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Echocardiographic screening of valvular heart disease in granulomatosis with polyangiitis: Do we need it?

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Rastreio ecocardiográfico de valvulopatia na granulomatose com poliangite: precisamos dele?

Systemic vasculitides are rare autoimmune-mediated disorders affecting various organs. Their clinical presentation is usually heterogeneous, with a long and difficult period until a diagnosis is finally established. They are classified according to the type of affected vessels, pathogenesis, demographics and clinical characteristics.[1] Granulomatosis with polyangiitis (GPA), formerly Wegener's granulomatosis, is included in the antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides and is characterized by necrotizing vasculitis of small and medium-sized vessels. Ear, nose and throat, lungs, and kidneys are mainly affected, and the disease occurs more frequently in patients in the fifth decade of life.[2]

Cardiovascular manifestations are a common cause of morbidity and mortality among patients with systemic vasculitis. Long-standing chronic inflammation leads to significant coronary, valvular and/or pericardial disease as well as myocarditis or aortic involvement. Among patients with GPA, cardiovascular involvement is nonetheless rare (3.3% in a cohort of 517 patients published on behalf of the Vasculitis Clinical Research Consortium[3]) and heterogeneous. Pericarditis and pericardial effusion are the most frequent cardiac complications seen in GPA.[4] The first cases of aortic valvular were described in the late 1980s.[5] Since then, small retrospective cohort studies and case reports constitute the only available evidence that drives clinical practice.

As in all rare systemic diseases, but especially in GPA, robust long-term prospective clinical evidence on the impact on the cardiovascular system is lacking. In addition, further evidence is needed to decide on the periodicity of cardiac clinical surveillance.

In the current issue of the *Journal*, Borowiec et al.[6] present a prospective observational single-center study on patients initially hospitalized with GPA and regularly followed in a university hospital in the Medical University of Warsaw, Poland, between February 2010 and November 2020. This is a case-control study of 105 patients analyzed at baseline and with a mean follow-up of up to 6.2 years. Variables analyzed included medical history, physical examination, laboratory studies and echocardiographic examination (mainly two-dimensional, flow and tissue Doppler).

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The included patients were mostly female (64%) and in the fifth decade of life. There was a high prevalence of cardiovascular risk factors in this population, with hypertension and dyslipidemia in 66% and 70% of the study population, respectively. Most patients were on regular glucocorticoids (84%).

The most frequent finding at baseline echocardiography was aortic regurgitation (43%); this was the only valvular dysfunction that increased significantly during follow-up, to 51% of the GPA group. Of these patients, only two underwent cardiac valve surgery. Other less frequent cardiac findings were aortic stenosis and mitral or tricuspid regurgitation, the rates of which were stable in follow-up.

Aortic regurgitation was also the dominant valvular finding in an observational study by the same clinical group,[7] in which 88 patients with GPA were compared with a control group of 40 age- and gender-matched patients (28% vs. 7.5%; p=0.03). Vegetations, leaflet thickening, valvular perforation and endocardial masses are the main mechanisms in heart valve lesions[8] described in ANCA-associated systemic vasculitis, particularly GPA.

In this long-term prospective study[6] the authors did not address the severity of aortic regurgitation or its progression in non-significant cases at baseline, which constitutes a substantial limitation to comprehending the full impact of GPA in aortic valve disease.

Additionally, the authors identified D-dimer levels as the only predictor of aortic regurgitation progression in this group of patients. The association of elevated D-dimers with inflammation and disease activity may explain this finding. Still, patients with aortic valve disease were older, and an input to the multivariate analysis for cardiovascular risk profile would help to further understand the differences found,[9] which I believe is an important limitation of the present analysis. Finally, only four (3.8%) of the included patients required aortic valve surgery during follow-up. Compared to the percentage of cases of symptomatic and significant heart valve disease identified in the systematic review published in 2011,[8] it might be argued that the long-term course may after all be less malignant than previously thought.

In this study, a small step was definitely taken to further understand the long-term impact of this rare systemic vasculitis on the cardiovascular system, specifically in cases of valve involvement. Surveillance is mandatory, but the current evidence raises several questions that require long-term prospective studies with the involvement of multiple high-volume centers to address these questions and strengthen the evidence that ultimately guides us in clinical practice.

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Conflicts of interest

The author has no conflicts of interest to declare.

References

1. Tani C, Bellando Randone S, Guiducci S, et al. Systemic sclerosis: a critical digest of the recent literature. Clin Exp Rheumatol. 2013;31(SUPPL.76).
2. Pagnoux C. Granulomatosis with polyangiitis. Rare Dis Immune Syst. 2020:97-129. doi:10.1007/978-3-030-02239-6_7
3. McGeoch L, Carette S, Cuthbertson D, et al. Cardiac involvement in granulomatosis with polyangiitis. J Rheumatol. 2015;42(7):1209-1212. doi:10.3899/jrheum.141513
4. Ahmed T, Meredith D, Klein AL. Granulomatosis with polyangiitis (Wegener's granulomatosis) complicated by pericarditis: our experience of two cases and comparative review of literature. Case. 2021;5(2):126-136. doi:10.1016/j.case.2020.11.008
5. Grant SCD, Levy RD, Venning MC, Ward C, Brooks NH. Wegener's granulomatosis and the heart. Br Heart J. 1994;71(1):82-86. doi:10.1136/hrt.71.1.82
6. Borowiec A, Rosinska M, Kowalik I, et al. Cardiac valvular involvement in granulomatosis with polyangiitis in long-term observation. Rev Port Cardiol. 2024;43;???-???.
7. Al-Habbaa A, Rawla P, