Ocular Immunology and Inflammation, 13:479–482, 2005

ISSN: 0927-3948 print; 1744-5078 online
DOI: 10.1080/09273940591004133

Taylor & Francis
Taylor & Francis Group

CASE REPORT

Masquerade Scleritis

Chrysanthi Kafkala, Yassine J. Daoud, Ian Paredes, and C. Stephen Foster
Ocular Immunology and Uveitis Service, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA, USA

ABSTRACT *Purpose:* To report two cases in which malignancy masqueraded as scleritis, delaying the diagnosis. *Methods:* Two patients initially diagnosed and treated for unilateral scleritis were referred for management of persistent inflammation. Additional evaluation uncovered underlying malignant processes. *Results:* The first patient presented with scleritis initially responsive to systemic corticosteroids, with relapse one month later. Upon referral, peripheral fundus examination revealed elevated lesions. Additional studies confirmed the diagnosis of choroidal melanoma. The patient was treated with proton-beam irradiation. The second patient developed necrotizing scleritis unresponsive to systemic steroids, methotrexate, and cyclophosphamide. A scleral biopsy disclosed an undifferentiated high-grade carcinoma, likely metastatic. Exenteration was performed. *Conclusions:* Scleritis can present a diagnostic challenge. It is often the sole initial manifestation of an occult systemic problem. Treatment-resistant scleritis should raise the suspicion of an infectious or malignant masquerade.

KEYWORDS Metastatic ocular carcinoma; scleritis; uveal melanoma

INTRODUCTION

The diagnosis of scleritis typically leads the ophthalmologist to obtain a detailed history, perform careful examination, and obtain laboratory tests in order to identify diseases associated with scleral inflammation. Half of the patients with scleritis have an associated systemic disease, and the scleritis is often the first clinical expression of that disease.[1] Identifying the underlying disease is critical for proper treatment and assessment of prognosis. Approximately 43% of scleritis cases are idiopathic, 48% are related to skeletal and connective tissue diseases, and an infectious agent is identified in 7%. Rarely does malignancy masquerade as scleritis. We report two cases, one a choroidal melanoma and the other an adenocarcinoma, which manifested initially as anterior diffuse and necrotizing scleritis, respectively.

Two important points are emphasized by this report: (1) a thorough initial examination and diagnostic evaluation are critical to achieve the correct diagnosis and (2) treatment-resistant scleritis should raise the suspicion of an infectious or malignant masquerade.

Accepted 24 April 2005.

Correspondence and reprint requests to: C. Stephen Foster, M.D., F.A.C.S., Immunology and Uveitis Service, Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston, MA 02114, USA. Tel: (617)-573-5549; Fax: (617)-573-3181; e-mail: fosters@uveitis.org

CASE REPORTS

Case 1

A 41-year-old Caucasian female was referred to the Ocular Immunology and Uveitis Service of the Massachusetts Eye and Ear Infirmary, in October 2002, for treatment of scleritis. Three months prior to presentation to our service, the patient complained of blurred vision, dull aching, and redness in her right eye. The ophthalmic examination performed at that time disclosed prominent scleral vessels superiorly, laterally, and inferiorly, and diffuse scleritis was diagnosed. The evaluation included complete blood count, fluorescent treponemal antibody absorption (FTA-Abs), rapid plasma reagin (RPR), erythrocyte sedimentation rate, rheumatoid factor, antinuclear antibodies, chest and sacroiliac x-ray, purified protein derivative (PPD), fasting blood sugar, and uric acid. The results of these studies were all normal or negative. The patient was treated with 80 mg prednisone daily. Her symptoms improved and prednisone was tapered over a period of three weeks. Three months later, the patient was referred to us because of recurrence of her scleritis. On presentation, she complained of redness and tenderness upon palpation of her right eye. The patient's visual acuities were 20/50 right eye and 20/20 left eye. Slit-lamp biomicroscopy disclosed a normal left eye. The right eye showed dilated scleral and episcleral vessels and 1+ cells in the anterior chamber. Dilated depressed peripheral fundus examination revealed elevated lesions just posterior to the lens temporally (Fig. 1). A submersion B-scan ultrasonogram showed a solid mass, 10.9 mm in height, in the region of the ciliary body (Fig. 2). Our retina oncology specialist concurred with our suspicion of melanoma. The patient refused enucleation. Tantalum rings were sutured around the borders defined with transillumination; the lesion measured 20 mm × 11 mm at the scleral surface. Proton-beam irradiation, 70 Gy over five sessions, was administered. Six months after the proton-beam irradiation, fundus examination showed that the tumor had regressed. One year after diagnosis of the choroidal melanoma, liver metastases were detected. The metastatic disease progressed rapidly, and the patient died in January 2004.

