CASE REPORT

Visual disturbance with systemic symptoms: old lessons revisited

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SUMMARY

We describe a retired physician who presented with visual disturbance and systemic symptoms. The presence of general malaise, headache and scalp tenderness, with raised inflammatory markers, suggested that giant cell arteritis (GCA) was the likely diagnosis. Rapid response to initial steroid therapy and histological evidence of inflammation in the temporal artery supported this diagnosis. The character of these visual symptoms was, however, atypical for GCA. The patient, who had heart valve disease, subsequently deteriorated and developed further symptoms warranting investigation of bacterial endocarditis. Retinal emboli are a recognised complication of endocarditis, which could account for these visual symptoms. Moreover, interpretation of the temporal artery biopsy is limited in the context of existing steroid therapy. Our patient was consequently diagnosed with bacterial endocarditis. This case reminds us to consider the wider differential diagnoses for headache, visual disturbance and systemic symptoms, where echocardiogram and blood cultures may be crucial to reach the diagnosis.

BACKGROUND

This case presents a number of important lessons. Most importantly, we are reminded to have a low threshold for performing echocardiography and blood cultures in a patient with visual disturbance, headache and systemic symptoms, especially with known valve disease. Infective endocarditis and vasculitis may mimic each other and can be difficult to differentiate clinically, as both may present with neurological and systemic features. There is also an important lesson with regard to the timing of temporal artery biopsy (TAB). Clinical guidelines recommend that high-dose steroids are started immediately on clinical suspicion of giant cell arteritis (GCA);¹ steroid therapy should not be delayed awaiting investigations. However, temporal artery biopsies performed after steroids have been started are difficult to interpret. This highlights the importance of early biopsy and not relying on this test as diagnostic. Symptomatic improvement with steroids is often taken as support of a diagnosis of GCA, while this case reminds us that endocarditis may also improve with steroids.

Finally, medically qualified patients may offer technical interpretations of their symptoms. It is important not to accept this uncritically, but to enquire further to ensure an accurate history is obtained. Our patient, a retired doctor, described his visual symptoms initially as 'homonymous hemianopia'.

However, on further questioning, it became apparent that his symptoms were monocular.

CASE PRESENTATION

A retired physician aged 74 years presented to his GP reporting of abrupt onset of generalised aches and pains, scalp tenderness, stiffness, lethargy and visual disturbance. He was previously fit and active. He had a 30-year history of migrainous aura, characterised by bilateral visual 'zig-zags' lasting a few minutes, without headache. This usually occurred monthly, but the frequency and duration had recently increased to several times a day, lasting 10–20 min each time. In addition, he had noted new visual symptoms of 'multi-coloured flower rosettes' and 'flashing lights' in both visual fields, altitudinal defects affecting the lower half of the visual field, central visual loss and a variety of scotomata. He described several episodes of brief (seconds) complete loss of vision. This occurred initially in the right eye, latterly the left, but never simultaneously. Although he described these as 'homonymous hemianopia', it later became clear that he was experiencing monocular symptoms.

He then developed an intermittent generalised headache, 'fuzzy' in nature, sometimes accompanied by feeling unsteady. On one occasion, he had an episode of acute vertigo lasting 30 min, leading to a fall. In the few days prior to presentation, he felt intermittently feverish.

He had long-standing bilateral tinnitus following barotrauma, right total hip replacement (2000), malaria and amoebic dysentery (1980) and childhood meningococcal meningitis. Mitral valve prolapse (requiring annual echocardiography) was identified in 2007. The onset of his recent symptoms coincided with his annual echocardiogram. This demonstrated mild to moderate mitral regurgitation, unchanged from previous assessments. His only medication was occasional paracetamol. He was a non-smoker, drank occasional alcohol and had no family history of note.

On examination, he looked well. His chest was clear and a 5/6 systolic murmur was noted in the mitral area, consistent with his known valve disease. There were no bruits in the carotid or subclavian areas and he was haemodynamically stable. He had pulsatile, non-tender temporal arteries. There were no other signs.

INVESTIGATIONS

Routine blood tests were undertaken by the GP, including FBC, U&Es, calcium, LFTs, glucose, C

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reactive protein (CRP) and ESR. White cell count was 13.2 (neutrophils 11.52), ESR 50 and CRP 153. Rheumatoid factor and anticyclic citrullinated peptide antibodies were negative.

