

CASE REPORT

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# A case of masquerade syndrome caused by metastatic iris tumor diagnosed by a high CEA level in the aqueous humor and iris biopsy

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## Abstract

**Background** With the advent of targeted therapies, the survival prognosis for metastatic tumors has extended, and it has become necessary to diagnose and consider treatment that takes into account Quality of Life for metastatic tumors of the eye. The reports of checking tumor marker in the aqueous humor for diagnosis of metastatic intraocular tumors are few. Here, we report a case of masquerade syndrome with secondary glaucoma in which a high carcinoembryonic antigen (CEA) level in the aqueous humor could assist diagnosis, and continuing targeted therapy and trabeculectomy were effective.

**Case presentation** A 73-year-old man was referred to us for iritis and high intraocular pressure (IOP) with severe eye pain in the left eye. He had Stage IVB lung adenocarcinoma treated with a molecularly targeted drug, Osimertinib. His best corrected visual acuity was 0.15, and IOP was 52 mmHg in the left eye. Anterior chamber cells (+), numerous small nodules in the iris, and small masses in the inferior angle were observed. In the aqueous humor, the CEA level was higher than in the blood. Napsin A and Thyroid Transcription Factor-1 (TTF-1) positive cells showed in the resected tissue at iridectomy performed during trabeculectomy. The pathological diagnosis of metastatic iris tumor of the lung adenocarcinoma was made, and we injected bevacizumab intravitreally once and continued Osimertinib. His IOP lowered to 8–10 mmHg, and the iris masses disappeared. He lost vision by metastasis to the left optic nerve after termination of Osimertinib one and a half years later. The metastasis shrank after restarting the drug. He passed away from an exacerbation of his primary lung cancer two years and nine months after the first visit. Although he lost vision in his left eye, the metastatic tumor in his left eye and optic nerve had disappeared, and his quality of life was maintained without any pain in his eye.

**Conclusions** Checking tumor markers in the aqueous humor can aid in diagnosis, and aggressive treatment of metastatic iris tumors must help maintain patients' Quality of Life.

**Keywords** Case report, CEA in the aqueous humor, Masquerade syndrome, Iris tumor, Trabeculectomy, Molecular targeted therapy

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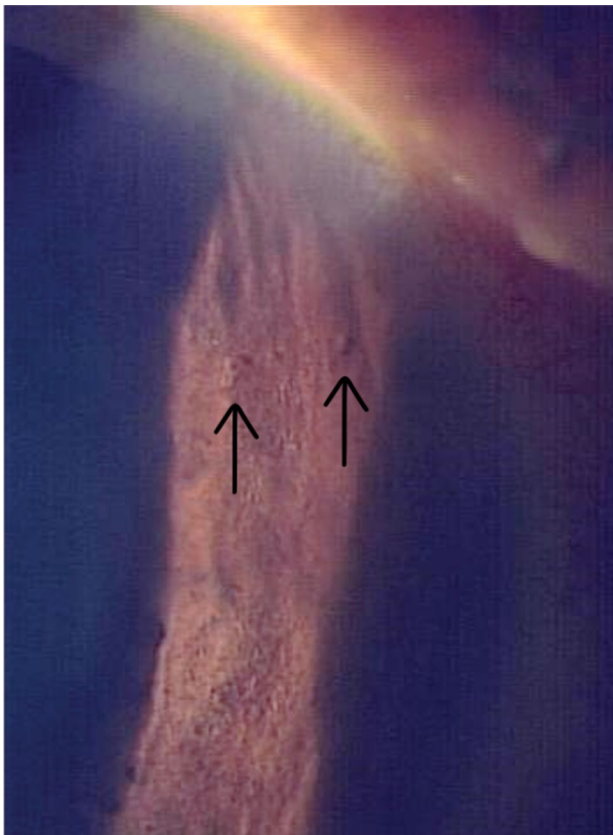
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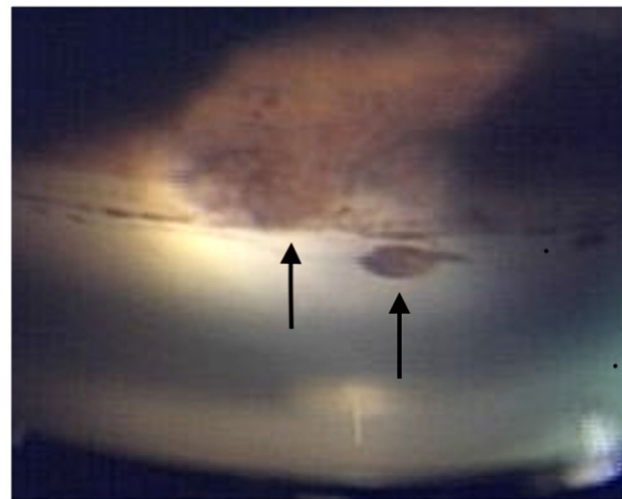


**Fig. 1** Slit-lamp photograph of the left eye showing small nodules. Arrows point to the iris nodules. Iris nodules were observed scattered on the iris surface

## Background

Since intraocular masquerade syndrome of neoplastic origin resembles iritis, differential diagnosis between them is crucial for ophthalmologists. Metastatic ocular tumors are relatively rare among all ocular tumors [1, 2], and iris metastasis was reported to account for 8% of all metastatic uveal tumors [3]. Moreover, a limited amount of iris tissue can be obtained by biopsy, and methods helpful for auxiliary diagnosis of iris malignancy are needed. On the other hand, recent advances in cancer treatment, such as molecular targeted therapies, have improved the prognosis of patients with malignancy, and that can increase the need for diagnosis and treatment of metastatic ocular tumors to maintain quality of life (QOL). There are few reports detailing tumor markers checked in the aqueous humor for auxiliary diagnosis of metastatic intraocular tumors.

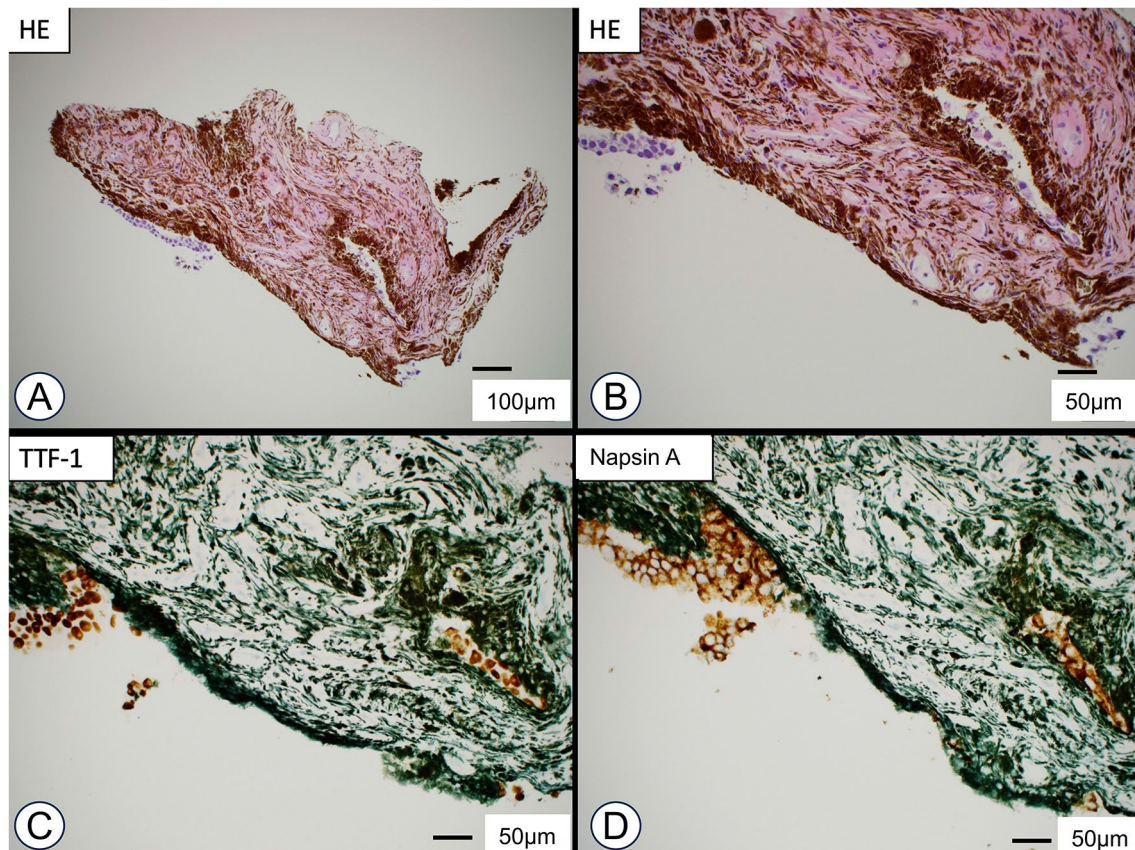
We present a case of intraocular masquerade syndrome who had severe eye pain caused by high ocular pressure and a tumor marker, carcinoembryonic antigen (CEA) level in the aqueous humor and pathology of the resected iris tissue of iridectomy during trabeculectomy led the diagnosis.



