

Case Report

# Intraocular Metastasis as the Presenting Symptom of NSCLC and the Role of Bevacizumab: A Case Report

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## Abstract

**Introduction:** Metastasis to the eye is a rare clinical entity accounting for about 2-9% ocular malignancies. Clinical awareness can lead to prompt diagnosis and appropriate management.

**Case presentation:** We here present a case of a 60-year-old patient who visited to several ophthalmologists with the complaint of blurry vision in his left eye. He was diagnosed with anterior uveitis and elevated intraocular pressure. A masquerade syndrome was suspected, and anterior chamber paracentesis was performed, which revealed metastatic non-small cell lung cancer (NSCLC). CT chest revealed a left lung mass with right paratracheal lymphadenopathy. No other evidence of metastatic disease was found on PET/CT scan and MRI of the brain. He received treatment for stage IV lung cancer with carboplatin, paclitaxel, and bevacizumab. The intraocular tumor cell infiltration was treated with intravitreal bevacizumab that resulted in subjective and objective improvement.

**Conclusion:** Metastasis to the eye may present in a masquerade-like fashion as intraocular inflammation. Tumor specific therapy directed locally within the eye may be a component of an overall treatment plan.

**Keywords:** Lung cancer; ocular metastasis; bevacizumab; non-small cell lung cancer

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**Consent:** Consent was taken from the patient for publication of this case report.

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## Introduction

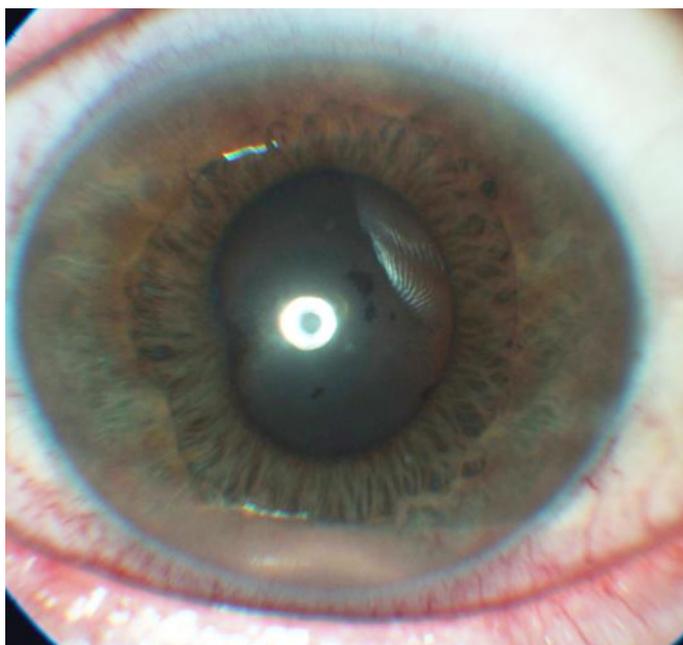
Metastasis to the eye though rare is the most common of all intraocular malignancies [1]. Out of these around 47–81% have breast cancer as the primary malignancy and 23% have lung cancer as the primary malignancy [1]. Further lung cancer is the most common cause of secondary intraocular malignancy in men, whereas breast cancer is the most common cause in women [2]. The choroid is the most common site for metastasis, whereas involvement of the ciliary body, retina, optic disc, vitreous and iris are rare. We discuss a patient who was diagnosed with metastatic NSCL (adenocarcinoma) after presenting with anterior uveitis and elevated intraocular pressure.

## Case presentation

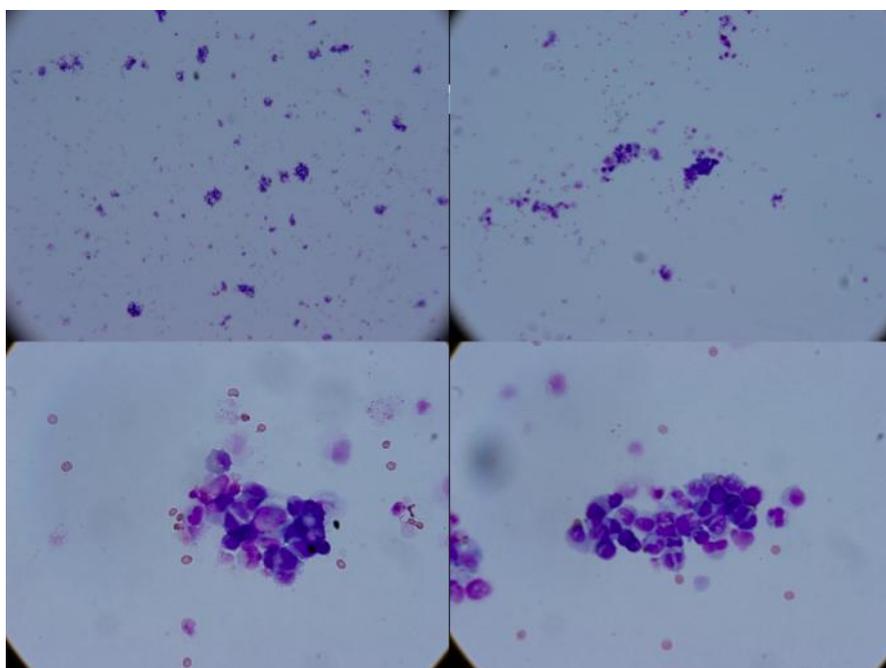
A 60 year old male active smoker with no significant past medical history presented with complains of redness and decreased vision in his left eye. Multiple optometrists and ophthalmologists had diagnosed him with anterior uveitis. His ophthalmological exam revealed his left eye (OS) visual acuity to be at 20/25 with an intraocular pressure of 46mmHg. Anterior segment exam revealed cellular precipitates, 1+ circulating cell, inferior anterior chamber debris, and engorged angle vessels on gonioscopy. The fundus exam was unremarkable. Metastatic infiltration of the iris and anterior chamber angle with secondary inflammation was suspected. Anterior chamber paracentesis was performed and histological exam showed metastatic NSCLC (Fig A and B). Post diagnosis his CXR showed a left sided mass. Remaining physical exam was normal. Laboratory studies including complete blood count and blood chemistry were within normal limits. Imaging studies including CT chest, abdomen and pelvis were significant only for heterogeneously enhancing mass in the left posterior medial lobe of lung measuring 9.4 cm by 7.8 cm along with a 1.1 cm right lower paratracheal lymph node. PET scan revealed a small focus of increased uptake SUV 3.5 along the medial aspect of left eye globe, without a discrete identifiable lesion on corresponding CT scan alongside a FGD avid left lung mass (SUV 8.1) and mediastinal lymphadenopathy (SUV 3.4). Left lung CT guided biopsy confirmed the mass to be adenocarcinoma with signet ring cell morphology. EGFR, ALK mutations were tested negative but K-ras mutation was positive.

