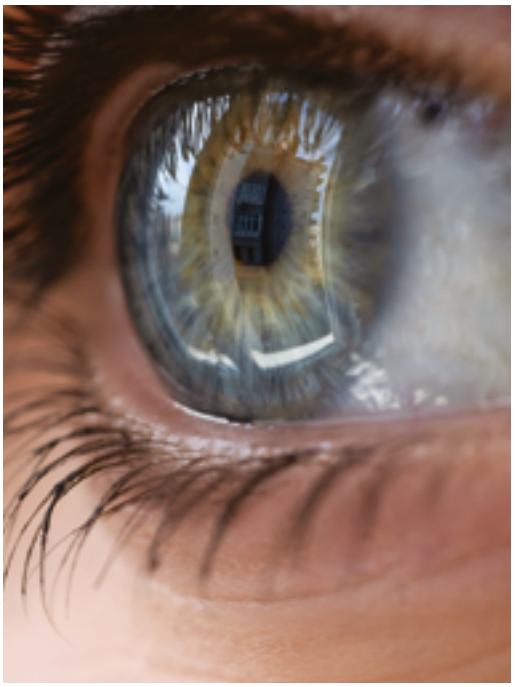
Giant cell arteritis presenting as a unilateral sixth nerve palsy



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CASE

A woman, aged 83 years, was referred by her general practitioner (GP) to an ophthalmology outpatient clinic with a two-week history of binocular horizontal diplopia.

The patient denied any ocular or orbital pain. She reported the onset of a headache, nausea, anorexia and fever over the same time period. She had jaw pain upon opening her jaw, but no definitive jaw claudication or other symptoms including scalp tenderness. There were no other focal neurological symptoms. She had no significant ocular history. Past medical history included previously resected bowel cancer.

QUESTION 1

Outline the key components of an initial approach to assessment of diplopia.

ANSWER 1

The first step is always to ensure the patient is experiencing binocular diplopia (ie the diplopia resolves upon closing either eye) as opposed to monocular diplopia, which is usually caused by refractive error or ocular media abnormalities such as cataract. Enquire about the direction of diplopia (horizontal vs vertical), course and associated symptoms (eg ocular pain, headache, giant cell arteritis [GCA] symptoms, any other focal neurological symptoms). A history of recent trauma (eg a fall) as well as past ocular and medical history should also be obtained.[1]

On general inspection, look for ptosis and proptosis. Best corrected visual acuity, pupil and eye movement examination should be recorded. Cranial nerve and other systemic examinations should be performed as appropriate.[1]

Investigations should be arranged based on the most likely differential diagnoses, and might include blood tests or neuroimaging.

CASE CONTINUED

On examination, best corrected visual acuity was 6/9.6 right eye and 6/7.5 left eye. Pupil examination and colour vision were normal. Eye movement examination revealed left lateral rectus underaction (Figure 1). The remainder of the eye and cranial nerve examination was unremarkable. The left temporal pulse was thready compared to the right on palpation.

QUESTION 2

What examination finding is demonstrated by the patient's eye examination?

QUESTION 3

What are the causes of this condition in adults?

ANSWER 2

The underaction of the left lateral rectus on eye movement examination is consistent with a left sixth nerve palsy.

ANSWER 3

The causes of a sixth nerve palsy in adults include:

- vascular (eg stroke, microvascular ischaemia [ie related to diabetes, hypertension, atherosclerosis], aneurysms, carotid-cavernous fistula)
- infective (eg syphilis, mastoiditis, meningitis, herpes zoster)
- neoplastic (eg skull-based tumours, infiltrative processes such as leukaemia)
- congenital (eg decompensated childhood strabismus)
- autoimmune (eg giant cell arteritis, multiple sclerosis, sarcoidosis, vasculitides)
- traumatic
- idiopathic
- any cause of raised intracranial pressure.[2]

Malignant aetiologies should be considered in any patient presenting with new onset diplopia and a history of malignancy, and appropriate neuroimaging should be arranged promptly.

CASE CONTINUED

In this case, the leading differential diagnosis was sixth nerve palsy secondary to GCA given the history of headache and constitutional symptoms. Inflammatory markers were elevated (erythrocyte sedimentation rate [ESR] 110 mm/h and C-reactive protein [CRP] 70 mg/L). Platelets were also mildly elevated at 433×10^9/L.

A magnetic resonance imaging (MRI) excluded any cranial or orbital causes of diplopia. Temporal artery ultrasound demonstrated a thickened left temporal artery, suggestive of arteritis. A temporal artery biopsy confirmed giant cell arteritis. The patient was treated with intravenous methylprednisolone and then tapered to oral prednisolone and weekly subcutaneous tocilizumab injections.

By three months postdiagnosis, prednisolone had been successfully weaned to 25 mg daily and inflammatory markers had normalised. The patient reported resolution of her headache and constitutional symptoms; however, her sixth nerve palsy was still present and symptomatic.

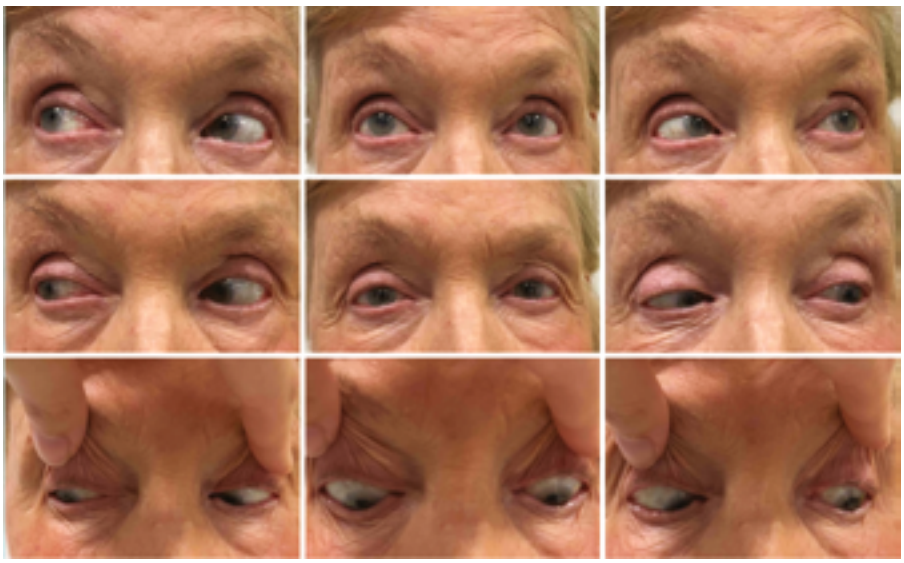

Figure 1. A nine-gaze photograph demonstrating left lateral rectus underaction. The left eye does not travel as far out in lateral gaze compared to the right eye. As a rule of thumb, the limbus should be able to go past the lateral canthus of the eyelids.

QUESTION 4

What are the ocular and systemic manifestations of GCA?

QUESTION 5

What investigations should be arranged when GCA is suspected? What treatments are currently available for the management of patients with ocular manifestations of GCA?

ANSWER 4

Ocular symptoms of GCA might include blurry vision, amaurosis fugax or loss of vision. Vision loss is usually unilateral and severe, but sequential in over one-third of patients with biopsy-proven GCA.[3] It usually occurs due to ischaemia secondary to vasculitis of vessels supplying the optic nerve or retina, although arteritis of the carotid or vertebral arteries might cause visual field defects or cortical blindness.[4]

Diplopia is seen in up to 19% of patients with GCA and can be due to central (ischaemia of cranial nerve nuclei or supranuclear gaze centres) or peripheral causes (ischaemic insult to the cranial nerves or extraocular muscles).[5,6]

Diplopia might precede severe visual loss. Therefore, GCA must be excluded in any patient aged >50 years with diplopia due to the risk of severe and sequential visual loss if untreated.

In terms of systemic manifestations, constitutional symptoms such as fever, night sweats, anorexia, weight loss, fatigue or myalgia are reported in up to 50% of patients with GCA.[7] Headache is reported in approximately 60%, whereas scalp tenderness, jaw claudication, temporal artery tenderness are also common.[8]

ANSWER 5

When GCA is suspected, initial investigations might include blood tests and ultrasound. Erythrocyte sedimentation rate, C-reactive protein and platelet counts are elevated in most patients with GCA, with a sensitivity of 65.5%, 66.9% and 71.2%, respectively.[9] Temporal artery ultrasound might demonstrate a 'halo sign' in GCA, where thickened hypoechoic tissue replaces the usual intima-media complex.[10] Temporal artery ultrasound is a less invasive diagnostic technique compared to temporal artery biopsy; however, temporal artery biopsy remains the gold standard of diagnosis due to higher sensitivity (77% vs 54%) and specificity (100% vs 81%).[11–13] Importantly, investigations should not delay commencement of steroids and early specialist referral is imperative where there is high clinical suspicion of GCA.

