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Case report

Noninfective Endocarditis in Microscopic Polyangiitis: Report of a Case With a Successful Response to Immunosuppressive Therapy[☆]

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ABSTRACT

Although antineutrophil cytoplasmic antibody (ANCA) vasculitis has a variety of clinical manifestations, valvular compromise is not common, especially in anti-myeloperoxidase (anti-MPO) antibody (perinuclear [P]-ANCA) vasculitis. We report the case of a 38-year-old woman with ANCA-associated vasculitis who was diagnosed with valve vegetation, that resolved with immunosuppressive therapy.

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Endocarditis no infecciosa en poliangitis microscópica: reporte de un caso con respuesta exitosa a inmunosupresión

RESUMEN

Aunque las vasculitis asociadas a ANCA tienen manifestaciones clínicas diversas, la afección valvular es infrecuente, especialmente en el contexto de una poliangitis microscópica. Reportamos el caso de una mujer de 38 años con vasculitis ANCA con características clínicas de poliangitis microscópica y anticuerpos anti-mieloperoxidasa positivos (MPO), que presentó una masa vegetante en la válvula mitral que resolvió con inmunosupresión.

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Palabras clave:

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Introduction

Valve involvement in antineutrophil cytoplasmic antibody (ANCA) vasculitis is rare. However, there are around 20 cases reported in the literature, most in the context of granulomatosis with polyangiitis and c-ANCA. Infective endocarditis and ANCA vasculitis can have similar clinical manifestations that include: purpura, glomerulonephritis, pulmonary and ocular involvement, elevated acute phase reactants and fever; these impede diagnosis and appropriate treatment. In addition, ANCA can be present

as an epiphenomenon in endocarditis which can add to diagnostic confusion. We describe the case of a patient with non-infective endocarditis associated with ANCA which, because of its clinical features and antibodies, behaved like a microscopic polyangiitis, and resolved with immunosuppression without requiring valve replacement.

Case

A previously healthy 38-year-old woman consulting with anasarca, on admission high blood pressure and gradual creatinine elevation (increase from 1 mg/dl to 6 mg/dl in one month) were recorded. The anti-nuclear antibodies were negative, complement was normal and no infections were revealed. Positivity for ANCA was found by indirect immunofluorescence (IIF) with P pattern 1:160, and the ANCA by ELISA anti-myeloperoxidase were

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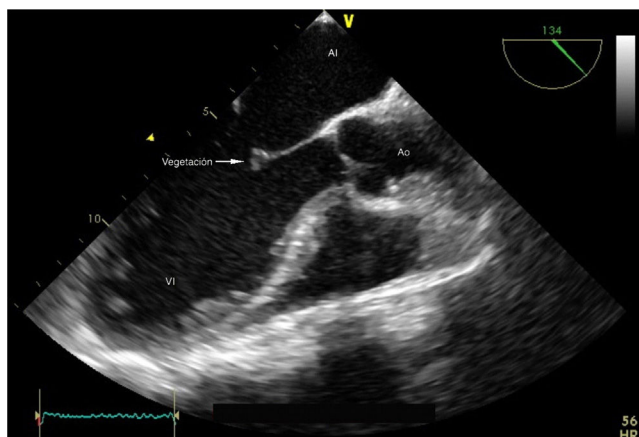


Fig. 1. Vegetation 4 × 5 mm in the A2 scallop of the anterior valve of the mitral valve with failure.

also positive. Kidney biopsy showed pauci-immune, focal segmental necrotising glomerulonephritis with extracapillary proliferation (30% fibrocellular crescents). No other organs were affected, CT of the thorax and transthoracic ultrasound were normal. Initially a diagnosis of ANCA vasculitis limited to the kidney was considered. Glucocorticoids were started: first, pulse methylprednisolone (500 mg intravenously/every day/3 days), followed by oral prednisolone 60 mg/day; in addition, plasma exchanges (she received 14 in total), and cyclophosphamide 500 mg intravenously on day 0 and day 15. After one month's hospitalisation the patient was discharged without requiring haemodialysis, with average creatinine levels of 2 mg/dl. The patient was prescribed an outpatient dose of prednisolone 50 mg/day, and a third dose of cyclophosphamide.

However, she was readmitted after 8 days with dyspnoea, cough and fever, and assured us that she had not stopped taking the glucocorticoids. Echocardiogram showed a vegetating mass of 4 × 5 mm in the A2 scallop of the anterior valve of the mitral valve with failure, which showed no independent movement (Fig. 1). Because of the suspicion of infective endocarditis, the patient was started on empirical broad-spectrum antibiotics (vancomycin and piperacillin-tazobactam, adjusted to her renal function), but her blood cultures were negative. On admission, CT of the thorax was

normal. Despite the antibiotic treatment the patient deteriorated clinically, with increased dyspnoea until she went into ventilatory failure and required admission to the intensive care unit. A further CT of the thorax showed findings suggesting alveolar haemorrhage, which was confirmed with bronchoalveolar lavage, and a repeat echocardiogram showed the persistence of the vegetative valve lesion and mitral failure. At that time repeat ANCA by ELISA were performed which were positive (anti-MPO).

Considering the patient's clinical deterioration despite management as infective endocarditis and the development of a new clinical manifestation attributable to vasculitis (alveolar haemorrhage) the possibility of valve involvement by ANCA vasculitis was considered, and that the combined clinical symptoms corresponded to a microscopic polyangiitis (MPA). After finding similar cases of valve involvement in ANCA vasculitis, the patient was given the third dose of cyclophosphamide (500 mg) and started on rituximab. The patient recovered, her blood cultures remained negative and on discharge echocardiography showed resolution of the vegetative lesion and the valve failure.

