Casos Clínicos

Odinofagia persistente como manifestação primária de Linfoma de Hodgkin

Hodgkin Lymphoma presenting as persistent sore throat.

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Resumen

As amígdalas palatinas podem ser afetadas por diversas patologias, incluindo doenças inflamatórias, infeciosas e neoplásicas. Apesar dos linfomas serem a segunda neoplasia maligna mais comum da cabeça e pescoço, o linfoma de Hodgkin extranodal é raro.

As manifestações mais comuns de doença de Hodgkin incluem o aparecimento de linfadenopatias e sintomas constitucionais. Os autores apresentam o caso raro de um linfoma de Hodgkin que se manifestou primariamente como uma massa amigdalina. Neste trabalho enfatizamos a importância do aspecto macroscópico das lesões amigdalinas que poderão ser importantes na suspeição de doença linfoproliferativa.

Palabras chave

doença de Hodgkin; linfoma; massa amigdalina.
Abstract

Several clinical conditions may affect the palatine tonsil, including inflammatory, infectious and tumoral diseases. Despite lymphomas are the second most common malignancy of the head and neck, extranodal Hodgkin lymphoma is a rare occurrence.

The most common manifestations of Hodgkin disease include enlarged lymph nodes and constitutional symptoms. We present the rare case of Hodgkin lymphoma presenting with a tonsillar mass. We emphasize the importance of the macroscopic appearance of tonsillar lesions that may yield the key to anticipate the diagnosis of this condition.

Keywords

Hodgkin disease; lymphoma; tonsillar mass.
Introduction

A considerable amount of pathological conditions may affect the palatine tonsil, including inflammatory, infectious and tumoral diseases. Lymphomas constitute a heterogeneous group of lymphoproliferative disorders that arise from the cells of the immune system, and are the second most frequent head and neck malignancy, after squamous carcinoma.\textsuperscript{(1,2)} They are broadly categorized into the most common non-Hodgkin lymphoma and the rarer Hodgkin disease (HD).

The term extranodal lymphoma has been applied in cases where neoplastic proliferation occurs at locations other than the lymph nodes, sometimes from sites that normally do not contain lymphoid tissue.\textsuperscript{(3,4)} This presentation can be seen in up to one-third of non-Hodgkin lymphomas but is rare in HD.\textsuperscript{(5)} Waldeyer ring is an extranodal site that encompasses the lymphoid tissue of the palatine tonsils, the base of tongue, nasopharynx and oropharynx.\textsuperscript{(6)} In these cases, the gastrointestinal tract is the most frequently reported extranodal site. However, head and neck extranodal lymphomas may affect the sinonasal tract, nasopharynx, tonsil, parotid gland, orbit and other even rarer locations.\textsuperscript{(7,8)}

The most frequent symptoms of HD at presentation include cervical lymph node enlargement and constitutional symptoms. Initial presentation with sore throat complaints is rare and may present a diagnostic challenge.\textsuperscript{(7,9)}

Case Report

A 69-year-old patient was referred to our department with a sore throat of two months duration that was progressively becoming more severe. Despite slight weight loss that the patient perceived to be associated with uncontrolled pain, he presented no other symptoms. His past medical history included controlled hypertension and type 2 diabetes mellitus, ischemic heart disease and ulcerative colitis medicated with azathioprine and mesalazine. He was a former smoker, without smoking habits over the past sixteen years.

He had been seen at another facility, where he was initially medicated with a seven-day course of amoxicillin-clavulanic acid, without improvement. He brought the results of a previously performed cervical computed tomography (CT) scan and a biopsy specimen. The former showed a right tonsillar mass with 3.5 X 2.4 cm, infiltrating the lateral pharyngeal wall and several enlarged lymph nodes, the larger with 2.6 X 1.6 cm with a necrotic core. The histology of the mass showed neutrophilic tonsillar infiltration suggestive of an acute suppurative condition.

Physical examination revealed an enlarged right tonsil covered with a white exudate (Figure 1.). Epithelial alignment looked friable and there was a sharp transition to normal mucosa near the palatoglossal and palatopharyngeal arcs. We also noticed an enlarged, consistent and painless jugular lymph node, with approximately 2cm on the right side. There were no other significant findings on physical examination.

![Figure 1: right tonsilar mass (1); uvula (2); soft palate (3); tongue (4). The lesion presented as tonsillar hypertrophy with ulcerative epithelia covered in a white exudate. Note the sharp transition to normal mucosa at the palatoglossal arch (arrow).](image-url)
Full blood count revealed a normocytic normochromic anemia of 12.4g/dl, biochemical tests, and serum lactate-dehydrogenase were normal, and erythrocyte sedimentation rate was 93 mm in the first hour. Human immunodeficiency virus type 1 and 2 and hepatitis B and C were negative.

Microbiological and mycobacterial tests were also negative. Repeated biopsy of the mass showed granulomas with polymorphonuclear infiltrate and rare cells Reed-Sternberg like. These cells were positive for CD30, CD15, and EBER and showed week positivity to CD20 and Pax 5.

Cervical lymph node excisional biopsy was performed in order to confirm the diagnosis and determine the disease subtype, and concluded to a nodular sclerosis variant Hodgkin lymphoma (Figure 2.). Tumor cells were positive for CD30 and CD15 and negative for CD45, CD3, and EMA. Few cells were positive for CD20 and Pax 5. EBER was detected in the tissue sample by in situ hybridization.