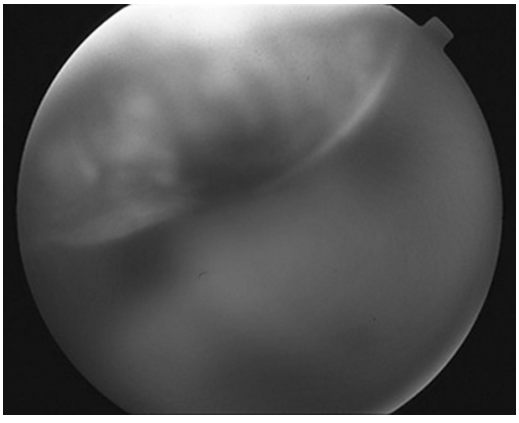

FIGURE 1 Dilated peripheral view of the retina with scleral depression. An elevated choroidal lesion is visible in the upper temporal area.

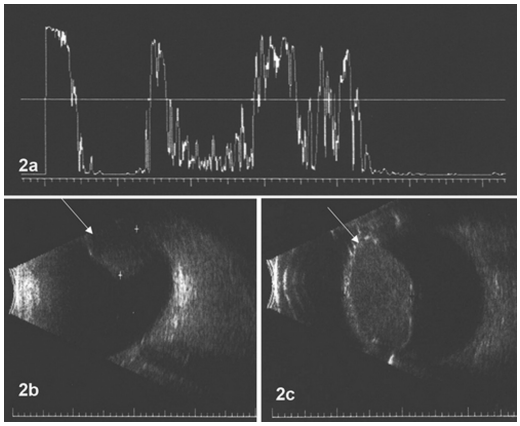

FIGURE 2 Right eye A-scan and submersion B-scan ultrasonogram of Case 1. (A) Non-standardized A-scan reveals a lesion with medium-to-low internal reflectivity and a fairly regular internal structure. (B, C) B-scan ultrasonography disclosed a very substantial tumor localized to the superotemporal anterior periphery (arrows).

Case 2

A 73-year-old Caucasian woman was first seen by us in January 2004, with a 10-month history of foreign-body sensation, redness, pain, and blurring of vision in her left eye. This had been treated with high-dose systemic corticosteroids, methotrexate, and subsequently cyclophosphamide. None of these treatments resulted in significant improvement. The patient was referred to our service for further management of her necrotizing scleritis. On examination, the patient's visual acuity was 20/25 in the right eye and 20/320 in the left eye. The left eyelid was swollen and slightly ptotic and scleral and episcleral injection was seen. We noted scleral thinning inferonasally, and material suggestive of a neoplastic tumor (Fig. 3). The pupil was ectopic nasally. A serologic evaluation was begun and a biopsy of the affected area was performed. During performance of the biopsy, we discovered an epibulbar mass and large areas of scleral necrosis. Histopathology disclosed numerous dysplastic malignant cells that were strongly positive

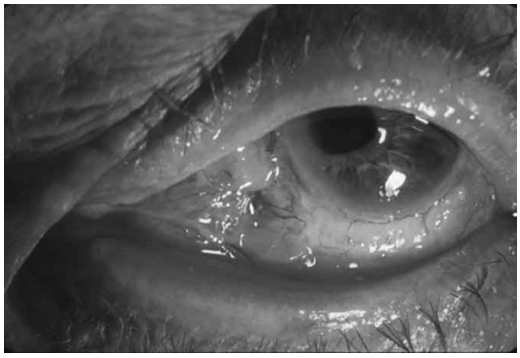

FIGURE 3 **Clinical picture of the affected left eye of Case 2. The lesion is seen inferonasally.**

for cytokeratin 903, pan-cytokeratin, and vimentin. These cells were also weakly positive for S100 and scattered cells were positive for calponin. CD68-positive macrophages were within the tumor (Fig. 4). These findings were consistent with an undifferentiated high-grade carcinoma of uncertain origin, likely metastatic. Orbital exenteration was subsequently performed.

