Occult Hematologic Malignancy in Routine Tonsillectomy Specimens

A Single Institutional Experience and Review of the Literature

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ABSTRACT

Objectives: Handling of tonsillectomy specimens often includes gross and histologic examination. The published incidence of occult malignancy in benign-appearing tonsils is vanishingly rare, and consequently some propose omitting histologic analysis in young patients without clinical risk factors for malignancy or grossly suspicious features.

Methods: At our institution, an occult Burkitt lymphoma in a grossly benign-appearing tonsil from an otherwise healthy 5-year-old prompted review of our cases. We retrospectively reviewed tonsillectomy findings over a 5-year period, excluding patients with known lymphoma or head and neck malignancies. A total of 740 patients were identified. All cases underwent gross and histologic examination.

Results: Four additional malignancies were diagnosed, including a clinically unsuspected lymphoma in a 14-year-old patient. In our experience, although most tonsillar malignancies present with suspicious clinical or gross findings, occult malignancies do occur.

Conclusions: Recognition of these occult findings may facilitate early diagnosis and treatment; thus pathologic study of these specimens may still be justified.

Routine tonsillectomy is performed for various nonneoplastic conditions including obstructive sleep apnea, snoring, and recurrent infection, among others. This procedure is common in the United States, with 737,000 procedures performed in 2006. Handling of these specimens varies and may be limited to gross examination or may also include histologic study because of concern for possible underlying malignancy or serious infection. A review of the literature shows the presence of occult malignancy in benign-appearing tonsils to be vanishingly rare, and based on this, some propose omitting histologic analysis based on patient age, the absence of clinical risk factors for malignancy, and absence of grossly suspicious features. The 1999 College of American Pathologists Q-Probes study of policies found that close to 43% of the 413 surveyed institutions conducted only gross evaluation of tonsils and adenoids, and these specimens were
entirely exempt from submission to pathology in up to 7% of institutions surveyed.\(^7\)

In our institution, gross evaluation of tonsils and/or adenoids is permitted when the patient is 16 years of age or younger and when requested by the surgeon. However, perhaps due to a relatively large number of immunocompromised pediatric patients in our patient population, this written policy is rarely applied. Our experience with a recent occult in situ Burkitt lymphoma diagnosed in a grossly benign-appearing tonsil from an otherwise healthy 5-year-old girl prompted a review of our cases to evaluate the incidence of unsuspected malignancy in routine tonsillectomy.

Materials and Methods

Findings on all purportedly routine tonsillectomies performed at our institution since 2007 were retrospectively reviewed. Patients with known lymphoma or malignancies of the head and neck region were excluded. Three cases from this period were excluded because they had undergone only a gross examination. Information regarding the histologic findings, patient age, and indication for surgery was compiled.

A total of 740 patients aged 1 to 79 years (570 children and 170 adults) were identified. The mean age at the time of procedure was 5.9 years for children and 35.3 years for adults. All cases had been subject to both gross and microscopic pathologic examination. Four malignancies were diagnosed, in addition to the index case Table 1, for an overall incidence of 0.67% (1.2% in adult patients and 0.52% in pediatric patients). Two of the five cases had no clinically suspicious features, for an overall incidence of occult hematologic malignancy of 0.27% (0% in adult patients and 0.35% in pediatric patients) Table 2.

This study was approved by the Loma Linda University Medical Center Institutional Review Board.

Results

Case 1 (Index Case)

A previously healthy 5-year-old girl underwent tonsillectomy for interrupted sleep and snoring. Gross examination revealed symmetrically enlarged tonsils with no ulceration or distinct lesions. Histologic evaluation revealed a follicle within the right tonsil that was effaced by a monotonous proliferation of medium-sized cells with round to polygonal nuclei, finely clumped chromatin, small nucleoli, and minimal cytoplasm Image 1. Although the identification of malignancy in a single follicle seems to be a stretch of diagnostic limits, in situ Burkitt lymphoma within this follicle was unequivocally confirmed with both immunohistochemistry (positive for CD20, CD10, Bcl-6, and \(\lambda\) protein, negative for Bcl-2 and kappa protein, and Ki-67 positive in 100% of cells) and fluorescence in situ hybridization, which demonstrated the \(C-MYC\) translocation. A complete staging workup showed no involvement of other sites.

