CASE REPORT

Atypical sarcoidosis-associated uveitis: diagnostic challenges

Jasmina Cehajic Kapetanovic,^{1,2} Nicholas P Jones,^{1,2} Laura R Steeples^{1,2}

¹Ophthalmology, Manchester Royal Eye Hospital and Manchester Academic Health Sciences Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK

²Faculty of Biology, Medicine and Health, Institute of Human Development, University of Manchester, Manchester, UK

Correspondence to Professor Nicholas P Jones, nicholas.jones@mft.nhs.uk

Accepted 15 May 2018

SUMMARY

Sarcoidosis is a multisystem disease of unknown aetiology with pulmonary involvement in most patients. Uveitis is common and often characteristic. We report a case of ocular sarcoidosis with grossly atypical contiguous optic neuropathy and choroiditis and describe the diagnostic challenges in this highly unusual presentation. High-dose systemic corticosteroid and immunosuppressive treatment was required for sustained control of intraocular inflammation.

BACKGROUND

Uveitis is reported in 30%–70% of patients with sarcoidosis and is often the first recognised manifestation.¹ Presentation is clinically variable but the signs compatible with sarcoidosis are internationally accepted.^{2,3} This patient presented with highly atypical aggressive uveitis and profound visual loss. We highlight the significant diagnostic challenges and demonstrate the application of investigation and imaging techniques, including recent developments, to establish a diagnosis and exclude serious differential diagnoses including masquerade conditions and infection.

CASE PRESENTATION

A 55-year-old Caucasian woman presented to the Manchester Uveitis Clinic with a 6-week history of progressive deterioration in vision in the right eye. Her right eye was amblyopic (best-corrected visual acuity (VA) 0.3 LogMAR). She had type 2 diabetes mellitus, systemic hypertension, migraines, depression, menorrhagia and previous ovarian cyst. She took metformin, alogliptin, propranolol and fluoxetine. There was no history of foreign travel, she was a non-smoker and was teetotaler. She had undergone BCG vaccination, had no history of tuberculosis (TB) and no known TB contacts.

There were no respiratory symptoms, no history of malignancy and no constitutional symptoms such as weight loss, fatigue or night sweats.

At presentation, VA was hand movements right and 0.1 LogMAR left. She had a right relative afferent pupillary defect (RAPD). The right blind spot was enlarged. There was moderate panuveitis and marked optic nerve head infiltration and oedema and contiguous large choroidal masses with overlying secondary serous retinal detachment extending to the macula (figure 1A). The left eye was normal. Full systemic examination was unremarkable.

INVESTIGATIONS

High-resolution swept-source optical coherence tomography (SS-OCT) showed multiple posterior pole choroidal and optic nerve lesions with exudation into the intraretinal and subretinal spaces (figure 2). Wide-field fundus fluorescein angiography revealed active papillitis but no retinal vasculitis. Ocular ultrasonography confirmed lobular choroidal and optic nerve masses with uneven surface and high internal reflectivity suspicious of choroidal metastases. Contrast-enhanced MRI brain and orbits demonstrated non-specific enhancement of the posterior globe but no intracranial lesions or convincing enhancement of the retrobulbar optic nerve; neither inflammation nor malignancy could be excluded.

Full blood count, renal and hepatic function and inflammatory markers were normal. Serum ACE was normal. Mantoux test (0 mm induration), gamma interferon, syphilis and HIV testing were negative. Tumour markers including CA 125 and 19-9 were negative. Ultrasound of abdomen and pelvis was normal. Chest X-ray was normal but CT of chest, abdomen and pelvis demonstrated mediastinal and hilar lymphadenopathy. 18F-Fluorodeoxyglucose positron emission tomography CT revealed multifocal enhancement within cervical, hilar, mediastinal, subcarinal, subdiaphragmatic, inguinal and left popliteal lymph nodes (figure 3). No pulmonary lesions were seen. Uptake in the left iliac bone was noted alongside non-specific uptake in the liver. These features were in keeping with sarcoidosis, but malignancy could not be excluded, particularly in the liver. Rapid tissue diagnosis was necessary and endobronchial ultrasound (EBUS)-guided biopsy was performed. Non-caseating granulomatous inflammation at three separate sites, entirely consistent with sarcoidosis, was identified. Cytology and culture showed no evidence of malignancy or TB.

