Isolated ocular metastases from lung cancer

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Non–small cell lung cancer constitutes 80%-85% of lung cancers, and 40% of NSCLC are adenocarcinoma. It is rare to find intra-ocular metastasis from lung cancer. In this article, we present the case of a patient who presented with complaints of diminished vision redness of the eye and was found to have intra-ocular metastases from lung cancer.

Case presentation and summary

A 60-year-old man with a 40-pack per year history of smoking presented to multiple ophthalmologists with complaints of decreased vision and redness of the left eye. He was eventually evaluated by an ophthalmologist who performed a biopsy of the anterior chamber of the eye. Histologic findings were consistent with adenocarcinoma of lung primary (Figures 1 and 2).

After the diagnosis, a chest X-ray showed that the patient had a left lower lung mass. The results of his physical exam were all within normal limits, with the exception of decreased visual acuity in the left eye. The results of his laboratory studies, including complete blood count and serum chemistries, were also within normal limits. Imaging studies – including a computed-tomography (CT) scan of the chest, abdomen, and pelvis and a full-body positron-emission tomography–CT scan – showed a hypermetabolic left lower lobe mass 4.5 cm and right lower paratracheal lymph node metastasis 2 cm with a small focus of increased uptake alone the medial aspect of the left globe (Figures 3 and 4).

An MRI orbit was performed in an attempt to better characterize the left eye mass, but no optic lesion was identified. A biopsy of the left lower lung mass was consistent with non–small-cell lung cancer (NSCLC). Aside from the isolated left eye metastases, the patient did not have evidence of other distant metastatic involvement.

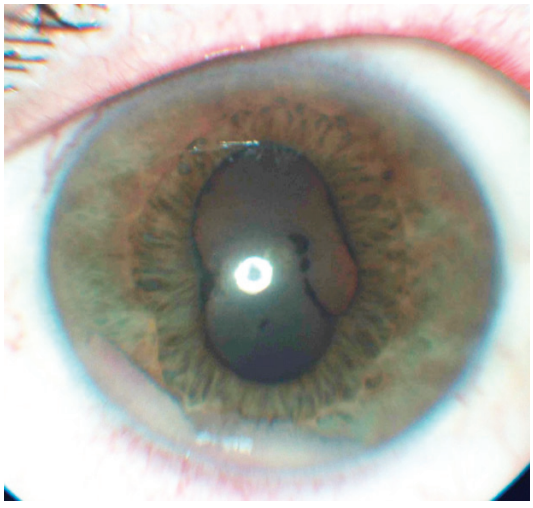

FIGURE 1 The anterior chamber of the eye, showing cellular keratin precipitates, 1+ cellular debris inferiorly, without any iris nodules or lesions.

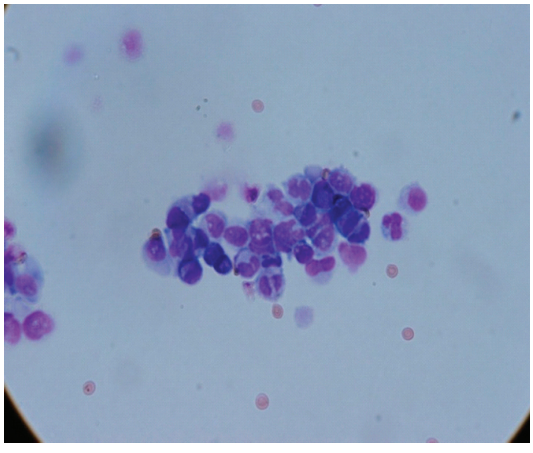

FIGURE 2 Histopathology of the anterior chamber fluid showing cellular debris and malignant cells consistent with adenocarcinoma of the lung. The stain was CK7 positive, CK20 negative, and TTF-1 positive.

