

Ciliary Body Metastasis Masquerading as Scleritis

Brian J. Lee, MD¹

Careen Y. Lowder, MD, PhD¹

Charles Biscotti, MD²

Lynn Schoenfield, MD²

Arun D. Singh, MD¹

Cole Eye Institute¹ and Department of Pathology and Laboratory Medicine,² Cleveland
Clinic, Cleveland, OH

Correspondence to:

Arun D. Singh, MD

Department of Ophthalmic Oncology, Cole Eye Institute, Cleveland Clinic,

9500 Euclid Avenue, Cleveland, OH 44195

Tel: +1 216 445 9479

Fax: +1 216 445 2226

E-mail: singha@ccf.org

Keywords: Scleritis, Ciliary body, Metastasis, Adenocarcinoma

Word count : 1282

Abstract

A 54 year old Caucasian male with a diagnosis of idiopathic anterior scleritis did not improve despite intensive treatment with topical steroids and oral indomethacin. Subsequently yellow gelatinous deposits were observed in the anterior chamber angle. Ultrasound biomicroscopy revealed an irido-ciliary mass. Transcorneal fine needle aspiration biopsy confirmed adenocarcinoma. As there was past history of testicular teratocarcinoma, metastasis was suspected but systemic evaluation did not reveal any primary tumor. One month after the completion of radiation therapy (40 Gy in 16 fractions) the patient developed neovascular glaucoma and the tumor had progressed. The right eye was enucleated. The present case highlights the role of ultrasound biomicroscopy in evaluation of patients with scleritis, indications of fine needle aspiration biopsy, and management of patients with uveal metastasis.

Case

A 54 year old Caucasian male presented to the Cole Eye Institute for a second opinion regarding a diagnosis of iritis. He described four months of ongoing redness, pain, and photophobia in the right eye. Initially, he was treated with topical prednisolone acetate 1% without improvement. Subsequently homatropine 5% and combined neomycin, polymixin B, and dexamethasone drops were prescribed without any relief. For a month prior to presentation, he had been off all medications and his symptoms had gradually worsened.

He denied any past ocular history of trauma, surgery, or inflammatory disease. His past medical history was significant for a left testicular teratocarcinoma in 1987. At that time, he underwent orchiectomy and chemotherapy for suspicion of pulmonary metastases. However, subsequent wedge resection of the lung confirmed the lesions to be hamartomas. His social history was significant for smoking (1.5 pack per day for the past 30 years) and the review of systems was negative.

On examination, the visual acuity was 20/20 in the right eye and 20/25 in the left eye. The intraocular pressures were 32 mmHg in the right eye and 16 mmHg in the left eye. Deep episcleral injection was observed inferotemporally in the right eye and a few cells were present in the anterior chamber. The iris and lens were normal. Dilated fundus examination of both eyes was normal. In addition, an ultrasound B scan mode was normal. Previously performed investigations were negative and included chest x ray, PPD, ACE level, RPR, FTA-ABS , Lyme antibody, ANA, and HLA-B27.

A diagnosis of idiopathic anterior scleritis of the right eye was made. Fluorometholone 0.25% topical drops hourly in the right eye and oral indomethacin 25 mg three times a day were prescribed. Additional workup included anti-neutrophilic cytoplasmic antibodies, complete blood count, complete metabolic panel, and chest CT with contrast were ordered.

Two weeks later, the patient returned for follow-up stating that his symptoms had improved. However, on examination the deep episcleral injection was still present. In addition, the iris was displaced anteriorly at the 7-8 o'clock position. Yellow gelatinous deposits were observed in the corresponding quadrant in the anterior chamber angle (**Figure 1**). Ultrasound biomicroscopy was performed to evaluate the angle and ciliary body region (**Figure 1**). Transcorneal fine needle aspiration biopsy was confirmatory (**Figure 2**).

QUESTIONS:

1. Describe the ultrasound biomicroscopic findings (**Figure 1**)
2. What is the diagnosis based upon fine needle aspiration biopsy (**Figure 2**)?
3. How would you manage this patient?

ANSWERS:

1. Describe the ultrasound biomicroscopic findings

The UBM revealed an elongated dome shaped irido ciliary mass that extends from the posterior aspect of the peripheral iris to the ciliary body (*). The mass was centered at 7 o'clock meridian and measured 8.5 mm circumferentially, 5.0 mm anteroposteriorly, and

2.4 mm in height. An incidental iris pigment epithelial cyst was also observed (arrow). Note anterior displacement of the peripheral iris and amorphous deposits in the angle.

2. What is the diagnosis based upon fine needle aspiration biopsy sample?

The cells are large and columnar with prominent nucleoli. The cytologic appearance is consistent with adenocarcinoma. Metastatic ciliary body adenocarcinoma is the most likely diagnosis. The differential diagnosis includes primary adenocarcinoma of the pigmented and nonpigmented ciliary epithelium. However, these lesions are extremely uncommon and are associated with minimal inflammation and appear as a circumscribed dark mass.

3. How would you manage this patient?

The approach to management of this patient is two fold; detection and treatment of the primary cancer and the management of the intraocular lesion. Further workup by his primary oncologists including serum tumor markers and whole body PET/CT scans failed to demonstrate recurrence or metastasis of the previously treated testicular tumor at other sites or additional primary cancer. The patient underwent radiation to the right globe (40 Gy in 16 fractions).

One month after the completion of radiation therapy, the patient complained of significant pain, the vision had reduced to 20/200, there was neovascular glaucoma with IOP of 28 mmHg, and tumor had progressed. The right eye was enucleated.

Histopathologically, adenocarcinoma involved the ciliary body, anterior surface of the iris (with associated neovascularization), trabecular meshwork, and posterior cornea

(**Figure 2**). There was also extension posteriorly into the adjacent choroid. Degenerative changes of the tumor cells due to prior radiation therapy were noted. Histologic features of a germ cell tumors were not present. Immunoperoxidase stains, performed to identify the possible primary site of this tumor, showed positivity for cytokeratins AE1/3, CK7, and CK 20 with negative staining for PSA (prostatic specific antigen) and TTF-1 (thyroid transcription factor-1). This immunohistochemical profile points most strongly to a primary adenocarcinoma in the gastrointestinal tract (colon, pancreas, stomach, appendix), lung, or bladder.¹

Discussion

Our case demonstrates the importance of considering intraocular malignancy in the differential diagnosis of a patient with persistent intraocular inflammation who does not respond to appropriate treatment with a negative laboratory and imaging workup for an underlying inflammatory disease. Meticulous examination is critical to making the correct diagnosis. In our patient, minimal anterior bowing of the peripheral iris and observation of yellow gelatinous deposits in the angle on the slit lamp examination led to a suspicion of an underlying mass lesion which was confirmed by UBM (**Figure 1**).^{2,3} In cases of persistent anterior scleritis, UBM can be very helpful to evaluate the posterior chamber and ciliary body region, which is otherwise not visible.²⁻⁴ Our patient had a normal B-scan ultrasound at his first visit. We recommend UBM evaluation in any patient with persistent anterior scleral inflammation even with no clinical findings to suggest a posterior chamber mass as this would allow earlier diagnosis and treatment of a potentially lethal ocular condition.²

Intraocular biopsy becomes a necessity when the systemic evaluation fails to offer alternative accessible sites for fine needle aspiration biopsy such as lymph nodes, lungs, and liver.⁵ We opted to perform transcorneal needle aspiration biopsy by using a 25 gauge needle instead of an incisional biopsy of the ciliary body as the latter would have been associated with significant ocular morbidity in the presence of pre-existing inflammation.⁵

Uncommonly, scleritis can be the presenting ocular finding even in patients with primary intraocular malignancy such as choroidal melanoma.⁶ More frequently, uveal metastasis is the underlying malignancy.⁷ Uveal metastases are most often observed in the uvea but iris and ciliary body can also be affected (about 2% of all uveal metastatic lesions) either solely or in combination with choroidal involvement.⁸ Other diagnostic possibilities include primary adenocarcinoma of the ciliary body that arise in the pigmented and non pigmented ciliary epithelium.⁹ Clinically, these tumors mimic melanomas because they appear as a slowly growing pigmented circumscribed mass.⁹ Histopathologically, the tumor cells are arranged in glandular pattern and exhibit prominent basement membrane.⁹

The recommended approach to the management of patients with suspected or proven uveal metastasis is to investigate for the primary as the nature of primary tumor has direct implications on the diagnosis, treatment and overall prognosis.¹⁰ In our patient with a history of smoking, adenocarcinoma of the lung cancer is the most likely source of the metastasis. The clinical suspicion of a metastasis of primary adenocarcinoma of the lung although not corroborated by extensive imaging studies is strongly suggested by the immunohistochemical profile. Other sources of primary adenocarcinoma such as

gastrointestinal tract or bladder are also being considered. Teratocarcinoma of the testis is a nonseminomatous germ cell tumor that spreads by lymphatics to the retroperitoneal nodes and is not known to metastasize to the uvea.¹¹ The patient will continue to be investigated periodically in the future. Despite all these efforts, in about 3-5% of metastatic lesions, the primary tumor may not be identified.¹²

Final diagnosis:

Iridociliary metastatic adenocarcinoma. Primary tumor undetected.

Legends

Figure 1.

A. Anterior segment photograph showing scleral injection in the inferotemporal quadrant. Note yellow gelatinous deposits in the corresponding anterior chamber angle region.

B. Ultrasound biomicroscopic photograph demonstrating an elongated dome shaped irido ciliary mass that extends from the posterior aspect of the peripheral iris to the ciliary body (*). The mass was centered at 7 o'clock meridian and measured 8.5 mm circumferentially, 5.0 mm anteroposteriorly, and 2.4 mm in height. An incidental iris pigment epithelial cyst was also observed (arrow). Note anterior displacement of the peripheral iris and amorphous deposits in the angle.

Figure 2.

A. Fine needle aspiration biopsy. The cells are large and columnar with prominent nucleoli. The cytologic appearance is consistent with adenocarcinoma. (Papanicolaou stain, 100 X). No particular site of origin of the tumor can be identified by cell morphology in this sample. The cytologic sample was insufficient to perform immunoperoxidase stains.

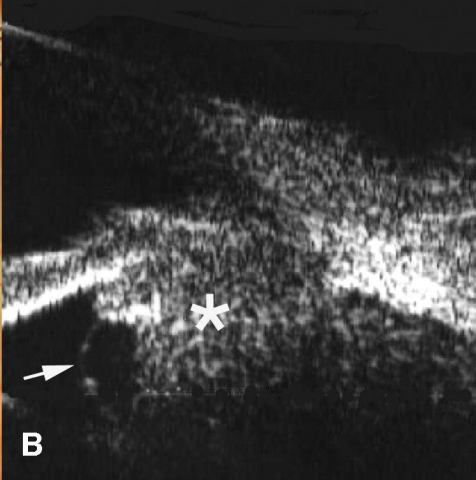
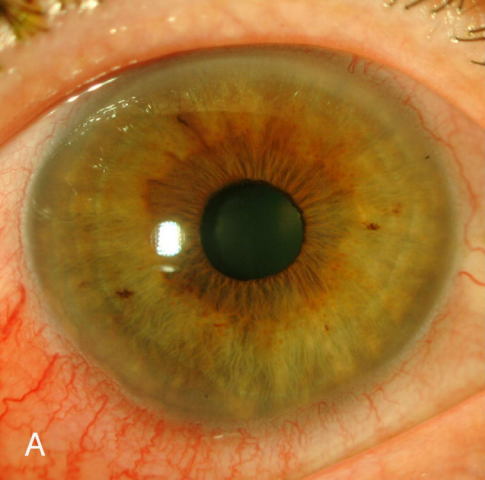
B. Histopathology of the enucleated globe. Adenocarcinoma in the angle and ciliary body (Hematoxylin and Eosin stain, 20 X). The tumor cells were weakly positive for CK

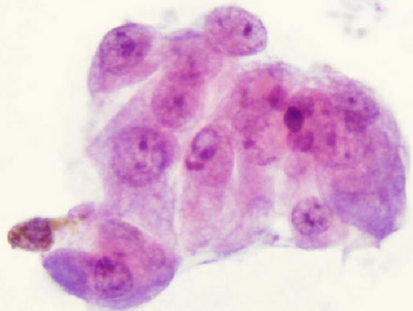
20 and strongly positive for CK7 suggesting adenocarcinoma arising in the gastrointestinal tract, lung, or bladder.

References

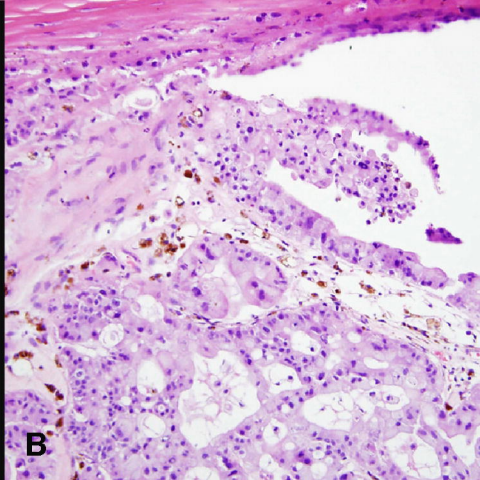
1. Chu PG, Weiss LM. Keratin expression in human tissues and neoplasms. *Histopathology* 2002;40:403-439.
2. Conway RM, Chew T, Golchet P, et al. Ultrasound biomicroscopy: role in diagnosis and management in 130 consecutive patients evaluated for anterior segment tumours. *Br J Ophthalmol* 2005;89:950-955.
3. Konstantopoulos A, Hossain P, Anderson DF. Recent advances in ophthalmic anterior segment imaging: a new era for ophthalmic diagnosis? *Br J Ophthalmol* 2007;91:551-557.
4. Heiligenhaus A, Schilling M, Lung E, et al. Ultrasound biomicroscopy in scleritis. *Ophthalmology* 1998;105:527-534.
5. Char D. Intraocular biopsy. In: Singh AD, Damato BE, Pe'er J, Murphree AL, Perry J, editors. *Clinical Ophthalmic Oncology*. Philadelphia: Elsevier-Saunders, 2007:334-340.
6. Yap EY, Robertson DM, Buettner H. Scleritis as an initial manifestation of choroidal malignant melanoma. *Ophthalmology* 1992;99:1693-1697.
7. Yeo JH, Jakobiec FA, Iwamoto T, et al. Metastatic carcinoma masquerading as scleritis. *Ophthalmology* 1983;90:184-194.
8. Shields CL, Shields JA, Gross NE, et al. Survey of 520 eyes with uveal metastases. *Ophthalmology* 1997;104:1265-1276.

9. Elizalde J, de la Paz M, Barraquer RI. Tumors of the ciliary pigment epithelium. In: Singh AD, Damato BE, Pe'er J, Murphree AL, Perry J, editors. *Clinical Ophthalmic Oncology*. Philadelphia: Elsevier-Saunders, 2007:366-371.
10. Bornfeld N. Uveal metastatic tumors. In: Singh AD, Damato BE, Pe'er J, Murphree AL, Perry J, editors. *Clinical Ophthalmic Oncology*. Philadelphia: Elsevier-Saunders, 2007:322-327.
11. Kinkade S. Testicular cancer. *Am Fam Physician* 1999;59:2539-2544, 2549-2550.
12. Pavlidis N, Fizazi K. Cancer of unknown primary (CUP). *Crit Rev Oncol Hematol* 2005;54:243-250.





A



B