Figure 1 Wide-field fundus images (Optos). (A) Optic nerve swelling and peripapillary choroidal granulomas at presentation and (B) at 6 months follow-up showing scarring and subretinal fibrosis.

To cite:

Cehajic Kapetanovic J, Jones NP, Steeples LR. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-225137

Figure 2 Colour fundus photographs (left) and OCT scans (right) with orientation of the OCT shown in green. (A) Superior to optic nerve showing large choroidal elevation and subretinal fluid. (B) Transecting the optic nerve demonstrating gross optic nerve swelling and choroidal elevation superior and inferior to the nerve due to choroidal granuloma and (C) temporal to the optic nerve, capturing the central macular area showing extensive subretinal fluid, choroidal elevation and disruption of the normal foveal appearance. OCT, optical coherence tomography.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included ocular metastatic disease, inflammation (in particular sarcoidosis and TB) and primary intraocular lymphoma.

TREATMENT

Following a diagnosis of biopsy-proven sarcoidosis and exclusion of infectious causes and underlying malignancy the patient was admitted for intravenous methylprednisolone (1 g/day for 3 days) followed by high dose oral prednisolone (80 mg/day). Oral

Figure 3 18F-Fluorodeoxyglucose positron emission tomography CT (PET scan). There is multifocal enhancement including cervical, hilar, mediastinal, subcarinal, subdiaphragmatic, inguinal and left popliteal lymph nodes but no pulmonary lesions were identified. Uptake in the left iliac bone was noted alongside with a non-specific uptake in the liver.

Figure 4 Serial OCT of the optic nerve demonstrating progressive resolution of swelling, choroidal elevation and subretinal fluid at: (A) 1 month; (B) 2 months and (C) 4 months post-treatment. Evidence of peripapillary chorioretinal scarring and subretinal fibrosis temporal to the nerve was seen on colour photography (D) and OCT (C). The macular structure was restored with resolution of choroidal elevation and subretinal fluid (E). OCT, optical coherence tomography.

azathioprine (50 mg twice daily) was given and steroids were tapered according to clinical response.

The response to treatment was rapid and 1 month later the right visual acuity (RVA) improved to 0.7 LogMAR and there was reduction in uveitis, papillitis and choroidal granulomas with partial resolution of intraretinal and subretinal fluid (figures 1B and 4A). Over the next 2 months optic nerve swelling and subretinal fluid progressively reduced (figure 4B).

OUTCOME AND FOLLOW-UP

Four months after presentation, RVA had improved further to 0.5 LogMAR. The choroidal granulomas had virtually disappeared with resolution of choroidal elevation (figure 4C) and restoration of normal macular appearance (figure 4E) on SS-OCT. The subretinal fluid had resolved and there was no evidence of intraocular inflammation. Peripapillary scarring progressively developed with subretinal fibrosis (figure 4C,D). After 6 months, the disease remains inactive off steroids but with ongoing azathioprine therapy. Functional improvement has been maintained; however the persistent RAPD reflects a degree of permanent optic nerve damage. The left eye remains unaffected.

DISCUSSION

Diagnostic criteria for ocular sarcoidosis were proposed by an International Workshop on Ocular Sarcoidosis (IWOS) in 2009.²

The criteria include seven clinical signs and five laboratory investigations. In our patient, the clinical signs were atypical: six of the seven criteria were not identified and the presentation with contiguous optic nerve granulomas and multifocal choroidal nodules differed from the IWOS clinical sign of 'optic disc nodule(s)/granuloma(s) and/or solitary choroidal nodule.' The variation from IWOS diagnostic signs, alongside absence of IWOS laboratory investigations, including elevated serum ACE and bilateral hilar lymphadenopathy on chest x-ray, mandated systematic investigation to exclude other causes.