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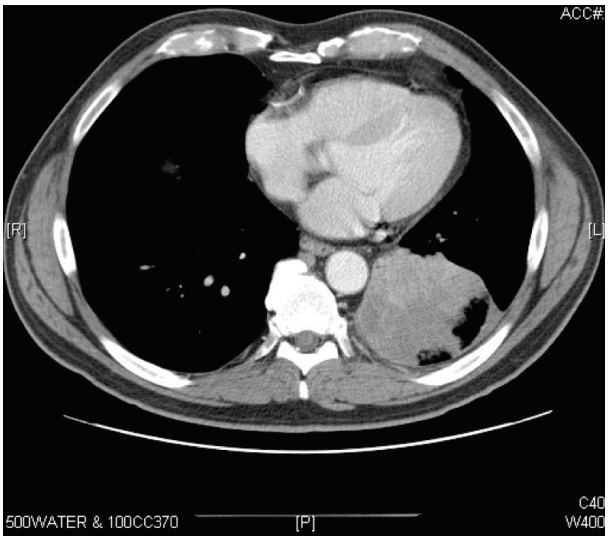

FIGURE 3 Computed-tomography chest scan with contrast demonstrating a left lower lung mass.

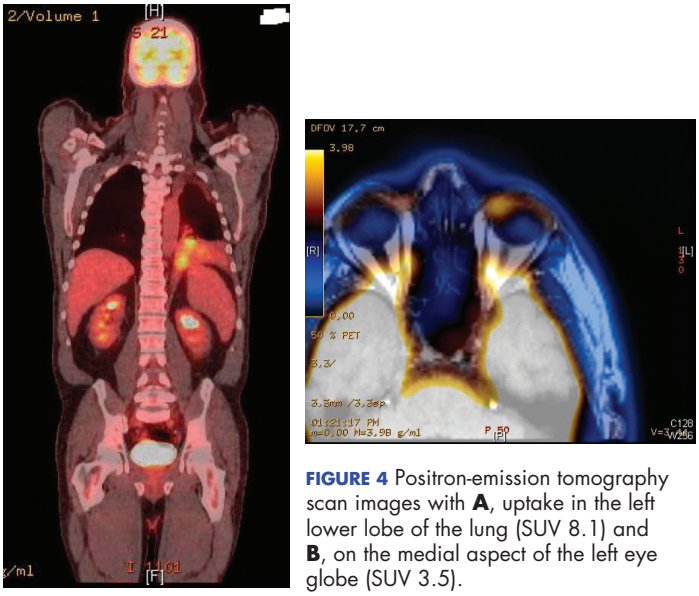

FIGURE 4 Positron-emission tomography scan images with **A**, uptake in the left lower lobe of the lung (SUV 8.1) and **B**, on the medial aspect of the left eye globe (SUV 3.5).

He was started on palliative chemotherapy on a clinical trial and received intravenous carboplatin AUC 6, pemetrexed 500 mg/m^2, and bevacizumab 15 mg/kg every 3 weeks. He received 1 dose intraocular bevacizumab injection before initiation of systemic chemotherapy as he was symptomatic from the intraocular metastases. Within 2 weeks after intravitreal bevacizumab was administered, the patient had subjective improvement in vision. Mutational analysis to identify if the patient would benefit from targeted therapy showed no presence of EGFR mutation and ALK gene rearrangement, and that the patient was K-RAS mutant.

After treatment initiation, interval imaging studies (a computed-tomography scan of the chest, abdomen, pelvis; and magnetic-resonance imaging of the brain) after 3 cycles showed no evidence of disease progression, and after 4 cycles of chemotherapy with these drugs, the patient was started on maintenance chemotherapy with bevacizumab 15 mg/kg and pemetrexed 500 mg/m^2.

Discussion

Choroidal metastasis is the most common site of intraocular tumor. In an autopsy study of 230 patients with carcinoma, 12% of cases demonstrated histologic evidence of ocular metastasis.[1] A retrospective series of patients with malignant involvement of the eye, 66% of patients had a known history of primary cancer and in 34% of patients the ocular tumor was the first sign of cancer.[2] The most common cancers that were found to have ocular metastasis were lung and breast cancer.[2] Adenocarcinoma was the most common histologic type of lung cancer to result in ocular metastases and was seen in 41% of patients.[3]

Decreased or blurred vision with redness as the primary complaint of NSCLC is rare. Only a few case reports are available. Abundo and colleagues reported that 0.7%-12% of patients with lung cancer develop ocular metastases.[4] Therefore, routine ophthalmologic screening for ocular metastases in patients with cancer has not been pursued in asymptomatic patients.[5] Ophthalmological evaluation is recommended in symptomatic patients.

