CASE REPORT

Bilateral Non-arteritic Anterior Ischaemic Optic Neuropathy as the Presentation of Systemic Amyloidosis

M. Z. Kanaan^a, A. R. Lorenzi^b, N. Thampy^c, R. Pandit^a, and Margaret Dayan^a

^aNewcastle Eye Centre, Royal Victoria Infirmary, Newcastle Upon Tyne, United Kingdom; ^bMusculoskeletal Department, Freeman Hospital, Newcastle Upon Tyne, United Kingdom; ^cDepartment of Cellular Pathology, Royal Victoria Infirmary, Newcastle Upon Tyne, United Kingdom

ABSTRACT

A 75-year-old hypertensive female with stable idiopathic intermediate uveitis presented with bilateral sequential optic neuropathy with optic disc swelling. The optic neuropathy in the first affected eye (right) was thought to be due to non-arteritic anterior ischaemic optic neuropathy (NAION). Asymptomatic left optic disc swelling was found at routine review 2 months later, and a diagnosis of giant cell arteritis (GCA) was sought. Temporal artery duplex ultrasound showed the “halo sign,” but a subsequent temporal artery biopsy showed light-chain (AL) amyloidosis with no signs of giant cell arteritis. In this case, bilateral sequential ischaemic optic neuropathy mimicking non-arteritic anterior ischaemic optic neuropathy was the presenting sign of systemic amyloidosis involving the temporal arteries.

ARTICLE HISTORY

Received 24 September 2016
Revised 5 May 2017
Accepted 6 May 2017

KEYWORDS

Giant cell arteritis; halo sign; ischaemic optic neuropathy; systemic amyloidosis; temporal artery ultrasound

Introduction

Amyloidosis is a systemic condition caused by deposition of insoluble abnormal amyloid fibrils intra- or extracellularly. There are few previously reported cases of optic neuropathy in the context of light-chain (AL) amyloidosis,^{1–3} none of which occurred without typical symptoms or laboratory findings suggestive of giant cell arteritis (GCA). We present a case of bilateral sequential optic neuropathy, presumed ischaemic, as the presenting manifestation of systemic amyloidosis.

Case presentation

A 75-year-old hypertensive female presented having woken with visual loss in the right eye 10 days earlier. She had no symptoms of GCA and was otherwise well. She had a history of bilateral idiopathic intermediate uveitis diagnosed 30 years previously. This had been fully investigated, was not associated with underlying systemic inflammatory disease, and had been inactive and not requiring any treatment for the preceding 2 years. The visual acuity in the right eye was hand movements and 6/9 in the left eye. She had a right relative afferent pupillary defect (RAPD), and

her Ishihara colour vision was 0/17 plates in the right eye compared with 17/17 plates in the left eye. There was superior and nasal loss of the visual field in the right eye on Goldmann visual field testing (Figure 1). Examination showed no active uveitis in either eye, but the right optic disc was swollen with haemorrhages (Figure 2) and the left optic disc was crowded with a “disc at risk” configuration. The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and platelet count were normal, and this was presumed to be a right non-arteritic anterior ischaemic optic neuropathy (NAION). The patient was reviewed 3 weeks later, by which time her right optic disc swelling was improving but her visual acuity and visual field remained unchanged. Six weeks after her initial presentation, she had her routine annual appointment in the uveitis clinic. She was kept under uveitis follow-up owing to the previous requirement for systemic immunosuppression to control her intermediate uveitis. She felt the vision in the right eye to be stable, and her left eye was asymptomatic with 6/12 vision. There was no sign of active uveitis in either eye. The right optic disc swelling had resolved, but the left optic disc was mildly swollen and there was a new left superior visual field defect (Figures 3 and 4). Her ESR and

Figure 1. Goldmann perimetry showing right visual field loss (OD) compared with normal left (OS).

Figure 2. Multi-colour photographs showing swollen right optic disc compared to normal left.

Figure 3. Goldmann perimetry showing persistent right visual field loss (OD) and new left superior visual field abnormality (OS).

CRP remained normal. Fluorescein angiography showed marginally delayed choroidal filling (12 seconds) from the time of injection, and the right temporal artery duplex ultrasound showed a hypoechoic area ("halo sign"). A diagnosis of possible GCA was made. The patient was treated with intravenous methylprednisolone 1 g daily for 3 days, followed by oral prednisolone 60 mg daily for 5 days then a slow oral taper. Subsequent right temporal artery

(TA) biopsy showed extensive deposition of amorphous eosinophilic material within the media. This material stained positively with Congo red and Sirius red with apple green birefringence, confirming amyloidosis (Figures 5 and 6). Further immunohistochemical staining undertaken at the National Amyloidosis Centre laboratory showed the amyloid stained with antibodies to kappa light chains, indicating amyloid of AL type. It is of note that the

Figure 4. Optic disc photographs showing resolution of right optic disc (OD) swelling and development of pallor, whereas left optic disc (OS) shows mild swelling and new haemorrhage (arrowed).