The patient was seen in the ophthalmology clinic, but investigation at this time was unremarkable.

A TAB was performed 6 weeks after steroid therapy was initiated. This delay was due to limited availability of the procedure. **Figure 1** shows the disrupted and partially destroyed internal elastic lamina (elastic Van Gieson) of the right temporal artery. There is intimal and medial thickening with scarring and oedema, but no active inflammation. Immunostaining of lymphocytes revealed the majority were CD3-expressing T-lymphocytes. The pathologist noted that the patient had been on steroids for 6 weeks, and in the context of the clinical history, concluded the biopsy was consistent with resolving/steroid-treated GCA.

DIFFERENTIAL DIAGNOSIS

The clinical picture suggested GCA, with new headache and scalp tenderness, accompanied by visual disturbance and systemic upset. However, his new visual symptoms were not typical of arteritic optic neuropathy (AON), as they were mainly positive and short-lived. AON typically leads to negative features, comprising visual impairment (usually developing over hours or days), pain (typically worse on eye movement) and dyschromatopsia. Yet, he described positive visual effects, additions to his vision such as 'flashing lights' and 'flower rosettes'. He specifically stated these were different from his previous migrainous symptoms.

Differential diagnoses for GCA include herpes zoster, migraine, transient ischaemic attack, cluster headache, sinus disease, temporomandibular joint pain and intracranial or ear-related pathology.¹ Retinal vasculitis, paraneoplastic retinopathy and other vasculides are the key potential diagnoses for our patient.

TREATMENT

Treatment was started in primary care with 60 mg once daily oral prednisolone, in accordance with guidelines, which recommend early empirical steroid treatment to prevent visual complications.¹ This led to rapid resolution of all symptoms. The dose was tapered by 10 mg twice weekly, to 20 mg. However, symptoms recurred as the dose was reduced and he was therefore referred urgently. Following rheumatology assessment, GCA was again considered the likely diagnosis, the dose of prednisolone was increased to 30 mg.

Figure 1 Temporal artery biopsy showing disrupted and partially destroyed internal elastic lamina (elastic Van Gieson) of the right temporal artery.

OUTCOME AND FOLLOW-UP

Unfortunately, after initial improvement following steroid therapy, our patient deteriorated, with increasing lethargy, night sweats, ongoing visual disturbance, rigours and transient loss of sensation in his hands and feet. Methylprednisolone was started. He described a nodule on his forehead above his left eyebrow, which was tender with purple skin discolouration. He also reported several tender red/purple lesions at the tips of his fingers. He became feverish and splinter haemorrhages were noted. Failure to improve with steroids, persisting inflammatory markers and a white cell count of 27 made us increasingly doubtful that GCA was the correct diagnosis. We considered other vasculitides, malignancy or infection. The presence of known valve disease, new splinter haemorrhages and fever suggested bacterial endocarditis. We arranged investigations, including urinalysis, immunology, serology, tumour markers, blood cultures, echocardiogram and CT imaging of the head, chest, abdomen and pelvis. Urinalysis was positive for blood and protein. Brain imaging was normal, but body imaging showed bilateral renal and splenic infarcts. Transthoracic echocardiogram revealed a 2.2×1.3 cm vegetation attached to the posterior mitral valve leaflet. **Figure 2** is the echocardiogram showing vegetation on the mitral valve (posterior leaflet). Transoesophageal echocardiogram showed a large vegetation and significant mitral regurgitation. Blood cultures grew streptococcus anginosus, confirming the diagnosis of bacterial endocarditis.

Steroids were withdrawn and he was treated with antibiotics. He underwent prosthetic mitral valve replacement, as his age, large size of vegetation and systemic embolism are indications for surgical intervention, which improves outcome.² His recovery was complicated by lumbar discitis and ongoing episodes of streptococcus anginosus bacteraemia. He is currently on long-term antibiotics, and is tolerating this well.

