *Streptococcus pyogenes*.<sup>9</sup> In this retrospective review, the authors aim to characterize risk factors implicated in patients with persistent or recurrent peritonsillar abscesses, with particular attention paid to the pathogens isolated from aerobic and anaerobic cultures.

### MATERIALS AND METHODS

#### *Study Population*

We performed an institutional review board-approved single-institution retrospective case series of patients who

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presented to our emergency department or outpatient clinic with suspicion for a deep neck space infection. Patients who were diagnosed with a peritonsillar or intratonsillar abscess (ITA) from 2000 to 2017 were included. Diagnostic criteria for the PTA included radiologist confirmation of debris or abscess within peritonsillar space, or evacuation of purulence from peritonsillar space either via bedside procedure or operative quinsy tonsillectomy, or clinical diagnosis of early peritonsillar abscess after failed evacuation attempt. Diagnostic criteria for the ITA included radiologist confirmation of debris or abscess within the tonsillar parenchyma, or evacuation of purulence from the intratonsillar parenchyma either via bedside procedure or operative quinsy tonsillectomy. Patients who did not have a diagnosis of PTA or ITA were excluded from the study, as were patients who had infections present within additional spaces of the neck (such as concomitant parapharyngeal or retropharyngeal abscesses). We excluded patients with diagnoses of viral pharyngitis or tonsillitis as interpreted from clinical reports. Herein, if there was no imaging performed or no evacuation of purulence after aspiration attempt, cellulitis was distinguished from “early” or “developing” abscess based off clinical interpretation of the treating provider. Demographics, clinical symptomatology, primary treatment modality, imaging characteristics, microbiological growth, and follow-up data were tabulated. Data were collected using clinical notes and imaging available in our electronic medical records system.

### Statistical Analysis

Standard descriptive statistics were tabulated, and bivariate associations with recurrent versus nonrecurrent cohorts were tested with chi-square tests and *t* tests where appropriate. Multivariable modeling was performed in two stages: First, all demographic, basic clinical factors, and symptomatology (listed in Tables I and II) were considered as potential predictors of recurrence in multivariable logistic regression models. Backward selection, with alpha criteria of 0.10, was performed. Second, additional factors for which we had subsets of patient information, such as white blood cell (WBC) count, rapid mononucleosis testing and rapid streptococcal testing, were tested for significance individually in addition to the parsimonious clinical model. Alpha of 0.05 was considered significant, and all analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC).

## RESULTS

Our study initially identified 1,335 patients with a diagnosis of PTA or ITA. Patients with diagnoses of viral

TABLE I.  
Demographic Information.

Patients N = 990	Overall (n, %)	No Recurrence	Recurrence	P Value
		(n, %) N = 834	(n, %) N = 156	
Age (mean, median, range)	24.3, 20.5, 1.2–88	24.8, 21.0, 1.2–88	21.8, 19.0, 6–65	< 0.001
Age group 0–12	82 (8%)	76 (9.1%)	6 (3.8%)	< 0.01
Age group 13–18	253 (26%)	195 (23.3%)	58 (37%)	< 0.001
Age group 19–30	432 (44%)	358 (43%)	74 (47%)	0.30
Age group 31–50	171 (17%)	156 (19%)	15 (9.6%)	< 0.001
Age group 51+	52 (5%)	49 (5.9%)	3 (1.9%)	< 0.01
Male gender	504 (51%)	426 (51%)	78 (50%)	0.80

TABLE II.  
Comparative Clinical Information for Recurrent and Nonrecurrent Groups.

Patients N = 990	Overall (n, %)	No Recurrence	Recurrence	P Value
		(n, %) N = 834	(n, %) N = 156	
Duration of symptoms	≤ 3 days	293 (30%)	256 (31%)	0.12
	4–7 days	479 (48%)	402 (48%)	0.81
	> 7 days	218 (22%)	176 (21%)	0.13
Fever	427 (43%)	363 (44%)	64 (41%)	0.56
Sore throat	990 (100%)	834 (100%)	156 (100%)	–
Worsening of symptoms	716 (72%)	592 (71%)	124 (79%)	0.03
Otalgia	577 (58%)	478 (57%)	99 (63%)	0.15
Trismus	561 (57%)	457 (55%)	104 (67%)	0.006
Cough	58 (6%)	51 (6%)	7 (5%)	0.43
Voice change	574 (58%)	472 (57%)	102 (65%)	0.04
Dysphagia	624 (63%)	512 (61%)	112 (72%)	0.01
Dyspnea	47 (5%)	40 (5%)	7 (5%)	0.87
Anorexia	468 (47%)	387 (46%)	81 (52%)	0.21
Neck pain	192 (19%)	160 (19%)	32 (21%)	0.70
Lymphadenopathy	573 (58%)	468 (56%)	105 (67%)	0.009

pharyngitis, tonsillitis, or other concomitant deep neck space infections were excluded. From this group, 990 patients were remaining. Demographics information for recurrent and nonrecurrent groups are shown in Table I. In all, 156 of the 990 patients developed recurrence of their abscess (16%). Patients were further subcategorized into age ranges: children were categorized as 0 to 12 years, adolescents into 13 to 18 years, young adults into 19 to 30 years, and adults were split into 31 to 50 and 50 + years as noted. The age ranges most susceptible to recurrent abscesses included the adolescent (23% recurrence rate) and the young adult groups (17% recurrence rate). Recurrent abscesses were uncommon in children (7.3% and the 50 + age group (5.8%).

Clinical information for the two cohorts is displayed in Table II. There were no significant differences in duration of symptoms between the recurrent and nonrecurrent groups. From a presenting symptomatology perspective, those who developed recurrences were more likely to have initially experienced acute progression of symptoms (79% vs. 71%, *P* = 0.03), trismus (67% vs. 55%, *P* = 0.006), voice changes (65% vs. 57%, *P* = 0.04), and dysphagia (72% vs. 61%, *P* = 0.01). They were also more likely to have clinical lymphadenopathy noted on initial examination (67% vs. 56%, *P* = 0.009).

Objective laboratory data and culture data are demonstrated in Table III. There was no statistically significant difference between the two cohorts in regard to elevated WBC count and development of recurrence. Rapid Epstein-Barr virus testing was found to be positive in a greater proportion of nonrecurrent patients (20% vs. 9%, *P* = 0.03). Overall, 494 (50%) patients were treated with amoxicillin-clavulanate, 493 (50%) with clindamycin, and three with a penicillin (0.4%) at their initial visitation. There was no statistically significant difference between the proportion of patients placed on

TABLE III.  
Objective Information for Recurrent and Nonrecurrent Groups.

Patients		Overall (n, %)	No Recurrence (n, %)	Recurrence (n, %)	P Value
White blood cell count (N = 734)	Normal (< 11.0)	184 (25%)	161 (26%)	23 (20%)	0.17
	Elevated (> 11.0)	550 (75%)	458 (74%)	92 (80%)	0.19
Rapid tests					
Mononucleosis (N = 451)	Positive	83 (18%)	76 (20%)	7 (9%)	0.03
Streptococcus, (N = 694)	Positive	124 (18%)	111 (19%)	13 (13%)	0.12

amoxicillin-clavulanate who experienced a recurrence versus those placed on clindamycin (17% vs. 15%, respectively,  $P = 0.39$ ).

Culture data is tabulated in Table IV; the microbiological data presented was obtained from the patient's initial visit to the hospital. Among the 990 patients with peritonsillar or intratonsillar abscesses, culture data was sent for 566 patients (58%). The remaining patients either did not have purulence aspirated with drainage attempt or no culture data was sent. The presence of *Fusobacterium necrophorum* (FN) (67% vs. 13%,  $P < 0.0001$ ) were significantly more prevalent in the recurrent group. There was no statistically significant association with presence of *Streptococcal* species, *Eikenella corrodens*, *Bacteroides fragilis*, *Prevotella* species, and *Staphylococcus aureus* species and recurrent PTA. Although not statistically significant, there was a large proportion of patients with *Streptococcus anginosus* (SA) with recurrent PTA (n = 32, 23%).

Further analysis of the relationship between FN and SA is demonstrated in Figure 1. For the patients for whom culture data was available, only 4% experienced recurrence in the absence of growth of FN or SA. For isolated bacteria, there was a 44% recurrence rate with presence of FN only and a 14% recurrence rate with presence of isolated SA. The recurrence rate for concomitant growth of FN and SA (42%) was similar to recurrence rates for FN only (44%).

A logistic regression model was utilized to assess odds of recurrence depending on isolated versus concomitant FN and SA growth, as demonstrated in Table V. This demonstrates that the odds of recurrence are significantly smaller for lack of growth of FN and SA and for the SA-positive only cohorts in comparison to the cohort with growth of both FN and SA. The odds of recurrence are similar for FN-positive only in comparison to FN and SA cohort.

TABLE IV.

Culture Data for Recurrent and Nonrecurrent Groups Obtained From Initial Hospital Visit.

Patients N = 566	Overall (n, %)	No Recurrence (n, %) N = 447	Recurrence (n, %) N = 119	P Value
Any streptococcus species	203 (35%)	159 (35%)	44 (37%)	0.68
Beta-hemolytic streptococcus group A	51 (9%)	42 (9.4%)	9 (7.6%)	0.61
Beta-hemolytic streptococcus group C	5 (<1%)	4 (0.9%)	1 (0.8%)	0.72
<i>Streptococcus agalactiae</i>	3 (<1%)	2 (0.4%)	1 (0.8%)	0.13
<i>Streptococcus pneumoniae</i>	3 (<1%)	2 (0.4%)	1 (0.8%)	0.13
<i>Streptococcus anginosus</i> group	140 (24%)	108 (24%)	32 (27%)	0.51
<i>Fusobacterium necrophorum</i>	176 (31%)	99 (22%)	77 (65%)	< 0.00001
<i>Prevotella</i> species	67 (12%)	55 (12%)	12 (10%)	0.52
No growth of organisms	76 (9%)	68 (15%)	8 (7%)	0.005
<i>Fusobacterium nucleatum</i>	27 (5%)	25 (5.6%)	2 (1.7%)	0.14
<i>Staphylococcus aureus</i>	20 (4%)	15 (3.4%)	5 (4.2%)	0.69
<i>Eikenella corrodens</i>	15 (3%)	11 (2.4%)	4 (3.4%)	0.58

## DISCUSSION

There exists a plethora of potential reasons for persistent or recurrent peritonsillar disease. Early recurrences, or persistence of disease, could be related to inadequate treatment (such as inadequate drainage of the peritonsillar space), extraperitonsillar spread of infection, or autoimmune deficiency.<sup>6,7,10</sup> Later recurrences could be related to autoimmune deficiency or prior history of tonsillitis or pharyngitis. In this retrospective review, our results indicated that those patients with persistent or recurrent disease were more likely to have presented with acutely progressive symptoms, trismus, voice changes, dysphagia, and lymphadenopathy. These findings are likely related to the probability that those with more severe symptoms, and resultant more severe infections, were more likely to present again with symptoms and abscesses that required repeat intervention. There further appeared to be a specific age range at which patients with pharyngeal abscesses were more likely to present with recurrent disease, specifically the age range of 13 to 18 years (23% recurrence rate) and the age range of 19 to 30 years (17%). This finding may be related to previous findings in the literature that those with a history of recurrent tonsillitis were more likely to develop PTAs and recurrent PTAs.<sup>6</sup>

The relationship of pathogenic organisms to peritonsillar abscess recurrence has not been previously well studied. Upon initial analysis, although not statistically significant, there did appear to be a potential association

### Comparison of *Fusobacterium Necrophorum* and *Streptococcus Anginosus* Growth in Culture

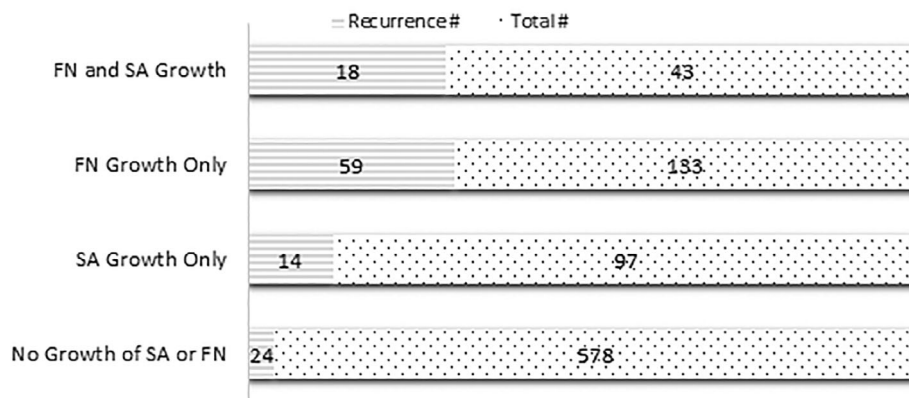


Fig. 1. Demonstration of overlap between *Streptococcus anginosus* and *Fusobacterium necrophorum*.

between *Streptococcus anginosus* growth and recurrent abscesses. However, further characterization demonstrated that the effect appeared to be attributable to concomitant growth of *FN* within those cultures. The *SA* group consists of morphologically similar strains, including *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*.<sup>9</sup> Previous studies have demonstrated no association between streptococcal species, including *SA*, and recurrent peritonsillar disease.<sup>11</sup>

In this study, the presence of *FN* species within such a large proportion of patients with previous peritonsillar abscesses or among those who eventually developed recurrent PTAs certainly suggests a relationship between *FN* and difficult-to-eradicate peritonsillar disease. Although this concept may be novel, the presence of *FN* within head and neck abscess aspirate is not.

*Fusobacterium* species, strictly anaerobic gram-negative rods, are primarily isolated from the oral cavity, although they can also be found in the abdomen and urogenital tract.<sup>12</sup> The publication of newer studies connecting *Fusobacterium* species with head and neck infections may be related to increased awareness of the potential devastating effects of this pathogen, with resultant increased testing. In a Danish study conducted on patient specimens collected between 2010 and 2014, the authors reported that *FN* was present on throat swab in 516 cases per million/year in the age range of 10 to 19 years and 302 cases per million/year

in the age range of 20 to 29 years.<sup>13</sup> In relation to aspirates from PTAs, *FN* was present in 168 and 116 cases per million/year in the age ranges of 10 to 19 and 20 to 29 years, respectively.<sup>13</sup> Additional studies offer support for routine anaerobic testing of patients with suspected pharyngotonsillitis, citing *FN* as the most prevalent cause of such infections in the age group of 15 to 30 years.<sup>14</sup> A large retrospective review of 847 patients demonstrated that *FN* was the most frequently detected bacteria in PTA culture (present in 23% of cultures), in addition to being significantly associated with a younger patient population (median age 18 years).<sup>15</sup> Although the long-term effects of *FN* are poorly elucidated, there is evidence to suggest that colonization of this organism may lead to a decrease in the diversity of the tonsillar microbiome.<sup>16</sup>

