Orbital manifestations of the Hematopoietic Tumors: Imaging Features and Differential Diagnosis.

Poster No.: C-1263
Congress: ECR 2014
Type: Educational Exhibit
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Keywords: Biopsy, CT, Eyes, Cancer
DOI: 10.1594/ecr2014/C-1263

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Learning objectives

Learning Objectives

- Review the spectrum of hematopoietic tumors involving the orbit.
- Illustrate the multi-modality imaging workup of such tumors.
- Increase awareness and recognition of uncommon presentations of hematopoietic tumors in the orbit.

Background

Visual problems in patients with hematological neoplasms are commonly observed by the ophthalmologists.

The affection of the orbits is not only due to neoplastic infiltration but also may be due to the complications of therapy (radio or chemotherapy) or the opportunistic infections. Lymphoma can affect any compartment of the orbit with secondary involvement more common than primary one. Although rare, Leukemic infiltration, extramedullary plasmacytomas and histocytosis of the orbit may also occur. Being infrequent, these lesions are commonly misdiagnosed; therefore special emphasis on these diseases & imaging features is of at most clinical importance.

Findings and procedure details

CT vs MRI in orbital imaging

Both CT and MRI are now widely used as primary orbital imaging techniques. Each modality has its strengths and weaknesses which affect selection of one or the other as the first choice

CT is more widely available, cheaper, provides quicker scans, is able to image bone directly, detects calcification better, and is the first choice in cases with suspected metallic orbital foreign bodies. Visualization of non metallic foreign bodies like wood is more problematic and both CT and MRI may have to be used. Recently multidetector CT is able to provide isotropic multiplanar imaging which has increased its ability to localize the site of orbital lesions.
On other side, MRI has advantages of lack of ionizing radiation, it has superior soft tissue contrast, its ability to image the orbit and intracranial structures free of beam hardening artifacts from the skull base/dental fillings. Selection of appropriate MRI protocols and use of the correct surface coils is important depending on clinical question. Use of gadolinium contrast enhancement and fat suppression aids in disease detection and characterization. The main disadvantage of MRI is long scan time, its higher cost, its inability to image bone or calcium directly, magnetic susceptibility artifacts, and claustrophobia in some patients.

**Diagnostic strategy**

Several approaches to the diagnosis of orbital pathology are in use. A common strategy is to localize the pathology to one of the defined compartments of the orbit. The orbit has 8 compartments: optic nerve, orbital apex, retroocular fat, extra ocular muscles, eye lid, eye globe, lacrimal system and the bony orbit. Another approach is to divide the orbit into intra and extraconal compartments. These have been described as the muscle cone, formed by the four rectus muscles, dividing the orbit into intraconal and extraconal compartments, with the optic nerve within the central part of the muscle cone. The extraconal compartment is bordered by the bony orbit and subperiosteal compartment. Recently, some authors have attempted to further refine this framework by using anatomical location, bone and sinus involvement, content, shape and associated features to increase diagnostic specificity.

The imaging findings are categorized into three groups: neoplastic infiltration, therapy induced changes, and the opportunistic infection.

**1. Neoplastic infiltration.**

Ocular problems in patients who have hematological malignancy are increasing in incidence because of the increased survival rate associated with more effective treatment. Direct invasion of the orbit with the neoplastic cells is common, and can affect any of the orbital compartments.

**1. Orbital lymphoma**

Lymphoma is reported to constitute between 6 and 8 % of orbital tumors. Orbital lymphoma either a part of systemic lymphoma or less commonly a primary lymphoma. it represents a small fraction of all systemic lymphomas that account for about 1-2 of non-Hodgkin lymphomas. Primary lymphoma of the orbit accounts for 0.01 % of all lymphomas. The most common lymphoma arising from tissues surrounding the eye is the low-grade B-cell lymphoma: so-called extra nodal marginal zone lymphoma (MALT lymphoma).
The clinical manifestations are non-specific including swelling and prolapses of the eyelid, painless but palpable masses, and exophthalmia. Early diagnosis can only be made with a needle biopsy.