Discussion

ANCA vasculitis has heterogeneous clinical manifestations, most of which are serious. Valve involvement is possible, as evidenced by this clinical case, and poses a diagnostic challenge, especially when establishing the difference with infective endocarditis. Manifestations by septic embolism and subacute bacterial endocarditis (SBE) can also simulate endocarditis associated with ANCA.¹ The literature reports 10%–33% positive ANCA in patients with infective endocarditis (generally c-ANCA by IIF and anti-proteinase 3 [anti-PR3] by ELISA).^{1–3}

It might help to establish the difference between infective endocarditis and ANCA vasculitis to consider that the majority of patients with SBE and ANCA as an epiphenomenon were positive for other antibodies and had evidence of circulating immune complexes such as hypocomplementaemia or vascular complement deposits, which are absent in ANCA vasculitis. It has also been described that ANCA in endocarditis become negative after antibiotic treatment and, contrary to the cases of ANCA vasculitis with valve lesions, the need for valve replacement is rare.¹

Table 1
Features of Reported Cases of Endocarditis Due to ANCA Vasculitis.

	Year of publication	Age	Sex	ANCA (ELISA)	ANCA (IIF)	Type of vasculitis	Type of valve involvement
Levine	1957	28	M	ND	–	GPA	Mitral regurgitation
Dabbagh	1982	16	M	ND	–	GPA	Aortic regurgitation
Gerbracht	1987	20	F	ND	ND	GPA	Aortic regurgitation
Yanda	1989	77	F	ND	ND	GPA	Aortic and mitral regurgitation
Fox	1994	20	M	ND	ANCA+ND of	GPA	Aortic and mitral regurgitation
Davenport 1	1994	19	M	PR3	c-ANCA	GPA	Aortic regurgitation
Davenport 2	1994	53	M	PR3	c-ANCA	GPA	Aortic regurgitation
Grant	1994	32	M	ND	c-ANCA	GPA	Aortic and mitral regurgitation
Goodfield	1995	25	M	ND	c-ANCA	GPA	Aortic regurgitation
Anthony	1999	48	M	PR3	c-ANCA	GPA	Aortic stenosis. Vegetation
Paik	1999	48	M	ND	c-ANCA	GPA	Aortic vegetation
Leff	1999	17	M	ND	c-ANCA	GPA	Aortic regurgitation
Bruno	2000	63	F	ND	ANCA+ND of	GPA	Aortic regurgitation
Mishell	2002	65	M	PR3	c-ANCA	GPA	Aortic and mitral vegetation
Stöllberger	2003	56	M	PR3	–	Unknown	Aortic regurgitation. Vegetation
Herbst	2003	56	F	ND	–	GPA	Mitral regurgitation. Mitral mass
Ramakrishnan	2004	44	F	ND	c-ANCA	GPA	Mass mitral prosthesis, atrial side
Attaran	2010	52	M	ND	ND	GPA	Mitral regurgitation and stenosis. Mitral mass
Koyalakonda	2010	52	M	ND	–	GPA	Aortic and mitral regurgitation - mitral stenosis. Mitral mass
Lacoste	2011	44	M	MPO	p-ANCA	GPA	Aortic regurgitation
Muñoz-Grajales	2017	38	F	MPO	p-ANCA	MPA	Mitral regurgitation. Vegetation

ANCA: antineutrophil cytoplasmic antibodies; IIF: indirect immunofluorescence; GPA: granulomatosis with polyangiitis; MPO: anti-myeloperoxidase; ND: no data; c-ANCA: cytoplasmic fluorescence pattern; p-ANCA: perinuclear fluorescence pattern; MPA: microscopic polyangiitis; PR3: proteinase 3; –: negative.

In the case we describe the diagnosis of MPA was based on the presence of lung/kidney syndrome, positivity to anti-MPO antibodies by ELISA and p-ANCA by IFI with no ENT involvement or demonstrated granulomatous disease.

In the cases of endocarditis due to ANCA vasculitis reported in the literature, valve involvement is most commonly aortic regurgitation, followed by mitral regurgitation (as in the case we describe), both secondary to: valve perforation, valve or septum thickening or the presence of masses or vegetations. We should highlight that vegetations have not been described in all cases.^{4,5}

Table 1 describes the main features of other cases reported in the literature on endocardial involvement in patients over the age of 16 due to vasculitis associated with ANCA.

In half of the reported cases of valvular disease due to ANCA vasculitis, valve involvement presented concomitantly with the diagnosis of vasculitis, but in almost 30% it presented when the patient was already receiving immunosuppression. An important difference with SBE with positivity for ANCA, mentioned earlier, is that in most cases due to vasculitis valve replacement has been required and only in 2 cases, such as ours, immunosuppression was enough to resolve the valve involvement.^{4–6}

We stress that as far as we know the reported cases of ANCA vasculitis with valve involvement presented in patients with a diagnosis of granulomatosis with polyangiitis, formerly Wegener's granulomatosis, and ours would be the first case described with microscopic polyangiitis.

Conclusions

Although rare, there are several cases in the literature that, like our case, highlight the possibility that vasculitis associated with ANCA might affect the heart valve apparatus. Establishing the difference between acute bacterial endocarditis and vasculitis associated with ANCA is a diagnostic challenge. Blood cultures, response to antibiotics, positivity to other antibodies, evidence of circulating

immune complexes, and the persistence of ANCA can help the clinician to establish the difference, an infective process favouring the former and an ANCA vasculitis the latter.

Ethical Disclosures

Protection of people and animals. The authors declare that no experiments were performed on humans or animals for this investigation.

Data confidentiality. The authors declare that they have followed the protocols of their work centre on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appears in this article.

Conflict of Interests

The authors have no conflict of interest to declare.

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