American Journal of Ophthalmology Case Reports 35 (2024) 102076

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Video

Paraneoplastic ocular sarcoid-like reaction in the setting of pulmonary sarcoid-like reaction and lung adenocarcinoma: A case report and literature review

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ARTICLE INFO

Keywords:
Sarcoidosis
Masquerade syndrome
Uveitis
Paraneoplastic syndrome
Lung adenocarcinoma

ABSTRACT

Purpose: To describe ocular sarcoid-like reaction as a unique manifestation of paraneoplastic syndrome in the context of concurrent pulmonary sarcoid-like reaction and lung adenocarcinoma.
Methods: Single case report and narrative review.
Results: A 59-year-old male patient presented with a year-long history of diminished vision and weight loss. Clinical examination revealed panuveitis and multiple chorioretinal lesions. A CT scan of the chest revealed mediastinal and hilar lymphadenopathy as well as a spiculated right lower lung nodule concerning for malignancy. Subsequent bronchoscopy and biopsy confirmed lung adenocarcinoma and non-caseating granulomas in sentinel lymph nodes.
Conclusion: Although pulmonary granulomatous reaction can be seen in the setting of lung malignancy, and ocular sarcoid-like reaction may present as a paraneoplastic manifestation of systemic malignancy, the presence of concomitant pulmonary and ocular sarcoid-like reactions distinguishes this case. The findings underscore the importance of a systemic workup for patients with concerning constitutional symptoms, as paraneoplastic syndromes and metastatic diseases may mimic uveitis. Recognition of paraneoplastic sarcoidosis as a potential clinical manifestation is essential, especially in patients with chronic illness indicators, necessitating a comprehensive evaluation for malignancy.

1. Introduction

Sarcoidosis is a multi-systemic disease defined by idiopathic non-caseating granulomas in affected organs.[1] Sarcoidosis has an established but complex association with cancer. It is unclear from the literature whether sarcoidosis precipitates malignancy or stems from the body's immune response to cancer cells.[2] Sarcoid-like reaction (SLR) is a granulomatous immune response that is histologically indistinguishable from sarcoidosis in patients who do not fulfill the diagnostic criteria for sarcoidosis.[1–4] SLR presenting as a paraneoplastic syndrome systemically independent of metastasis or direct invasion of cancer is referred to as paraneoplastic sarcoidosis in this report. This phenomenon is associated with multiple types of cancers, with the most common including gastrointestinal, hematological, pulmonary, gynecological, and head/neck tumors.[2] The granulomatous reaction can be found both in the sentinel lymph nodes of solid tumors, and in distant locations such as the spleen, liver, or bone.[5] While systemic paraneoplastic sarcoidosis has been described, ocular SLRs as a manifestation of a paraneoplastic syndrome is reportedly rare.[6,7] The current study is that of a patient presenting with panuveitis and chorioretinitis secondary to paraneoplastic sarcoidosis in the setting of subsequently diagnosed lung adenocarcinoma.

2. Case

A 59-year-old male presented as a referral for panuveitis after experiencing declining vision and floaters for a year. He endorsed an 85-pack year smoking history with current use of a half pack per day. His

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https://doi.org/10.1016/j.ajoc.2024.102076
Received 8 November 2023; Received in revised form 9 April 2024; Accepted 29 April 2024
Available online 15 May 2024

ocular history included bilateral open angle glaucoma for which he had undergone a glaucoma valve procedure in the right eye a year prior to presentation. He endorsed a strong family history of cancer; his brother was diagnosed with lung cancer and his twin sister was diagnosed with throat cancer. Of note, he was cachectic with temporal wasting on presentation, and his wife noted dramatic weight loss in the past year.

His visual acuity was significantly decreased to light perception in the right eye and 20/200 in the left eye, with intraocular pressures of 4 and 14 mmHg in the right and left eyes, respectively. Bilateral anterior chambers appeared normal with the Ahmed glaucoma valve still well positioned on the left side. The view to the posterior segment in the right eye was significantly hindered by dense vitreous haze. Although fundus photos showed some view into the posterior pole, primary vision loss is presumed to be due to optic nerve damage indicated by the optic nerve pallor. Relative afferent pupillary defect was not noted because the pupils were nonreactive secondary to iris atrophy and synechiae. The view in the left eye was clearer and multifocal yellow chorioretinal lesions were noted (Fig. 1A). On fluorescein angiography, vascular leakage including a small amount of angiographic cystoid macular edema (CME) was visible in the left eye. No obvious CME was noted on OCT. On indocyanine green angiography, hypocyanescent lesions were visualized in the left eye (Fig. 1B). Previously ordered laboratory studies from the referring physician were notably negative for syphilis (T. pallidum), tuberculosis (QuantiFERON gold), and birdshot chorioretinopathy (HLA-A29). His angiotensin converting enzyme was elevated to 75.