It can occur at any age but more common in the old patients are between 50 and 70 years of age, and no gender predilection is recognized.

**Imaging features**

Orbital lymphoma usually appears as a soft tissue mass, can affect any of the orbital components. It involves the conjunctiva (especially in the case of orbital adnexal MALT lymphoma (OAML) (Fig.1) or elsewhere in the orbit, frequently in the upper outer quadrant, closely associated with the lacrimal gland.

Although the extraocular muscles may be surrounded or displaced by the mass, they can usually be identified as not being the origin of the tumour, helpful in distinguishing lymphomas from other orbital masses.

In study done by Gema Priego.,et 2012 , they found that lymphomas have a characteristic location in the orbit that can assist radiologists to reach a proper diagnosis. This typical location consists of the involvement of superior quadrants; specifically, the superior-lateral one. The most commonly infiltrated structures are found within the superior-lateral quadrant, such as the superior rectus muscle, lateral rectus muscle, lacrimal gland and eyelid. Involvement of intra-conal space is usually associated with the extra-conal one, and is related with large size of the tumour. Therefore, an intra-conal involvement alone will not be the main pattern of lymphoma in the orbit. In addition, low prevalence is described within occupation of lower quadrants and contact with the optic nerve.

**CT**

On non-contrast CT, the mass is usually homogeneous in density, either isodense or slightly hyperdense when compared to the extraocular muscles. Following administration of contrast, only mild to moderate enhancement is seem (Fig.2), similar again to the extraocular muscles and lacrimal gland. Spiral (CT) using a dual-phase contrast-enhancement protocol report that lymphomas have a decrease in density on delayed images, as opposed to orbital pseudotumours, whose density increases on delayed images.

**MRI**

Similar to intracranial lymphoma, the densely cellular nature of these tumours with high nucleus-to-cytoplasm ratio results in relatively specific appearances: This tumour has been described as a mass with distinct margins, which shows an isointense signal on T1wi and iso-hyperintense on T2wi. Variable enhancement has been reported after
contrast administration. Moreover, low values in the apparent diffusion coefficient on diffusion-weighted study have been found helpful to discriminate lymphoma from other orbital lesion (Figs.3&4).

b. Leukemia

Leukemia is the most common malignancy of childhood, with acute lymphoblastic leukemia accounting for 80% of all cases and acute myeloid leukemia (AML) accounting for 20%. Foal myelogenous leukemic infiltration called granulocytic sarcomas or myeloid sarcomas, previously described as choloroma. These lesions are more common in children with the peak age prevalence is 7 years. Granulocytic sarcoma may occur prior or after the diagnosis of AML and can be sign of replase in treated patients.

Clinically: most common presenting symptoms of orbital disease are proptosis, periorbital swelling and a mass in the lacrimal gland or eyelid. Orbital involvement is bilateral more than unilateral.

Imaging Features:-

Granulocytic sarcomas of the orbit can affect any of its compartments yet it usually arises from the lateral orbital wall. These lesions tend to encase, rather than invade, normal structures, including bone and sclera.

Plain radiography have a limited role as the granulocytic sarcoma usually appears as a soft-tissue mass. Less commonly, bone erosion or demineralization or periosteal reaction may be seen.

US: - a nonspecific, homogeneous, hypoechoic or echogenic solid mass is seen. The borders may appear infiltrative.

CT: - these lesions appears homogeneously isoattenuating to slightly hyperattenuating relative to muscle with homogenous enhancement. Invasion of the orbital fat and extension to the eyelid are commonly observed with no calcification.

MRI: - granulocytic sarcomas are iso- to hypointense relative to gray matter or muscle on T1wi and heterogeneously iso- to slightly hyperintense on T2wi with homogeneous enhancement (Fig.5).