Figure 5. Histopathology slide showing a cross-section of the biopsied temporal artery with amyloid deposition.

Figure 6. Histopathology slide showing Congo red stain highlighting amyloid deposition.

patient had no predisposing conditions for the development of amyloidosis and no laboratory findings to suggest Waldenström macroglobulinaemia or monoclonal gammopathy. Serum autoantibodies (antinuclear antibody [ANA], double-stranded DNA [dsDNA], extractable nuclear antigen [ENA], anti-cardiolipin), ESR, CRP, serum angiotensin-converting enzyme (ACE), immunoglobulins, serum electrophoresis, complement levels, and treponemal and hepatitis serology taken before starting steroid treatment were all normal or negative. Contrast-enhanced magnetic resonance imaging (MRI) of brain and orbits, performed a few days following steroid treatment, was normal.

The patient was worked up for other end-organ damage from amyloid deposition, and her skeletal survey showed no lytic lesions. There were no visceral amyloid deposits on serum amyloid P component scintigraphy. Screening for cardiac involvement with cardiac MRI, echocardiography, and biomarkers was normal.

The steroids were tapered and discontinued, and the patient completed six cycles of chemotherapy for amyloidosis (Velcade, cyclophosphamide, and dexamethasone five weekly cycles), after which she achieved a complete biochemical remission. The visual field loss in the left eye recovered almost completely over 2 months following the initiation of chemotherapy, and visual acuities remained at counting fingers in the right eye and 6/9 in the left eye.

Discussion

This was an unusual case in which bilateral sequential optic neuropathy was the presenting manifestation of AL amyloidosis involving the temporal arteries. We suspect that this is most likely to have been anterior ischaemic optic neuropathy due to vascular compromise from amyloid infiltration given the typical onset during sleep in a hypertensive elderly patient and the resolution of the optic disc swelling over the following 6 weeks without treatment. The “disc at risk” configuration may have facilitated the ischaemic insult to the prelaminar optic nerve head.

Vascular involvement in amyloidosis can lead to ischaemic complications such as angina⁴ and ischaemic stroke⁵ and produce symptoms mimicking polymyalgia rheumatica and giant cell arteritis.^{3,6} In our patient, vascular stenosis caused by amyloid deposition in the vessels walls may have combined with an element of hyperviscosity in an already predisposed individual to cause an ischaemic optic neuropathy.

Ischaemic optic neuropathy has been described in a patient who had already been treated for primary systemic amyloidosis in whom treatment had to be withheld owing to hepatic toxicity 2 months prior to developing visual complications.¹ In that case, the patient had raised inflammatory markers (ESR, fibrinogen, and D-dimer), in keeping with possible GCA followed by bilateral simultaneous optic neuropathy, whereas in our case the optic neuropathy was sequential and predated the diagnosis of amyloidosis. There has also been a report of a 67-year-old patient who presented with fatigue, headache, jaw claudication, and visual disturbance, was suspected to have GCA and treated with high-dose corticosteroids, but later developed nodular stricture of his lips and a persistently elevated ESR leading to a lip biopsy that confirmed systemic amyloidosis.² Ischaemic optic neuropathy was not established as the cause of the visual disturbance because the patient died from a myocardial infarction prior to temporal artery biopsy. Ischaemic optic neuropathy has also been described in familial amyloidotic polyneuropathy.⁷

More recently, Ghinai et al. reported two patients with underlying diagnoses of Waldenström macroglobulinaemia and monoclonal gammopathy of undetermined significance, respectively, who presented with

acute visual loss and clinical features of GCA but were found later to be due to systemic amyloidosis. In their second case, as here, a temporal artery ultrasound was performed, showing the “halo sign.” Persistence of symptoms despite high-dose steroid in this patient led to the decision to obtain a temporal artery biopsy from which the diagnosis of systemic amyloidosis was made.³

The detection of a “halo sign” on temporal artery duplex ultrasound suggests vascular inflammation and in the correct clinical context has a good specificity for the diagnosis of GCA.⁸ In our case, sequential optic neuropathy, which is typical of GCA, was not accompanied by other symptoms or signs of GCA despite the positive temporal artery duplex scan. However, the sequential loss of vision in both eyes required that a diagnosis of AION be considered and a temporal artery biopsy was performed. In the second of Ghinai et al.’s cases,³ the clinical features at presentation, a positive “halo sign” on temporal artery duplex ultrasound and raised inflammatory markers, were in keeping with giant cell arteritis. Importantly, their patient failed to respond to treatment, prompting a review of the diagnosis. In both cases, TA biopsy was performed, and in our case the histological appearance of extensive deposition of amorphous eosinophilic material within the media has prompted consideration of systemic amyloid. In both cases, infiltration of the temporal arteries was found to have led to a false-positive temporal artery duplex ultrasound. The use of temporal artery ultrasound is increasing as a non-invasive test in the investigation of patients with suspected giant cell arteritis. However, its true sensitivity and specificity as a diagnostic test is difficult to determine in the absence of a “gold standard” test for the diagnosis of GCA and reported values vary widely.^{9,10} There are few reported cases of “false-positive” test results in the literature, but other cases of non-GCA vasculitis have been documented.¹¹ It is most useful in the context of high and low clinical pre-test probability of GCA. Thus, where classical symptoms and signs of GCA are absent, inflammatory markers are normal, or a patient fails to respond to treatment as expected, a temporal artery biopsy adds valuable information when examined by an experienced histopathologist.

