Metastatic orbital dermatofibrosarcoma protuberans fibrosarcomatous variant treated with radiotherapy

Carlthan J. M. Ling, MD,[a] Erika Wheeler, MD,[b] and Shannath L. Merbs, MD, PhD[c]
Baltimore, Maryland

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INTRODUCTION

Dermatofibrosarcoma protuberans (DFSP) is a rare, locally-invasive soft-tissue tumor typically presenting as a plaque on the trunk of young adults.[1] Fibrosarcomatous transformation is associated with local recurrence, metastasis, and histologic loss of CD34 expression.[2,3] The authors describe an unusual case of a metastatic DFSP with fibrosarcomatous transformation presenting with proptosis from a large orbital mass that was treated with radiotherapy.

Abbreviation used:

DFSP: Dermatofibrosarcoma protuberans

CASE REPORT

37-year-old man with a history of DFSP presented to the emergency department for 3 weeks of painless right eye protrusion and intermittent blurry vision. On examination, vision in the right eye was 20/25, and pupils and color vision were normal. External examination was remarkable for superior and anterior displacement of his right eye with limited eye movement (Fig 1, *A*). Dilated examination revealed no evidence of optic nerve compression. Magnetic resonance imaging of the orbit and computerized tomography of the face with contrast showed a right inferior-lateral orbit mass measuring $4.0 \times 2.8 \times 3.1$ cm^3 that was causing displacement of the eye and associated straightening of the optic nerve (Fig 2).

The patient had an extensive oncologic history. He was initially diagnosed with DFSP at the age of 31, with a 20-cm lower left back mass that was treated with a wide local excision with 2 cm as the closest peripheral specimen margin (superior). The deep margin of the main specimen was < 0.5 mm, and a separately submitted additional periosteal deep margin was negative for tumor cells. He was lost to follow-up but remained disease-free for 5 years, until he developed shortness of breath and was found to have multiple right-sided pleural masses on computerized tomography of the chest, without evidence of local recurrence in the lower lumbar region. Metastatic DFSP was confirmed by bronchoscopy. The biopsy was positive for platelet-derived growth factor subunit B and 22q 13 translocation, but negative for CD34. The patient was started on imatinib 400 mg daily; however, he self-discontinued the treatment after 8 months due to side effects. Twenty-one months later, he developed a jaw mass in the right side that underwent fine-needle aspiration, revealing malignant spindle cells with loss of CD34 (Fig 3). He presented to the emergency department with right-sided proptosis and blurry vision 2 weeks later.

Given the tumor's location and size and the good vision in the right eye, extensive discussion about management of the orbital mass included both exenteration and palliative radiation and the risk of vision loss associated with both treatments. The patient decided on palliative radiation, receiving 40.05 Gy to the right orbit in 15 fractions. He was

From the Department of Ophthalmology and Visual Sciences[a]; and Department of Pathology, University of Maryland Medical Center, Baltimore[b]; and Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore.[c]

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Correspondence to: Shannath L. Merbs, MD, PhD, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, 419 W Redwood St Ste 420, Baltimore, MD 21201. E-mail: smerbs@som.umaryland.edu.

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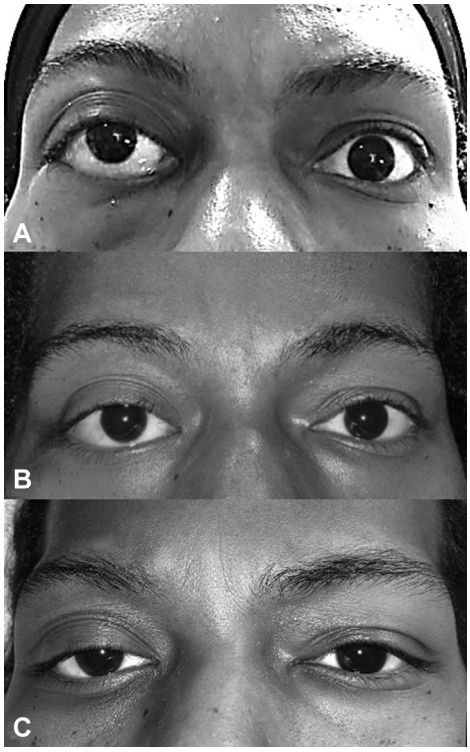

