



# RETINAL METASTASES AS THE INITIAL PRESENTATION OF ADVANCED LUNG ADENOCARCINOMA

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## ABSTRACT

**Introduction:** Most lung cancers are diagnosed at an advanced stage. Common metastatic sites include the brain, bone, liver and adrenal glands. Ocular metastases, however, are extremely rare. We present a case of advanced lung adenocarcinoma presenting exclusively with photopsias attributable to retinal metastases.

**Case description:** We describe a woman in her fifties, a lifetime non-smoker with an unremarkable medical and family history, who presented to the emergency department with photopsias for a week. Ophthalmology evaluation revealed decreased visual acuity bilaterally, and a fundus examination disclosed lesions suggestive of bilateral retinal metastases. A comprehensive evaluation diagnosed a stage IVb lung adenocarcinoma with exon 19 mutation on epidermal growth factor receptor gene. Subsequently, she developed complaints of headaches and dizziness. She received frontline osimertinib 80 mg daily, preceded by upfront whole-brain radiation therapy with partial orbital inclusion for symptomatic ocular and brain metastases. After ten radiation therapy sessions, her complaints were resolved and an ophthalmology reevaluation revealed improvement in visual acuity and resolution of photopsia complaints. The patient is currently on osimertinib and preserves an ECOG score of 0.

**Conclusion:** Retinal metastases usually indicate advanced disease, so presenting with isolated ocular symptoms is exceedingly rare. Especially in cases of uncommon metastases, a multidisciplinary approach is fundamental for a prompt diagnosis and timely treatment, impacting prognosis and quality of life.

## KEYWORDS

Retinal metastases, lung cancer, EGFR mutation

## LEARNING POINTS

- Ocular metastases in lung cancer are usually a sign of advanced disease.
- Advanced lung adenocarcinoma presenting solely with retinal metastases is extremely rare.
- A multidisciplinary team is essential for the diagnosis and treatment of lung cancer with uncommon metastases.



## INTRODUCTION

Non-small cell lung cancers (NSCLC) represent 85% of all lung cancers. Adenocarcinoma is the most common type, accounting for 40% of all lung cancers<sup>[1]</sup>. Most lung cancer patients are diagnosed with advanced disease, and the major metastatic sites include the brain, bone, liver and adrenal glands. Ocular metastases, however, are extremely rare, with a reported incidence of 0.1%<sup>[2]</sup>. Here, we report a case of retinal metastases as the initial presentation of a stage IV lung adenocarcinoma.

## CASE DESCRIPTION

We describe a woman in her fifties, a lifetime non-smoker, with an unremarkable medical and family history. She presented to the emergency department complaining of seeing flashing lights for a week. The remaining clinical history and physical examination were normal. Ophthalmology evaluation revealed a best-corrected visual acuity of 5/10 on the right and 2.5/10 on the left. A fundus examination uncovered various retinal masses with subretinal fluid and exudative retinal detachment in both eyes, suggesting retinal metastases. A cranial computed tomography (CT) revealed multiple hypodensities evocative of peritumoral oedema and lytic lesions in the skull. The chest X-ray showed an opacified left hemithorax. A thoracoabdominal CT scan was conducted given the suspicion of a metastasised malignancy, and evidenced a left superior lobe atelectasis with left superior lobar bronchus lumen reduction suspected of a bronchopulmonary malignant lesion (Fig. 1) and various lesions suspected of secondary infiltration. The patient was admitted to the internal medicine ward for continuing investigation. A bronchofibroscopy showed neoplastic infiltration of bronchial mucosa at the level of secondary carina and left superior lobar bronchus. Pathology analysis revealed adenocarcinoma with acinar and micropapillary patterns, and diffuse expression of TTF1 in the immunohistochemistry study. These findings established the diagnosis of advanced lung adenocarcinoma, and the patient was discharged to a priority pneumology consultation. She continued staging while immunohistochemistry and molecular analysis were ongoing. A whole-body FDG PET scan described a left bronchopulmonary malignancy with metastases in the bilateral supraclavicular, mediastinal and hilar ganglia, liver lobes, adrenal glands and multiple sites in the skull and appendicular skeleton. Cerebral magnetic resonance imaging revealed countless brain and ocular metastases with peritumoral oedema (Fig. 2). The patient was evaluated in consultation in one week and was diagnosed with a lung adenocarcinoma stage IVb (cT4N3M1c). She maintained photopsias and reported new-onset headache and right leg pain. A venous duplex ultrasound confirmed a lower extremity deep venous thrombosis, and she was readmitted on therapeutic anticoagulation. She also started dexamethasone 4 mg four times daily and levetiracetam 500 mg twice daily due to symptomatic peritumoral oedema. Following discussion in the lung cancer multidisciplinary



Figure 1. Thoracoabdominal computed tomography, coronal, showing a left upper lobe atelectasis with reduction of the lumen of the left superior lobar bronchus, and a heterogeneous contrast uptake suspected of a bronchopulmonary malignant lesion.