In conclusion, amyloidosis can involve the temporal arteries to give an ischaemic optic neuropathy and this may present in a variety of ways. Our case

adds to the literature by demonstrating that systemic amyloidosis should also be considered in cases of rapidly sequential anterior ischaemic optic neuropathy in patients who do not fit the typical profile for developing NAION in terms of age, risk factors, or optic disc configuration. Furthermore, our case also adds to the limited literature confirming infiltration of the temporal artery by amyloid as a cause of a false-positive temporal artery duplex scan.

Acknowledgement

This case was presented in the UK Neuro Ophthalmology Society Interest Group Meeting, March 2016.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

References

- [1] Neri A, Rubino P, Macaluso C, Gandolfi SA. Light-chain amyloidosis mimicking giant cell arteritis in a bilateral anterior ischemic optic neuropathy case. *BMC Ophthalmol* 2013;13:82.
- [2] Emmungil H, Kalfa M, Başarık B, Kahraman, Tanhan F, Yaman B, Öztürk A, Erdemir, Kandiloğlu G, İnal V, Kabasakal Y. Primary systemic AL amyloidosis presenting as temporal arteritis. *Case Rep Rheumatol* 2014;2014:549641.
- [3] Ghinai RAM, Mahmood S, Mukonoweshuro P, Webber S, Wechalekar AD, Moore SE. Diagnosing light chain amyloidosis on temporal artery biopsies for suspected giant cell arteritis. *J Neuro-Ophthalmol* 2016. doi: [10.1097/WNO.0000000000000447](https://doi.org/10.1097/WNO.0000000000000447).
- [4] Al Suwaidi JI, Velianou JL, Gertz MA, Cannon RO 3rd, Higano ST, Holmes DR Jr, Lerman A. Systemic amyloidosis presenting with angina pectoris. *Ann Intern Med* 1999;131:838–841.
- [5] Zubkov AY, Rabinstein AA, Dispenzieri A, Wijidicks EF. Primary systemic amyloidosis with ischemic stroke as a presenting complication. *Neurology* 2007;69:1136–1141.
- [6] Salvarani C, Gabriel SE, Gertz MA, Bjornsson J, Li C-Y, Hunder GG. Primary systemic amyloidosis presenting as giant cell arteritis and polymyalgia rheumatic. *Arthr Rheumatol* 1994;37(11):1621–1626. doi: [10.1002/art.1780371111](https://doi.org/10.1002/art.1780371111).
- [7] Hamann S, Jensen PK, Fledelius HC. Bilateral optic neuropathy in a patient with familial amyloidotic polyneuropathy. *BMJ Case Rep* 2013;2013:bcr2013200445. doi: [10.1136/bcr-2013-200445](https://doi.org/10.1136/bcr-2013-200445).
- [8] Schmidt W, Kraft H, Vorpahl K, Völker L, Gromnica-Ihle E. Color duplex ultrasonography in the diagnosis of temporal arteritis. *N Engl J Med* 1997;337:1336–1342.
- [9] Aranda-Valera IC, García Carazo S, Monjo Henry I, De Miguel Mendieta. Diagnostic validity of Doppler ultrasound in giant cell arteritis. *Clin Exp Rheumatol* 2017;35;Suppl 103(1):123–127.
- [10] Luqmani R, Lee E, Singh S, Gillett M, Schmidt WA, Bradburn M, Dasgupta B, Diamantopoulos AP, Forrester-Barker W, Hamilton W, Masters S, McDonald B, McNally E, Pease C, Piper J, Salmon J, Wailoo A, Wolfe K, Hutchings A. The role of ultrasound compared to biopsy of temporal arteries in the diagnosis and treatment of giant cell arteritis (TABUL): a diagnostic accuracy and cost-effectiveness study. *Health Technol Assess* 2016;20:1–238.
- [11] Dasgupta B, Borg FA, Hassan N, Alexander L, Barraclough K, Bourke B, Fulcher J, Hollywood J, Hutchings A, James P, Kyle V, Nott J, Power M, Samanta A, on behalf of the BSR and BHPR Standards Guidelines and Audit Working Group. BSR and BHPR Guidelines for the management of giant cell arteritis. *Rheumatol* 2010;49(8):1594–1597.