Differential Diagnosis

The main differential diagnosis of an orbital mass in a patient known to have leukemia is: abscess, hematoma, or secondary malignancy. Abcess shows ring like enhancement on
background of cellulitis whereas the granulocytic sarcomas shows diffuse enhancement on other hand, the hematomas do not enhance at all. DWI may also help to identify the abscess by its notable restricted diffusion (Fig5).

The differential diagnosis of an orbital mass in patients with no history of leukemia is much more wider and challenging, including rhabdomyosarcoma which is the most common extraocular malignancy of the orbit in children. Rhabdomyosarcoma is much more likely than granulocytic sarcoma to cause bone erosion.

Because the granulocytic sarcoma may present with inflammatory signs including redness and swelling of the orbit, the differential diagnosis of orbital cellulitis is considered, however the infiltration of the conal fat, and diffuse enhancement at imaging suggest the much more common condition of orbital cellulitis.

When the orbital granulocytic sarcomas are bilateral, the differential diagnosis of LCH and metastatic neuroblastoma is considered, however the presence of more concomitant lytic bony lesions in other bones can help in proper diagnosis.

LCH lytic lesion usually has beveled edges in the skull and associated with diabetes insipidus related to involvement of the infundibulum.

The metastatic lytic bony lesions from neuroblastoma also have a predilection for the orbits, are frequently bilateral, and also originate in the osseous walls of the orbits. But this tumor contains calcifications and may be accompanied by aggressive periosteal reaction, lytic lesions elsewhere in the skeleton, abdominal masses, and excess urinary levels of catecholamines.

c. Histiocytosis

Histiocytosis is a group of disorders characterized by abnormal proliferation of histocytes. Langerhans cell histiocytosis is a histiocytic lesion that behaves aggressively in children. Orbital involvement occurs in 23% of children with LCH and always involves the bone, since it originates in bone and spreads directly into the orbit.

LCH is ranging from benign unifocal bone disease to more aggressive multisystem disease. Eosinophilic granuloma, the most localized and benign form of LCH, usually presents in children less than 4 years of age as unifocal bone disease with possible orbital involvement. LCH has been reported to have a higher male predominance, commonly involves the superotemporal orbit, and manifests with proptosis, ptosis, erythema, and enlarging palpebral fissures.

Imaging can help define the extent of disease and osseous destruction. On CT, LCH manifests as lytic bony lesion with clear cut edges associated with soft-tissue lesion, can
be well-defined or diffusely homogeneous, and shows moderate to marked enhancement after contrast administration. The soft-tissue mass may extend into the orbit, temporal fossa, forehead, face, and epidural space (Fig 6&7). MR should be used to better evaluate intracranial extension of disease. The mass replaces the normal bright signal of marrow with heterogeneous signal on T1WI, can be hyperintense or hypointense on T2WI, and demonstrates enhancement on T1-weighted post-contrast images.

The differential diagnosis of orbital Langerhans cell histiocytosis is orbital rhabdomyosarcoma with bone invasion, although bone destruction in the former is typically more pronounced. Both of these entities may spread into adjacent paranasal sinuses or intracranial contents. The unusual clinical finding of diabetes insipidus due to involvement of the infundibulum or the presence of additional bone lesions suggests Langerhans cell histiocytosis, although rhabdomyosarcoma may metastasize to bone as well.

Erdheim-Chester Disease (ECD) is a rare form of non Langerhans’ cell histiocytosis originally described as "Lipid Granulomatosis" orbital involvement may be uni or bilateral intraconal masses at presentation. The masses may be large and extending to the extraconal space. These orbital lesions had mainly a hypointense signal on both T1-and T2wi and intense enhancement on post contrast images (Fig.8).

d. Multiple myeloma

Multiple myeloma is a subgroup of plasma cell dyscrasias in which there is neoplastic proliferation of plasma cells or their precursors. Mean age at presentation is between 40-70 yrs with peak in the 7th decade. It accounts for about 10% of all hematological malignancies.

Orbital involvement in multiple myeloma is a very rare finding. It accounts for 0.1 - 0.5 % of all orbital tumors.

Unilateral slowly progressing proptosis, pain, visual impairment and dioplopia are the commonest reported clinical presentation. Bilateral proptosis with multiple soft tissue masses is an extremely rare presentation of multiple myeloma.

Orbital involvement can occur in one of the following ways.

a. As a part of systemic multiple myeloma with local bone destruction from an isolated plasmacytoma.

b. Extramedullary plasmacytoma from orbital soft tissue.

c. Secondary extension to the orbit of a sinus.
Imaging features of orbital multiple myeloma

**In CT:** Orbital myeloma most commonly presents as a unilateral solitary soft tissue intraorbital tumor which is an extension of bony deposit and is associated with bone destruction.

**MRI** shows low signals on T1 wi and high signals in T2 images with variable enhancement on post contrast images.

### 2. Therapeutic complication

**Radiation-induced optic neuropathy**

Radiation-induced optic neuropathy represents ischemic injury to the optic nerve, typically occurring 4-60 months after radiation therapy. The diagnosis is often difficult and usually one of clinical exclusion. The patients typically presents with sudden, painless, monocular visual loss. The symptoms progress over several weeks, and may be bilateral depend on the radiation port. The injury can occur anywhere from the extraocular, intraorbital optic nerve to the optic chiasm. Visual field examination shows abnormality depends on the location of involvement. In optic nerve injury, nerve fiber bundle defects are expected. Whereas with chiasmal injury, bitemporal visual field defects are found. The pathogenesis of radiation optic neuropathy is not fully understood. The most accepted theory is small vessel disease related to endothelial cell proliferation, thickened vessel walls, and subsequent occlusion. These regions of radiation-induced vascular injury may coalesce, resulting in a perivascular coagulative necrosis.

Most useful imaging MRI finding is pathologic segmental contrast enhancement in the optic nerve confined to the radiotherapy port. This abnormal segment usually shows

isointense signal on T1WI and hyperintensity on T2WI( Fig.9). On the chronic stage atrophic changes of such segment are noted.

### 3. Opportunistic infection

Patient with hematological malignancy have suppressed immunity as a result of disease as well as the immunosuppressive drugs. These patients are usually victims of many opportunistic infections. Orbital involvement in such cases may be in the form of cellulitis.

**Imaging features**

Urgent imaging is indicated to assess the anatomic extent of disease, including postseptal, cavernous sinus involvement; evaluate for sources of contiguous spread,
such as with sinusitis or trauma; and identify orbital abscesses that require exploration and drainage.

The orbital infection is described with respect to the orbital septum as either preseptal (periorbital) or postseptal (orbital). The septum is a thin sheet of fibrous tissue that originates in the orbital periosteum and inserts in the palpebral tissues along the tarsal plates. It provides a barrier against the spread of periorbital infections into the orbit proper. This distinction between periorbital and orbital processes is of clinical importance because postseptal infections are treated more aggressively.

Periorbital cellulitis is a preseptal process limited to the soft tissues anterior to the orbital septum; most commonly arises from the contiguous spread of infection from adjacent structures such as the face, teeth, and ocular adnexa. Clinically it present by swelling and erythema of the eyelids, chemosis, and, in severe cases, limitation of eye movement without proptosis.

Cross-sectional imaging demonstrates diffuse soft-tissue thickening and areas of enhancement anterior to the orbital septum are seen on periorbital cellulitis. It is very difficult to differentiate between preseptal oedema and periorbital cellulitis. (Fig 1)

Orbital cellulitis is a postseptal infectious process most commonly caused by paranasal sinusitis (Fig 2), which spreads to the orbit via perivascular pathway. Thus, bone destruction is not necessarily seen. Clinically it present as the periorbital infection yet may present with proptosis.

**On cross sectional images:** The orbital cellulitis is associated with poor definition of orbital planes, inflammatory stranding in the intraconal fat and intraconal or extracanal soft tissue mass.

