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CLINICAL CASE

Results of radiotherapy in extranodal MALT lymphoma. A case report and literature review

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KEYWORDS
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Abstract Mucosa-associated lymphoid tissue (MALT) represents 8% of non-Hodgkin lymphomas (NHL), with 2% affecting the conjunctiva. The case is presented of a 19-year-old patient diagnosed with conjunctival MALT lymphoma of the right eye, treated with external radiotherapy (ERT), and showing a complete, 100% response. At 18 months, no signs of relapse.

The treatment of choice for MALT type extranodal lymphoma is ERT. It has shown excellent results in controlling the disease, overall survival, progression-free survival and relapse-free survival. The relapse rate is 6–27% and the transformation to a higher grade lymphoma between 18% and 23%, consequently patients must have adequate follow-up. If the above is confirmed, reirradiation, chemotherapy and/or molecular target-directed therapy should be considered.

PALABRAS CLAVE
Linfoma;
MALT;
Conjuntiva;
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Electrón

Resultados de tratamiento con radioterapia en linfoma MALT extraganglionar. Reporte de un caso y revisión de la literatura

Resumen El linfoma asociado a tejido mucoso (MALT) representa el 8% de los Linfomas No Hodgkin (LNH), afectando a la conjuntiva en el 2%. Se presenta el caso de paciente de 19 años de edad diagnosticada con linfoma MALT en conjuntiva de ojo derecho, tratada con radioterapia externa (RTE), mostrando respuesta completa del 100%. A 18 meses de seguimiento, sin datos de recaída.

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El tratamiento del elección en linfoma MALT extraganglionar es con RTE, ha demostrado excelentes resultados en control de la enfermedad, sobrevida global, sobrevida libre de progresión y sobrevida libre de recaída. La recaída es del 6–27% y la trasformación a un linfoma de mayor grado ente 18–23%; motivo por el cual los pacientes deben tener un adecuado seguimiento, en caso de confirmarse lo anterior se deberá considerar re-irradiación, quimioterapia y/o terapia dirigida a blanco molecular.

Introduction

NHL was first described in 1983 by Isaacson and Wright.[1] It has an incidence of 4.3% and a mortality rate of 3.2% according to the surveillance, epidemiology, and end results program (SEER) statistics.[2] In the United States it occupies fifth place in terms of incidence in both men and women, and ninth place in terms of mortality.[3,4] More frequently among women, with an incidence peak at between 50 and 70 years of age.[5]

The presentation of mucosa-associated lymphoid tissue (MALT) in conjunctiva represents approximately 2–8% of cases.[5–7] The most frequent location being the palpebral conjunctiva (64–70%), lacrimal gland (18%) and less frequently retrobulbar tissue or extraocular muscles.[6,8,9]

Some infectious agents are involved in the aetiology of MALT lymphomas, such as *Chlamydia psittaci*, *Hepatitis B Virus and Chlamydia pneumoniae*. This varies according to geographical region. In Europe, it presents at a rate of 87%, however, this association has not been clearly observed in America,[6,10,11] given the above and based on the results of a meta-analysis it was concluded that the association between chronic *C. psittaci* infection and the development of orbital MALT lymphoma varies considerably.[8] Furthermore, it is related to autoimmune processes such as thyroiditis and Sjögren's syndrome, increasing the relative risk to 70 and 40 times respectively among the general population.[8,9,12]

The form of presentation is indolent, it is characterised by frequent relapses that may transform into a diffuse large-B-cell lymphoma.[13,14]

In the majority of patients it presents unilaterally, although it presents bilaterally in 15% of cases.[15–17]

The diagnosis of orbital MALT lymphomas is based on the analysis of morphology, immunophenotype and genetic analysis of the biopsy material.

Histopathologically it is characterised by a heterogeneous morphology with irregular nuclei. Plasmacytoid cells with intranuclear pseudoinclusions of immunoglobulin may present, which are also known as Dutcher bodies, or acidophil spheres in the cytoplasm or Russell bodies may present.[2,18,19]

The immunohistochemical panel includes positivity for CD19, CD20 (more common), CD79a, CD53, CD21[12] and overexpression of BCL2 Figures 1–5.

For the genetic analysis, studies such as fluorescent in situ hybridisation (FISH) are useful for determining translocations *t*(11;18), *t*(11;14), *t*(3;14). Of these, *t*(11;18) produces genetically stable MALT lymphomas, which do not transform into B lymphocyte lymphomas.[12,18–20]

PET-CT is an imaging technique being increasingly used. This is performed with the radiotracer 18 FDG (fluorodeoxyglucose) to determine pathological progression, which can be present in up to 73% of cases in orbital or conjunctival sites.[21] Other imaging techniques such as magnetic resonance do not have greater diagnostic precision.[3,14,17]

One of the most recent studies of orbital MALT lymphoma is DNA methylation. It has been demonstrated that a differentiated methylation exists between the different genes with respect to the *C. psittaci* infection status and the response to doxycycline, with IRAK1 and CXCR6 being the most associated genes.[22]

The treatment options are surgery, ERT, chemotherapy (CT) alone or concomitantly and molecular target-directed therapy.

ERT is indicated where response to antibiotics is poor or null, the dose studied is in the range of 25–36 Gy with electrons or photons, giving good results in controlling the disease, overall survival and relapse-free survival.

The indications for CT or targeted therapy with anti CD-20 monoclonal antibodies (rituximab) are patients with a marked symptomatic disease or systemic disease with pulmonary and/or hepatic invasion.

Patients who present transformation to a high grade lymphoma (diffuse large-B-cell lymphoma), are candidates for treatment with rituximab-cyclophosphamide, doxorubicin, vincristine, prednisone (R-CHOP).[23–25]

Case report

Female patient, 19 years of age, originating from Estado de México, student, negative background for cancer or autoimmune disease susceptible genetic profile, no surgery, chronic-degenerative or trauma history.

The patient's symptoms commenced 4 months before the physician's assessment, with the presentation of a tumour in the right lower eyelid of less than 1 cm, accompanied by asthenia, adynamia, general deterioration, with no weight loss, euthermic. The patient consulted the ophthalmologist who performed an excisional biopsy, resulting in the histopathological report of marginal zone B lymphoma associated with MALT mucosa.

The immunohistochemical panel was positive for CD20, BCL2 and Lambda chain and negative for CD5, CD43