

# A Case of Orbital Metastasis as Disease Progression of Anaplastic Lymphoma Kinase-Positive Lung Cancer Treated with Crizotinib

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## Key Words

Orbital metastasis · Crizotinib · Adverse event · Anaplastic lymphoma kinase · Lung cancer · Lung adenocarcinoma

## Abstract

Orbital metastasis of lung cancer is rare. It often causes visual disorder. To date, there are only a few case reports. Crizotinib is an anaplastic lymphoma kinase (*ALK*) tyrosine kinase inhibitor that leads to responses in most patients with *ALK*-positive non-small-cell lung cancer. Visual disorder is one of the popular adverse events of crizotinib, but the symptom almost decreases over time. We report a case of orbital metastasis as the disease progression of *ALK*-positive lung cancer treated with crizotinib. It should be kept in mind that orbital metastasis can be the disease progression of lung adenocarcinoma with *ALK* translocation treated with crizotinib. When physicians encounter a patient receiving crizotinib with visual disorder, we must distinguish between adverse events and orbital metastasis.

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## Case Report

A 64-year-old woman who never smoked was diagnosed with a lung nodule in the right lower lobe at her medical checkup. She underwent a VATS (video-assisted thoracic surgery) right lower lobectomy with an ND2a-1 procedure. A surgical biopsy of the lung tumor confirmed adenocarcinoma with metastasis to the hilar lymph nodes (pT1aN1M0; pStageIIA) and revealed the presence of anaplastic lymphoma kinase (*ALK*) rearrangement. She re-

ceived adjuvant platinum-based chemotherapy. Twenty months after her surgery, she presented with recurrent disease in the form of multiple mediastinal lymphadenopathies, so crizotinib (250 mg twice daily) was administered orally. A week later, she complained of bilateral visual disorder. A head MRI before crizotinib therapy showed nothing in particular. We diagnosed this symptom as an adverse event of crizotinib and continued to prescribe crizotinib. Four weeks later, a chest CT scan showed a good partial response of multiple lymph node metastases.

Five months after starting crizotinib, she complained of a progression of her visual disorder and developed a left eye movement disorder and eyelid ptosis. A head MRI showed multiple brain metastases and an orbital metastasis (fig. 1). At the same time, a chest CT showed multiple lung metastases, so we diagnosed a progression of the disease. The brain metastases were treated with whole-brain radiation therapy, and the orbital metastasis with Gamma Knife radiotherapy. The lung metastases were treated with platinum-based chemotherapy. After the treatments, she noticed a partial improvement of the visual disorder and continued the platinum-based chemotherapy for 3 months.

## Discussion

Here, we report a case of orbital metastasis as the disease progression of *ALK*-positive lung cancer treated with crizotinib. The incidence of ocular metastases in lung cancer was reported to be 1–7%; however, clinically significant ocular metastases were rare and occurred in less than 1% of patients [1]. There is only one case report about ocular metastasis of lung cancer with *ALK* rearrangement [2].

Crizotinib has marked clinical response for the treatment of non-small-cell lung cancer positive for *ALK* rearrangement [3]. Visual disorder is one of the common adverse events of crizotinib. According to previous reports [3, 4], crizotinib causes 60–64% (all grade) visual disorders, but in most cases, this symptom is not progressing in severity and cures itself naturally.

There are some case reports about the response to crizotinib in brain metastases to *ALK*-positive lung cancer [5, 6], but crizotinib generally exhibits poor blood-brain barrier (BBB) penetration [7]. Several reports have been described about the development of brain metastases in patients receiving crizotinib [8, 9].

In our case, the patient complained of visual disorder soon after starting crizotinib, and the symptoms continued. Five months after starting crizotinib, she complained of a progression of her visual disorder and it was the initial sign of a progressing disease. It may be affected by a poor BBB penetration of crizotinib, but with multiple brain metastases and an orbital metastasis, multiple lung metastases also appeared concurrently. We considered her progressing disease was the result of a resistance to crizotinib.

