THERAPEUTIC SUCCESS WITH BRENTUXIMAB IN ADVANCED MF WITH MAJOR SKIN INVOLVEMENT. CLINICAL CASE

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Summary

Mycosis fungoides is the commonest type of primary, a form of non-Hodgkin characterised clinically by lesional progression from patches to plaques to tumours.It can begin as chronic itching, even before the appearance of clinical signs of the disease. Specific serological investiga-tions, lymph node biopsy and imaging may be required if there is concern the skin lesions are secondary to a systemic lymphoma or in advanced disease (ie, extracutaneous spread).We are presenting the case of a 54-year-old female patient, smoker, known with mycosis fungoides since 2007 and diagnosed in our Clinic in 2014, currently being treated with acitretin 40 mg per day, who presented for control due to the appearance of a left submandibular tumefaction with pre and retroauricular extension, imprecisely delimited, with a firm consistency and slightly painful to the touch, with modified overlying skin (ulcerated tumour plaque, with thick serohematic crust on the surface).A puncture-biopsy was performed on the left submandibular lymphadenopathy, the appearance being of aggressive non-Hodgkin's lymphoma (ki67=70%), CD30+, reason why it was decided to initiate the therapy with Brentuximab vedotin, a targeted antibody-drug conjugate (ADC) active against CD30-positive cancer cells.

Key words: *mycosis fungoides, cutaneous T-cell lymphomas, non-Hodgkin's lymphoma, Brentuximab vedotin.*

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Introduction

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL), accounting for approximately 40% of all cutaneous lymphomas and 54%–65% of CTCL cases [1].

The etiology of CTCL is largely unknown. Infectious agents, ultraviolet (UV) radiation, or occupational exposure are being discussed as possible triggers [2].

Mycosis fungoides can have an indolent evolution. Mycosis fungoides clinically presents with progressive lesional stages from patches to plaques, and tumors.Associated features include pruritus, poikiloderma and ulceration of tumours [2].

There are multiple treatments for mycosis fungoides with uncertain benefits that target only certain areas (local therapy) or the entire body (systemic therapy). Treatments include creams, ointments, oral or injected medicines, light therapy, radiotherapy and chemotherapy [3].

The introduction of highly-targeted antibody-drug conjugates (ADC) in the last decade represents an important advance in treatment algorithms for some cancers, with ADC designed to provide highly-selective killing of tumour cells with minimal effects on normal tissue. One such ADC is brentuximab vedotin, which targets the CD30 membrane receptor, a tumour necrosis factor receptor superfamily member [4].

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CD30 is an ideal therapeutic target because it is expressed in many lymphomas, having high selectivity for tumor tissue with low expression on normal tissue. [5].

Case report

We are presenting the case of a 54-year-old female patient, smoker, known with mycosis fungoides since 2007, with a certain diagnosis since 2014, currently being treated with Acitretin 40 mg per day, who was referred first to our Clinic for the presence of a generalized facial eruption constituted by well-defined erythematous tumour plaques and placards, with a histopathological picture compatible with lymphoma. Soon she developed tumours with ulcerations, purulent secretions and serohematic crusts on the surface, generalized pruritus and scratching lesions. She was treated both by dermatologists and oncologists. At the last presentation, there is a left submandibular tumefaction with pre and retroauricular extension, imprecisely delimited, with a firm consistency and slightly painful to the touch, with modified overlying skin (ulcerated tumour plaque, with thick serohematic crust on the surface). A **puncture-biopsy** was performed on the left submandibular lymphadenopathy, the appearance being of aggressive **non-Hodgkin's lymphoma** (ki67=70%), CD30+, reason why the hematologist who cared for the patient decided to initiate the **COP regimen** (cyclophosphamide, vincristine and prednisone). Considering the lymphoma refractory to COP regimen, the hematologist decides to initiate therapy with **Brentuximab vedotin**. The administered dose was 1.8 mg/kg in infusion every 3 weeks, minimum 8 cycles.

