Title

Primary Ocular Adnexal Extranodal Marginal Zone Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma Presenting as Orbital Apex Syndrome

Journal

Neuro-Ophthalmology, 41(2)

ISSN

0165-8107

Authors

Yuen, Carlen A

Pula, John H

Mehta, Milap

Publication Date

2017-03-04

DOI

10.1080/01658107.2016.1263343

Peer reviewed

NEURO-OPHTHALMOLOGY
2017, VOL. 41, NO. 2, 94–98
http://dx.doi.org/10.1080/01658107.2016.1263343

Taylor & Francis
Taylor & Francis Group

CASE REPORT

Primary Ocular Adnexal Extranodal Marginal Zone Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma Presenting as Orbital Apex Syndrome

Carlen A. Yuen[a], John H. Pula[b], and Milap Mehta[c]

[a]Department of Neurology, University of Chicago, Chicago, Illinois, USA; [b]Department of Neurology, NorthShore University HealthSystem, Chicago, Illinois, USA; [c]Department of Ophthalmology, NorthShore University HealthSystem, Chicago, Illinois, USA

ABSTRACT

A 75-year-old female with a past medical history significant for prior stroke and atrial fibrillation presented with acute onset of orbital apex syndrome with chemosis and periorbital ecchymosis. Following initial treatment to relieve intraocular pressure, she began spontaneously haemorrhaging retro-orbitally. Preliminary investigation with neuroimaging demonstrated a left orbital mass with extension into the orbital apex. A provisional diagnosis of cavernous haemangioma was made. She was treated with transorbital resection of the orbital mass. Subsequent histopathology revealed a diagnosis of ocular adnexal non-Hodgkin lymphoma of histologic type extranodal marginal zone of mucosa-associated lymphoid tissue (MALT lymphoma). MALT lymphoma should be considered in cases of orbital apex syndrome.

ARTICLE HISTORY
Received 23 October 2016
Revised 17 November 2016
Accepted 17 November 2016

KEYWORDS
MALT lymphoma; ocular adnexal extranodal marginal zone; orbital apex syndrome

Introduction

Ocular adnexal lymphomas (OALs) are localised lymphomas that are confined to the orbit, lacrimal glands, conjunctiva, and lids.[1] Approximately 70–90% of OALs are primary.[1] They are 1% of non-Hodgkin lymphomas.[2] The majority of OALs are primary extranodal B-cell lymphomas of the marginal zone (ENMZ)[3] mucosa-associated lymphoid tissue (MALT) lymphomas.[1,4] OALs are predominantly diagnosed in females between the 5th and 7th decades of life,[4] primarily unilateral,[3,4] and indolent in their natural history course.[1] Presenting signs and symptoms include progressive exophthalmos, ophthalmoplegia, decreased visual acuity, diplopia,[4] and chemosis.[5] OALs that extend into the orbital apex can present with orbital apex syndrome (OAS).

The orbital apex is a confined space, representing 13–17 mm of the pyramidal-shaped posterior orbit.[6,7] The annulus of Zinn, a fibrous ring at the entrance of the orbital apex, is a confined space with high compression risk that serves as the attachment point for cranial nerves (CN) II, III, and VI[6,7] and also contains the ophthalmic artery and nasociliary nerve, a branch of CN V_1.[6] First described in 1945 by Kjoer,[8] OAL can manifest as OAS with exophthalmos, ophthalmoplegia, and decreased visual acuity.[6,9] Additional symptoms of periorbital pain, ptosis, ipsilateral hypaesthesia of the forehead, upper eyelid, and impaired corneal reflex can also occur.[6,9]

Here, we discuss a case of primary unilateral OAL that presented atypically as OAS and illustrate the importance of early diagnosis to improve visual prognosis. We further describe specific distinguishing diagnostic characteristics and localising features of OAS, and treatment modalities for OAL. OAL should be considered in patients that present with OAS.