Further testing was performed to rule out vitreoretinal lymphoma. MRI of the brain was negative. Uveal lymphoma was also on the differential, as was sarcoidosis, and CT chest/abdomen/pelvis was performed to evaluate further for these conditions. CT of the abdomen/pelvis returned negative. However, CT chest demonstrated a 1.5 cm right lower lung spiculated nodule in addition to partially calcified mediastinal and hilar lymphadenopathy.

The patient was referred to interventional pulmonology and received an endobronchial ultrasound-guided fine-needle aspiration biopsy of the right lower lobe nodule and sentinel lymph nodes (Fig. 2A and B). The nodule stained positive for TTF-1 and Napsin-A confirming the diagnosis of lung adenocarcinoma. Cytology of biopsied lymph nodes demonstrated non-caseating granulomas. PET-CT also demonstrated less uptake of the nodes relative to the lung mass, making them more likely secondary to granulomatous inflammation.

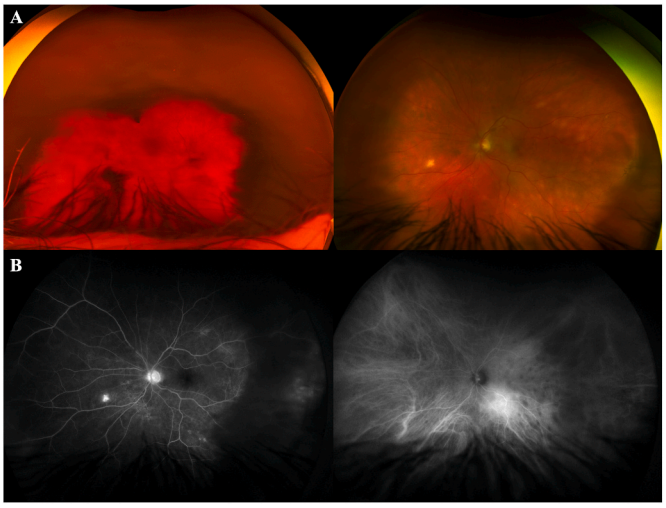

Fig. 1. A) Fundus photo of the right eye demonstrates an obstructed posterior segment view secondary to synechiae and vitreous haze, and deep yellow chorioretinal lesions in the left eye. B) Fluorescein angiography of the left eye (left) demonstrates hyperfluorescence of the optic disc and retinal vascular leakage. The indocyanine green angiography of the left eye (right) shows hypocyanescent areas corresponding to the chorioretinal lesions.

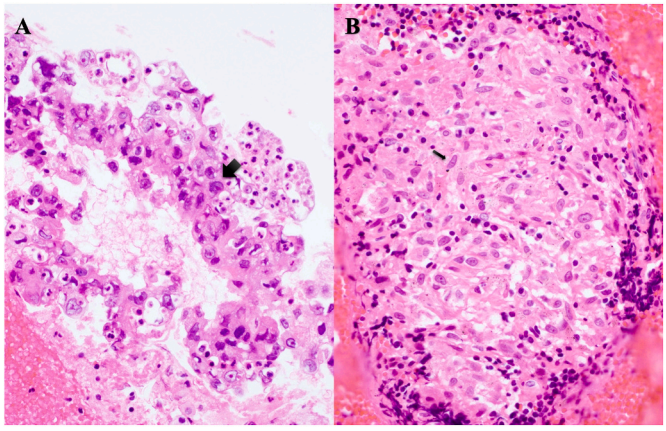

Fig. 2. Histopathology of biopsies (Hematoxylin and eosin, 400x).
A) Right lower lobe lung mass showing adenocarcinoma with markedly atypical cohesive epithelial cells with atypical nuclei and prominent nucleoli (arrow) and mixed inflammation. B) Station 12R lymph node showing a non-caseating granuloma composed of epithelioid histiocytes (arrow) and scattered small lymphocytes.

The clinical manifestation of the patient's uveitis was most consistent with SLR uveitis given the presence of multifocal choroidal lesions, and this in concert with the patient's pulmonary granulomatous inflammation made secondary paraneoplastic sarcoidosis the most likely diagnosis. The recommendation was made for the patient to undergo systemic radiotherapy and surgical excision of the lung mass, with the use of local steroid therapy for treatment of uveitis in the meantime.

