CASE STUDY

Subglottic MALT Lymphoma of the Larynx in a Patient With Rheumatoid Arthritis

Linfoma MALT subglótico en un paciente con artritis reumatoide

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Clinical Case

A 41-year-old woman was referred to our hospital presenting dysphonia, shortness of breath on moderate exertion and a one year history of stridor, with a history of RA diagnosed in 2002, and being treated with hydroxychloroquine and NSAIDs. Nasofibrolaryngoscopy revealed a reddish growth compromising 70% of the subglottic lumen, with oedema and major hyperaemia of the supraglottic region and aryepiglottic folds. MRI (Fig. 1) showed a subglottic lesion with posterior base of 2.5 cm × 1.5 cm. The tumour was resected via laryngofissure and tracheotomy.

Histopathological examination (Fig. 2) leads to a diagnosis of MALT-type lymphoma, immunophenotype CD20 (+), CD43 (+), CD10 (−) and CD3 (−).

Physical examination, blood count, imaging and bone marrow biopsy did not reveal any extralaryngeal spread of disease; therefore, the patient was assessed as a stage IE (localised disease) of the Ann Arbour system. It was decided that the treatment should start with six cycles of R-CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisolone plus rituximab) and the patient is currently undergoing local adjuvant radiotherapy. Ten months after the surgical resection, the patient is decannulated and with no evidence of recurrence.

Discussion

Laryngeal lymphomas represent less than 1% of primary neoplasms in this location, and the most common are
diffuse B lymphoma and MALT (mucosa-associated lymphoid tissue),\textsuperscript{1,5} probably developing in lymphoid collections of the supraglottic lamina propria and laryngeal ventricles; however, MALT has not been identified in the subglottis.\textsuperscript{1,5} Only anecdotal cases have been published since the first description of a primary laryngeal MALT lymphoma in 1990.\textsuperscript{4,6,7}

The location of primary laryngeal lymphomas is predominantly supraglottic. Subglottic, as in our case, or transglottic presentations, are rare. The age at which they appear varies, between 4 and 81 years of age. Studies are contradictory in terms of gender predominance. Laryngoscopy usually reveals a submucous polyloid mass with no ulceration. The main symptoms include dysphagia, dysphonia, dyspnoea and stridor.\textsuperscript{1,5}

The pathogenesis of MALT lymphomas suggests a response to antigenic stimuli due to chronic inflammation or autoimmune processes. Gastric MALT lymphomas have been associated with \textit{Helicobacter pylori} infection in the salivary gland with Sjøgren's syndrome, and in the thyroid glands with Hashimoto’s thyroiditis. An inflammatory process as a precursor to the disease has not been described in the larynx. Gastroesophageal reflux disease can cause secondary chronic laryngitis and, as a consequence, the formation of lymphoid tissue; however, more studies are required on this association.\textsuperscript{4,5}

Recent studies have demonstrated genetic alterations in 60% of MALT lymphomas: translocations t(1;14) with trisomy 3, t(11;18)(q21;q21), t(14;18)(q32;q21), and mutations of the p53 gene (17p13) and c-myc (8q;24).\textsuperscript{1,5}

According to various studies, patients with RA have 2–3 times greater incidence of lymphomas than the rest of the population; however, there is still heterogeneity in terms of results. Some authors refer to an increased risk in patients who have been treated with corticosteroids or immunosuppressants, suggesting that the drug treatment of the disease plays a major role in the development of lymphomas.\textsuperscript{1,5,7}

Mikuls et al. published a case and control study in 2006 on patients with a diagnosis of NHL with no history of RA, and when they assessed survival, they found similar results in both situations. In patients with RA the evolution time was on average 10 years, prior to a diagnosis of NHL. In addition, they noticed that the majority of cases had received treatment with disease-modifying drugs, principally hydroxychloroquine or gold injections, followed by methotrexate and sulfasalazine. Our patient was treated with hydroxychloroquine; nonetheless, additional studies are required to determine the relationship between this drug and NHL.\textsuperscript{8}

In the case of methotrexate this relationship was observed in patients with a history of treatment of more than 8 years, with a total ingestion exceeding 180 mg.\textsuperscript{8} An important fact is that when the natural course of the RA becomes complicated with a lymphoma, other comorbidities (coronary heart disease, for example) are determinants of survival and should be addressed in treatment.\textsuperscript{6}

The majority of laryngeal lymphomas are treated with radiotherapy for localised disease and chemotherapy in cases of spread or recurrence of disease. Both are considered effective treatments, and have demonstrated better results used in combination.\textsuperscript{1,5} Some patients have benefited from the local use of IFN α2a, or the systemic use of the monoclonal anti-CD20 antibody, rituximab.\textsuperscript{1,3,5} Surgical excision has been proposed recently as an initial method of treatment.\textsuperscript{2,4} The prognosis for MALT lymphomas is favourable compared to other types of B lymphomas, with a survival of up to 86%–100% at 5 years, even when 25% of

\textbf{Figure 2} Histopathological examination: diffuse proliferation of atypical lymphoid cells causing lymphoepithelial lesion (A, haematoxylin-eosin) with intense CD20 immunoreactivity (B), and focally for CD43 (C), citoqueratine (D) was positive only in glandular structures.
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the patients present with disease that has already spread on diagnosis.2-5

Conflict of Interests

The authors have no conflict of interests to declare.

References