Case report

A 75-year-old female with a past medical history significant for prior stroke and atrial fibrillation, anticoagulated with rivaroxaban, presented to the emergency department with acute onset of a progressively worsening left atraumatic, erythematous, oedematous, ophthalmalgic orbit. She denied prior malignancy, headache, ocular discharge, or photophobia. Right eye ocular examination was normal. Left eye ocular examination

CONTACT Dr. John H. Pula jpula1@uic.edu Department of Neurology, NorthShore University HealthSystem, 2050 Pfingsten Road, Suite 280, Glenview, IL 60026, USA.

revealed exophthalmos, periorbital ecchymosis, chemosis, visual acuity of 20/25, ophthalmalgia, ophthalmoplegia (supraduction 30%, infraduction 70%, adduction 40-50%, and abduction 30% limitation), and normal pupil reaction, and left eye intraocular pressure (IOP) of 40 mm Hg. Topical timolol 5% administration was ineffective in controlling IOP, which precipitously increased to 65 mm Hg. Attainment of IOP reduction to 23 mm Hg required emergent lateral canthotomy and cantholysis (LCC) with subsequent extension. Left haemorrhagic chemosis was observed secondary to steadfast spontaneous retrobulbar haemorrhaging. Reversal of anticoagulative effects with four-factor prothrombin complex concentrate was attempted given the patient's persistent haemorrhage. Computed tomography (CT) orbit and head demonstrated findings characteristic of a retro-orbital cavernous haemangioma (Figure 1a). Magnetic resonance imaging (MRI) without and with contrast findings revealed a homogeneous linear antral conal enhancing 18 × 21 × 19 mm isointense T1 and T2 superior mass (Figure 1b and c).

She was administered 60 mg oral prednisone and topical erythromycin ointment. A preoperative diagnosis of haemorrhagic cavernous haemangioma was made based on radiologic findings, symptomatology, and insidious growth pattern. Subtotal transorbital excision was performed due to the proximity of the mass to the optic nerve. The residual mass remained superior to the optic nerve. Histopathological examination established a diagnosis of non-Hodgkin lymphoma of ocular adnexa, ENMZ MALT lymphoma. Flow cytology revealed positivity for CD19, CD20, CD45, Bcl-2, and lambda.

Postoperative CT imaging revealed partial resection of the prior left superior intraorbital mass 0.8 × 1.1 × 1.1 cm (previously 2.4 × 1.77 cm) with associated moderate left periorbital swelling and mild exophthalmos.

Discussion

Diagnosis and treatment of OALs requires a multidisciplinary approach with the involvement of