DISCUSSION

Scleritis is a rare inflammatory ocular disorder. Most ophthalmologists may encounter one or two new cases of scleritis each year.[2] Scleritis can potentially have serious ocular complications, and about 50% of scleritis cases are associated with systemic or local infectious diseases, some of which may have lethal consequences.[1] The most common systemic diseases associated with scleritis are rheumatoid arthritis, Wegener's granulomatosis, polyarteritis nodosa, systemic lupus erythematosus, relapsing polychondritis, and inflammatory bowel disease.[1] Infections with organisms such as pseudomonas, aspergillus, herpes (simplex or zoster), or tuberculosis may cause severe scleritis that is difficult to treat.[2] Albeit rare, malignancies can masquerade as scleritis. Effective therapy is dictated by the diagnosis of the associated systemic or the infectious etiology. Therefore, every patient with scleritis must be evaluated by means of a detailed medical history, the performance of an eye and general physical examination, and the pursuit of appropriate laboratory and imaging investigation. Biopsy must be performed in treatment-resistant and in suspected masquerade cases.

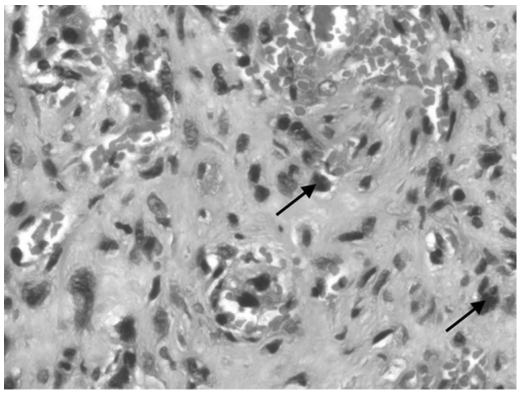

FIGURE 4 **Photomicrograph of the mass biopsy from Case 2. Numerous dysplastic malignant cells are evident (arrows). Stain: hematoxylin-eosin; original magnification: ×200.**

Choroidal melanoma is the most common primary intraocular tumor in adults. It is most common in Caucasians, 55–60 years of age. This tumor is often a fatal malignancy since it spreads hematogenously, mainly to the liver. Early diagnosis and treatment, therefore, are critical. Melanomas are often misdiagnosed or the diagnosis is delayed. Bove and Char[3] reported a notable number of patients with symptomatic uveal melanomas in whom the diagnosis was not established on initial ophthalmic examination.

Ocular inflammation can be the initial manifestation of choroidal melanomas. Fraser and Font[4] reported 22 of 450 cases of melanoma that presented initially as episcleritis, uveitis, endophthalmitis, or panophthalmitis. In our first patient, reported above, choroidal melanoma mimicked scleritis. That patient presented with pain and dilated episcleral and scleral vessels, cells in the anterior chamber, and blurred vision, all consistent with a usual presentation of diffuse scleritis. The inflammation responded to systemic corticosteroid treatment, with all the symptoms and findings in complete remission. Relapse of the disease one month later was also consistent with scleritis, which is typically characterized by recurrences. Yap et al.[5] reported three cases of plaque-like choroidal melanoma which, like our case, manifested initially as scleritis and the inflammatory component responded to treatment with corticosteroids. When scleritis recurred and the patient was referred to us, a peripheral fundus examination with scleral depression revealed an exudative retinal detachment associated with a pigmented multidomed-shaped choroidal mass. The A- and B-scans clearly demonstrated the tumor and supported the clinical suspicion of choroidal melanoma.

Diagnosing a choroidal melanoma as early in the course as possible is critical since prognosis is related to tumor size.[6,7] Our patient was treated with proton-beam irradiation, a procedure that preserves the eye in 75% of patients and useful (better than 20/200) visual

acuity in 49% of cases[8] and is associated with a 75.6% five-year survival.[8] At the follow-up visits, examination showed the tumor regressing. Nevertheless, the patient died two and a half years after initial presentation from melanoma metastasis to the liver.

