

## Diplopia and Extraocular Muscle Enlargement as an Initial Presentation of Breast Cancer

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**Keywords:** *diplopia, exophthalmos, extraocular muscle, orbital metastasis, breast cancer, invasive lobular carcinoma.*

### Introduction

Diffuse extraocular muscle enlargement is a rare condition that can be encountered by neurologists or neuromuscular specialists. Thyroid ophthalmopathy is the leading cause, but many other etiologies may account for such a presentation.<sup>1-4</sup> Here we describe a patient presenting with diffuse extraocular muscle enlargement on imaging who was later found to have metastatic breast cancer through further workup.

### Case description

A 28-year-old female presented with progressive diplopia, asymmetrical proptosis left being worse than right, right sided headache, and right facial numbness for three months. Her past medical history was notable for intracranial hemorrhage secondary to a ruptured left posterior communicating artery aneurysm having occurred four years prior to presentation, and tobacco use. On physical examination, she was alert and oriented, without aphasia or dysarthria. Her visual fields were full, and her visual acuity was 20/200 OD and 20/70 OS. Pupils were sluggishly reactive to light, without afferent pupillary defect. Extraocular movement of both eyes was severely restricted to no movement in all directions. Bilateral exophthalmos was present with significant conjunctival injection on the left side. Facial sensation to pinprick was reduced in the territories of the second and third branches of the right trigeminal nerve. The remaining neurological examination was unremarkable. A non-contrast brain CT revealed marked thickening of all extraocular muscles bilaterally.

Initial differential diagnoses included thyroid ophthalmopathy, neurosarcoidosis, idiopathic orbital inflammatory disease, immunoglobulin G4 (IgG4) related disease, granulomatosis with polyangiitis, and orbital lymphoma or metastasis. Her serum complete blood count,

complete metabolic panel and thyroid function tests were unremarkable. Serum thyroid stimulating immunoglobulin was undetectable. Serum angiotensin converting enzyme, soluble interleukin-2 receptor was and IgG4 were all normal. Cerebrospinal fluid (CSF) studies revealed the following finding: white blood cells 3 cells/ $\mu$ l, protein 150 mg/dl (normal range: 15 to 45 mg/dl) and glucose 47 mg/dl (normal range: 40 to 70 mg/dl). The CSF cytological examination revealed clusters of atypical cells with plasmacytoid to epithelioid morphology.

Cerebral arterial angiogram showed the presence of a 3 mm right middle cerebral artery aneurysm without evidence of cavernous carotid fistula or cavernous sinus thrombosis. Subsequent brain MRI exhibited diffuse enlargement of all extraocular muscles in both eyes with uniform contrast enhancement (Figure). MRI also revealed an infiltrative process affecting the retro-orbital fat and extending into the right cavernous sinus. Chest CT showed a 1.3 cm nodular density in the left breast, as well as enlarged bilateral axillary lymph nodes. Subsequent positron emission tomography-computed tomography confirmed hypermetabolic lesions in both breasts with asymmetric cutaneous thickening of the left breast, diffuse hypermetabolic lymphadenopathy, and hypermetabolic lesions in the axial and appendicular skeleton. Exam revealed peau d'orange appearance on the skin of the left breast and a punch biopsy showed invasive lobular carcinoma. The previously noted atypical cells found in her CSF matched the breast carcinoma morphologically. Her orbital lesions were thought to represent metastasis from the breast carcinoma. She underwent palliative whole brain and orbit radiotherapy while hospitalized with significant improvement in her visual symptoms and radiographic appearance of the extraocular muscles. (Figure). One month following discharge, her diplopia and headache had entirely resolved. Hormonal therapy was planned on discharge.

### Discussion

The differential diagnosis for diffuse extraocular muscle enlargement is wide. Non-neoplastic etiologies include thyroid ophthalmopathy, idiopathic orbital inflammatory disease, IgG-4 related disease, sarcoidosis, granulomatosis with polyangiitis and others.<sup>1-4</sup> Solid tumor metastasis is a rare but well recognized cause of extraocular muscle enlargement. Our patient's presenting symptoms of progressive and asymmetrical proptosis, blurred vision, and diplopia by themselves could not reliably differentiate between these etiologies. Breast exam, breast biopsy

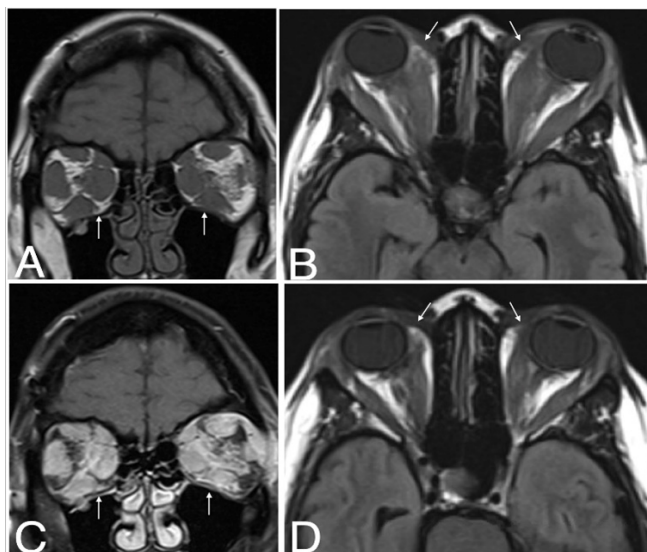


Figure. Diffuse enlargement of extraocular muscles on magnetic resonance imaging. Enlargement of extraocular muscles, proptosis and soft tissue enlargement (arrows) is seen on coronal T1 pre-contrast (A) and axial T2 FLAIR (B) images. Diffuse enhancement involving retro-orbital fat (arrows) is seen on coronal post contrast T1 image (C). Follow-up MRI (D) one month later shows marked improvement in proptosis and extraocular muscle infiltration (arrows).

and CSF cytology were instrumental in establishing the final diagnosis of metastatic breast cancer to the orbits. Metastases to the trigeminal nerve and the CSF signaled meningeal involvement (meningeal carcinomatosis) in addition to the orbital metastasis.

Breast cancer is the most frequent primary tumor to metastasize to the orbit, representing 29 to 48% of metastatic cases. Metastasis from prostate, melanoma, lung and renal cell carcinoma occurs less frequently.<sup>5-7</sup> In addition to the extraocular muscles, other sites of orbital metastasis included intraocular structures such as the uveal tract, retina, lacrimal glands or surrounding fat. Orbit metastasis from breast cancer is often a late-stage finding, and the average duration from diagnosis of breast cancer to presentation with orbital disease is 4 to 8.5 years.<sup>5,8-10</sup> While rare, extraocular metastasis as the initial presentation of breast cancer similar to our patient have been previously described.<sup>11-13</sup> Bilateral orbital metastasis is often less frequent than unilateral disease, representing 6 to 25% of cases.<sup>2,8-9</sup> However, bilateral orbit involvement tends to occur more frequently in breast cancer.<sup>14</sup>

In this report we have shown that metastatic disease should be considered in the evaluation of diffuse, bilateral extraocular muscle infiltration causing proptosis and

diplopia, even in a patient without prior known history of malignancy. A timely diagnosis is needed as patients may respond well to palliative radiotherapy. Radiotherapy with or without chemotherapy is the preferred therapy for diffuse orbital metastasis and may improve vision.<sup>14-15</sup>

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