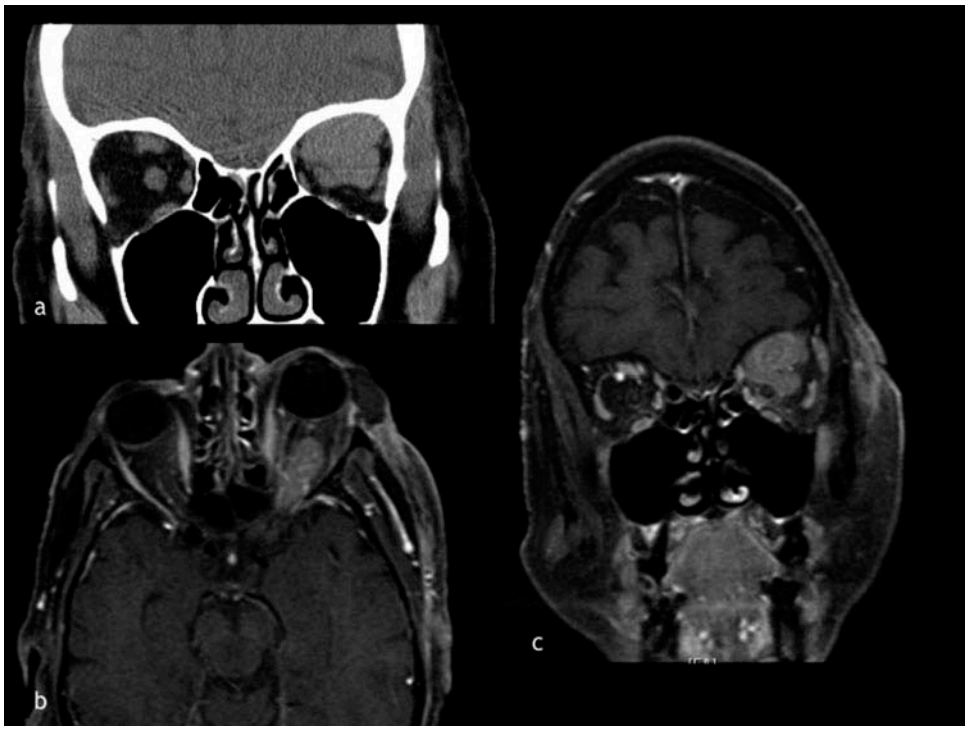

Figure 1. (a) Coronal CT without contrast on admission demonstrating the lesion in the mid-superior aspect of the left orbit. No right orbital soft tissue abnormality was noted. (b) Axial and (c) coronal T1 fat saturation sequences with gadolinium MRI demonstrated a left 18 × 21 × 19 mm isointense superior predominantly intraconal mass extending into the orbital apex, principally involving the superior rectus muscle.

ophthalmology, neurosurgery, radiology, pathology, and haematology-oncology.

Our patient presented with progressive left exophthalmos, ophthalmalgia, ophthalmoplegia, and chemosis, fitting the demographics and presenting signs of OAL.[5] Diagnosis of OAL can be complicated by similar symptomatology and similar insidious growth pattern with cavernous haemangioma (CH),[10] as was the case in our patient. Further complicating the diagnosis was the patient's acute onset of erythaema, oedema, and periorbital ecchymosis, likely secondary to spontaneous haemorrhage. Gradual onset of presenting symptoms is typically seen in OAL. In addition, spontaneous haemorrhage is typically observed in CH, as described in a case series by Zenobii et al.,[11] leading to the establishment of a preoperative diagnosis of CH. Our patient's anticoagulation use was considered as a predisposing factor for haemorrhage.

Initial assessment with collective neuroimaging (CT and MRI) should be obtained in patients with orbital masses to identify imaging patterns, location, and affected structures and to aid in diagnosis.[4,9] OALs demonstrate isointense signal on T1 MRI and iso-hyperintense signs on T2 MRI, providing an advantage in differentiating orbital lymphoma from other orbital masses, such as cavernous haemangiomas.[4] In our patient, an 18 × 21 × 19 mm isointense T1 and T2 superior intraconal mass was consistent with imaging patterns of OAL. Differential diagnoses of intraconal masses include OAL, meningioma, cavernoma, and glioma.

Location is another discerning feature of OALs.[4] Priego et al. report that the superolateral quadrant represents the most frequent location for orbital lymphomas (59%), whereas the superomedial (26%) and inferior (15%) represented smaller percentages.[4] However, on axial CT imaging, our patient demonstrated high density in mid-superior aspect of the left orbit. In this same study, the superior rectus muscle was most common structure infiltrated (74%), followed by the lateral rectus (59%), lid (53%), and lacrimal gland (47%). Although supraduction was impaired in our patient, this was secondary to mass effect. Optic nerve involvement was less represented (11%), which was consistent with our patient, who did not demonstrate any pupillary defects on admission.

The pathogenesis of ENMZ MALT lymphoma is unknown. One theory proposes a chronic inflammatory process secondary to a microbial source serves as a provoking factor for malignant transformation.[3] Although one European study identified an association of ENMZ MALT with *Chlamydia psittaci*,[3,5,12] these results were unsubstantiated in a subsequent American study.[3] MALT lymphomas are also observed in *Helicobacter pylori* gastric infections; however, a definitive association has not been established.[3] Our patient's history was negative for these risk factors and did not report prior history of *Chlamydia psittaci* and *Helicobacter Pylori* infections, or peptic ulcer disease.