Fig 1. A, Initial patient presentation with proptosis and superior displacement of the right eye seen in primary gaze. **B,** Improvement of proptosis and superior displacement 2 weeks after radiotherapy. **C,** Maintenance of the improved right eye position 7 months after radiotherapy.

also started on sunitinib 37.5 mg daily, which he self-discontinued after 3 months due to intolerance. He was seen in the ophthalmology clinic 2 weeks after he started his radiotherapy with reduced proptosis (Fig 1, *B*) and a right visual acuity of 20/40. Six months after radiotherapy to the orbit, a total body 18F-flurodeoxyglucose positron emission tomography scan revealed no focal abnormal hypermetabolic activity in the orbit and no residual tumor. Seven months following radiotherapy, the patient was 20/25 on the right eye with a normal eye position and a slight limitation of adduction (Fig 1, *C*).

DISCUSSION

DFSP is a rare, locally-aggressive soft-tissue tumor with intermediate malignancy that presents as a slow-growing flesh-colored plaque on the trunk (50% of the cases), extremities (20%-30% of the cases), and head and neck (10%-15% of the cases).[1] The incidence of the disease is estimated to be 0.8-5 cases per 1 million persons, with a 4% rate of distant metastasis.[1] Primary orbital DFSP is rare with few published case reports.[4] Hematoxylin-eosin staining shows a fibroblastic proliferation of spindle cells arranged in a storiform pattern.[1] In DFSP, immunohistochemical staining is positive for CD34 and negative for factor XIIIa.[5] DFSP fibrosarcomatous variant characteristics include enlarged atypical nuclei, cytologic atypia, high mitotic count, fascicular arrangement, and loss of CD34.[2,3] In a review by Liang et al,[2] compared to DFSP, fibrosarcomatous variant of DFSP has a higher rate of local recurrence (29.8% vs 13.7%), metastasis (14.4% vs 1.1%), and death from disease (14.7% vs 0.8%). Our patient displayed fibrosarcomatous changes with metastases to lungs, face, and orbit over a period of 6 years.

While this patient was treated before the most recent guidelines were established, current clinical guidelines require Mohs surgery or surgery with peripheral and deep *en-face* margin assessment with 6-month follow-up examinations.[5] Tyrosine kinase inhibitors, including imatinib and sunitinib, target platelet-derived growth factor receptors and are used in locally advanced and unresectable DFSP.[3,6] Radiotherapy with 50-60 Gy has helped control recurrence in patients with conservative resections and positive margins.[7]

Metastatic DFSP to the orbit is very rare with only 1 published case report.[8] Orbital metastasis may present with proptosis, restricted eye movements, pain, decreased vision, and double vision. In general, orbital metastases are not candidates for therapeutic surgical intervention given the underlying systemic disease; however, if patients are nonresponsive to palliative chemotherapy and radiotherapy, then palliative surgery may be an option.[9] The previously published case of metastatic DFSP to the orbit[8] with very poor vision was managed with radiation and palliative chemotherapy. The tumor responded poorly to therapy, and orbital exenteration was performed for persistent discomfort and worsening disfigurement.[8] On presentation, our patient had excellent vision but with stretching of the optic nerve seen on imaging; with no intervention, continued growth of the lesion would have led to a compressive optic neuropathy with progressive visual loss.[10]

Our patient received a palliative dose of radiation to the orbit and a trial of chemotherapy, though this was discontinued due to intolerance. Two weeks following initiation of his treatment, he had decreased proptosis, almost complete normalization of right eye movements, and good vision. Six months later, the tumor could no longer be seen on imaging (Fig 2, *C*), and 7 months later, he had continued to maintain good vision in the right eye. To the authors' knowledge, this is the first case report of metastatic orbital DFSP that showed radiographic and clinical response to radiotherapy.

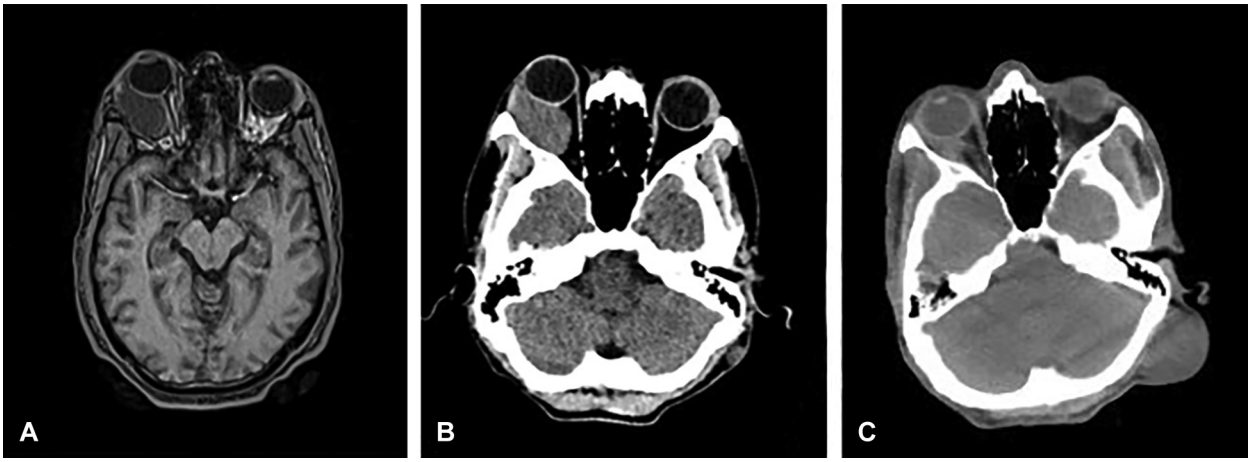

Fig 2. A, T1-weighted magnetic resonance imaging of the orbit without contrast showing a right hypointense lesion with intraconal and extraconal components, straightening of the optic nerve and tenting of the posterior globe. **B,** Computerized tomography (CT) of the face with contrast showing enhancing soft-tissue density in the extraconal and intraconal space of the right orbit. **C,** CT scan 6 months following radiotherapy showing no residual tumor, a small amount of fibrotic residual tissue with no mass effect, and a new left posterior auricular subcutaneous mass. *CT*, Computerized tomography.