**Fig. 2** Small masses located at the inferior angle. Arrows indicate the small masses located in the inferior angle of the left eye observed with a Gonioscope

## Case presentation

A 73-year-old man had had blurred vision in the left eye for a month, and he was diagnosed with iritis and secondary glaucoma by a local clinic. Patient was referred to our hospital for high intraocular pressure (IOP) with severe eye pain in the left eye. He had stage IVB lung adenocarcinoma with multiple metastases including bone, and had a targeted drug, osimertinib, for two months. The drug was effective in stabilizing his systemic condition. While his best corrected visual acuity (BCVA) was 1.2 and IOP was 16 mmHg in the right eye, his BCVA was 0.15, and IOP was 52 mmHg in the left eye. A slit lamp examination showed anterior chamber cells (+) and numerous small nodules in the iris (Fig. 1). A gonioscopy examination showed small masses and peripheral anterior synechia on the inferior angle (Fig. 2). Since we suspected secondary glaucoma caused by a metastatic iris tumor, we performed a trabeculectomy and iris biopsy in the left eye to lower the IOP and to make a pathological diagnosis. The pathological examination result was negative for malignancy. The intraocular pressure temporarily decreased to 10 to 13mmHg but rose again to 30mmHg one month after surgery. During this period, we received information that his primary lung cancer was a lung adenocarcinoma of TTF-1 positive and a tumor marker CEA level was high from an internist treating lung cancer. We performed a trabeculectomy with anterior aqueous humor sampling and pathological examination using iris tissue obtained at iridectomy. The CEA level in the aqueous humor was 75.6 ng/mL, higher than 17.3 ng/mL in the blood. Napsin and TTF-1 positive cells were observed in the iris tissue (Fig. 3), and the pathological diagnosis was metastasis of the lung adenocarcinoma. The surgery resulted in a decrease in IOP. We injected Bevacizumab



**Fig. 3** Pathological picture of the iris tissue taken at the peripheral iridectomy during the trabeculectomy. **A, B:** Hematoxylin and eosin staining (HA) showing different magnification. **C:** Immunostaining for Thyroid Transcription Factor-1 (TTF-1). Positive cells stain brown. **D:** Immunostaining for Napsin A. Brown-stained positive cells are observed on the surface of the iris. TTF-1 and Napsin A are markers for lung adenocarcinoma. The black line in **A** indicates 100 µm, and the black lines in **B-D** indicate 50 µm

intravitreally once and continued the targeted drug osimertinib. The anterior chamber became clear, the iris tumor shrank, and the iris nodules disappeared. Since then, his IOP has been controlled to 8mmHg-10mmHg, and his eye pain has disappeared. One and half years later, Osimertinib was terminated due to the systemic condition maintained stable, and metastases were observed at the left optic nerve. Although the optic nerve metastases shrank with the resumption of osimertinib, the BCVA decreased to no light perception. He died two years and nine months after the first visit because of an exacerbation of his primary lung cancer. Although he lost vision in his left eye, the metastatic tumor in his left eye and optic nerve had disappeared, and his QOL was maintained without any pain in his eye.

### Discussion

We presented a case of painful secondary glaucoma caused by masquerade syndrome. High CEA level in the aqueous humor and pathological examination of iridectomy tissue during trabeculectomy led to the diagnosis of metastatic iris tumor from lung adenocarcinoma. His

severe pain in the eye disappeared by controlling intraocular pressure with trabeculectomy. Anterior cells and iris nodules disappeared with a vitreous injection of molecularly targeted drug and continued targeted therapy systemically.

