



# Paraneoplastic ocular sarcoidosis in the setting of recurrent rectal carcinoid tumor diagnosed by F<sup>18</sup>-fluorodeoxyglucose PET CT

Elizabeth D. Marlow, M.D.<sup>a,\*</sup>, Lisa J. Faia, M.D.<sup>a</sup>, Dafang Wu, M.D., Ph.D.<sup>b</sup>, Nathan Farley, M.D.<sup>a</sup>, Sandeep Randhawa, M.D.<sup>a</sup>

<sup>a</sup> Associated Retinal Consultants, P.C., Royal Oak, MI, USA

<sup>b</sup> Department of Nuclear Medicine, William Beaumont Hospital, Royal Oak, MI, USA

## ARTICLE INFO

### Keywords:

FDG PET

Nuclear medicine

Paraneoplastic ocular sarcoidosis

## ABSTRACT

**Purpose:** Nuclear medicine imaging can provide a noninvasive means of distinguishing inflammatory mass lesions from oncologic intraocular tumors.

**Observation:** We report a case of paraneoplastic ocular sarcoidosis with choroidal mass lesions that was initially concerning for choroidal metastasis of a primary carcinoid tumor. PET CT was utilized with two different tracers to characterize the choroidal mass as being FDG-avid, consistent with a sarcoid-like lesion, and lacking the Gallium (Ga-68) DOTATATE uptake of carcinoid tumor metastases.

**Conclusions and Importance:** Functional imaging is valuable to distinguish clinically similar inflammatory versus oncologic intraocular pathology.

## 1. Introduction

Paraneoplastic sarcoid reactions involving the eye are rare. Despite a well-established association between sarcoidosis or sarcoid-like reactions and malignancy in the medical literature, there are few previously published cases on paraneoplastic ocular sarcoidosis.<sup>3</sup> We report a case of ocular sarcoid-like reaction associated with recurrent rectal carcinoid tumor. The patient's presentation was notable for a choroidal mass initially concerning for metastasis. Position emission tomography (PET) distinguished the choroidal mass as a manifestation of a sarcoid-like reaction rather than a metastasis by applying Gallium (Ga-68) DOTATATE to screen for carcinoid tumor and F<sup>18</sup>-fluorodeoxyglucose (FDG) for sarcoidosis.

## 2. Case report

A 63-year-old woman with a history of rectal carcinoid tumor presented with bilateral decreased vision and new photophobia. Exam was notable for subnormal vision (best corrected visual acuity 20/50 both eyes), unremarkable intraocular pressures (7 mmHg right eye, 6 mmHg left eye), and bilateral 1+ cells in the anterior chamber, trace vitreous cells, and choroidal folds. The left eye had a raised, choroidal, amelanotic lesion in the midperiphery with surrounding subretinal fluid.

Ultrasound of both eyes revealed choroidal thickening in the macula. The dome-shaped avascular mass had an irregular surface contour and diffuse margins with medium to high reflectivity (Fig. 1). There was no extraocular extension.

The patient's history was notable for biopsy-proven grade-1 (carcinoid) neuroendocrine tumor of the rectosigmoid colon in 2007 that was treated with resection. Ten years after achieving initial remission, a local metastasis to presacral and perirectal lymph nodes were detected on surveillance imaging. Following another surgical resection, she was again considered in remission. A whole-body PET CT in 2018 showed no evidence of somatostatin receptor-avid malignancy or metastasis.

The patient also had a history of multiple sclerosis previously treated with methotrexate and rituximab. These were stopped at the time of her carcinoid tumor recurrence to avoid concurrent immunosuppression and increased risk of hematologic malignancy. At the time of her presentation with bilateral uveitis, she remained off immunosuppression.

Upon her presentation with new panuveitis in both eyes and a choroidal mass in the left eye, concern was for spread of carcinoid tumor versus a paraneoplastic reaction, namely sarcoidosis. To clarify the etiology of her choroidal lesion, she underwent two PET scans including the abdomen, chest, and head. One scan was conducted with Gallium (Ga-68) DOTATATE to image somatostatin-expressing neuroendocrine tumor, and the other with FDG to screen for sarcoidosis. The PET scan

\* Corresponding author. Associated Retinal Consultants, P.C. 3555 West 13 Mile Road, Royal Oak, MI, 48073, USA.

