CASE REPORT

Unusual cause of flare in antineutrophil cytoplasmic antibody-associated vasculitis

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SUMMARY

A 53-year-old woman attended for a routine outpatient appointment for follow-up of antineutrophil cytoplasmic antibody-positive vasculitis. Her disease had relapsed despite appropriate medical management with mycophenolate mofetil (MMF), as evidenced by rising acute phase response and antimyeloperoxidase titre with ongoing symptoms. On further questioning, she had been taking oral charcoal as part of a detoxification diet, which we postulate was causing significantly impaired MMF absorption. This case report summarises the presentation and highlights the importance of a thorough drug history, and should prompt the reader to keep an open mind with regard to drug interactions and treatment regimen adherence when treatment is, unexpectedly, seemingly failing.

BACKGROUND

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a term representing a wide-ranging spectrum of diverse, chronic, autoimmune, multisystem diseases.^{1–3} They share a common pathology and are characterised by the presence of ANCA and focal necrotising lesions, leading to small vessel vasculitis.² ANCAs are reactive to either proteinase-3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA). A number of clinically and pathologically defined diseases have developed, including: granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) and microscopic polyangiitis (MPA).³

AAV is rare, with annual incidence estimated to be 19.5 per million, prevalence 255 per million and peak age of onset at 65–74 years.³ When there is major organ involvement, these diseases can be life-threatening and warrant substantial immunosuppression (remission induction) followed by more long-term maintenance therapy (maintenance of remission).³ Organ involvement classically includes capillaritis causing alveolar haemorrhage in the lungs, crescentic glomerulonephritis causing acute kidney injury, and purpuric rash or vasculitic ulceration in the dermis, with both GPA and EPA also causing granulomatous lesions, as their names suggest.¹ Longstanding treatment includes corticosteroids and cyclophosphamide, with recent additions including azathioprine, methotrexate, mycophenolate mofetil (MMF) and, in refractory disease, rituximab.³ Modern therapy has enabled a shift from previously fatal conditions, to those with a more relapsing and remitting course.

CASE PRESENTATION

A 53-year-old woman attended the Arthritis Centre at Northwick Park Hospital, Harrow, for a routine connective tissue disease clinic outpatient follow-up. Her medical history included AAV, which was diagnosed in 2013, with mononeuritis multiplex, constitutional symptoms and an elevated MPO-ANCA titre, warranting a 12-day admission to hospital. Additionally, she had previous cervical carcinoma (treated with radiotherapy), left hydronephrosis (thought to be secondary to the radiotherapy) with ureteric (JJ) stent in situ as well as bronchiectasis. Her regular medication included aspirin, Adcal-D3, cyanocobalamin injections and ferrous sulfate. She had been on MMF for 3 years to control her vasculitis (which was in remission prior to this attendance), following an adverse effect with cyclophosphamide (haemorrhagic cystitis). She always reported excellent adherence to her medication regimen.

During this attendance, she was suffering with symptoms of a chest infection, as evidenced by fever and a cough productive of sputum, which her general practitioner had treated with a short course of oral antibiotics the month before. She had recurrence of her typical vasculitis symptoms with constitutional symptoms including generalised weakness, anorexia and lethargy as well as relapse of her previously severe paraesthesia (described by her as ‘pins and needles’) in her lower limbs bilaterally, mostly affecting the feet. Things were progressing despite antimicrobial treatment.

General examination was unremarkable aside from a few inspiratory crackles at the left base and the patient’s weight remained stable. There was no focal neurological deficit except sensory loss in the left anterior leg and dorsal aspect of both feet, in the distribution of the superficial peroneal nerve (L5 nerve root). There were no peripheral stigmata of vasculitis. Distal pulses were intact bilaterally.

Interestingly, on further questioning, the patient volunteered that between 7 and 8 months prior to this appointment, she had started the ‘Goop’ diet. This is a healthy lifestyle diet, as advocated by celebrity Gwyneth Paltrow on <http://goop.com>, a weekly lifestyle publication, which she also curates.⁴ The patient had been taking oral charcoal as part of a detoxification process with the aim of ‘flushing out toxins’. This was bought from either a specialist health food shop or on the internet, and came in liquid form, as 200 mL bottles. Unfortunately, the exact dose is not available; however, she was taking it on an ‘as needed’ basis. On average, she would drink around a third of a bottle per day.

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INVESTIGATIONS

Routine bloods showed chronic and stable iron deficiency anaemia (haemoglobin 81 g/L and mean corpuscular volume 77.7 fL) with otherwise normal full blood count. Liver and bone profiles were normal but the patient had developed an acute kidney injury (urea 12.0 mmol/L, creatinine 172 µmol/L (baseline 100 µmol/L) and estimated glomerular filtration rate 28 mL/min/1.73 m²). She had a moderate inflammatory response with an erythrocyte sedimentation rate of 61 mm/h and C reactive protein level of 26 mg/L. Complement (C3/C4) was normal. Autoantibody profile was negative, except perinuclear ANCA (pANCA), which was positive, with MPO-ANCA and PR3-ANCA titres 27.0 (normal range 0–5) and 0.2 (normal range 0–3) IU/mL, respectively. The MPO-ANCA titre at time of initial diagnosis (2013) was 123 IU/mL, falling to 6.7 IU/mL 12 months before. Sputum microscopy, culture and sensitivity were unremarkable. Urinalysis showed blood and leucocytes, and the patient's albumin to creatinine ratio as being 11.7 µg/mg, which were all normal for her and had remained unchanged. Interestingly, the previous year, she had had a suppressed acute phase response. CT of her chest showed an area of upper lobe consolidation, however, broncho-alveolar lavage revealed no organisms or acid-fast bacilli.

