CASE REPORT

Aortitis and pachymeningitis: an unusual combination in granulomatosis with polyangiitis (myeloperoxidase-associated vasculitis)

Konstantinos Parperis,^{1,2} Yasir Abdulqader³

¹Medicine, Maricopa Medical Center and University of Arizona College of Medicine, Phoenix, Arizona, USA

²Medicine, University of Cyprus Medical School, Nicosia, Cyprus

³Internal Medicine, Maricopa Integrated Health System, Phoenix, Arizona, USA

Correspondence to

Dr Konstantinos Parperis, kparperi@email.arizona.edu

Accepted 30 December 2018

SUMMARY

Aortitis and pachymeningitis are uncommon manifestations of the antineutrophil cytoplasmic antibody-associated vasculitides, a group of systemic autoimmune diseases mainly affecting small vessels. We present a case of a 71-year-old woman with a remote history of idiopathic chronic granulomatous pachymeningitis complicated with aortic thickening due to autoimmune aortitis.

BACKGROUND

Our case illustrates an unusual presentation of granulomatosis with polyangiitis (GPA) and highlights the importance of considering aortic involvement in patients with a history of pachymeningitis and positive for the myeloperoxidase antibody (MPO). Early recognition and surveillance might prevent complications like aortic dissection and rupture.

CASE PRESENTATION

A 71-year-old Hispanic woman with a medical history of hypertension, hyperlipidaemia, diabetes mellitus, coronary artery disease, left eye blindness admitted to the hospital with worsening acute on chronic headache.

In 1998, the patient experienced acute onset of a severe headache, associated with subacute vision loss in the left eye and MRI of the brain demonstrated a left retro-orbital mass without any other abnormal findings. Biopsy of the lesion in a different institution revealed granulomas associated with necrosis, with negative cultures for bacterial, fungal or mycobacterial infections. Given the pathology results and negative infectious workup, the patient was diagnosed with idiopathic granulomatous pseudotumour and she was treated with prednisone with the improvement of her symptoms. For several years, the patient had no complaints, so she did not follow up with her medical provider and she stopped the prednisone. No follow-up imaging studies were performed.

In 2016, she developed recurrent headaches and an MRI of the brain demonstrated diffuse thickening of the meninges (figure 1). The patient underwent a right frontal dural biopsy that showed fibrosis and chronic inflammation, with the presence of histiocytes, lymphocytes and less than 10 IgG₄ positive plasma cells/high power field were stained positive for IgG₄, without evidence of granulomas or

necrotising vasculitis (figure 2). Given the lack of storiform features of fibrosis and obliterative phlebitis and the presence of a small number of IgG₄ plasma cells, the diagnosis of IgG₄-related disease is unlikely.

INVESTIGATIONS

During this admission, the patient had a lumbar puncture with normal cerebrospinal fluid findings. Laboratory studies showed elevated erythrocyte sedimentation rate and C reactive protein (CRP), positive perinuclear antineutrophil cytoplasmic antibody (p-ANCA) and elevated level of MPO antibody of 159 (normal <0.4). The proteinase-3 antibody, urinalysis, serum protein electrophoresis, thyroid function tests were all normal. The IgG₄ serum level was 24 mg/dL (normal range 2.4–121.0 mg/dL) and the eosinophil count was 0 on the complete blood count. In order to rule out syphilis as a possible aetiology of the aortitis, the rapid plasma reagin test was performed and it was negative. CT of the sinuses demonstrated right mastoid air cells under pneumatized with trace fluid within chronic changes. CT angiogram of the chest and abdomen showed thickened ascending aorta and aortic arch, plus multiple areas of calcifications at the thoracic aorta, brachiocephalic artery, celiac and left main coronary artery (figure 3).

Figure 1 MRI brain showed diffuse pachymeningeal enhancement (white arrow).