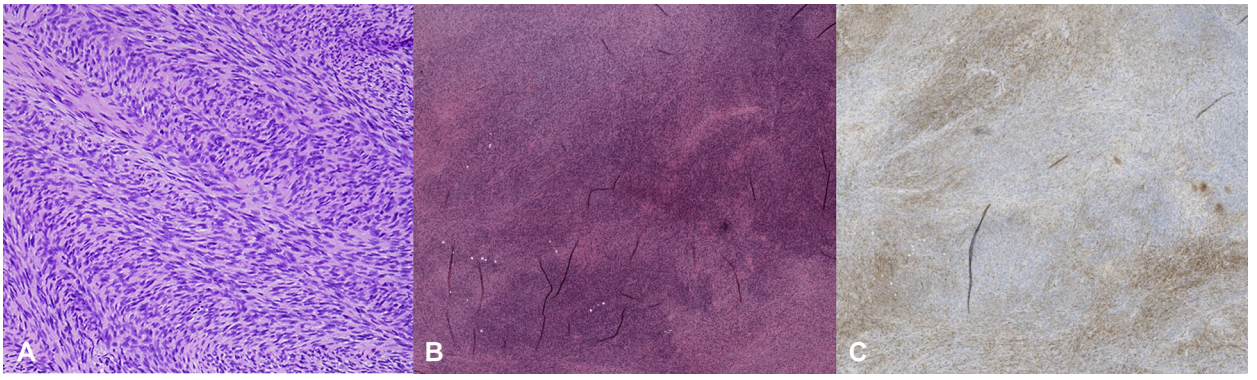

Fig 3. A, Histopathology of right jaw mass showing fibrosarcomatous transformation of dermatofibrosarcoma protuberans (DFSP) with characteristic herringbone growth pattern and hypercellularity. **B,** Denser, hyperchromatic areas consistent with the regions of fibrosarcomatous transformation. **C,** Hypercellular areas with fibrosarcomatous transformation lack CD34, while the areas of DFSP without fibrosarcomatous transformation retain CD34. DFSP, Dermatofibrosarcoma protuberans. (**A** and **B**, Hematoxylin-eosin stain; original magnifications; **C** brown staining: **A**, ×400; **B**, ×40, **C,** ×40.)

Conflicts of interest

None disclosed.

REFERENCES

1. Gloster HM Jr. Dermatofibrosarcoma protuberans. *J Am Acad Dermatol*. 1996;35(3 Pt 1):355-374; quiz 375-376. https://doi.org/10.1016/s0190-9622(96)90597-6. Erratum in: *J Am Acad Dermatol*. 1997;36(4):526.
2. Liang CA, Jambusaria-Pahlajani A, Karia PS, Elenitsas R, Zhang PD, Schmults CD. A systematic review of outcome data for dermatofibrosarcoma protuberans with and without fibrosarcomatous change. *J Am Acad Dermatol*. 2014;71(4):781-786. https://doi.org/10.1016/j.jaad.2014.03.018
3. Thway K, Noujaim J, Jones RL, Fisher C. Dermatofibrosarcoma protuberans: pathology, genetics, and potential therapeutic strategies. *Ann Diagn Pathol*. 2016;25:64-71. https://doi.org/10.1016/j.anndiagpath.2016.09.013
4. Sharma D, Singh G, Kakkar N, Jha V. Orbital dermatofibrosarcoma protuberans with frontal and ethmoid sinus involvement: A case report and brief review of literature. *Indian J Ophthalmol*. 2017;65(9):892-894. https://doi.org/10.4103/ijo.IJO_770_16
5. National Comprehensive Cancer Network (NCCN). *NCCN Clinical Practice Guidelines in Oncology Version 1. 2022-November 17, 2021: Dermatofibrosarcoma Protuberans*. Accessed on February 6 https://www.nccn.org/guidelines
6. Fu Y, Kang H, Zhao H, et al. Sunitinib for patients with locally advanced or distantly metastatic dermatofibrosarcoma protuberans but resistant to imatinib. *Int J Clin Exp Med*. 2015;8(5):8288-8294.

7. Ballo MT, Zagars GK, Pisters P, Pollack A. The role of radiation therapy in the management of dermatofibrosarcoma protuberans. *Int J Radiat Oncol Biol Phys*. 1998; 40(4):823-827. https://doi.org/10.1016/s0360-3016(97)00895-x
8. Nakra T, Cook T, Douglas RS, Goldberg RA. Dermatofibrosarcoma protuberans metastatic to the orbit. *Arch Ophthalmol*. 2004;122(8):1240-1241. https://doi.org/10.1001/archopht.122.8.1240
9. Goldberg RA, Rootman J, Cline RA. Tumors metastatic to the orbit: A changing picture. *Surv Ophthalmol*. 1990;35(1):1-24. https://doi.org/10.1016/0039-6257(90)90045-w
10. Behbehani R. Clinical approach to optic neuropathies. *Clin Ophthalmol*. 2007;1(3):233-246.