Computerized axial tomographic scan of chest, abdomen, and pelvis, positron emission tomography and bone marrow biopsy allowed the disease to be staged as IIB.\(^{(10)}\)

Treatment consisted of chemotherapy (doxorubicin, bleomycin, vinblastine and dacarbazine) and the patient completed six cycles with disease remission. He remains in remission two years after completing therapy.

**Discussion**

Hodgkin disease is a lymphoproliferative disorder caused by the multiplication of a B cell clone. The disease usually manifests as lymph node enlargement and constitutional symptoms.\(^{(5,6)}\) Unlike non-Hodgkin lymphomas, an extranodal manifestation of HD is very rare.\(^{(7,9)}\)
In this atypical location, secondary involvement is more frequent than a primary tonsillar disease.(7) Although a few cases of primary Waldeyer ring Hodgkin lymphoma are described in the literature, many studies did not include immunohistochemical workup.(6) Indeed, NHL may be mistaken by HD and a full workup is necessary to allow an accurate classification of lymphoproliferative disorders.\(^{(6,8)}\)

The variant most frequently described in this setting is mixed cellularity, although in one study lymphocyte-rich and nodular sclerosis types of HD were more frequent.\(^{(6)}\)

When HD presents with oropharynx and cervical lymph node involvement, as in our case, it may be difficult to determine the primary site of origin.\(^{(7)}\) Primary nodal disease with secondary tonsil involvement is more frequent in Hodgkin disease. However, several factors, in this case, may be consistent with an extranodal presentation. First, the only symptom reported was a sore throat, which was present for at least two months, while the cervical lymph node was only noted on physical examination. Second, clinical evolution favored a tonsillar origin. Though cervical lymph nodes remained stable throughout vigilance until treatment was started, the tonsillar mass presented several changes. Initially, it enlarged and later regressed, with visible necrosis, exposing the tonsillar bed, which was suggestive of an intense proliferative focus.

Immunodeficiency and EBV are possible explanations for Waldeyer ring involvement in HD.\(^{(6)}\) Waldeyer lymphoid tissue is a known reservoir of EBV and due to its oncogenic potential, some authors propose it as a possible explanation for Waldeyer ring lymphomas.\(^{(6,7,11)}\)

One study showed that EBV latent membrane protein expression by Reed Sternberg cells was more frequent in neck nodes compared with other site nodes, reflecting oropharynx drainage pathways.\(^{(11)}\)

The diagnosis of lymphoproliferative disorders presenting as tonsillar masses is not always straightforward. Not infrequently, several biopsy specimens are necessary before the diagnosis is highlighted.\(^{(3,4)}\) Immunohistochemical studies and flow cytometry are needed to establish a definitive diagnosis and analysis of a representative amount of fresh tissue is necessary to examine the architecture of the proliferative lesion.\(^{(8)}\)

Although constitutional symptoms are more frequent among HD patients, in most cases these are absent. Also, lymph node enlargement may be absent or indistinguishable from other types of malignancy or non-malignant disorders, which may further delay the diagnosis.\(^{(4)}\) Although fine needle biopsy can usually differentiate between a carcinoma and a lymphoma, a high index of suspicion is necessary to provide sufficient amount of tissue to allow a complete and prompt diagnostic workup of the later.\(^{(6)}\) Factors that may be helpful include patients’ age and habits, immune status and inconclusive previous biopsies.\(^{(2,8,9)}\) In our experience, the presence of a well-demarcated mass with a sharp transition to normal mucosa, along with lymphoid hypertrophy is suggestive of a lymphoma, when a neoplastic cause is suspected. Constitutional symptoms and lymph node enlargement are inconsistent features among HD patients and, when present, may be indistinguishable from those associated with other malignant and non-malignant conditions. Table 1 summarizes the main findings of Waldeyer ring Hodgkin lymphomas in previous studies.

Hodgkin lymphoma may rarely present as a tonsillar mass and the clinical picture may not differ from the much more common head and neck carcinoma. Detailed macroscopic inspection of the lesion may reveal factors such as lymphoid hypertrophy and a lesion confined to the lymphoid elements that may provide a clue to a lymphoproliferative disorder. Also, the negative nature of previously performed biopsies may be characteristics to be taken into account in the suspicion of lymphomas of the Waldeyer’s ring.
Table 1. Resume of the main findings in Waldeyer ring Hodgkin lymphomas(6,12-18).

<table>
<thead>
<tr>
<th>Report</th>
<th>Patients’ characteristics</th>
<th>Symptoms/ Clinical Findings</th>
<th>Histology</th>
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<tr>
<td>Quiñones-Avila et al. (n=22)</td>
<td>Male preponderance, median age of 48 years, history of NHL in 14%.</td>
<td>Tonsil enlargement in 18% Lymph node enlargement in 14%</td>
<td>lymphocyte-rich classical (36%), nodular sclerosis (32%), mixed cellularity (18%), lymphocyte depletion (5%).</td>
<td>Localized to Waldeyer ring in 32%. Waldeyer ring and cervical lymph nodes in 50%.</td>
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<tr>
<td>Prudhomme-Lacroix F et al. (n=3)</td>
<td>Male, &gt;40 years.</td>
<td>Mixed cellularity.</td>
<td></td>
<td>Tonsil.</td>
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<tr>
<td>Oluwasanmi AF et al.</td>
<td>Female, 52 years.</td>
<td>Tonsil enlargement.</td>
<td>Lymphocyte-rich classical.</td>
<td>Tonsil.</td>
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**Conflict of interest**

None declared.
References


