Case report

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Double hit: Mantle Cell Lymphoma associated with squamous cell carcinoma or chalazion? A case report

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Abstract

A few cases of ocular adnexal neoformations related with MCL have been reported in the literature. We present a rare case of tumour duplicity: mantle cell lymphomas (MCL) associated with squamous cell carcinoma (SCC) localised at the level of the ocular adnexa, on left upper eye lid mass since two years of 18 mounth duration in a 57-year-old man who had previously been diagnosed with stage IV MCL for 14 months. The patient had been treated according to the R-DHAP scheme for 4 cycles, in anticipation of a possible autologous HSC transplant, which was not carried out due to a positive diagnosis at the end-of-cycle osteomedullary biopsy (BOM) check. Ophthalmological examination was performed, and afther surgical removal histological examination proved to be squamous cell carcinoma (SCC).

The aim of this case report is to decode the signs, symptoms and factors associated with the formation, that appear to be a chalazion, at an early stage in order to prevent the overgrowth of the mass that could invade the surrounding tissues by infiltrating them, as well as negative aesthetic outcomes of the surgery due to the excessive size of the mass, which could compromise the patient's quality of life. ***Clin Ter 2023; 174 (5):390-394 doi: 10.7417/CT.2023.2455***

Key words: *Mantle cell lymphoma, eye lid, chalazion, squamous cell carcinoma*

Introduction

Mantle cell lymphoma (MCL) constitutes a subtype of non-Hodgkin lymphoma (NHL) associated with considerable morbidity and mortality. Studies regarding the clinical and histopathological features of MCL have shown that it often involves the ocular adnexal region (the orbit, eyelids, conjunctiva, lacrimal gland and lacrimal sac). The case we are describing is a form of SCC in the adnexal region of the eye, which is a rare occurrence, as reported in the literature, that presents as the first sign of MCL, a very aggressive lymphoma subtype that causes severe morbidity and death in patients (1)(Péčová T). Initially, due to its characteristics, the neoformation, which is most frequently found in the eyelid, falls within the differential diagnosis with chalazion, however a correct early diagnosis of the SCC lesion is necessary both because of its malignancy characteristics but above all because in these patients it appears to be the first sign associated with MCL, which is associated with an inauspicious prognosis.

A 57-year-old man with a neoformation on the upper eyelid of his left eye for two years, who had previously been diagnosed with stage IV MCL for 14 months, came to our attention. Due to the diagnosis he received, the patient underwent chemotherapy according to the guidelines, which is why he neglected the aforementioned neoformation, which nevertheless increased in size over time.

The diagnosis of SCC located at the level of the ocular adnexa was made after located at the level of the ocular adnexa was performed after surgical removal of the same and subsequent histological examination that confirmed it to be G2 squamous cell carcinoma.

The purpose of this rare clinical case is to emphasise how the correct differential diagnosis is essential for early treatment in these patients with i to avert the associated complications due to its location and appearance, which places it in differential diagnosis with chalazion, often delaying dianosis and subsequent surgical removal with the risk that this neoformation may spread to surrounding tissues. Due to its clinical presentation, it represents a diagnostic challenge that requires teamwork to enable a diagnosis as early as possible.

Case report

A 57-year-old white man, came to our observation, at the Fiorini Hospital in Terracina, Latina, Italy, Department of Ophthalmological Sciences, "La Sapienza" University of Rome, for ocular neoformation since two years, which had previously been assessed and diagnosed as chalazion that had increased in size over the past four month.

At the general anamnesis the patient reported being affected by mantellar cell lymphoma at stage IV MCL for

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14 months diagnosis (February 2022) for which he had been treated according to the chemo-immunotherapy R-DHAP scheme for 4 cycles from 27/04/2022 to 14/09/2022.

Subsequently on 19/10/2022 patient has undergone on mobilisation to HSC with Nivestim 1 flx2, collection of HSC after administration of Mozobil 20 mg 1fl and collection of 3.14/μL CD34+.

Since the follow-up bone marrow biopsy performed on 06/10/2022 was still positive, in view of the failed mobilisation and collection of stem cells for autologous transplantation the patient underwent mobilisation with high-dose Rituximab ARA and subsequent re-collection on 7/11/2022.

Subsequently on 18/11/2022 the patient was admitted due to the onset of fever and neutropenia, blood culture examination showed positivity for Pseudomonas aeruginosa infection and during admission the patient continued HSC mobilisation with Nivestim 30MUI 2 times/day. On 20/12/2022 he received HD-ARAC chemotherapy.

In particular, the control head TC scan performed on 27/09/2022 was negative: it did not show any areas of altered contrastographic impregnation of the encephalic tissue. Periencephalic CSF spaces and ventricular system within limits. Midline structures in axis. Major salivary glands within limits. Preserved amplitude of the para- and retropharyngeal spaces. No evidence of lymphadenopathy in the latero-cervical region. Regular pneumatisation of the cavities, where except fluid obliteration of maxillary seeds. Symmetrical eyeballs with regular representation of retrobulbar fat (Fig.1)

PET-TC performed post R-DHAP on 30/09/2022 compared with the previous analogue on 15/03/2022 deposes for complete metabolic response to treatment (score 2 according to Deauville Lymphoma scale) Fig. 1.

At the ophthalmological anamnesis the patient reported about two years earlier the appearance in the upper lateral third of the eyelid, desquamation accompanied by secretion that had been treated with local Tobramycin, which led to improvement with recurrence occurring more and more frequently over time. So in June 2021 the patient underwent a dermatological examination and an eye examination with a diagnosis of blepharitis. At subsequent ophthalmic examinations, following the growth in the site of the neoformation, the patient was given therapy for a diagnosis of chalazion. He reported progressive growth of the neoformation from September 2022 (Fig. 2). In February 2022 the patient was diagnosed with lymphoma and started chemo-immunotherapy. At the end of the course of treatment the patient reports rapid growth in the neoformation from January 2023 for which on 22/02/2023 he receives a diagnosis of "carcinoma in situ of the eyelid extending to the eyelid corner" and subsequently listed for blepharoplasty surgery.

Following rapid growth of the above-mentioned neoformation, the patient presented to our emergency department:

The complete ophthalmological examination of our patient on 14/04/2023 included the valuation of best correct visual acuty (BCVA) which was 10/10 in both eye. The adnexa were intact in right eye. In left eye there was appreciated neoformation lateral third upper eyelid of nonreducible nonmobile solid content with respect to the tarsal plane, on eyelid eversion the tarsus does not appear infiltrated. The anterior segment was normoconformed and the intraocular pressure (IOP), measured with a Goldmann applanation tonometer was 12 mmHg in both eyes. Fundus examination showed normalexavated optic disc, the macular region was uninjured, the retina in the periphery was uninjured and on the plane.

In view of the signs of malignancy of the neoformation, surgical removal was immediately scheduled: "after disinfection of the surgical field, removal of a neoformation on the upper left eyelid with reconstructive sliding plastic, Prolene 5.0 intradermal suture and detached silk 5.0 stitches" Fig. 2.

On histopathological examination the lesion was compatible with G2 squamous cell carcinoma.

The figures 3 shows the post-operative course at one week, and how at one month the scarring outcomes were satisfactory from an aesthetic point of view. The patient recovered good static and dynamic upper eyelid function. Simultaneously with the ophthalmic post-operative course, the patient followed a maintenance chemotherapy schedule

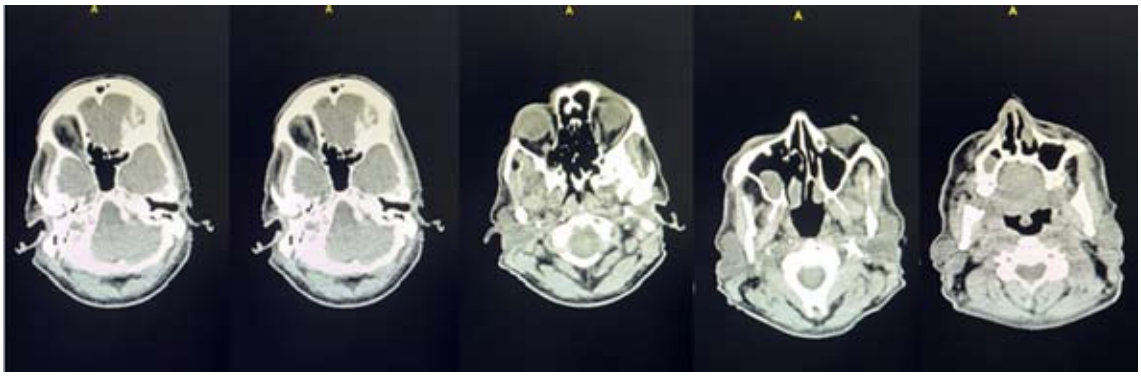

Fig. 1. TC scan performed on 27/09/2022: no signs of infiltration or metastasis

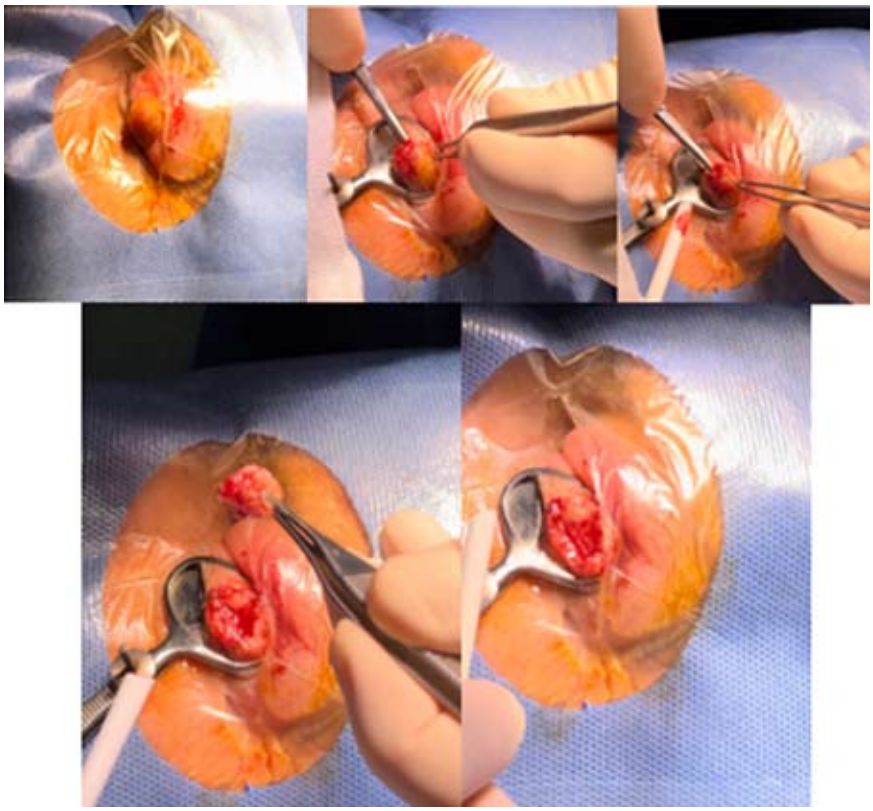

Fig. 2. Neoformation removal surgery

Fig. 3.
A. One week after surgery
B. One month after surgery

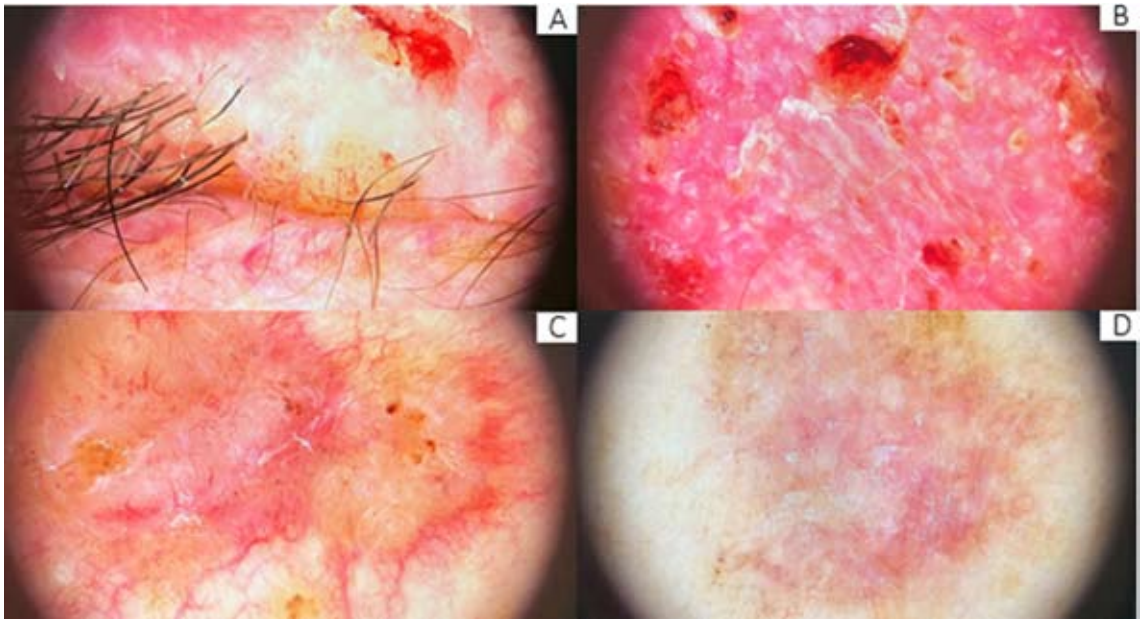

Fig. 4. Dermatoscopies A. Upper left eyelid after surgery. B. left auricle. C. left scapula. D. left arm

with Rituximab every two months for two yearswith Rituximab schedule showing an absolute lymphocyte value of 1.67 10^3/uL (normal range values) on 11/05/2023 after the second administration of maintenance chemotherapy.

After the histological diagnosis of SCC the patient was referred to an oncodermatological monitoring pathway and on 16/05/2023 the patient underwent dermoscopy that found SCC lesions on the left auricle, left scapula and left arm (Fig 4 A-D). Therefore on 18/05/2023 the patient underwent biopsy of these lesions to set the appropriate therapy.

Discussion

MCL represents 2.5–10% of all non-Hodgkin's extranodal lymphomas and are the most common malignant tumours of the orbit (2)(Shields et al. 2004). MCL appears to be among the two most common subtypes of high-grade ocular adnexal lymphoma, accounting for 1-5% of ocular adnexal lymphomas and is generally associated with considerable morbidity and mortality.

The orbit is the most commonly involved site of MCL involvement, followed by the lacrimal gland and the eyelid, similar to extranodal marginal zone lymphoma in this region (3) (Looi A).

Epidemiologically MCL is 2-3 times more frequent in males than in females. It occurs in elderly patients with an average age of 60 and orbit and eyelid are frequently involved. High proportion of systemic involvement is presented in general with MCL of the orbital and adnexal region. Seventy percent of patients pesented with stage IV disease and had multiple relapses and short survival tim. Its biological behaviour is very aggressive, with a mean survival of 3–4 years. Ocular (extra- and intraocular) adnexal damage is extremely rare, with 4% histologically confirmed damage diagnosis. (3).

In this patients simultaneous cutaneous localisations are very rare. Up to 2006, only 17 cases of skin metastases of MCL (4) (Singh AK) had been described. A recent study identified 14 patients with MCL involving the skin (1%); in 50% of these patients the skin was the primary clinical site (5) (Wehkamp U,). Skin cancers are the second most common malignancy in patients with lymphoma, and vice versa; in patients with skin cancers, malignant lymphomas are the most frequent secondary associated neoplasia (1,6) ((Péčová T, Manusow D). According to the literature, therefore, even if very rarely tumour duplicity would seem to co-exist in these immunocompromised patients (7).

The clinical and pathological features of lymphoma involving the ocular adnexa region is scarce. There is a very high proportion of systemic involvement in general with MCL of the orbital and adnexal region. Most patients presented with stage IV disease and had multiple relapses and short survival time. The clinical evolution of patients with MCL is relatively aggressive with a poor response to the treatment. Complete remission is obtained in 6–35% of the patients and the disease-free survival period is short, between 10 and 18 months (3) (Looi A). Treatment with rituximab-containing chemotherapy improved survival significantly compared with combination chemotherapy without rituximab (8) (Messineo D). There is a study with modifi ed R Hyper CVAD without R-MTX/ARA C followed by maintenance rituximab for 2 years, achieving high response rates with 59% PFS, 77% OS after 2 years (9) (Kahl BS). This therapy regimens such as RFCM (rituximab, fl udarabine, cyclophosphamide and mitoxantrone) have proved to be effective in relapses and with an improvement in terms of survival compared to the same scheme without rituximab; considered by a number of centres as a treatment standard in relapses (10) (Rasmussen P). In fact, our patient is also receiving maintenance therapy with Rituximab every two months for two years.

We present a rare case of tumour duplicity In line with this, our case although had initially presented with SCC on the conjunctiva, but due to inadequate workup by ophthalmologist and loosing follow up, subdividing our case to primary or secondary was not possible.

Since most patients with MCL initially present to the ophthalmologist, the current subdivision into primary or secondary lymphomas, based on limited ocular involvement (by imaging) and evidence of coexisting disease or a previous history of lymphoma, is not practical. Therefore, it is not yet possible to state that there is a higher frequency of occurrence of SCC at the time of diagnosis of MCL in patients presenting with initial ocular disorders.

A rigorous approach to the initial diagnosis and staging of squamous cell carcinomas of the ocular adnexa is necessary in this type of patient, in fact in order to guarantee a correct differential diagnosis with ocular alterations such as chalazio, interdisciplinary collaboration between specialists is essential. In particular, the ophthalmological framing of these oncohaematological patients is of primary importance in order to guarantee a timely diagnosis of MCL, which is important due to the high degree of malignancy of this type of lymphoma.

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