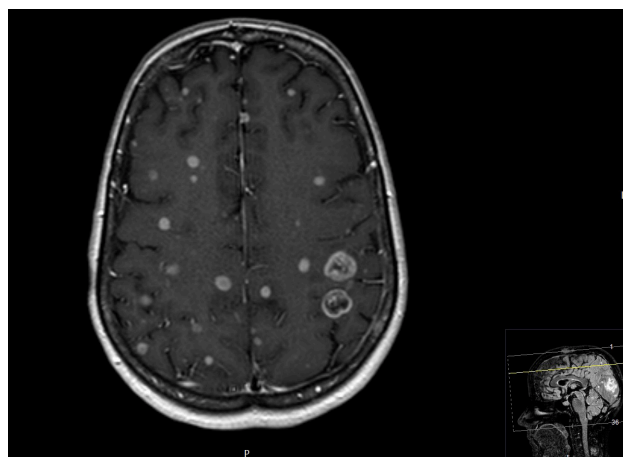


Figure 2. Cerebral magnetic resonance, axial, revealing multiple ring-enhancing lesions scattered at both cerebral hemispheres.

group, the patient initiated upfront whole-brain radiation therapy (WBRT), with partial orbital inclusion (total dose of 30Gy, 3Gy a day for ten sessions), for symptomatic brain and orbital metastases. The patient had never reported respiratory complaints or respiratory failure. Meanwhile, the results of PD-L1 expression were positive, and molecular analysis revealed a mutation on exon 19 of the epidermal growth factor receptor (EGFR) gene. Therefore, she initiated EGFR tyrosine kinase inhibitors (TKI) osimertinib 80 mg daily, three weeks after the initial presentation. After completing ten radiation therapy (RT) sessions, the headaches and dizziness were resolved, and the patient noted an improvement in visual acuity and photopsias. Follow-up ophthalmology evaluation revealed improved visual acuity and resolution of the retinal detachment bilaterally. Currently, the patient is on systemic therapy and preserves an eastern cooperative oncology group (ECOG) score of 0. To date, no treatment-related adverse effects have been reported. The long-term impact of brain and orbital irradiation is yet to be assessed.

## DISCUSSION

We describe a rare case of advanced lung adenocarcinoma presenting solely with ocular symptoms attributable to retinal metastases. The eye is an uncommon metastatic site, and most metastases occur in the posterior choroid due to its rich vascular supply<sup>[3]</sup>. On the other hand, retina involvement is rare as it is only supplied by the single central retinal artery, with its occurrence confined to case reports and small series<sup>[3]</sup>. The most common sites for retinal metastases are cutaneous melanoma, followed by lung, breast and gastrointestinal carcinomas<sup>[3,4]</sup>. Retinal invasion from primary lung adenocarcinoma has only been reported in a handful of cases<sup>[4,5]</sup>. Retinal metastases from carcinoma usually present with decreased visual acuity, floaters, photopsia and ocular pain. Examination findings are yellow-white masses with occasional subretinal fluid, exudation, retinal haemorrhage or vitreous seeds<sup>[3]</sup>. Other findings include exudative retinal detachment and secondary glaucoma<sup>[5]</sup>. Retinal invasion is usually diagnosed later in the disease course, and most patients have disseminated metastases by the time they are recognised<sup>[2]</sup>. For this reason, presenting solely with ocular symptoms in a patient with multi-organ metastases is exceedingly rare. In our case, prompt identification of these lesions elicited a comprehensive evaluation for a primary extraocular malignancy, which led to the diagnosis of stage IVb lung adenocarcinoma with *EGFR* gene exon 19 mutation. These mutations are observed in approximately 15% of NSCLC adenocarcinomas and occur primarily in women and non-smokers<sup>[6]</sup>. The patient received frontline *EGFR* TKI osimertinib, preceded by upfront WBRT with partial orbital inclusion for symptomatic ocular and brain metastases. Osimertinib is the preferred initial treatment for advanced lung cancer with *EGFR* mutation, including when central nervous system involvement is present, given its significant intracranial activity and improved outcomes compared with earlier-generation TKI<sup>[7]</sup>. This patient also underwent upfront local RT with good clinical response. Although the RT deferral in patients with brain metastases who start on osimertinib is being questioned, additional studies are necessary to evaluate this alternative<sup>[8]</sup>. Moreover, some authors suggest that local treatment, in addition to systemic therapies, could improve outcomes for selected patients with ocular metastases, but this is limited to retrospective cohorts and case series<sup>[2,9,10]</sup>. Nevertheless, it is essential to consider the potential RT-related complications, such as neurocognitive defects and cataracts, when making treatment decisions for these patients.

Hence, we describe a rare presentation of one of the most incidental cancers. Retinal metastases are usually indicative of advanced disease, but patients may benefit from systemic and local therapies. Especially in cases of uncommon metastases, a multidisciplinary approach is fundamental for a prompt diagnosis and timely treatment, impacting prognosis and quality of life.

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