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A NOT SO PREDICTABLE CASE OF PRIMARY ORBITAL B-CELL LYMPHOMA: IMAGING FINDINGS AND REVIEW OF LITERATURE

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Absract – *Lymphoma represents only 6-8% of all orbital masses. Its incidence is estimated to have been rising over the last two decades. We describe the imaging feature of small and large diffuse B-cell primary lymphoma, which was found in the extra-conal orbital space. Imaging findings of lesion, depicted on Computed Tomography and Magnetic Resonance were suggestive of the presence of a soft-tissue neoplasm: the isolated appearance of our single orbital lesion made this a challenging diagnosis for radiologists and clinicians.*

A brief review – emphasizing imaging features – is reported in this manuscript, in order to increase diagnostic confidence of clinicians, radiologists and surgeons.

INTRODUCTION

Only a small percentage (6-8%) – among single orbital lesions – is represented by lymphomas. In two-third of cases it is a primary location particularly in Non-Hodgkin lymphoma[1].

Literature reports that the most frequent histological type of orbital lymphoma is represented by mucosa-associated lymphoid tissue (MALT) lymphomas; the typical location is supero-lateral region of intra- and extraconal spaces, namely in cases of large tumors[1,2]. We report a case of small and large diffuse B-cell lymphoma, located in the supero-medial extra-conal space with involvement of levator palpebrae superioris muscle. Main imaging features of orbital lymphoma are described in this case report, in order to increase the diagnostic confidence of clinicians, radiologists and surgeons.

CASE REPORT

In November 2013, a 64-year-old woman required ophthalmologic examination for left superior eyelid's swelling, referred since July. There were no visual field deficits and no other symptoms at the ophthalmologic examination.

An Ultrasound exam, performed in another diagnostic center, revealed the presence of a lesion located in the left supero-medial periorbital tissues (size 1.5 cm). This lesion presented an inhomogeneous ultrasound pattern, with moderate to high vascular signal at power-color-Doppler.

To better investigate the orbital lesion, the patient was admitted to the neuro-surgery department of our hospital in January 2014.

Neurological examination demonstrated indolent periorbital swelling, outward proptosis and palpebral ptosis.

Magnetic Resonance Imaging (MRI) scan was performed in our radiology department, using a 1.5 Tesla Magnetic Resonance scanner; conventional head sequences were acquired in order to evaluate the presence of neurological disease. In addition, for the orbital evaluation we acquired high-resolution images using Fast Spin Echo (FSE) and Gradient Echo (GRE) sequences (thickness 3 mm,

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320x256 matrix, Number of Excitation 3), even with fat spatial saturation. Diffusion Weighted Imaging (DWI) was also acquired, using Single Shot Echo Planar Imaging (SSEPI) technique.

MRI examination revealed a soft-tissue mass (27 mm x 24 mm x 9 mm) located in the extraconal space at the orbital roof, slightly hyperintense on both T1- and T2-weighted images (Figure 1).

This mass was contiguous to the superior rectus/levator palpebrae superioris complex - showing, on coronal images (Figure 2), no clear cleavage with these muscles. In addition, it was close to superior oblique muscle.

The lesion showed homogeneous enhancement after intravenous gadolinium injection (Figure 3); no signal drop out was observed on fat-suppressed enhanced T1-weighted images.

On DWI, the lesion was hyperintense, with clear signal restriction on Apparent Diffusion Coefficient (ADC) map (Figure 4); this finding suggested high cellularity of the lesion.

The patient's evaluation was completed performing a Multidetector Computed Tomography (MDCT) examination, in order to assess bone involvement. MDCT acquisitions included also coronal multiplanar reconstruction images.

The lesion was confirmed by MDCT scan, with no evidence of bone involvement (Figure 5).

These findings were suggestive of a soft-tissue neoplasm located in the extra-conal space, with periorbital supero-medial extension and malignant behaviour-muscle infiltration.

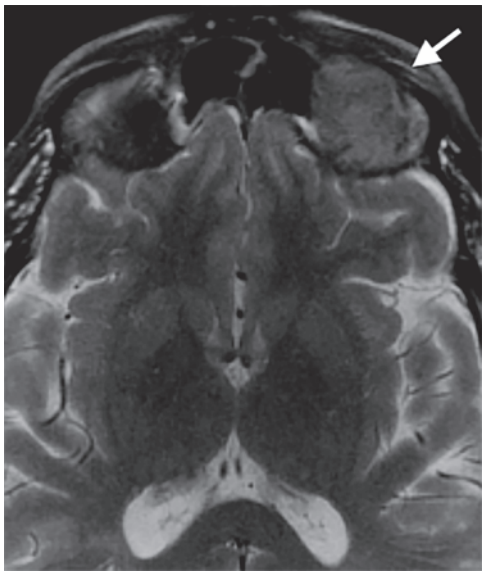

Figure 1. Axial Fat-suppressed T2-weighted image shows soft-tissue mass *(white arrow)* located in the orbital roof, in the supero-medial extra-conal space, with slightly hyperintense signal.