E-mail address: [emarlow@bayarearetina.com](mailto:emarlow@bayarearetina.com) (E.D. Marlow).

<https://doi.org/10.1016/j.ajoc.2020.100887>

Received 11 May 2020; Received in revised form 9 August 2020; Accepted 16 August 2020

Available online 20 August 2020

2451-9936/© 2020 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

with Gallium (Ga-68) DOTATATE revealed uptake exclusively in the rectum without evidence of metastasis. An MRI of the pelvis later confirmed a 12mm enhancing focus in the presacral region most consistent with recurrence of the carcinoid tumor (image not shown). The FDG PET showed focally increased tracer activity corresponding to a soft-tissue density within the left globe and orbit, suggesting that the choroidal mass was a sarcoid-like lesion (Fig. 2B). There was no discrete abnormal FDG uptake in the chest, abdomen, or pelvis (imaging not shown).

Following the imaging, she was advised to restart rituximab for her choroidal sarcoid-like granuloma. The patient declined oral steroids due to previous intolerance but showed improvement in her intraocular inflammation and resolution of the choroidal lesion on rituximab (Fig. 1F).

### 3. Discussion

Paraneoplastic sarcoidosis has been described in the setting of hematologic and solid malignancies with rates of association as high as 20% with lymphoma and 4% with carcinomas.<sup>1</sup> Sarcoidosis remains a diagnosis of exclusion based on nonnecrotizing granulomas in multiple organ systems, negative testing for other granulomatous diseases, and histopathologic confirmation, when available. In paraneoplastic sarcoidosis, the granulomas may be isolated, most often occurring in lymph nodes and tissue adjacent to the malignancy, and may lack the multiorgan involvement of systemic sarcoidosis.<sup>2,3</sup> Although distant nonnecrotizing granulomas due to sarcoid-like reactions have been documented to affect a variety of organs, it has rarely been described to affect the eyes.<sup>3</sup>

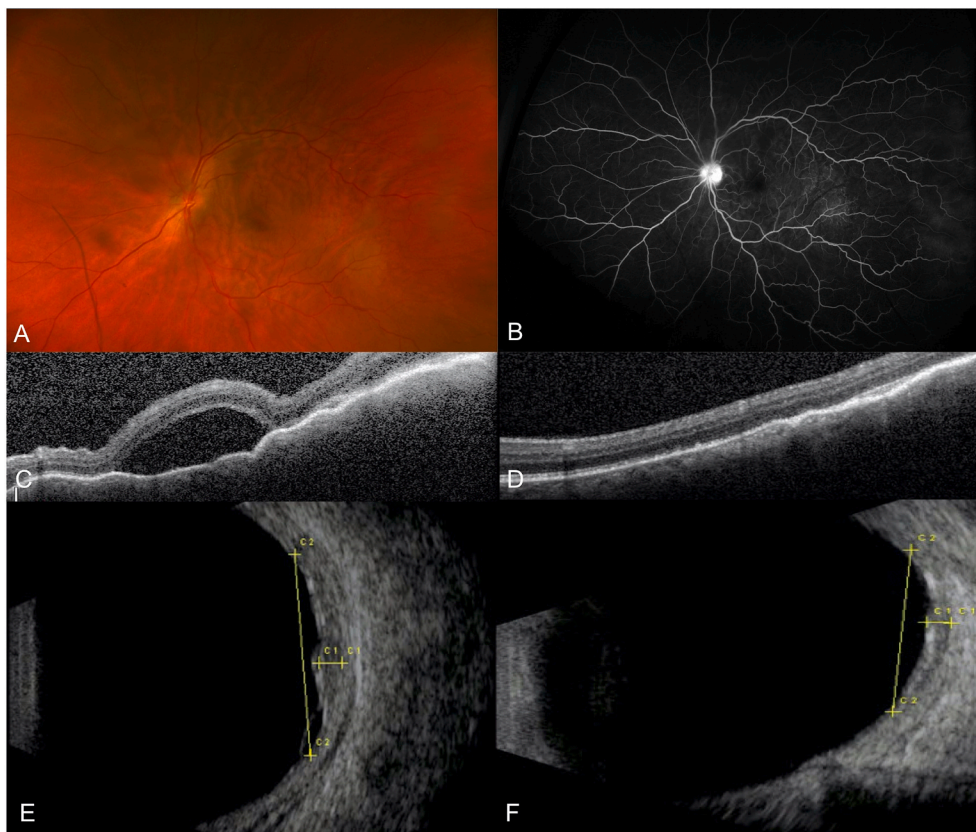
The relationship between paraneoplastic sarcoidosis and malignancy remains unclear. One postulated mechanism is that tumor cells release antigens or metabolites into systemic circulation that stimulate a T-cell-mediated host response prompting granulomatous inflammation in

genetically susceptible individuals.<sup>2</sup> Another possibility is that sarcoidosis may be indicative of a dysregulated immune system that is permissive of malignancy.<sup>1</sup>