Patients with ocular manifestations of GCA must be referred to an ophthalmologist promptly for formal eye examination and commencement of appropriate steroid treatment to prevent progression to severe and bilateral visual loss. A temporal artery biopsy is usually performed within a week of commencing steroids, with specimen length of at least 20 mm to ensure a sufficient sample to avoid shrinkage or a false negative result because of skip lesions.[13,14] Contralateral temporal biopsy might be considered if the initial biopsy is negative but high clinical suspicion for GCA remains.[15]

Patients with ocular manifestations of GCA are usually treated with IV methylprednisolone for 3–5 days followed

by a prolonged tapering course of oral prednisolone over 1–2 years.[16] Adjunctive steroid-sparing immunomodulatory treatments such as methotrexate or biologic agents might be used in consultation with rheumatology or immunology teams to reduce steroid dose and side effects. Tocilizumab, an anti-interleukin-6, is increasingly used as it has demonstrated superior results to prednisolone in achieving sustained remission as well as higher quality of life scores among patients.[17,18]

Key points

- The causes of new onset binocular diplopia are wide-ranging and require further investigation.
- New onset of diplopia in any adult aged >50 years should prompt consideration and work-up of GCA.
- Corticosteroids are the mainstay of GCA management; however; the treatment landscape is evolving to include steroid-sparing agents.

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References

1. Jain S. Diplopia: Diagnosis and management. Clin Med (Lond) 2022;22(2):104–06. doi: 10.7861/clinmed.2022-0045.
2. Dinkin M. Diagnostic approach to diplopia. Continuum (Minneap Minn) 2014;20(4 Neuro-ophthalmology):942–65. doi: 10.1212/01.CON.0000453310.52390.58.
3. Liu GT, Glaser JS, Schatz NJ, Smith JL. Visual morbidity in giant cell arteritis. Clinical characteristics and prognosis for vision. Ophthalmology 1994;101(11):1779–85. doi: 10.1016/S0161-6420(94)31102-X.
4. Simon S, Ninan J, Hissaria P. Diagnosis and management of giant cell arteritis: Major review. Clin Exp Ophthalmol 2021;49(2):169–85. doi: 10.1111/ceo.13897.
5. Vodopivec I, Rizzo JF 3rd. Ophthalmic manifestations of giant cell arteritis. Rheumatology (Oxford) 2018;57 Suppl 2:ii63–72. doi: 10.1093/rheumatology/kex428.
6. Ye JJ, Bouffard MA, Brooks E, Hung YP, Kimchi EY. Giant cell arteritis presenting with multiple cranial neuropathies – Case report. Neurohospitalist 2023;13(2):188–91. doi: 10.1177/19418744221139893.
7. Healey LA, Wilske KR. Presentation of occult giant cell arteritis. Arthritis Rheum 1980;23(6):641–43. doi: 10.1002/art.1780230605.
8. Hunder GG, Bloch DA, Michel BA, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum 1990;33(8):1122–28. doi: 10.1002/art.1780330810.
9. Chan FLY, Lester S, Whittle SL, Hill CL. The utility of ESR, CRP and platelets in the diagnosis of GCA. BMC Rheumatol 2019;3(1):14. doi: 10.1186/s41927-019-0061-z.
10. Muratore F, Pipitone N, Salvarani C, Schmidt WA. Imaging of vasculitis: State of the art. Best Pract Res Clin Rheumatol 2016;30(4):688–706. doi: 10.1016/j.berh.2016.09.010.
11. De Miguel E, Beltran LM, Monjo I, Deodati F, Schmidt WA, Garcia-Puig J. Atherosclerosis as a potential pitfall in the diagnosis of giant cell arteritis. Rheumatology (Oxford) 2018;57(2):318–21. doi: 10.1093/rheumatology/kex381.
12. Luqmani R, Lee E, Singh S, et al. 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(90):1–238. doi: 10.3310/hta20900.
13. Allison MC, Gallagher PJ. Temporal artery biopsy and corticosteroid treatment. Ann Rheum Dis 1984;43(3):416–17. doi: 10.1136/ard.43.3.416.
14. Murchison AP, Bilyk JR, Eagle RC Jr, Savino PJ. Shrinkage revisited: How long is long enough? Ophthalmic Plast Reconstr Surg 2012;28(4):261–63. doi: 10.1097/IOP.0b013e31824ee720.
15. Boyev LR, Miller NR, Green WR. Efficacy of unilateral versus bilateral temporal artery biopsies for the diagnosis of giant cell arteritis. Am J Ophthalmol 1999;128(2):211–15. doi: 10.1016/S0002-9394(99)00101-4.
16. Hellmich B, Agueda A, Monti S, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2020;79(1):19–30. doi: 10.1136/annrheumdis-2019-215672.
17. Stone JH, Tuckwell K, Dimonaco S, et al. Trial of tocilizumab in giant-cell arteritis. N Engl J Med 2017;377(4):317–28. doi: 10.1056/NEJMoa1613849.
18. Strand V, Dimonaco S, Tuckwell K, Klearman M, Collinson N, Stone JH. Health-related quality of life in patients with giant cell arteritis treated with tocilizumab in a phase 3 randomised controlled trial. Arthritis Res Ther 2019;21(1):64. doi: 10.1186/s13075-019-1837-7.

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