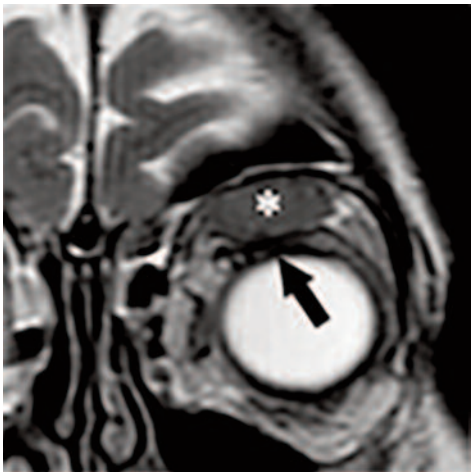

Figure 2. Coronal Fast Spin Echo T2-weighted image confirms the presence of the lesion *(white asterisk)*; no clear cleavage was observed to the superior rectus/levator palpebrae superioris complex *(black arrow)*.

Biopsy – in order to better characterize the lesion – was achieved via antero-superior orbitotomy by the neuro-surgeons. Extemporaneous intra-operative examination demonstrated "small and large diffuse B-cell lymphoma".

Immunohistochemistry showed that the malignant cells were positive for CD20, CD79a and Bcl-2 and negative for CD3, CD30; their proliferative index (Ki67) was 30%.

Subsequently, the patient was admitted to the hematology department to perform a MDCT for staging disease. MDCT exam demonstrated no evidence of systemic disease and a primary localization of orbital lymphoma.

DISCUSSION

The orbit is an uncommon site of onset of lymphoproliferative diseases, which include benign lesions (lymphoid hyperplasia), atypical lymphoid hyperplasia and malignant lesions (lymphoma)[1]. Lymphoma represents 6-8% of all orbital masses, but its incidence is estimated to have been rising over the last two decades[1,3].

Orbital lymphoma can be primary in two-third of cases, with no evidence of concurrent systemic disease and without any history of lymphoma[2,4]. Up to 75% of these patients will develop systemic disease[5].

Only a small part of all systemic lymphomas involve the orbital site, representing about 1-2% of non-Hodgkin lymphomas[1].

A peculiarity of our case is the presence at histological examination of small and large diffuse B-cell lymphoma. In fact, among orbital lymphomas, the most frequently reported type is

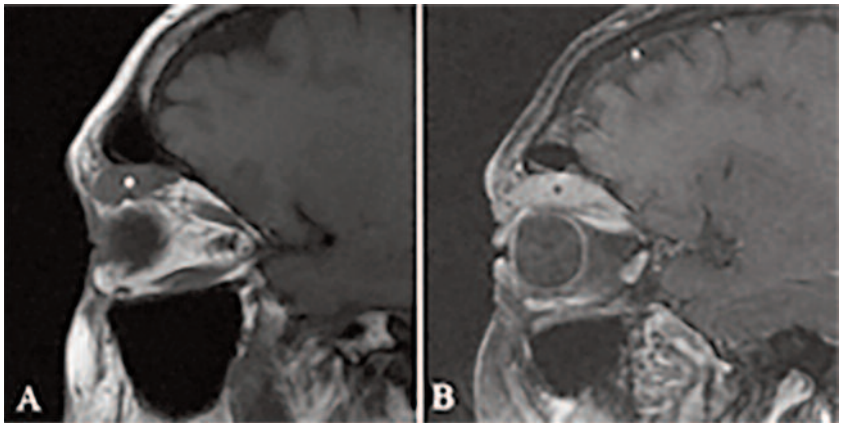

Figure 3. Sagittal T1-weighted image (4a) reveals a mass (asterisks) with slightly hyperintense signal; sagittal T1-weighted scan after fat suppression and gadolinium administration (4b) shows marked homogeneous enhancement of the lesion.

MALT lymphomas, followed by follicular lymphomas, diffuse large B-cell lymphomas and mantle cell lymphomas[6,7].

The etiology of orbital lymphoma is uncertain[3]. These diseases seem to arise in extranodal sites with chronic inflammation or autoimmune disorders[1]. Recent studies demonstrated the association of lymphoma with Chlamydia psittaci infection[1,8]. Orbital lymphomas arise more commonly in the fifth to seventh decade with a slight predominance for female gender[1].

Clinical presentation is characterized by a palpable, firm or rubbery mass associated with painless periorbital swelling, progressive proptosis, ptosis, visual impairment, diplopia and motility disturbance. Occasionally conjunctival irritation - "salmon eye" - tearing and minimal pain can occur[1,9,10].

According to a previous report published by Gerbino et al[6], the majority of orbital lymphomas involve both intra- and extra-conal spaces; they involve less frequently only the extra-conal space, and rarely are they found only in the intra-conal space.

In the orbital space, the most encountered location for the lesion is the superior quadrant, specifically the superior-lateral one[1] (Figure 6). Involvement of lower quadrants has been less commonly reported; in this site, it can be also associated with contact of optic nerve[1].

In our patient, the lesion was recognized in the extra-conal space with supero-medial periorbital expansion; this is a rare finding.

Disease progression is generally associated with infiltration of the extrinsic eye muscles, particularly the superior rectus-levator muscle complex, followed by medial rectus and lateral rectus muscles, and, rarely, inferior oblique muscle[6]. In addition, the lesion could also infiltrate bone structure, lacrimal sac and lacrimal gland[6,11].

The diagnosis of orbital lymphomas initially takes advantage of CT and MRI examinations, subsequently a definitive histological type is obtained by performing a biopsy.

Characteristically, on CT and MRI, the neoplasm presents itself as a solitary mass that molds around orbital structures without signs of infiltration[11,12].

CT acquisitions show a moderate and homogeneous high-density lesion - similar to the skeletal muscle in appearance – with well circumscribed margins[11]. After contrast agent injection, this lesion reveals mild enhancement that decreases on delayed images[1]. Furthermore, CT is the instrument required to identify bone involvement.

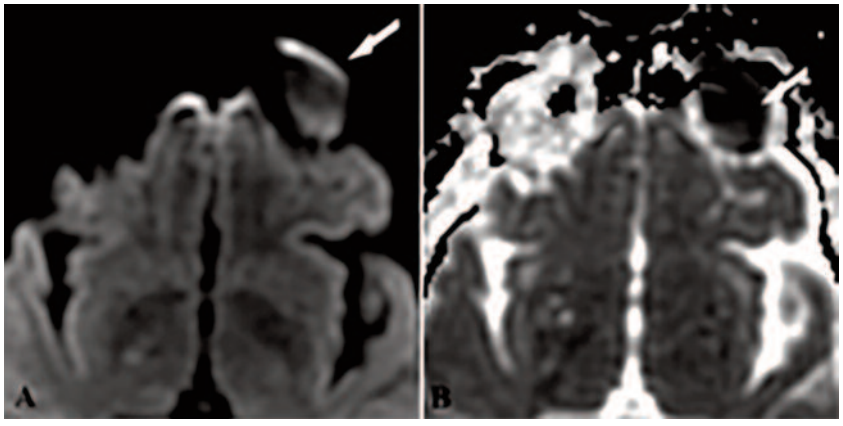

Figure 4. Axial diffusion-weighted single-shot echo-planar images (5a, 5b) demonstrate a restricted diffusion *(high signal)* of the lesion *(white arrow)*; apparent diffusion coefficient map confirm the restriction of diffusion *(low signal)* of the neoplasm *(white arrow)*.

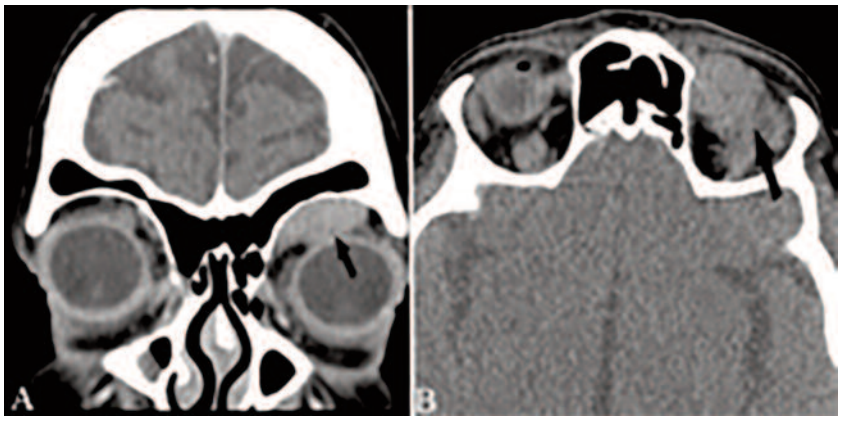

Figure 5. On figure 1A, CT coronal multiplanar reconstruction image demonstrates neoplasm *(black arrow)*, without signs of bone involvement; on figure 1B, axial CT scan confirms the absence of bone erosion from the lesion.

MRI demonstrates a well-defined lesion isointense (relative to the brain) on T1-weighted sequences, and iso-hyperintense on T2-weighted images[2]. In opposition to CT scan, post-gadolinium MR images exhibit a moderate to marked homogeneous enhancement[2].