3. Discussion

In paraneoplastic systemic manifestations of SLR, non-necrotizing granulomas often occur adjacent to the tumor in nearby tissue or sentinel lymph nodes, and less frequently present with the multisystemic reaction seen in systemic sarcoidosis. Eye involvement in paraneoplastic sarcoidosis is uncommon but has been reported. Balasubramaniam et al. reviewed four cases of ocular SLR secondary to systemic malignancies of hematologic origin (two patients), endometrial carcinoma (one patient), and renal cell carcinoma (one patient).[7] All patients had non-necrotizing granulomas confirmed on biopsy. The patients in this series demonstrated a variety of ophthalmic findings including conjunctival follicular reaction, vitreitis, retinal vascular leakage, and chorioretinitis. As in the case described herein, two of the patients had SLR that preceded their malignancy diagnosis. Marlow et al. also described a patient presenting with decreased vision, photophobia, and a choroidal lesion and found to have recurrent rectal carcinoid tumor. F18-Fluorodeoxyglucose PET-CT was used to determine that the choroidal lesion was more likely a SLR rather than metastasis of the primary malignancy.[6] In addition, Salman et al. performed a retrospective observational study of chronic lymphocytic leukemia in which seven patients developed ocular SLR after malignancy diagnosis and one patient with ocular SLR prior to the malignancy diagnosis.[8] Diagnosis of ocular SLR was determined either clinically or by concurrent liver biopsy with non-necrotizing granulomas in these eight cases.

Although these cases have described SLR in the setting of systemic malignancies, SLR uveitis in the setting of simultaneous pulmonary SLR and lung adenocarcinoma by histopathology have not been extensively reported in the existing literature. This observation is based on a literature review conducted on April 2, 2024, utilizing PubMed and Google Scholar using the key words sarcoidosis, sarcoid-like reaction uveitis, ocular sarcoid-like reaction, pulmonary sarcoid-like reaction, paraneoplastic sarcoidosis, and lung adenocarcinoma. Furthermore, only three other cases apart from this report describe ocular SLR leading to the

diagnosis of cancer.[7,8] This case serves as an example of paraneoplastic sarcoidosis as a masquerade with systemic findings that, if not pursued further, might have been misdiagnosed as presumed isolated pulmonary sarcoidosis. As described in the aforementioned case report by Marlow et al., paraneoplastic sarcoidosis that presents as an isolated choroidal lesion can also create uncertainty of the diagnosis by masquerading as a metastatic lesion.

The exact etiology of paraneoplastic sarcoidosis is unknown. One theory that represents a better prognosis for the patient, is that paraneoplastic sarcoidosis is the body's manifestation of an immune response to the cancer.[2] The notable difference in management of primary ocular sarcoidosis as compared to paraneoplastic sarcoidosis is that the former often requires systemic immunosuppressive therapy for long-term control, while the latter is managed by treatment of the primary malignancy. In our case, there is no long-term follow-up data on resolution of SLR with malignancy treatment because unfortunately the patient had subsequent spinal metastasis which limited his mobility and clinic follow-up. A causal relationship is not able to be concretely established; thus, it is important to acknowledge the possibility that these findings may have been incidental. However, the temporal onset of concomitant cachexia and vision loss provides greater support that the ocular and pulmonary SLRs are interrelated paraneoplastic phenomena.

In conclusion, the case described in this report demonstrates the complexity of diagnosing ocular SLR and the importance of a complete systemic workup for patients with concerning constitutional symptoms, as paraneoplastic and metastatic conditions can masquerade as uveitis. Paraneoplastic sarcoidosis should be considered in the differential diagnosis for patients with typical ocular findings in the setting of weight loss or other indicators of chronic illness. Diagnosis of paraneoplastic sarcoidosis requires a systemic evaluation for malignancy, including ancillary testing such as PET-CT and diagnostic biopsy when appropriate. Treatment of the systemic malignancy in many cases leads to resolution of the SLR.[7]

Data

Data not available due to no datasets being generated in this report.

CRediT authorship contribution statement

Grace L. Casado: Writing – review & editing, Writing – original draft, Validation, Resources, Conceptualization. **Erika Robinson:** Writing – review & editing, Writing – original draft, Visualization, Validation, Conceptualization. **Noreen Khan:** Writing – review & editing, Writing – original draft, Data curation. **Vishak John:** Validation, Supervision, Data curation. **Arthi G. Venkat:** Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors report there are no competing interests to declare.

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