Sinusitis in patients concurrently on tumor necrosis factor alpha inhibitors
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Abstract

Objective: Tumor necrosis factor alpha (TNF-α) inhibitors have revolutionized treatment of many impairing inflammatory diseases. We aim to characterize the features of sinusitis in patients concurrently on anti-TNF-α therapy and their treatment course.

Methods: This is a retrospective chart review of 28 patients diagnosed with sinusitis by a Duke otolaryngologist while on a TNF-α inhibitor. Descriptive statistics and bivariate analysis were performed with SPSS (Version 22, Chicago, IL). Phi correlation coefficients greater than r = +/- 0.3 and p ≤ 0.05 were considered significant.

Results: Of the 28 patients studied, 12 (42.9%) had a history of sinusitis prior to initiation of anti-TNF-α therapy and 16 (57.1%) had no prior history. 71.4% (n=20) of patients were diagnosed with chronic rhinosinusitis without polyps and 17.9% (n=5) had recurrent acute sinusitis. In the group with no prior history of sinusitis, the median time from drug initiation to diagnosis of sinusitis was 22.5 months (IQR: 2.25-111.75). Overall, 14.3% (n=4) of the cohort stopped, changed, or held doses of the drug due to sinusitis. 35.7% (n=10) of patients required a surgery or procedure, which included functional endoscopic sinus surgery (FESS) (25%, n=7) and balloon dilation (10.7%, n=3).

Conclusion: Anti-TNF-α therapy can be associated with development of sinusitis, especially chronic sinusitis. While surgery was sometimes necessary, discontinuation of anti-TNF-α therapy due to recurrent sinusitis was not necessary in most cases.

Background

• Tumor necrosis factor alpha (TNF-α) inhibitors have revolutionized the treatment of many immune-related chronic inflammatory diseases.
• There are five agents approved for use: infliximab, etanercept, adalimumab, certolizumab pegol, and golimumab
• TNF-α is a key proinflammatory cytokine in the pathogenesis of many inflammatory and autoimmune diseases
• Its inhibition has shown to reduce inflammation¹.
• TNF-α also plays a role in host immune defenses and responses to local injury.
• Thus, TNF-α inhibitors have been associated with a number of adverse effects, including an increased risk of serious infections².
• However the frequency and characteristics of less serious infections, such as sinusitis, are not as well understood.
• The development of sinusitis after initiation of TNF-α antagonists has been observed³,⁴, but its clinical features and disease course are not well characterized in literature. In this study, we aim to characterize sinusitis, both new onset and preexisting, in patients concurrently on anti-TNF-α therapy.

Methods

• Retrospective study of 28 patients diagnosed at Duke University with acute or chronic sinusitis by an otolaryngologist between October 1, 2010 and October 1, 2014 while concurrently receiving TNF-α inhibitor therapy.
• Demographics, pertinent medical and social history were collected
• Characteristics of the patients’ sinusitis and treatment course including subjective symptoms, endoscopic findings, computed tomography (CT)/magnetic resonance imaging (MRI) findings and sinus culture results were collected
• Sinus disease at time of initial diagnosis was classified into acute rhinosinusitis - single episode (ARS-single), acute sinusitis - >1 episode (ARS-multiple), chronic sinusitis without nasal polyps (CRSwNP), and chronic sinusitis with nasal polyps (CRSwNP).
• Statistical analysis was performed with SPSS (Version 22, Chicago, IL).
• Associations between categorical variables were examined using chi-squared tests. Phi coefficients greater than r = +/- 0.3 and p ≤ 0.05 were considered significant.

Results

Table 1: Sinusitis types in patients without a prior history of sinusitis and in entire cohort. ARS-single = acute rhinosinusitis-single episode, ARS-multiple= acute sinusitis - >1 episode, CRSwNP= chronic sinusitis without nasal polyps, CRSwNP+ chronic sinusitis with nasal polyps.

<table>
<thead>
<tr>
<th>Sinusitis type</th>
<th>Patients without a prior history of sinusitis (n=16, n, %)</th>
<th>Total cohort (n=28, n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARS-single</td>
<td>1.0 (63)</td>
<td>1.0 (36)</td>
</tr>
<tr>
<td>ARS-multiple</td>
<td>6.0 (31.3)</td>
<td>5.0 (17.9)</td>
</tr>
<tr>
<td>CRSwNP</td>
<td>10.0 (62.5)</td>
<td>20.0 (71.4)</td>
</tr>
<tr>
<td>CRSwNP+</td>
<td>0.0 (0)</td>
<td>2.0 (7.2)</td>
</tr>
</tbody>
</table>

Table 2: Changes in therapy in patients with and without a history of sinusitis, while on anti-TNF-α therapy

<table>
<thead>
<tr>
<th>Changes in TNF-α therapy</th>
<th>Patients with prior history of sinusitis (n=12, n, %)</th>
<th>Patients without prior history of sinusitis (n=16, n, %)</th>
<th>Total cohort (n=28, n, %)</th>
<th>Phi correlation coefficient (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinued</td>
<td>1.0 (8.3)</td>
<td>6.0 (37.5)</td>
<td>1.0 (36)</td>
<td></td>
</tr>
<tr>
<td>Switched to another agent in same class</td>
<td>0.0 (0)</td>
<td>1.0 (6.3)</td>
<td>1.0 (36)</td>
<td></td>
</tr>
<tr>
<td>Held due to sinusitis then restarted</td>
<td>0.0 (0)</td>
<td>2.0 (12.5)</td>
<td>2.0 (7.1)</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

• This is the largest study to date reporting the association of anti-TNF-α inhibitor therapy with sinusitis.
• The most common types of sinusitis were CRSwNP and ARS-multiple.
• The median time from initiation of therapy to diagnosis of sinusitis was 22.5 months.
• Discontinuation of the drug, switching to another agent in the same class, or holding doses occurred in 14.3% of patients, suggesting that cessation of TNF-α antagonist may not always be necessary, contrary to prior reports³-⁴.
• Patients with no prior history of sinusitis were more likely to discontinue anti-TNF-α therapy and/or undergo surgical management. However, this was not statistically significant.
• The limitations of this study:
  • Small sample size and retrospective study design
  • Unable to determine incidence of sinusitis after starting anti-TNF-α therapy.
  • Overestimation of percentage of chronic and recurrent acute sinus disease.
  • Cannot isolate the effect of TNF-α antagonists from the effect of concurrent immunosuppressants on the development of sinusitis.

Conclusion

• This study provides further evidence that anti-TNF-α therapy can be associated with the development of sinusitis, especially chronic rhinosinusitis without nasal polyps.
• While surgery was sometimes included in the treatment regimen, discontinuation of anti-TNF-α therapy due to sinusitis was not deemed necessary in most cases.
• Further studies with a larger sample size will be required to fully characterize the effects of anti-TNF-α therapy on the course of sinusitis.

Acknowledgments

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References