TREATMENT

The patient was diagnosed with a flare of her AAV and was started on oral corticosteroids: prednisolone 30 mg daily for 2 weeks, then reduced to 20 mg for 2 weeks, 10 mg for 2 months, then reduced by 5 mg/month, then stopped. The MMF was temporarily discontinued in view of the acute kidney injury, but was later restarted without problem.

OUTCOME AND FOLLOW-UP

The patient attended for 2-weekly blood tests and the acute phase response had normalised; in addition, she had resolution of the acute kidney injury. Her paraesthesia and chest symptoms also improved, and she now continues on maintenance MMF. She no longer takes charcoal supplementation and 2 months later is symptom free.

DISCUSSION

Activated charcoal is commonly used in medicine, in the management of drug overdose or poison ingestion, as it has the ability to adsorb a wide variety of substances thus preventing their gastrointestinal absorption.⁵ MMF is converted to mycophenolic acid (MPA), the active form, by first pass metabolism. MPA undergoes enterohepatic circulation, and interruption of this by charcoal would reduce MPA levels (as seen with cholestyramine).⁶ It would seem that self-medication with charcoal for around 7 months had allowed relapse of this patient's vasculitis that had previously been well controlled on MMF as a single agent.

One consideration is that the constellation of symptoms described could have been due to intercurrent infection. At the time of presentation, we were unable to identify a defined source of sepsis, as evidenced by absent microbial growth from the urine, sputum and broncho-alveolar lavage samples sent to microbiology. The MPO-ANCA titre on this attendance was approximately four times higher than that of the previous year, when the patient was well. Furthermore, inflammatory markers were rising despite antibiotic therapy, which then normalised on the initiation of oral corticosteroids.

A further consideration is that this patient simply relapsed while on MMF and the charcoal ingestion was coincidental rather than causative. Indeed, the IMPROVE trial showed that 55.3% of patients on MMF therapy for maintenance of remission in AAV were shown to relapse.⁷ In this patient, while we did not measure MMF levels, it would have been very interesting to see the concentration at the time of flare diagnosis and again following cessation of charcoal ingestion. We feel that, in view of no convincing evidence to confirm infection, coupled with deterioration of the patient both clinically and biochemically despite antibiotic therapy, as well as a rapid improvement on starting oral corticosteroids, that this flare of AAV was due to reduced gastrointestinal absorption secondary to ingestion of oral charcoal.

The acute kidney injury identified was likely to have been pre-renal in origin, rather than due to active vasculitis. Of course, a renal biopsy would have clarified this situation. The preserved urine albumin to creatinine ratio suggests that the rise in serum urea and creatinine were related to inflammatory burden elsewhere. In this context, a renal biopsy would be invasive and would be expected to yield no further diagnostic benefit; hence no biopsy was performed.

In our centre, we do not routinely measure MMF levels in patients on this treatment, but this clinical scenario raises the question as to whether we should be doing so in these patients, as this may have alerted us to a potentially subtherapeutic MMF concentration. Further work is needed to identify high-risk patients (such as those with pre-existing malabsorption), and to determine if and when we should be measuring MMF levels, such as at times of disease flare.

Fortunately, in this case, the patient was able to volunteer the information needed to ascertain the cause of her worsening symptoms, and her disease was brought under control using short term oral corticosteroids and reintroduction of MMF as a single agent. While there is a health disclaimer on the website for the users of the Goop diet,⁴ clearly this is an area of concern for both patients and clinicians. Such celebrity-endorsed diets may promote the use of charcoal and other food stuffs or medications that can clearly cause altered or unpredictable absorption of medications. We have presented an unusual case of vasculitis flare, which serves to highlight the importance of a thorough drug history, as well as the importance of patient education. Good communication skills are paramount to fostering an effective doctor–patient relationship to allow patients to inform the clinician of any new medications or supplements, whether prescribed or over-the-counter/internet, to ensure there are no adverse effects.

Learning points

- ▶ Activated charcoal prevents absorption of medication.
- ▶ Always take a thorough drug history, including prescribed, over-the-counter/internet, complementary therapy and recreational/party drugs.
- ▶ Keep an open mind when a patient has ongoing disease activity despite optimal medical treatment, thinking about interactions and adherence with treatment regimen.
- ▶ Consider measuring blood mycophenolate mofetil concentration in patients presenting with possible disease flare.

Competing interests None declared.

Patient consent Obtained.

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