Although lymphoma was identified as the causative factor for OAS in our patient, other primary orbital apical tumours include carvernous haemangiomas, gliomas, meningiomas, neurofibromas, schwannomas, and pituitary tumours.[6] Lymphomas in the orbital apex characteristically arise secondarily from local invasion of the paranasal sinuses, skull base, or metastasis,[6] although primary lymphoma was identified in our patient. Risk of systemic involvement with primary ENMZ MALT lymphomas is low,[13] and our patient was free of systemic disease. Non-neoplastic aetiologies responsible for OAS include trauma, inflammation, infection, and fistulas.[9]

The orbital apex is contiguous with the superior orbital fissure and cavernous sinus.[14] OAS, superior orbital fissure syndrome (SOFS), and cavernous sinus syndromes (CSS) collectively constitute a set of syndromes known as orbital apex disorders and are classified by anatomical location.[6]

Cranial nerve (CN) III, IV, and VI palsies can be seen in all orbital apex disorders along with ptosis and mydriasis.[6] Although our patient demonstrated ophthalmoplegia, she did not demonstrate ptosis or mydriasis. Discerning OAS from SOFS and CSS is accomplished by localising the affected region by clinical manifestation. Exophthalmos and V_1 palsy are observed predominantly in OAS and SOFS.[6,9] Exophthalmos is secondary to retrobulbar processes, venous congestion, or laxity resultant from extraocular muscle

impairment.[6] Although our patient exhibited exophthalmos, V_1 palsy was absent.

One differentiating feature of OAS is CN II impairment[6,9,15] secondary to injury to the optic disc or optic nerve,[6] although our patient lacked an afferent pupillary defect. However, lack of CN IV palsy did help with diagnosis. CN IV is external to the annulus of Zinn[6,16] and travels through the lateral portion of the superior orbital fissure.[15] As a result, CN IV compression or injury occurs less frequently in OAS.[16]

Positioned laterally within the cavernous sinuses are CN III, IV, V_1, and V_2.[6] CSS presents with distinguishing characteristics of CN V_2 and sympathetic nerve injury.[9] With no signs of ipsilateral buccal hypaesthesia or miosis in our patient, CSS was not suspected.

Treatment of choice for acute OAS is rapid orbital decompression with lateral canthotomy and cantholysis to decrease intraocular pressure and preserve vision,[6] as was performed in our case.

Our patient was treated with surgical resection. At 1-week follow-up, she was scheduled for combination radiation therapy. Eckardt et al. advises against surgery as a single treatment modality due to increased risk of relapse secondary to incomplete resection.[2] However, surgical resection for decompression is not without complications and can result in direct injury or indirect vascular injury to the optic nerve and visual loss.[17] A subtotal resection was performed in our patient due to proximity of the mass to the optic nerve.

In OAS cases where the diagnosis is equivocal, the principal treatment options include observation, corticosteroids, and surgical biopsy.[18] Corticosteroids can be administered in cases where there are no signs of an infectious aetiology.[18] Acartürk et al. report a case series of 11 traumatic OAS patients who attained complete symptom resolution following administration of high-dose intravenous methylprednisolone followed by oral prednisone.[19] In cases of advancing ophthalmoplegia and visual loss, repeat imaging and a biopsy are indicated.[18]

Flow cytology in our patient's tumour exhibited CD20 positivity. Recent studies describe responsiveness to rituximab for CD20-positive[5] extranodal ENMZ lymphomas in both multimodality and primary single-agent treatment modalities.[1] Disease progression and recurrence with rituximab treatment is not yet understood.[1] Portell et al. suggest that rituximab is a viable option for bilateral ENMZ OAL to avoid the toxic effects induced by radiotherapy.[12]

Here we have presented a unique case of a primary unilateral OAL presenting with OAS to illustrate the importance of early diagnosis in improving visual prognosis.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

References

[1] Rootman DB, Mavrikakis I, Connors JM, Rootman J. Primary, unilateral ocular adnexal lymphoma: disease progression and long-term survival. *Ophthal Plast Reconstr Surg* 2011;27:405–409.