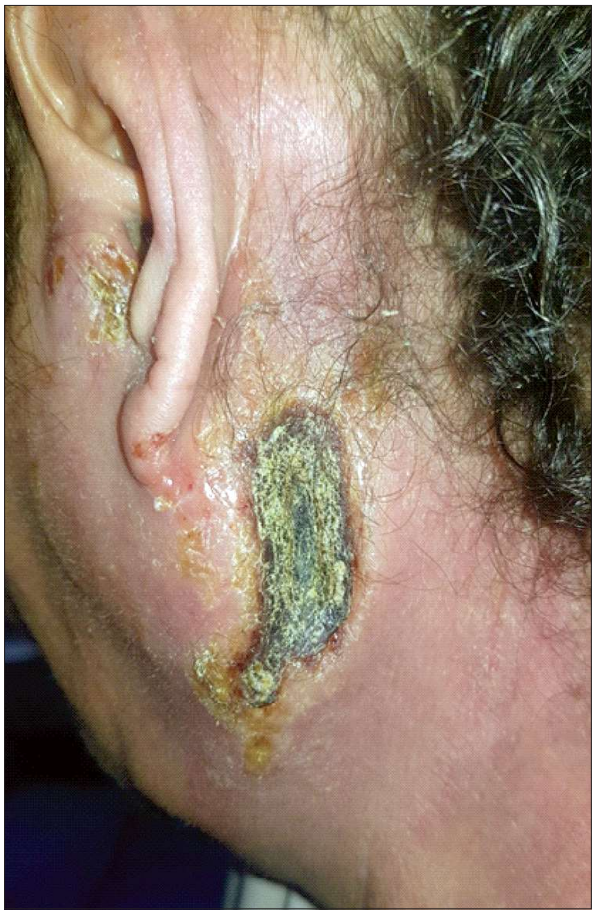

Figure 1. Before Brentuximab

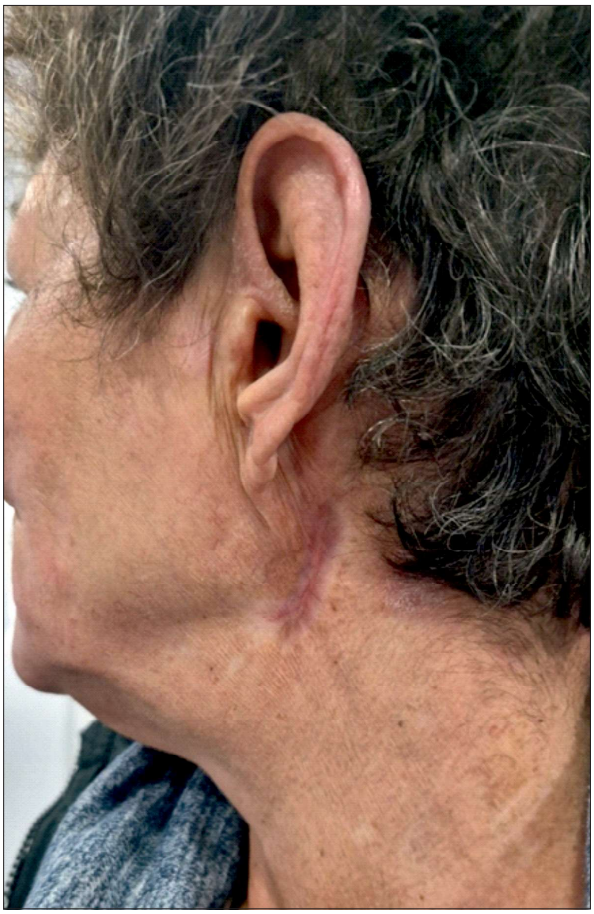

Figure 2. After Brentuximab

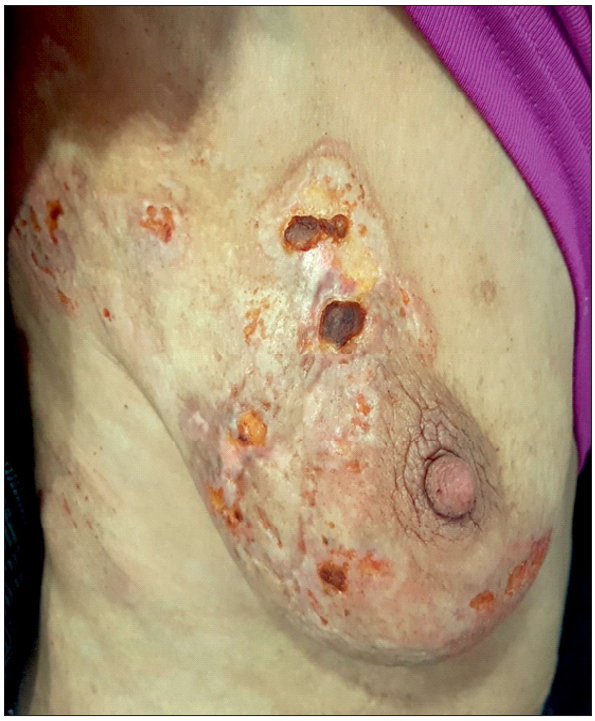

Figure 3. Before Brentuximab

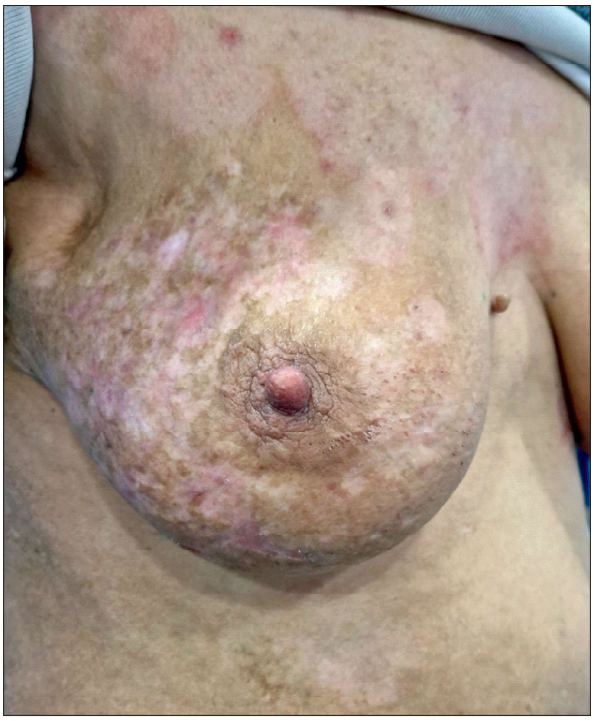

Figure 4. After Brentuximab

The patient responded favorably, both cutaneously and systemically to the administration of Brentuximab vedotin treatment, without notable adverse effects.

In parallel, the patient also underwent local treatment with imiquimod for two of the ulcerated tumor-type skin lesions, unresponsive to the systemic and local treatments used. Therapeutic benefit was evident, but the patient discontinued topical therapy.

Previous treatments: 10 sessions of PUVA phototherapy (2014), external radiotherapy – "whole body" technique from 2014 to 2016, with periods of complete remission.

Personal pathological history revealed the presence of non-insulin-dependent (type II) diabetes mellitus and ischemic cardiomyopathy. On clinical examination we detected a normal-weight patient, cardio-respiratory normal, palpable lateral cervical, occipital, axillary and inguinal lymph nodes, confirmed by **thoracic-abdominal-pelvic contrast-enhanced CT**: supradiaphragmatic lymphadenopathy, without abdominal lymphadenopathy, homogeneous hepatomegaly.

Laboratory analyses have revealed inflammatory syndrome, leukocytosis with neutrophilia, mild thrombocytosis, increased IgE immunoglobulin.

Discussions

The presented case is interesting both for the delayed diagnosis of lymphoma initially diagnosed as lupus erythematosus and treated with hydroxychloroquine, thus leading to disease progression and for its refractory nature to multiple conventional treatments.Successful use of topical imiquimod therapy may be an option in selected cases of MF, and aggressive forms may benefit from modern ADC therapies.

CD30 is an ideal target for ADC-based therapy, given its high levels of expression on specific tumour cells and limited expression on normal cells (restricted to a small population of cells, predominantly activated B cells and T cells) [4].

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Conflict of interest
NONE DECLARED

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