He was diagnosed with stage IV NSCLC, T2a N2 M1b and was enrolled in a clinical trial for the treatment of his metastatic NSCLC; he received a total of four cycles of intensive chemotherapy with paclitaxel, carboplatin and bevacizumab. Patient achieved stable disease and was thereafter started on maintenance regimen with bevacizumab and pemetrexed. He was diagnosed two years ago and currently his disease is stable on maintenance treatment.

He received one dose of intraocular bevacizumab injection (1.25 mg) prior to initiation of systemic chemotherapy. Within 2 weeks post intravitreal bevacizumab administration, the patient's intraocular inflammation and pressure improved.



**Fig. A** Picture of the anterior chamber of the eye showing cellular precipitates without any iris nodules or lesions.



**Fig. B** Histopathology of the anterior chamber fluid showing cellular debris and malignant cells consistent with adenocarcinoma of the lung.



Fig. C CT chest with contrast demonstrating left lower lung mass.

## Discussion

The incidence of ocular metastasis from lung cancer is reported to be 2-7% [1]. Choroid is the most commonly involved site followed by iris and the ciliary body [2, 8]. Patients presenting with this kind of lesion are usually in the late stages of their primary disease [9]. The vascularity of the uveal tract is thought to predispose it to metastasis though no clear etiology has been postulated [3]. These lesions can present either posteriorly as posterior segment lesions, or anteriorly as anterior uveitis as seen in our patient; other presentations include iris nodules, and neovascularization of the iris [10]. With regards to the iris, metastasis is usually unilateral whereas bilateral choroid involvement is sometimes seen. Further iris metastasis tends to involve the irido-corneal angle with resultant secondary glaucoma [12].

Shields *et al* reported that, in 56% of patients with intraocular lung cancer metastasis, the diagnosis of the primary tumor was made afterwards, highlighting the importance of early recognition of intraocular metastasis [4]. However it was estimated in a study by Kreusel *et al* that in patients with metastatic lung carcinoma, just 7.1% presented with ocular involvement [15]. The symptomology can range from blurry vision, photopsia, red eye, floaters and visual field defects [9].

The diagnosis of ocular metastasis is based primarily on clinical findings supported by imaging studies. The various diagnostic procedures include ultrasonography, fluorescein angiography, computed tomography/MRI and fine needle aspiration [2].

There are various treatment modalities available for the treatment for intraocular metastasis, including systemic chemotherapy, radiotherapy and lately progress has been made in molecular targeted therapies. In general ocular metastasis respond favorably to systemic chemotherapy; however, local therapy is warranted when there is enlargement of the lesion, pain or visual disturbance [1, 13].

With increasing knowledge of the oncogenes involved in the pathogenesis of NSCLC, targeted therapies are now proving to provide greater therapeutic advantages. EGFR, k-RAS and ALK are the oncogenes most commonly associated with NSCLC. All of these mutations are more commonly found in adenocarcinoma and are involved in cellular survival and neoplastic proliferation [1, 7].

Solid tumor growth and metastasis is dependent on neovascularization. Thus the use of molecular targets of therapy that inhibit angiogenesis halts tumor growth. VEGF and EGFR are such targets [8]. Bevacizumab is an anti VEGF monoclonal antibody that has shown promising results [11, 13]. It inhibits endothelial cells from responding to angiogenic protein VEGF. This is the underlying principle with regards to its use in tumors expressing high levels of VEGF. When used via intraocular injections it inhibits neo-vascularization and eventually tumor growth. Reports have been cited of patients presenting with choroid mass that underwent complete regression along with subjective and objective improvement after the use of intravitreal bevacizumab [5, 6, 8]. Further erlotinib, a reversible, orally available, highly selective epidermal growth factor receptor tyrosine kinase inhibitor, has also demonstrated encouraging results in the treatment of intraocular NSCLC metastasis [8, 13]. Maturu et al in their systemic review talk about 9 cases that received intravitreal bevacizumab primarily due to choroid metastases, with improved vision and regression of metastases in 6 out of 9 patients further supporting the use of molecular targets of therapy [16].

With combined local and systemic therapy, patient achieved reduction in intraocular inflammation and improved intraocular pressure.

## Conclusion

Intraocular metastasis is a potential masquerade and should be considered in the differential diagnosis of uveitis. Intravitreal bevacizumab is a promising molecular target of therapy that inhibits neovascularization and tumor growth with resultant clinical benefits in patients presenting with intraocular metastasis.

## Consent

Patient's consent was taken prior to submission for peer review.

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