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Exophthalmos as a First Manifestation of Small Cell Lung Cancer: A Long-Term Follow-Up

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Key Words

Lung cancer · Orbital metastasis · Exophthalmos

Abstract

Small cell lung cancer is characterized by rapid growth and early metastasis. Despite its sensitivity to cytotoxic therapy, until now treatments have failed to control or cure this disease in most patients. Orbital metastases are a rare manifestation of systemic malignancies. Breast and lung cancers represent more than two thirds of the primary cancer sites. Metastases to the eye and orbit develop in approximately 0.7–12% of patients with lung cancer. Here, we report a rare case of exophthalmos as the first manifestation of a metastatic carcinoma due to small cell lung cancer, and a 6-months follow-up with complete exophthalmic response to chemotherapy.

Introduction

Small cell lung cancer (SCLC) represents 13–20% of all new lung cancer diagnoses. It is the most aggressive histological subtype of lung cancer, with a strong predilection for early metastases [1]. The brain is a common site of metastasis in SCLC. At the initial diagnosis, at least 10% of the patients with SCLC already have brain metastases, brain metastases signal stage IV disease and generally herald an ominous prognosis, but neuro- and radiosurgical therapeutic evolution has resulted in effective therapeutic approaches, leading to improvements in neurological status and survival [2, 3].

Case Report

A 69-year-old Caucasian man was admitted to the emergency unit, complaining of progressive exophthalmos over the past 15 days ([fig. 1](#)). His medical history included heavy smoking (108 pack-years, until the day of admission). The patient reported fatigue without loss of weight for the last 6 months. On physical examination, auscultation of the lungs revealed diminished breath sounds and dullness to percussion in the upper left lung field.

Blood tests disclosed anemia, hematocrit 33.1% and hemoglobin 10.4 g/dl, with a pattern of chronic diseases. The serum chemistry findings were normal. Ophthalmologic examination confirmed profound exophthalmos of his right eye. Best corrected visual acuity was 20/20 in both eyes. Pupils were equal, round and reactive to light. The results of a neurologic examination were within normal limits. Chest X-ray ([fig. 2a](#)) showed a sizable mass in the left upper lobe of the lung in contact with the pleura. Chest computed tomography (CT) revealed a large round solid tumor with hilar and pre-vascular lymph node enlargement. The patient underwent magnetic resonance imaging (MRI) of the brain and orbits to enable further evaluation. The MRI revealed a soft-tissue mass in the outer posterolateral wall of the right orbital cavity with infiltration of the subcutaneous fat, muscles and skin ([fig. 3a](#)). There were no further lesions in the brain parenchyma. A CT of the upper and lower abdomen also showed no metastatic lesions. In an attempt to determine the exact histopathological nature of the lesion, bronchoscopy was performed. The findings included a bleeding multilobar mass infiltrating the main carina and projection of the adjacent bronchial mucosa due to external pressure at the rising of the right main bronchus. Bronchial washings and transbronchial needle biopsies of the lung were performed. The specimen showed malignant cells consistent with SCLC cells. The patient additionally underwent an orbital biopsy (CT-guided fine needle aspiration biopsy) [[4](#), [5](#)]. The histological findings were identical to those of the lung mass.

The patient was referred to the pulmonary department (oncology unit) for first-line chemotherapy with six regimens of cisplatin and etoposide, showing an initial complete response both at the primary site and the orbital metastasis ([fig. 2b](#), [3b](#)).

Due to subsequent relapse to the lung, after the 4th cycle the patient underwent second-line chemotherapy with topotecan and carboplatin. At his last follow-up, a complete resolution of the exophthalmos was observed ([fig. 4](#)). He concluded six cycles with an initial partial response, but died 2 months after the last session. Written informed consent was obtained from the patient upon discharge for publication of this case report and all accompanying images.

Discussion

SCLC represents 13–20% of all new lung cancer diagnoses [[2](#)]. It is the most aggressive histological subtype of lung cancer, with a strong predilection for early metastases [[1](#)]. The brain is a common site of metastasis in SCLC, accounting for approximately 70% of cases [[2](#), [3](#)]. At diagnosis, at least 10% of the patients already have brain metastases, and the majority of these will be symptomatic. They can lead to significant morbidity, and therefore effective therapeutic approaches are required. Central nervous system metastases signal stage IV disease and generally herald an ominous prognosis, but neuro- and radiosurgical advances have resulted in effective treatments of brain metastases, leading to improvement in neurological status and survival [[6–8](#)].