© BMJ Publishing Group Limited 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Parperis K, Abdulqader Y. *BMJ Case Rep* 2019;**12**:e226795. doi:10.1136/bcr-2018-226795

Figure 2 Right frontal dural biopsy revealed thickened and fibrotic dura with mild chronic inflammation.

DIFFERENTIAL DIAGNOSIS

Meningitis, vasculitis, aortitis, migraine headache, stroke.

TREATMENT

Given the above findings of chronic granulomatous pachymeningitis, aortitis and the presence of high titre of MPO, the

Figure 3 CT angiogram of the chest revealed thickened ascending aorta and aortic arch wall (blue arrow).

diagnosis of GPA was made. The patient was treated with prednisone 60 mg daily and methotrexate 20 mg weekly with folic acid 1 mg daily and noted significant improvement of her headache. Rituximab and cyclophosphamide were considered as possible treatment options but due to lack of insurance and income, the patient decided to proceed with an affordable regimen that included prednisone and methotrexate.

OUTCOME AND FOLLOW-UP

During a follow-up appointment in the rheumatology clinic 6 months after discharge from the hospital, she was doing well with no new episodes of headache, normal level ESR, CRP and the prednisone was gradually decreased to 5 mg daily.

DISCUSSION

GPA is a systemic autoimmune disease characterised by the presence of inflammatory white blood cells in the vessel walls, mainly involving small to medium-sized vessels. Pathological hallmarks of GPA are granulomatous inflammation and necrotising vasculitis affecting of arteries, capillaries, venules that may result in organ ischaemia and dysfunction. GPA has been associated with the presence of ANCA in the serum. Although GPA is primarily linked with specific ANCA for proteinase-3 (90% of cases), 10% of patients have antibodies against the MPO.¹ The incidence of GPA is 8.5 cases per million based on a population-based study from UK.² The disease has a large variation in clinical presentation, ranging from mild disease affecting the upper respiratory tract to severe involvement leading to respiratory or renal failure.

Central nervous complications include cranial neuropathies, pituitary Central Nervous System (CNS) vasculitis leading to cerebrovascular accidents, pituitary intraparenchymal mass lesions and pachymeningitis.³ Chronic pachymeningitis in GPA has been frequently reported with the onset of GPA, occurs in the brain rather than in the spinal cord, manifested with severe headache which only resolved with the administration of corticosteroids.^{4,5} There are approximately 48 case reports or case series describing pachymeningitis as a complication of GPA.⁴⁻⁶ Di Comite *et al* observed that 37.1% of a total of 37 patients with GPA and meningeal involvement were cytoplasmic ANCA positive and 14.3% were positive for p-ANCA.⁴ Orbital involvement is commonly seen in with GPA and one of the manifestation might be a retro-orbital pseudotumour and proptosis.^{7,8} GPA is classified as a small-vessel vasculitis and aortic involvement is very unusual. Indeed, the presence of aortitis can create a diagnostic confusion with other large vasculitides like giant cell arteritis or Takayasu's arteritis. To our knowledge, there are only two case reports connecting pachymeningitis with aortitis in MPO-associated vasculitis. Nguyen *et al* described a case of a 64-year-old woman who presented with joint pain and workup revealed anti-MPO antibody and evidence of pachymeningitis and aortitis on F-18 fluorodeoxyglucose-positron emission tomography/CT.⁹ In addition, Takenaka *et al* reported a case of a 47-year-old Japanese woman that developed aortitis and pachymeningitis due to MPO-associated vasculitis, successfully treated with tocilizumab.¹⁰

Furthermore, Nakabayashi *et al* reported three cases of Japanese women that developed aortitis and two patients found to have high titres of MPO.¹¹ Both patients had renal involvement consistent with glomerulonephritis and none of the patients had CNS manifestations. The pathogenesis of aortitis, although not well defined, may be a result of the invasion of the aortic wall by inflammatory cells and granulomas resulting in granulomatous

aortitis.¹² Alternatively, necrotising vasculitis involving the vasa vasorum of the aortic wall, leading to chronic aortitis has been suggested as a possible mechanism of the disease.¹³