The implication of *FN* as a pathogenic driver for recurrent peritonsillar infections and abscesses fits within the continuum of our increasing awareness of *FN* presence with pharyngotonsillar infections and well-established knowledge of *FN* generation of Lemierre syndrome.<sup>17</sup> It is thus theorized that *FN* acts to colonize the oropharynx and result in recurrent infections/abscesses.<sup>18,19</sup> There is increasing evidence that *FN* preferentially colonizes or manifests in a specific age range; in this study, we note that the age range at greatest risk for recurrence is the 13- to 18-years-old category. Previous studies have demonstrated that *FN*-driven tonsillitis preferentially affects a similar 10- to 19-years-old age category.<sup>13</sup> Similarly, the population at greatest risk for *FN*-driven Lemierre syndrome is in the 14- to 24-years-old age range, with one study demonstrating a median age of 18 years.<sup>20,21</sup> Treatment strategies in this young patient population may need to be reconsidered. Initially, based off the findings in this study of the potential significance of certain pathogens, we would recommend that all PTA aspirate be sent for aerobic and anaerobic culture. In the event of *FN* growth, the literature as it pertains to antibiotic treatment and duration is largely theoretical and empiric. Penicillins, metronidazole, and clindamycin are known to have low minimal inhibitory concentrations for *FN*, and resistance is rare.<sup>14</sup>

TABLE V.

Odds Ratio Estimates for Recurrence Risk With *Streptococcus anginosus* and *Fusobacterium necrophorum*.

Effect	Point Estimate	95% Wald Confidence Limits	
<i>FN</i> - and <i>SA</i> -negative versus <i>FN</i> - and <i>SA</i> -positive	0.060	0.029	0.125
<i>FN</i> -positive only versus <i>FN</i> - and <i>SA</i> -positive	1.107	0.552	2.221
<i>SA</i> -positive only versus <i>FN</i> - and <i>SA</i> -positive	0.234	0.102	0.537

*FN* = *Fusobacterium necrophorum*; *SA* = *Streptococcus anginosus*.



In the absence of pertinent clinical studies, it is difficult to make specific recommendations for treatment type and duration. There does appear to be a role for close and dedicated follow-up for these patients and possible low threshold to consider tonsillectomy. Although none of the recurrent patients in our cohort with *FN* developed Lemierre syndrome, it is certainly a known and severe possibility.

### Study Limitations

The limitations of this study are related to its retrospective nature. As discussed in the Methods section, the diagnosis of PTA was based off radiographic, procedural, or clinical findings. Whereas diagnoses derived from imaging or evacuation of purulence are largely objective, there is inherent bias in diagnosing an abscess in the absence of imaging findings or confirmation via evacuation of purulence from an abscess cavity. This relegates the diagnosis of “early” or “developing” abscess versus cellulitis to the treating practitioner, which can be inconsistent and potentially incorrect. Thus, this introduces the possibility that some of the recurrent PTA cases may have simply represented cellulitis at the time of initial treatment, or that the provider may have missed the abscessed cavity on intervention. Further limitations stem from the lack of standardized workup and treatment of suspected PTA cases. This is demonstrated in the non-uniform performance of CT imaging, rapid streptococcus testing, Epstein-Barr virus testing, and even obtainment of culture data from aspirate. Although custom analyses were performed for the subset of patients who did have the aforementioned testing performed, it is difficult to determine definitive conclusions due to this nonstandard workup.

### CONCLUSION

Peritonsillar abscess is the most common neck space abscess; the clinical course and treatment results in significant patient distress, lost school/work days, and specialized care. Recurrent PTAs have been previously linked to extraperitonsillar spread on imaging, prolonged hospital stays, prior hospitalizations, and younger age range. In this retrospective review, we describe increased prevalence of *FN* within PTA aspirates in the recurrent PTA population. Given this finding, it would be prudent for all practitioners to send aspirate for anaerobic growth to screen for *FN*. In addition, we would recommend close and dedicated follow-up with a low threshold to pursue tonsillectomy in this patient population. Future prospective studies can better help elucidate the ideal type of antibiotic and duration of treatment to implement.

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### Contributor Statement

All the authors have made substantial contributions to this project, including contributions to conception and design, or acquisition of data, or analysis and interpretation of data. All authors were involved in drafting the article or revising it critically for important intellectual content. All authors have given final approval of the article, as submitted for publication and take responsibility for content. The authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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