[2] Eckardt AM, Lemound J, Rana M, Gellrich NC. Orbital lymphoma: diagnostic approach and treatment outcome. *World J Surg Oncol* 2013;11:73.

[3] Lagoo AS, Haggerty C, Kim Y, Hammons M, Neufeld K, Redher C, Woodward J, Klintworth GK. Morphologic features of 115 lymphomas of the orbit and ocular adnexa categorised according to the world health organization classification: are marginal zone lymphomas in the orbit mucosa-associated lymphoid tissue-type lymphomas? *Arch Pathol Lab Med* 2008;132:1405–1416.

[4] Priego G, Majos C, Climent F, Muntane A. Orbital lymphoma: imaging features and differential diagnosis. *Insights Imaging* 2012;3:337–344.

[5] Kharod SM, Herman MP, Morris CG, Lightsey J, Mendenhall WM, Mendenhall NP. Radiotherapy in the management of orbital lymphoma: a single institution's experience over 4 decades. *Am J Clin Oncol* 2015 Sep 20 [Epub ahead of print]. doi: 10.1097/COC.0000000000000229

[6] Warburton RE, Brookes CC, Golden BA, Turvey TA. Orbital apex disorders: a case series. *Int J Oral Maxillofac Surg* 2016;45:497–506.

[7] Linnau KF, Hallam DK, Lomoschitz FM, Mann FA. Orbital apex injury: trauma at the junction between the face and the cranium. *Eur J Radiol* 2003;48:5–16.

[8] Kurzer A PM. Superior orbital fissure syndrome associated with fractures of the zygoma and orbit. *Plast Reconstr Surg* 1979;64:715–719.

[9] Aryasit O, Preechawai P, Aui-Aree N. Clinical presentation, aetiology and prognosis of orbital apex syndrome. *Orbit* 2013;32:91–94.

[10] Yamamoto J, Takahashi M, Nakano Y, Saito T, Kitagawa T, Ueta K, Miyaoka R, Nishizawa S.

Spontaneous hemorrhage from orbital cavernous hemangioma resulting in sudden onset of ophthalmopathy in an adult—case report. *Neurol Med Chir (Tokyo)* 2012;52:741–744.

[11] Zenobii M, Galzio RJ, Lucantoni D, Caffagni E, Magliani V. Spontaneous intraorbital hemorrhage caused by cavernous angioma of the orbit. *J Neurosurg Sci* 1984;28:37–40.

[12] Portell CA, Aronow ME, Rybicki LA, Macklis R, Singh AD, Sweetenham JW. Clinical characteristics of 95 patients with ocular adnexal and uveal lymphoma: treatment outcomes in extranodal marginal zone subtype. *Clin Lymphoma Myeloma Leuk* 2014;14:203–210.

[13] Rose GE Verity DH. Neuro-ophthalmology of orbital disease. *Handb Clin Neurol* 2011;102:467–491.

[14] Li Y, Wu W, Xiao Z, Peng A. Study on the treatment of traumatic orbital apex syndrome by nasal endoscopic surgery. *Eur Arch Otorhinolaryngol* 2011;268:341–349.

[15] Lenzi GL, Fieschi C. Superior orbital fissure syndrome: review of 130 cases. *Eur Neurol* 1977;16:23–30.

[16] Chen CT, Wang TY, Tsay PK, Huang F, Lai JP, Chen YR. Traumatic superior orbital fissure syndrome: assessment of cranial nerve recovery in 33 cases. *Plast Reconstr Surg* 2010;126:205–212.

[17] Kim BS, Im YS, Woo KI, Kim YD, Lee JI. Multisession Gamma Knife radiosurgery for orbital apex tumors. *World Neurosurg* 2015;84:1005–1013.

[18] Yeh S, Foroozan R. Orbital apex syndrome. *Curr Opin Ophthalmol* 2004;15:490–498.

[19] Acartürk S, Seküçoğlu T, Kesiktäs E. Mega dose corticosteroid treatment for traumatic superior orbital fissure and orbital apex syndromes. *Ann Plast Surg* 2004;53:60–64.