Case 2

A previously healthy 14-year-old boy underwent routine tonsillectomy. Gross examination revealed symmetrically enlarged tonsils with no ulceration or distinct

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y</th>
<th>Suspicion for Malignancy</th>
<th>Suspicious Features</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>No</td>
<td>None</td>
<td>Burkitt lymphoma (unilateral)</td>
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<tr>
<td>2</td>
<td>14</td>
<td>No</td>
<td>None</td>
<td>Follicular lymphoma, grade 3 (bilateral)</td>
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<td>3</td>
<td>15</td>
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<td>Asymmetry, distinct lesion, ulceration</td>
<td>Diffuse large B-cell lymphoma (unilateral)</td>
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<tr>
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<td>68</td>
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<td>Asymmetry, airway obstruction, age</td>
<td>Mantle cell lymphoma (bilateral)</td>
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<tr>
<td>5</td>
<td>79</td>
<td>Yes</td>
<td>Marked enlargement, airway obstruction, age</td>
<td>Mantle cell lymphoma (bilateral)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>No. of Malignancies</th>
<th>No. of Suspicious Features</th>
<th>No of No Suspicious Features</th>
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</thead>
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<td>All patients</td>
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<td>48</td>
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<tr>
<td>Meta review (Randall)(^2)</td>
<td>13547</td>
<td>6 (0.044%)</td>
<td>4</td>
</tr>
<tr>
<td>Current series</td>
<td>740</td>
<td>5 (0.67%)</td>
<td>3</td>
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<tr>
<td>Pediatric patients</td>
<td>570</td>
<td>3 (0.52%)</td>
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</tr>
<tr>
<td>Meta review (Randall)(^2)</td>
<td>13547</td>
<td>6 (0.044%)</td>
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<tr>
<td>Current series</td>
<td>740</td>
<td>5 (0.67%)</td>
<td>3</td>
</tr>
</tbody>
</table>

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\(^1\)Table 1
Cases of Hematologic Malignancy in Tonsillectomy Specimens in our Review

\(^2\)Table 2
Summary of Number and Incidence of Tonsillar Malignancy (Suspected and Unsuspected) in the Literature and at Our Institute
lesions. Histologic evaluation revealed focal atypical lymphoid nodules in both tonsils consisting of large cleaved and noncleaved cells with prominent nucleoli, loss of polarization, lack of tingible body macrophages, and lack of well-demarcated mantle zones that were easily distinguished from adjacent normal reactive germinal centers [Image 2]. Further immunohistochemical studies confirmed the presence of follicular lymphoma, grade 3 (neoplastic follicles positive for CD20, PAX-5, CD10, Bcl-6, and Bcl-2) within both tonsils (approximately 20%-30% of the right tonsil and 5% of the left tonsil). A complete staging workup showed no involvement of other sites.

Case 3
A previously healthy 15-year-old boy underwent tonsillectomy for unilateral tonsillar enlargement of 2 months’ duration. Gross examination revealed marked asymmetric enlargement of the left tonsil (15-g left tonsil vs 6-g right tonsil) that was ulcerated and contained a distinct 3-cm firm grey mass. On histologic evaluation, about 90% of the left tonsil was found to be effaced by a diffuse lymphoid infiltrate of large cells with irregular or angulated nuclei with vesicular chromatin and multiple nucleoli, and moderate amount of cytoplasms. A diagnosis of diffuse large B-cell lymphoma, germinal center B-cell subtype (positive for CD20, CD10, Bcl-6, MUM1, and Bcl-2, with Ki-67 positive in about 85% of cells) was rendered based on immunohistochemistry. A complete staging workup showed no involvement of other sites.

Case 4
A previously healthy 68-year-old man had an 8-month history of progressively enlarging left neck mass which eventually caused partial airway obstruction. Only the
Image 2 A, Large fused follicles that lack tingible body macrophages or well-demarcated mantle zones (H&E, ×20). B, The follicles contain both large cleaved and noncleaved cells, some with prominent nucleoli (H&E, ×400). C-E, On immunohistochemistry, the abnormal follicles stain positive for CD20 (C, ×200), CD10 (D, ×100), and Bcl-2 (E, ×200).
left tonsil was removed. Histologic evaluation showed complete effacement of the normal tonsillar parenchyma by a monotonous lymphoid infiltrate of intermediate-sized cells with oval to slightly irregular nuclei with dispersed chromatin and occasional prominent nucleoli, and small amount of cytoplasm. Further immunohistochemical and flow cytometric studies (positive for CD20, CD22, PAX-5, CD5, CD43, FMC7, Bcl-2, cyclin D1, and λ protein, negative for CD23 and κ protein, and Ki-67 positive in 70%-80% of cells) confirmed a diagnosis of mantle cell lymphoma. A complete staging workup showed involvement of other lymph nodes in the head and neck region, but no bone marrow or distant organ involvement.

Case 5
A previously healthy 79-year-old man had a 4-month history of bilateral progressive enlargement of the tonsils. He showed initial mild improvement with antibiotic therapy but soon developed partial airway obstruction and underwent tonsillectomy. Gross examination revealed bilateral marked enlargement (both >25 g), but no surface ulceration or distinct lesions. Histologic evaluation showed complete effacement of the bilateral normal tonsillar parenchyma by a mostly diffuse lymphoid infiltrate consisting of monotonous, small- to intermediate-sized cells with slightly irregular nuclei with dispersed chromatin and inconspicuous small nucleoli, and scanty to small amount of cytoplasm. Immunohistochemical studies confirmed a diagnosis of mantle cell lymphoma, blastoid variant (positive for CD20, CD5, Bcl-2, and cyclin D1, negative for CD23, and Ki-67 positive in about 65% of cells). A complete staging workup revealed involvement of the gastrointestinal tract, but no bone marrow involvement.

Discussion
Currently US hospitals do not have a standardized approach to processing tonsillectomy specimens. A survey of the American Academy of Otolaryngology Head and Neck Surgery in 2001 showed a declining preference for histologic examination. The most common reasons cited for this change were cost savings, medical literature, or a combination of factors. Criteria for omitting histologic examination are most often based on patient age, absence of any clinical suspicion for malignancy, risk factors (ie, history of immunosuppression, various environmental exposures), and lack of suspicious gross findings (ie, asymmetry, ulceration, or distinct lesions). Attention to these criteria would have detected 3 of our 5 cases, but not the remaining 2. Also, even with formal criteria in place to exclude a specimen from histologic examination, potentially these criteria can be inappropriately applied. Q-Probe studies have shown a persistent lack in communication of pertinent clinical information to surgical pathology; nearly 30% of surgical pathology reports were found to be amended because of a lack of clinical-pathologic correlation. Of these, nearly 9% of errors were discovered when new clinical information was provided.

A review of published studies involving 54,901 adult and pediatric patients showed a 0.087% incidence of tonsillar malignancy overall. Most patients with malignancy (88%) had recognized risk factors preoperatively, with only 6 patients (0.011% of cases) receiving an entirely unsuspected malignant diagnosis (Table 2). Studies that analyzed 13,547 pediatric patients separately from adults showed a 0.044% prevalence of malignancy, with 2 (0.015%) being entirely unsuspected (Table 2).

Lymphoma is one of the most common head and neck malignancies in children and lymphoma of the tonsils and adenoids accounts for about 9% of non-Hodgkin lymphoma cases registered for pediatric oncology group protocols. Although many of these cases are suspected clinically before surgery, a number are discovered incidentally on gross and histologic examination, highlighting the importance of pathology review even of grossly normal-appearing tissues. One review series that specifically focused on pediatric tonsillar lymphoma reported 2 cases of unsuspected Burkitt lymphoma at their institution. That translated to an incidence of occult lymphoid malignancy of 0.18% in their series, more similar to that found in our pediatric cases. Anecdotal case reports of unexpected tonsillar malignancies, both hematologic and nonhematologic, which are not part of a series review can also be found in the literature.

In conclusion, the literature and our experience suggest that most tonsillar malignancies present with suspicious clinical or gross findings; however, occult malignancies do occur and many of these are in the pediatric population. Although the incidence is very low, recognition of occult malignancy in tonsillectomy specimens may facilitate early diagnosis and treatment, as seen in 2 of our cases. The cost-benefit ratio is not addressed by our review; however, we believe that the rate of occurrence of tonsillar lymphoma in the pediatric population and the possibility of unsuspected malignancy should be carefully considered when implementing formal “gross-evaluation-only” policies for surgical pathology specimens. The histologic examination of these specimens may still be justified. Further characterization of unexpected subtle lesions with immunohistochemistry and/or molecular/cytogenetic analysis is often helpful in confirming the diagnosis.

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References
2. Randall DA, Martin PJ, Thompson LDR. Routine histologic examination is unnecessary for tonsillectomy or adenoidectomy. Laryngoscope. 2007;117:1600-1604.
7. Zarbo RJ, Nakhleh RE. Surgical pathology specimens for gross examination only and exempt from submission. a College of American Pathologists Q-probes study of 413 institutions. Arch Pathol Lab Med. 1999;123:133-139.