The pathogenesis of aortitis, although not well defined, may be a result of the invasion of the aortic wall by inflammatory cells and granulomas resulting in granulomatous aortitis.¹² Alternatively, necrotising vasculitis involving the vasa vasorum of the aortic wall, leading to chronic aortitis has been suggested as a possible mechanism of the disease.¹³

Most of the patients are treated with corticosteroids and the addition of immunosuppressive agents like rituximab, tocilizumab, disease-modifying antirheumatic drugs may be indicated in patients with severe disease.^{10 14}

Learning points

- ▶ Aortitis, although a rare complication of granulomatosis with polyangiitis (GPA), can be a manifestation of the antineutrophil cytoplasmic antibody-associated vasculitis.
- ▶ Aortic aneurysms, dissection, rupture and death are potential complications of aortitis.
- ▶ The presence of pachymeningitis and aortitis may be suggestive of an underlying diagnosis of GPA.

Contributors Both authors, KP and YA, contributed equally to this manuscript including planning, conduct, reporting, conception and design, acquisition of data and interpretation of data.

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 for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Hoffman GS, Specks U. Antineutrophil cytoplasmic antibodies. *Arthritis Rheum* 1998;41:1521–37.
- 2 Watts RA, Carruthers DM, Scott DG. Epidemiology of systemic vasculitis: changing incidence or definition? *Semin Arthritis Rheum* 1995;25:28–34.
- 3 Seror R, Mahr A, Ramanoelina J, et al. Central nervous system involvement in Wegener granulomatosis. *Medicine* 2006;85:53–65.
- 4 Di Comite G, Bozzolo EP, Praderio L, et al. Meningeal involvement in Wegener's granulomatosis is associated with localized disease. *Clin Exp Rheumatol* 2006;24:S60–S64.
- 5 Katrib A, Portek I, Corbet AJ, et al. Meningeal involvement in Wegener's granulomatosis. *J Rheumatol* 1998;25:1009–11.
- 6 Holle JU, Gross WL. Neurological involvement in Wegener's granulomatosis. *Curr Opin Rheumatol* 2011;23:7–11.
- 7 Bullen CL, Liesegang TJ, McDonald TJ, et al. Ocular manifestations of Wegener's granulomatosis. *Ophthalmology* 2001;108:1535–154.
- 8 Kubal AA, Perez VL. Ocular manifestations of ANCA-associated vasculitis. *Rheum Dis Clin North Am* 2010;36:573–86.
- 9 Nguyen T, Vanderghyest F. Pachymeningitis and aortitis in a patient with antineutrophil cytoplasmic antibody-associated vasculitis. *Mayo Clin Proc* 2014;89:e115.
- 10 Takenaka K, Ohba T, Suhara K, et al. Successful treatment of refractory aortitis in antineutrophil cytoplasmic antibody-associated vasculitis using tocilizumab. *Clin Rheumatol* 2014;33:287–9.
- 11 Nakabayashi K, Kamiya Y, Nagasawa T. Aortitis syndrome associated with positive perinuclear antineutrophil cytoplasmic antibody: report of three cases. *Int J Cardiol* 2000;75:S89–94.
- 12 Chirinos JA, Tamariz LJ, Lopes G, et al. Large vessel involvement in ANCA-associated vasculitides: report of a case and review of the literature. *Clin Rheumatol* 2004;23:152–9.
- 13 Vaglio A, Corradi D, Manenti L, et al. Evidence of autoimmunity in chronic periaortitis: a prospective study. *Am J Med* 2003;114:454–62.
- 14 Mukhtyar C, Guillevin L, Cid MC, et al. EULAR recommendations for the management of primary small and medium vessel vasculitis. *Ann Rheum Dis* 2009;68:310–7.

Copyright 2019 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-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