When a lymphoproliferative lesion is suspected on CT and MR images, an open-sky biopsy is necessary to obtain an accurate diagnosis[6]. Only for selected patients with particular anatomic location of the neoplasm, it is possible to perform a biopsy using a computer-assisted navigation platform.

Histological examination first takes advantage of hematoxylin and eosin stained paraffin sections, and later of immunohistochemical staining for immunologic phenotyping.

After diagnosis confirmation, it is necessary to stage the disease according to the Ann Arbor classification[13].

Differential diagnosis of orbital masses depends on their location: intra- and/or extra-conal space.

Intraconal tumours include optic nerve sheath meningioma, glioma and cavernoma.

Meningioma is a solid fusiform lesion with homogeneous enhancement post-contrast, in opposition to the non-enhancing optic nerve; occasionally, meningioma shows intralesional calcification. Optic glioma is an aggressive tumour of the adult patients; generally, the mass involves adjacent muscles and may also destroy orbital bones. It is typically unilateral, with moderate inhomogeneous enhancement and involvement of any part of the optic nerve (from the globe to the optic chiasm)[11].

Cavernoma is common in adult patients with slowly progressive proptosis. Images show a sharply circumscribed, rounded intraconal mass that commonly extends to the extraconal space, without lytic destruction of the bony orbit. On MDCT images, the lesion may have intralesional "microcalcifications", which are usually pathognomonic for cavernoma[1]. Dynamic enhancement is characteristic, because it becomes complete on delayed images[13]. On MR images, they appear as homogeneously hyperintense lesions, also after spatial fat suppression.

The presence of both intra- and extra-conal compartment lesion may include inflammatory/metabolic disease, neoplasm and lymphoproliferative disorder.

Inflammatory pseudotumor is a frequent cause of proptosis, and it is often similar to orbital lymphoma. It characteristically shows fat infiltration, associated with perilesional edema[14]. MRI reveals low signal on T2-weighted sequences, and delayed enhancement after intravenous gadolinium administration. Diffusion weighted Imaging (DWI) has recently been used to differentiate pseudotumor from lymphoma. Lymphoma is a hypercellular tumour, indeed it typically exhibits high signal on DWI images, with low apparent

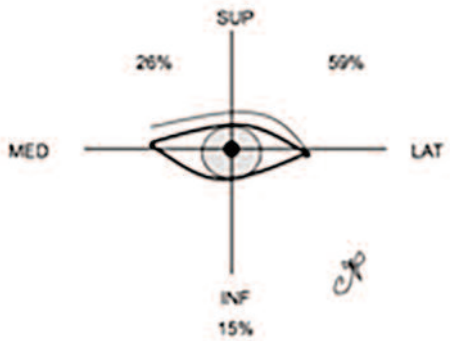

Figure 6. Graphic for distribution of lesions in the orbital space; the most encountered location for the lesion is the superior quadrant, specifically the superior-lateral one (data from paper by Prigo et al)[1].

diffusion coefficient (ADC) values. Inflammatory lesion shows intermediate DWI signal and ADC value (comparable to normal lacrimal gland)[14].

Thyroid orbitopathy is represented by a thickening of common rectus muscles over 4 mm and by enlargement of intra-conal fat[1]. Sarcoidosis determines diffuse infiltration of orbital structure and dural thickening[1].

Malignant lesions of orbital structures are usually constituted by metastasis. They typically arise from carcinoma (breast, lung, prostate, melanoma, carcinoid, gastrointestinal, renal cell) in adult patients, with involvement of anterior compartment. Metastases appear hyperintense on T2-weighted images, with irregular enhancement after intravenous contrast administration. Bony destruction is often seen[11].

Lymphoproliferative diseases include a spectrum of disorders (lymphoid hyperplasia, atypical hyperplasia and lymphoma) that is difficult to differentiate for their similar imaging features[15].

Treatment of orbital lymphoma is controversial. For stage I and II of localized disease, radiotherapy is recommended; however, the site of irradiation could involve radiosensitive structures such as lens, lacrimal gland and retina. Chemotherapy, or a combination of chemo and radiotherapy, is indicated in patients with disseminated and advanced tumours[16]. The introduction of Rituximab, a chimeric monoclonal antibody against B-cell-specific antigen CD20, reported a clinical efficacy in the treatment of follicular lymphomas. In the last few years the use of antibody was admitted also for other subtypes of non-Hodgkin lymphomas with important results[13]. Surgery is not recommended except for initially biopsy[16].

CONCLUSIONS

The diagnosis of orbital lymphomas may be challenging, because lymphoproliferative diseases have similar characteristics by imaging. The suspicion of orbital lymphoma needs adequate imaging studies, with a combination of CT and MRI, followed by early surgical biopsy. A multidisciplinary approach is recommended for disease management[17]; only a correct diagnosis, obtained by histological report, could lead to the opportune treatment of the disease.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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