Orbital metastases are a rare manifestation of systemic malignancies and account for only 1–13% of all orbital tumors [[9–11](#)]. However, the precise incidence of these lesions is difficult to estimate. It has increased in recent years because improvements in treatment modalities have resulted in improved survival in cancer patients. Published reports indicate breast and lung tumors to be the most common primary neoplasms leading to eye metastasis, and metastases to the eye or orbit develop in approximately

0.7–12% of patients with lung cancer [9–11]. Ophthalmologic symptoms may be preceded by systemic symptoms, especially if the primary site is the lung, gastrointestinal tract, thyroid or kidney [2].

The most common manifestations of orbital metastases are diplopia, exophthalmos, inflammation, decreased visual acuity, pain, chemosis and eyelid swelling, depending on the site affected. Symptoms usually occur acutely and progress rapidly, over the course of weeks to months [9–11].

The aim in treating orbital metastases is to relieve discomfort. Surgical removal of the mass is not recommended. Regardless of the primary tumor type, prognosis is poor because patients with orbital metastases are usually at an advanced stage of the disease. In one report, the mean survival time was 7.4 months. In another report, the median survival time was 1.3 years, and the two-year survival rate was 27% [4, 5]. The survival duration was not significantly different among patients with different types of primary neoplasms.

Available treatment options of orbital metastasis are external beam radiotherapy, plaque radiotherapy and newer methods like surgical resection, transpupillary thermotherapy and intravitreal chemotherapy. Additionally, anti-vascular endothelial growth factor therapy can be used to slow the progress of maculopathy and neuropathy as well as spare vision after local radiotherapy [12–14].

Systemic chemotherapy alone can also be used to treat metastatic tumors to the eye and orbit [15]. However, chemotherapy of the primary cancer alone is not recommended in patients in whom the orbital lesion does not resolve with chemotherapy alone. In this case report, a thorough follow-up of the orbital lesion is presented radiographically, in combination with chemotherapy administration.

Conclusion

A great index of suspicion is essential when an orbital lesion appears. Even though reduction in visual acuity due to orbital metastasis is rarely the first sign of lung cancer, the clinician should be alert. Routine annual or biannual ophthalmic examination is recommended for patients with underlying primary cancers to allow early detection of metastasis and early intervention to protect vision and maintain quality of life.

Disclosure Statement

The authors declare that they have no competing interests.



Fig. 1. Left: MRI of the orbits. Coronal, T₂-weighted MR image demonstrates an ovoid mass-like lesion with high signal intensity, corresponding to lung cancer metastasis. The lesion provokes a globe displacement (arrow). Right: photograph of the patient.

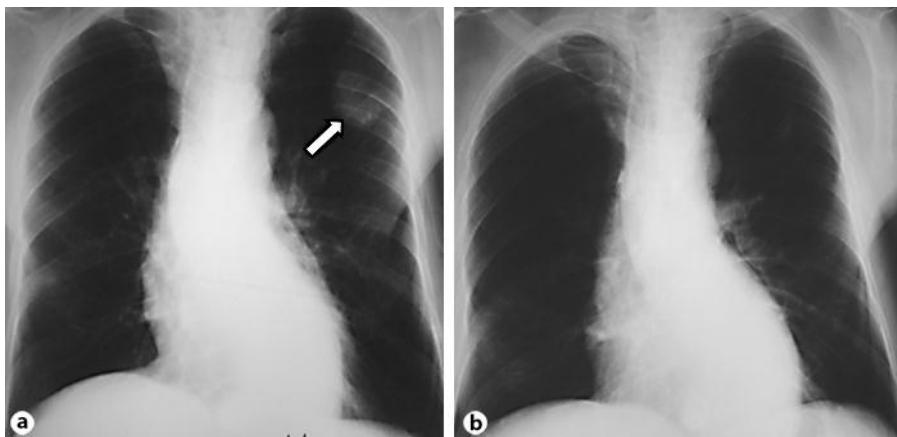


Fig. 2. Posterior-anterior chest X-rays. **a** Before treatment, a round mass corresponding to lung cancer is seen in the upper lobe of the left lung (arrow). **b** Six months after treatment, the round mass is not visible.