Metastatic involvement of two or more other organs was found to be a risk factor for development of choroidal metastasis in patients with lung cancer though in our patient no evidence of other organ involvement was found.[5] The most common site of metastases in patients with NSCLC with ocular metastases was found to be the liver. Choroidal metastases was reported to be the sixth common site of metastases in patients with lung cancer.[5]

Treatment of ocular manifestations has been generally confined to surgical resection or radiation therapy, but advances in chemotherapy and development of novel targeted agents have shown promising results.[7] Median life expectancy after a diagnosis of uveal metastases was reported to be 12 months in a retrospective study, which is similar to the reported median survival in metastatic NSCLC.[8]

Our patient was enrolled in a clinical trial and was treated with a regimen of carboplatin, paclitaxel, and bevacizumab. On presentation, he had significant impairment of vision with pain. He was treated with intravitreal bevacizumab yielding improvement in his visual symptoms. Bevacizumab is a vascular endothelial growth factor receptor monoclonal antibody approved for use in patients with metastatic lung cancer. Other pathways that have been reported in development of lung cancer involve the ALK gene translocation, and EGFR and K-RAS mutations, and

TABLE NSCLC patients treated with targeted therapy

Case	Patient age, y (sex)	Mutations	Chemotherapy	Clinical outcomes
Kim[11]	57 (F)	No mention	Intravitreal bevacizumab and oral erlotinib	Improved vision, regression of metastases
George[12]	42 (F)	No mention	Systemic chemotherapy with carboplatin/paclitaxel/bevacizumab	Improved vision, regression of metastases
Inoue[13]	68 (F)	No mention	Oralgeftinib	Improved vision, regression of metastases
Singh[6]	42 (F)	No mention	Systemic chemotherapy with cisplatin, paclitaxel with intravitreal bevacizumab, followed by gefitinib for disease progression	Patient lost to follow-up, but eye symptoms improved after intravitreal bevacizumab
Singh[6]	53 (M)	No mention	Systemic chemotherapy with cisplatin, permetrexed and intravitreal bevacizumab, followed by systemic bevacizumab and oral erlotinib on disease prrogression	Vision did not improve due to retinal detachment. Patient died after 16 mo with disease progression
	52 (F)	EGFR+	Oral geftinib	Improved vision
Feng[15]	62 (F)	ALK+	Systemic chemotherapy with carboplatin and pemetrexed with radiation to the eyes with no response; crizotinib started when ALK results were positive.	Improvement in vision with complete resolution of ocular lesions on imaging
Current case	60 (M)	EGFR–, K-RAS+, ALK translocation negative	Systemic chemotherapy with carboplatin, paclitaxel and bevacizumab; intravitreal therapy with bevacizumab	Improvement in vision after first intravitreal bevacizumab injection and regression of systemic metastases

targeted therapy has shown good results in cancer patients with these molecular defects. Randomized clinical trials in patients with advanced NSCLC and an EGFR mutation have shown significant improvement in overall survival with the use of erlotinib, a tyrosine kinase inhibitor targeting the epidermal growth factor receptor.[9] Similarly, crizotinib has shown promising results in patients with metastatic NSCLC who have ELM-ALK rearrangement.[10] As our patient's tumor did not have either of these mutations, he was initiated on chemotherapy with bevacizumab. The presence of a K-RAS mutation in this patient further supported the use of front-line chemotherapy given that it may confer resistance against agents that target the EGFR pathway.

In our review of the literature, we found cases of patients with ocular metastases who responded well to therapy with targeted agents (Table). Singh and colleagues did a systematic review of 55 cases of patients with lung cancer and choroidal metastases and found that the type of therapy depended on when the diagnosis had been made in relation to the advent of targeted therapy: cases diagnosed before targeted therapy had received radiation therapy or enucleation.[6] As far as we could ascertain, there have been no randomized studies evaluating the impact of various targeted therapies or systemic chemotherapy on ocular metastases, although case reports have documented improvement in vision and regression of metastases with such therapy.

Conclusion

The goal of therapy in metastatic lung cancer is palliation of symptoms and improvement in patient quality of life with prolongation in overall survival. The newer targeted chemotherapeutic agents assist in achieving these goals and may decrease the morbidity associated from radiation or surgery with improvement in vision and regression of ocular metastatic lesions. Targeted therapies should be considered in the treatment of patients with ocular metastases from NSCLC.

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