Development of an orbital subperiosteal abscess is most commonly associated with ethmoid sinusitis. DWI can easily detect abscess formation as it shows restricted diffusion with marked reduced ADC value. The Urgent drainage of the abscess may be necessary to avoid a rapid elevation of intraorbital pressure and resultant visual impairment. (Fig 11).

Another rare complication of therapy is retro-ocular lipomatos which is usually presents as a localized hypertrophy of the adipose tissue. This phenomenon is recorded after prolonged administration of moderate to high doses of oral corticosteroids. Often asymptomatic, they can also be revealed by worrying symptoms usually due to a compressive syndrome. CT and MRI are the most helpful diagnostic means, appears as increased amount of the retroocular fat with starching of the optic nerves (Fig.12). Interestingly, these lipomatos have regressed after cessation of the therapy.
70 year old male with recurrent Lymphoma

Diffuse infiltration of the left conjunctiva showing diffuse CT enhancement. It eliciting iso to hypointense on T1WI & T2WI with uniform enhancement.

Fig. 1
4 year male patient with NHL

An ill defined solid enhanced mass lesion is seen at the supralateral aspect of the left orbit extending intracranially into the left temporal region, also extending to the involve the left temporalis muscle yet the lateral orbit bony wall is intact

Fig. 2
13 year old male with Hodgkin Lymphoma

An ill defined retro-ocular solid lesion is seen at the inferior half of the left orbit involving the inferior rectus elicits isointense signal on both T1 & T2wi with heterogenous enhancement.

Fig. 3
63 year old female with mantle cell Lymphoma

Diffuse infiltration of the left temporalis muscle, bilateral retro-ocular mass entangling the optic nerve. These masses are iso to hypointense on T1WI & T2WI with uniform enhancement.

Fig. 4
10 year old female presented with AML

Bilateral rather symmetrical infiltration of both lacrimal glands and superior recti. It elicits iso intense signal on both T1&T2wi with uniform enhancement on post contrast series with restricted diffusion and reduced ADC value on ADC map.

Fig. 5
3 year male patient with LCH

A well defined lytic lesion with punched out edge seen at the lateral orbital wall. Marked regression is noted after therapy.

Fig. 6
5 year female patient with LCH

A well defined lytic lesion involving the orbital roof associated with large intra-orbital enhanced soft tissue mass lesion.

Fig. 7
12 year old male patient with Erdheim-Chester disease

Diffuse infiltration of the extra ocular muscles with diffuse bony lytic lesion at skull base.

Fig. 8
61 male patient with history of nasal lymphoma treated by radiotherapy, presented after 4 years with right visual deficit.

MRI revealed marked enhancement of the intracranial segment of the right optic nerve (arrow) radiotherapy induced optic neuropathy. The patient pursued hyperbaric oxygen with the vision in his right eye improved slightly.

Fig. 9
70-year-old patient with CLL presented with severe eye pain and progressive visual loss due to herpes zoster reactivation.

MRI shows abnormal enhancement around the left optic nerve sheath complex with blurred perineural fat and abnormal enhancement along the supratrochlear nerve. Intracranially there is abnormal enhancement of cranial nerves III. Patient symptoms improved on antiviral therapy.

Fig. 10
1 year male with NHL presented with left eye throbbing pain

A well defined retro-ocular cystic lesion is seen showing thick uniform wall (a& b) with marginal enhancement (c & d). The lesion is hyper intense on DWI (e) with marked reduced ADC value on ADC map (f).

Orbital abscess

Fig. 11
25 years old male with lymphoma after chemotherapy presented with proptosis and visual deficit.

CT & MRI show prominent retro-ocular fat with stretched optic nerves without masses or abnormal enhancement. Findings impressive of retro-ocular lipomatosis.

Fig. 12
Conclusion

The patients with hematological neoplasms has orbital affection by many ways, the imaging modalities (CT and more accurate MRI) are effective in diagnose and characterize the orbital affection in cases of hematological neoplasms. The differentiation the neoplastic infiltration, infectious processes and the therapeutic toxicity need more clinical and laboratory correlation.

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References