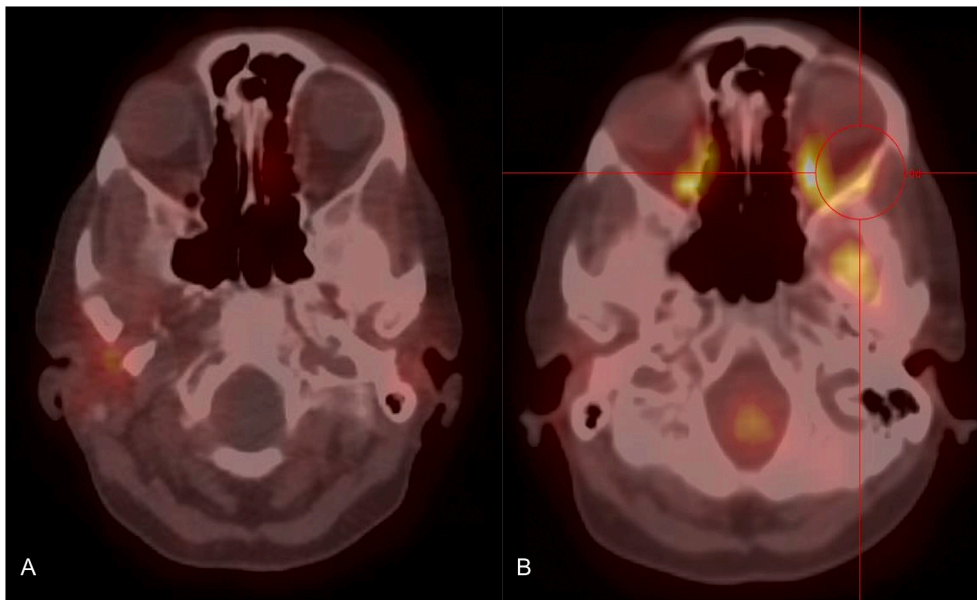
Distinguishing localized sarcoid-like reactions from tumor recurrence is of critical importance in initial tumor staging and surveillance imaging for recurrence. It has been shown that PET imaging with In-111 pentreotide radiotracer can distinguish the somatostatin-avid carcinoid tumors from FDG-avid sarcoid granulomas and aid in accurate imaging interpretation.<sup>4</sup> Our hospital utilizes Gallium (Ga-68) DOTATATE, a somatostatin analogue, to screen for carcinoid tumors. Gallium (Ga-68) DOTATATE has also been shown to detect sarcoid lesions, though with less sensitivity and specificity compared to FDG.<sup>5,6</sup>

Ocular sarcoid-like reactions associated with malignancy are particularly rare. Balasubramaniam et al. described a series of 5 cases in which ocular-sarcoid reactions were shown to present before, during, or following cancer.<sup>3</sup> In our own case, the sarcoid-like reaction occurred in the setting of remission but prompted further work-up revealing a tumor recurrence. The gold-standard for diagnosis of sarcoid and sarcoid-like intraocular lesions is vitrectomy with biopsy. However, this diagnostic technique is invasive and may be limited by the location of lesions of interest. Non-invasive functional imaging allows the opportunity to avoid chorioretinal biopsy and potentially allow greater visual recovery.