There were reports of detecting tumor markers in the aqueous humor [4–6]. High levels of Interleukin10 in the aqueous humor are known to occur in primary vitreoretinal lymphoma, and higher Interleukin10 level than Interleukin6 levels has diagnostic value [7, 8]. On the other hand, there are few reports of metastatic ocular tumors with CEA measurements of aqueous humor [9]. In the current case, we obtained information on the tumor marker in the blood that showed high levels in the primary tumor and compared that with the values in the aqueous humor. The aqueous humor CEA level was four times higher than the serum CEA level. Since limited tissue can be obtained from an eye by biopsy, it causes the result of false negatives. Thus, if a tumor marker that shows a high level in the primary tumor is known, it must be informative to check the tumor marker in the aqueous

humor for auxiliary diagnosis of metastatic intraocular tumors.

The effectiveness of intravitreal bevacizumab injection for glaucoma secondary to metastatic iris tumor was reported [9], and we performed a single intravitreal injection in the present case. The iris metastatic tumor remained in remission after only one injection of bevacizumab, suggesting that the intravitreal injection contributed to the regression of the iris tumor and that the systemic administration of the molecular targeted drug contributed to the maintenance of remission after the filtration surgery.

Surgical treatments were reported to be performed rarely in metastatic iris tumors. In a clinical study of 104 cases, management of iris metastasis included systemic chemotherapy ( $n=18$ , 22%), external beam radiotherapy ( $n=34$ , 41%), plaque radiotherapy ( $n=20$ , 24%), surgical excision ( $n=4$ , 5%), enucleation ( $n=3$ , 4%), or observation ( $n=4$ , 5%) [10]. A previous review of glaucoma secondary to intraocular tumors has suggested that minimally invasive glaucoma surgery (MIGS) could be considered to manage secondary glaucoma in the absence of iris or ciliary body involvement and for eyes with treated and regressed posterior ocular malignancies [11]. On the other hand, MIGS, filtering, or shunting surgery in eyes with active intraocular tumors should be avoided to prevent tumors from spreading out of the eye. In the present case, the cancer did not originate in the eye, and the molecular targeted drug controlled the multiple metastases outside of the eye. Since we considered that the targeting drug could prevent the spread of tumor cells even if the iris nodules were metastatic iris tumors, we performed trabeculectomy with iris biopsy for diagnosis and to relieve his eye pain. Death after iris metastasis diagnosis is reported to occur in 87% at a median of 10 months [10], and we believe that two years and nine months in the present case is not short. However, effective molecular targeted drugs may be discontinued due to side effects or high prices, and filtration surgery may spread malignant cells out of the eye, so filtration surgery in the eye with masquerade syndrome should be avoided as much as possible. If filtration surgery is necessary, patients should be advised of the possibility that the tumor may spread outside the eye.

Although the visual function of the affected eye could not be maintained in the current case, the QOL maintained fine until his death without any pain in his eye. Since survival can be extended with targeted therapy, considering the treatment of metastatic iris tumors may be crucial to maintain patients' QOL. Strength of the current case report is pathologically confirmed case and observation period of more than two and half years and limitation is a case report.

We reported a masquerade syndrome caused by a metastatic iris tumor complicated with secondary glaucoma, which could be diagnosed by the CEA level of the aqueous humor and iris pathology. Obtaining information about tumor markers that are elevated in the primary tumor and comparing their concentrations in the blood and in the aqueous humor can aid in diagnosing of metastatic intraocular tumors. A trabeculectomy was effective in controlling the IOP and iris tumor together with systemic targeted therapy. Aggressive treatment for metastatic iris tumors may contribute to maintaining patients' QOL.

#### Abbreviations

BCVA	Best Corrected Visual Acuity
CEA	Carcinoembryonic Antigen
HA	Hematoxylin and eosin staining
IOP	Intraocular Pressure
QOL	Quality of Life
TTF-1	Thyroid Transcription Factor-1

#### Author contributions

Analyzed and interpreted the patient data: SK, RK. Treatment: RK. Pathological diagnosis: SY. Manuscript drafting: SK, RK. Manuscript revision: SK, RK. All authors reviewed and approved the final manuscript.

#### Funding

No funding or grant support was received.

#### Data availability

No datasets were generated or analysed during the current study.

#### Declarations

##### Ethics approval and consent to participate

This article does not contain any studies with human participants or animals.

##### Consent for publication

Written informed consent for publication of this case and accompanying images was obtained from the patient prior to his death.

##### Competing interests

The authors declare no competing interests.

Received: 31 July 2024 / Accepted: 17 September 2024

Published online: 27 September 2024

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