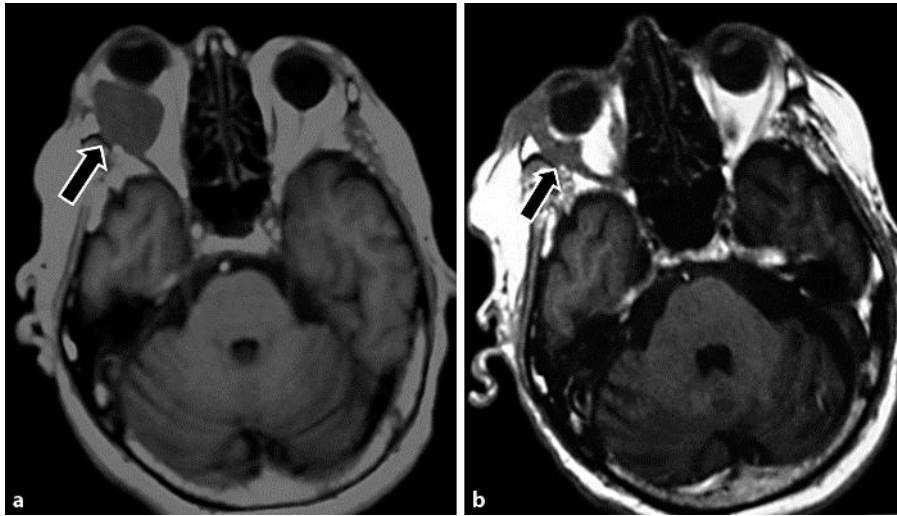


Fig. 3. Axial, enhanced, T₁-weighted MR images of the orbits. **a** Before treatment, an ovoid well-circumscribed, mass-like lesion which enhances homogeneously is seen within the right orbit (arrow). The lesion is attached to the lateral rectus muscle and is extended to the intraconal space. A severe globe proptosis can be noticed. **b** After the treatment, the mass has been decreased in size dramatically (arrow). The globe proptosis has been resolved.

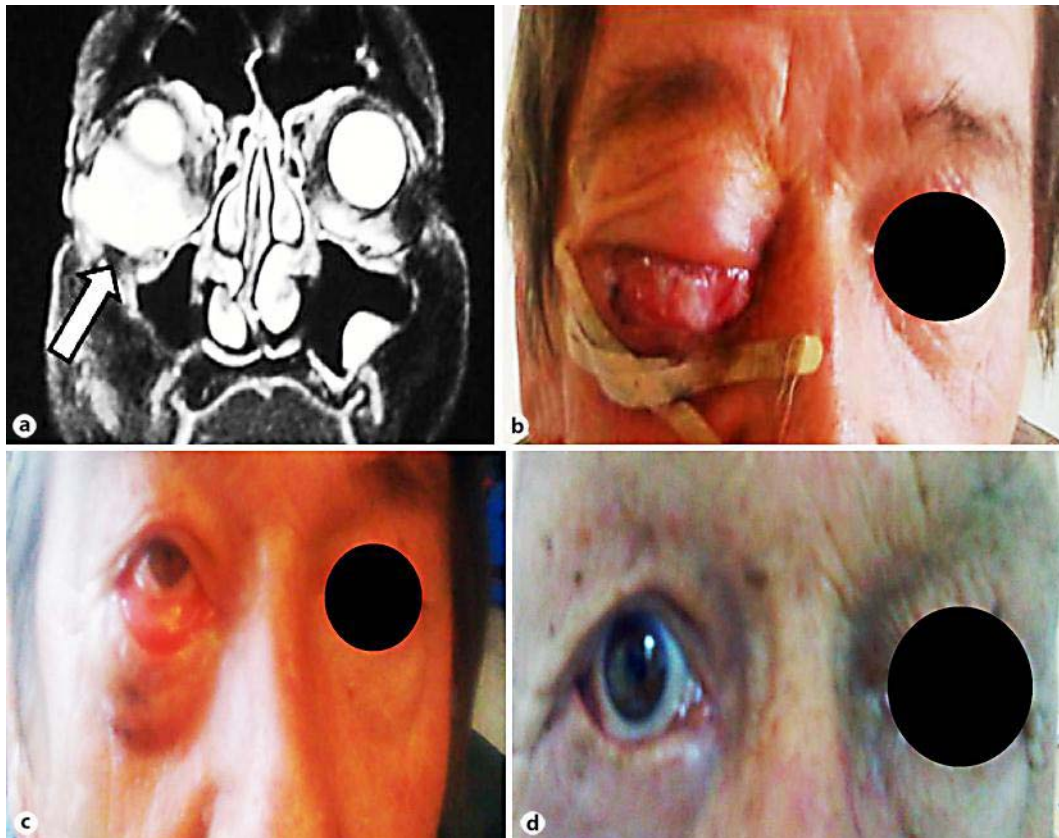


Fig. 4. MRI upon admission (a), photograph upon admission (b), photograph after 3 months of treatment (c), and photograph after 6 months of treatment (d).

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