In patients with malignancy who were screened for paraneoplastic sarcoidosis by FDG PET, sarcoid-like reactions were present in 1.1% of cancer patients and was most often noted in the setting of recurrence rather than initial staging.<sup>7</sup> All of the cases of paraneoplastic sarcoidosis reported in Chowdhury et al.'s study had FDG-avid mediastinal lesions.<sup>7</sup> In contrast, only 3 of the 5 cases of ocular sarcoid-like reactions previously published were described as having mediastinal or hilar adenopathy. Our patient showed isolated FDG-uptake in the left globe without uptake in the chest, abdomen, or pelvis. Mediastinal or hilar adenopathy is a key diagnostic criterion for the diagnosis of systemic and ocular sarcoidosis, and its absence in cases of paraneoplastic ocular sarcoid is of



**Fig. 1.** Baseline and follow-up imaging for choroidal mass in paraneoplastic ocular sarcoidosis. **A.** Wide-field fundus photographs of the left eye revealing choroidal folds. Left eye shows disc hyperemia and an amelanotic choroidal lesion. **B.** Fluorescein angiography confirms choroidal folds and reveals granular hyperfluorescence overlying the choroidal lesion. There is late leakage at the disc. **C.** Optical coherence tomography (OCT) shows subretinal fluid overlying the choroidal mass. **D.** These changes are resolved on follow-up imaging after initiating Rituximab. **E.** Ultrasonography of choroidal lesion, which displayed medium to high internal reflectivity. C1 = 1.54mm, C2 13.72mm. Lesion measured 13.7 mm × 12.4 mm × 1.7mm in its greatest dimensions. **F.** Follow-up ultrasonography after treating with Rituximab shows decreased size; C1 1.25mm, C2 12.21mm.



**Fig. 2.** PET CT imaging of choroidal mass to distinguish paraneoplastic sarcoidosis from metastases. Head imaging on combined PET CT with Gallium (Ga-68) DOTA-TATE (A) was negative for both the globe and orbit while F<sup>18</sup>-fluorodeoxyglucose (FDG) (B) demonstrated increased FDG radiotracer uptake in the left globe and orbit. The signal denoting FDG-avidity in the left lateral orbit is surrounded by a red circle. There is bilateral, asymmetric FDG-avidity overlying the medial aspect of both orbits marked by yellow signal greater on the left (maximum standard uptake value (SUV) 7.1) than the right (maximum SUV 5.7). . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

unclear significance.<sup>8</sup>

#### 4. Conclusions

This is the first published case of ocular sarcoid-like reaction in the setting of rectal carcinoid tumor recurrence and demonstrates that functional radiography can characterize intraocular lesions as a paraneoplastic process rather than metastases. It remains to be determined whether imaging can supplant histopathology of ocular structures to confirm the diagnosis of ocular sarcoid-like reactions.

#### Patient Consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

#### Declaration of competing interest

This paper has not been previously presented or published.

There is no funding or grant support.

The following authors have no financial disclosures: EM, LF, DW, NF, SR.

All authors attest that they meet the current ICMJE criteria for

Authorship.

#### Acknowledgements

None.

#### References

1. Brinker H. Solid tumors preceding or following sarcoidosis. *Med Pediatr Oncol.* 1987; 15:82–88.
2. Brinker H. Sarcoid reactions in malignant tumours. *Canc Treat Rev.* 1986;13:147–156.
3. Balasubramanian S, Salomao D, Davies J, et al. Paraneoplastic sarcoid-like reactions in the eye. *Retina.* 2015;35(4):789–797.
4. Avram A, Mackie G, Schneider B, Kalemkerian G, Shulkin B. Differentiation between carcinoid and sarcoid with F-18 FDG PET and In-111 pentreotide. *Clin Nucl Med.* 2006;31:197–200.
5. Sharma S, Singh A, Sharma S, Tripathi M, Das C, Kumar R. Gallium-68 DOTA-NOC PET/CT as an alternative predictor of disease activity in sarcoidosis. *Nucl Med Commun.* 2018;39(8):768–778.
6. Keijsers RG, Grutters JC, Thomeer M, et al. Imaging the inflammatory activity of sarcoidosis: sensitivity and interobserver agreement of (67) Ga imaging and (18)F-FDG PET. *Q J Nucl Med Mol Imaging.* 2011;55(1):66–71.
7. Chowdhury FU, Sheerin F, Bradley KM, Gleeson FV. Sarcoid-like reaction to malignancy on whole-body integrated <sup>18</sup>F-FDG PET/CT: prevalence and disease pattern. *Clin Radiol.* 2009;64:675–681.
8. Herbert CP, Rao NA, Mochizuki M. Members of the scientific committee of first international workshop on ocular sarcoidosis. International criteria for the diagnosis of ocular sarcoidosis: results on the first international workshop on ocular sarcoidosis (IWOS). *Immunol Inflamm.* 2000;17(3):160–169.