In most cases, visual disorders during crizotinib treatment is an adverse event, but it rarely happens as the presentation of orbital metastasis. We should observe the change of condition carefully and distinguish between adverse events and ocular metastases during the treatment with crizotinib.

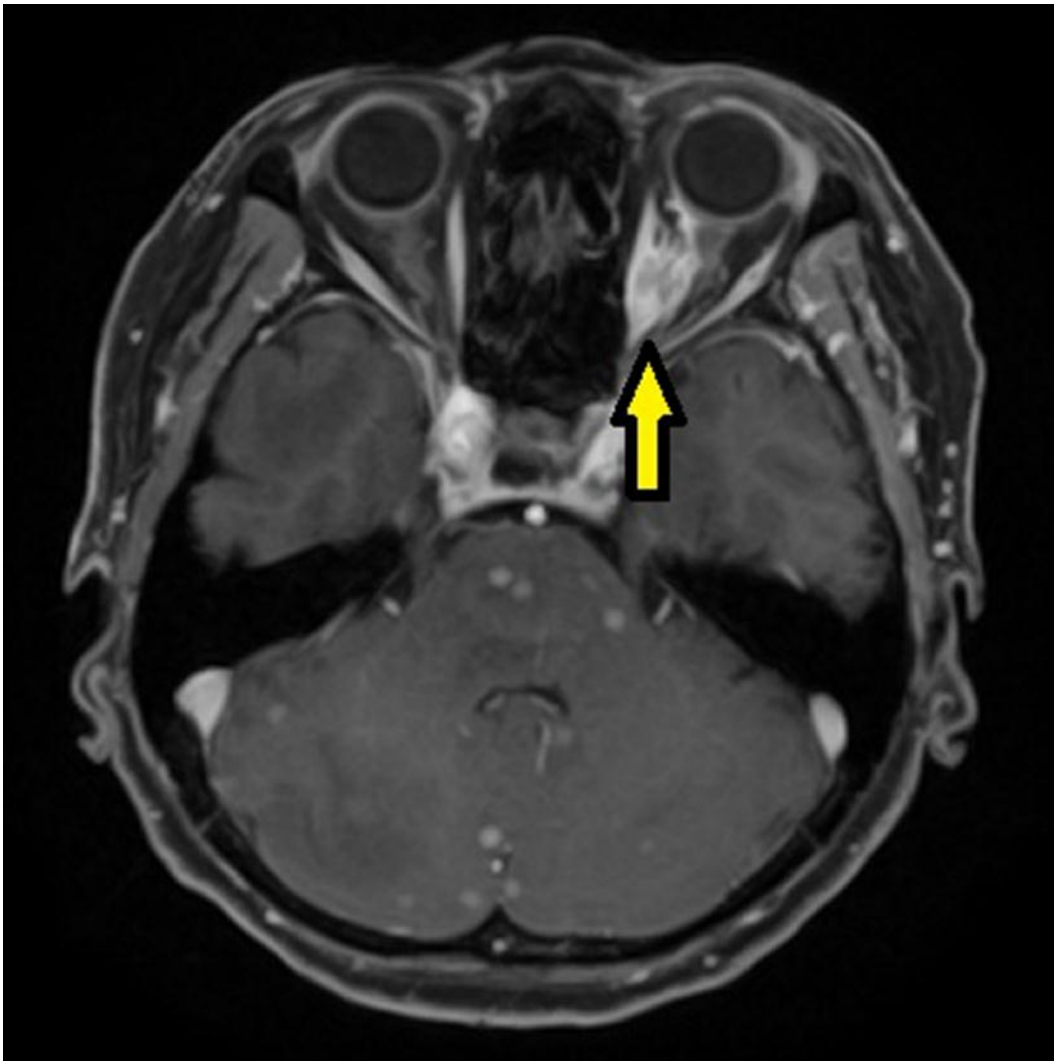
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**Fig. 1.** A head MRI at 5 months after starting crizotinib showed a left orbital metastasis with multiple brain metastases.