DISCUSSION

The presence of general malaise, headache and scalp tenderness, with raised inflammatory markers, suggested a diagnosis of GCA in our patient. Initial rapid response to steroid therapy supported this. Headache is the most common clinical feature in GCA, usually unilateral and/or temporal but sometimes diffuse or bilateral. Approximately 50% of patients have other symptoms: jaw claudication, scalp tenderness and systemic manifestations such as fever, anorexia, weight loss and polymyalgia. Visual symptoms (transient monocular visual loss/blurring and

Figure 2 Echocardiogram showing vegetation on the posterior leaflet of the mitral valve.

diplopia) are due to anterior ischaemic optic neuropathy or, less commonly, retinal artery occlusion.³ Examination findings may include a tender, thickened and/or beaded (alternating areas of palpable thickening) superficial temporal artery, with reduced or absent pulsation. Neurological signs may include upper cranial nerve palsies or visual field defects. Funduscopy may show disc pallor and oedema, which can progress to cotton-wool patches, haemorrhages and optic atrophy.³ Inflammatory markers—ESR, plasma viscosity, CRP—are usually elevated. GCA can occur with normal ESR or CRP, but it is unusual for both to be normal.⁴

None of these clinical features are pathognomonic for GCA and a significant minority of patients present with atypical symptoms. The American College of Rheumatology criteria for the classification of GCA states patients must fulfil at least three out of five criteria (box 1).

These criteria are a classification and not diagnostic criteria. Classification criteria have a lower sensitivity, and hence, there is a greater risk of false negatives. Nevertheless, while our patient presented with some atypical features for GCA, his symptoms certainly reflect the above criteria to suggest a diagnosis of GCA.

TAB is the gold standard investigation and should be performed as soon as possible. Common clinical findings of headache and scalp tenderness have poor positive predictive value (PPV) for positive biopsy. Jaw claudication with visual disturbance has the highest PPV, but the proportion of patients in which both features occur is <1%.⁶ Moreover, false-negative biopsies may occur in the presence of 'skip lesions' or prior steroid treatment.⁷

The recommendation to start high-dose steroids immediately following clinical suspicion of GCA is to minimise risk of long-term visual complications and should not be delayed waiting for further investigations.¹ However, it has been argued that the 'potential for identifying alternative conditions is seriously hampered by the earlier treatment decision'.⁶ The histological findings are not diagnostic; there were no specific histological features which confirm that inflammatory damage to the vessel wall was certainly due to GCA. The presence of resolving inflammation on a background of existing steroid therapy, in the context of the clinical picture, was felt to be consistent with partially treated GCA. There is evidence to suggest, at least within the first 2 weeks of treatment, steroid therapy does not affect the positive biopsy rate in suspected GCA.⁸ This reasserts the guideline to avoid any delay to treatment prior to biopsy.

Bacterial endocarditis should always be suspected in the presence of widespread symptoms with raised ESR and known valve disease. A lower threshold of suspicion may have prompted

earlier blood cultures and cardiac imaging, despite the recent reassuring echocardiogram. The rapid response to steroids was misleading and may reflect attenuation of the immune response in bacterial endocarditis. Retinal emboli are a recognised complication of endocarditis,⁹ which may account for his visual symptoms. Similarly, the inflammation seen in the TAB may be due to embolic events.

Learning points

- ▶ Giant cell arteritis is not the only cause of headache and visual disturbance with systemic symptoms and raised inflammatory markers: consider malignancy or systemic infection. With known valve disease and systemic symptoms, blood cultures and echocardiogram are imperative.
- ▶ Infective endocarditis and vasculitis mimic each other and are difficult to differentiate clinically.
- ▶ Temporal artery biopsy (TAB) should ideally be obtained before steroids are started, or as soon as possible afterwards. Delay in this investigation in our patient was due to early rapid response to therapy, consistent with the clinical picture. However, steroid-treated biopsy is difficult to interpret, which highlights the importance of early TAB and not relying on this test as diagnostic.
- ▶ Symptomatic improvement with steroids is often taken as support of a diagnosis of vasculitis, but patients with endocarditis may also improve with steroids.
- ▶ Medically qualified patients may offer technical interpretations of their symptoms. It is important to enquire further to ensure an accurate history is obtained.

Contributors The manuscript was written by MEH and KM, with the assistance of PMF. EM and RD provided editing and oversaw the process.

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Box 1 The American College of Rheumatology criteria for the classification of GCA⁵

1. >50 years of age
2. New-onset localised headache
3. Temporal artery tenderness or decreased pulsation
4. Elevated ESR >50 mm/hour
5. Abnormal temporal artery biopsy

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