The second case we presented is that of a metastatic carcinoma disguised as necrotizing scleritis. Metastatic carcinoma is the most common intraocular tumor. When the incidence of intraocular metastasis is viewed in relation to the calculated number of cancer cells delivered via the arterial route, the uveal tract is the most highly favored target site for the development of metastasis per unit of delivered cancer cells.[9] Duke-Elder stated that the vast majority of tumor emboli preferentially course through the 20 short posterior ciliary arteries to lodge in the posterior pole rather than transversing the two long posterior or five anterior ciliary arteries to reach the anterior segment of the eye.[10] Ferry and Font reported that the lung is the most frequent primary site of ocular metastatic cancer, followed by the breast.[11,12]

Necrotizing scleritis is a severe form of scleritis in which inflammation of the sclera leads to the destruction of the sclera itself. It is more common in women and is more often discovered in the context of rheumatoid arthritis, Wegener's granulomatosis, polyarteritis nodosa, or relapsing polychondritis. The usual symptoms are pain (the predominant feature), redness, decrease in vision, and photophobia.

Yeo et al.[13] described the common ocular symptoms and signs produced by metastatic tumors to the eye: decreased vision (80%), visible mass (72%), redness of the eye (56%), pain (56%), glaucoma (56%), iridocyclitis (44%), and hyphema (24%), obviously similar to our patient's signs and symptoms. In rare instances, ocular metastasis may be the first sign of a systemic primary.[14]

In order to prevent ocular morbidity from scleritis or mortality from the underlying malignancy, early diagnosis is obviously an important part of scleritis management. In instances of malignant or infectious scleritis masquerade, the ophthalmologist is best able to establish an early diagnosis and direct proper treatment by harvesting tissue for histopathologic analysis in those instances in which the inflammation is atypical and/or fails to respond in the expected way to anti-inflammatory therapy.

REFERENCES

[1] Akpek EK, Thorne JE, Qazi FA, Do DV, Jabs DA. Evaluation of patients with scleritis for systemic disease. *Ophthalmology.* 2004;111:501–506.

[2] Goldstein D, Tessler HH. Episcleritis, scleritis, and other scleral disorders. In: Yanoff M, Duker JS, editors. *Ophthalmology*. St. Louis, MO: Mosby Inc., 2004;511–519.

[3] Bove R, Char DH. Nondiagnosed uveal melanomas. *Ophthalmology.* 2004;111:554–557.

[4] Fraser Jr DJ, Font RL. Ocular inflammation and hemorrhage as initial manifestations of uveal malignant melanoma: incidence and prognosis. *Arch Ophthalmol.* 1979;97:1482–1486.

[5] Yap EY, Robertson DM, Buettner H. Scleritis as an initial manifestation of choroidal malignant melanoma. *Ophthalmology.* 1992;99:1693–1697.

[6] Panigel K, Hedelin G, Speeg-Schatz C, Sahel J, Brini A. Prognostic factors of choroidal melanoma: an anatomo-clinical retrospective and statistical study of 76 enucleated cases. *J Fr Ophtalmol.* 1992;15:410–414.

[7] Reader S, Grigg J, Billson FA. Choroidal melanoma: a review of the experience of the Sydney Eye Hospital Professorial Unit 1979–1995. *Aust NZ J Ophthalmol*. 1997;25:15–24.

[8] Fuss M, Loredo LN, Blacharski PA, Grove RI, Slater JD. Proton radiation therapy for medium and large choroidal melanoma: preservation of the eye and its functionality. *Int J Radiat Oncol Biol Phys.* 2001;49:1053–1059.

[9] Weiss L. Analysis of the incidence of intraocular metastasis. *Br J Ophthalmol.* 1993;77:149–151.

[10] Duke-Elder S, editor. *System of ophthalmology. Vol. IX: Diseases of the uveal tract*. St. Louis, MO: CV Mosby Co., 1966; 917.

[11] Ferry AP, Font RL. Carcinoma metastatic to the eye and orbit. I. A clinicopathologic study of 227 cases. *Arch Ophthalmol.* 1974;92:276–286.

[12] Ferry AP, Font RL. Carcinoma metastatic to the eye and orbit. II. A clinicopathologic study of 26 patients with carcinoma metastatic to the anterior segment of the eye. *Arch Ophthalmol.* 1975;93:472–482.

[13] Yeo JH, Jakobiec FA, Iwamoto T, Brown R, Harrison W. Metastatic carcinoma masquerading as scleritis. *Ophthalmology*. 1983;90:184–194.

[14] Tang RA, Kellaway J, Young SE. Ophthalmic manifestations of systemic cancer. *Oncology.* 1991;5:59-66; discussion 66-71.