Ocular sarcoidosis can mimic other inflammations or malignancy. The clinical appearance of large multifocal choroidal and optic nerve head lesions associated with exudative retinal detachment mimicked intraocular tumour. Choroidal inflammation is common in sarcoidosis, with often small, multifocal peripheral chorioretinal lesions² and solitary choroidal granulomas² described in the IWOS criteria but in this case the large, multifocal choroidal lesions and ultrasound appearance raised concern of infiltrative tumour. Optic nerve head granuloma(s) are also recognised in sarcoidosis but in the absence of known disease warrant systemic investigations.^{4,5}

Tissue biopsy remains the gold standard of diagnosis in sarcoidosis but intraocular biopsy may be blinding; biopsy is therefore usually from hilar/mediastinal lymph nodes or accessible cutaneous or subcutaneous lesions.^{2,3} In this case, EBUS biopsy with rapid on-site evaluation provided prompt tissue

diagnosis and allowed us to proceed with corticosteroid therapy. The technique is a recent valuable development in establishing the diagnosis of sarcoidosis with a pooled diagnostic accuracy of 78.2% (95% CI 75.6% to 80.4%)⁶ and superior diagnostic yield in stage I and II sarcoidosis to transbronchial needle aspiration (83.3 vs 53.8%, $p < 0.05$).⁷

Corticosteroids are the mainstay of initial therapy; use of high-dose systemic treatment reflected the severity of inflammation and was followed by azathioprine therapy for long-term disease control and prevention of further ocular disease in either eye.

Acknowledgements Imaging Department, Manchester Royal Eye Hospital.

Contributors JCK acquired clinical information regarding the case, wrote the manuscript, revised it and approved the final version of the work for publishing. LRS acquired clinical information regarding the case, revised the manuscript and approved the final version of the work for publishing. NPJ revised the manuscript and approved the final version of the work for publishing.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Jones NP. Sarcoidosis. *Curr Opin Ophthalmol* 2002;13:393–6.
- 2 Herbert CP, Rao NA, Mochizuki M. International criteria for the diagnosis of ocular sarcoidosis: results of the first International Workshop On Ocular Sarcoidosis (IWOS). *Ocul Immunol Inflamm* 2009;17:160–9.
- 3 Acharya NR, Browne EN, Rao N, *et al.* Distinguishing features of ocular sarcoidosis in an international cohort of uveitis patients. *Ophthalmology* 2018;125:119–26.
- 4 Ganesh SK, Kaduskar AV. Optic nerve head granuloma as a primary manifestation of ocular sarcoidosis - a tertiary uveitis clinic experience. *Oman J Ophthalmol* 2015;8:157–61.
- 5 Hickman SJ, Quhill F, Pepper IM. The evolution of an optic nerve head granuloma due to sarcoidosis. *Neuroophthalmology* 2016;40:59–68.
- 6 Wahidi MM, Herth F, Yasufuku K, *et al.* Technical aspects of endobronchial ultrasound-guided transbronchial needle aspiration: CHEST guideline and expert panel report. *Chest* 2016;149:816–35.
- 7 Tremblay A, Stather DR, MacEachern P, *et al.* A randomized controlled trial of standard vs endobronchial ultrasonography-guided transbronchial needle aspiration in patients with suspected sarcoidosis. *Chest* 2009;136:340–6.

Learning points

- Ocular sarcoidosis clinical manifestations may be atypical and can cause profound visual loss.
- Ocular sarcoidosis should be strongly considered in intraocular inflammation with multitissue involvement.
- This case highlights the clinical utility of positron emission tomography-CT and endobronchial ultrasound techniques for the diagnosis of sarcoidosis.
- Aggressive immunosuppression may be necessary and can achieve good control of inflammation and favourable visual recovery.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow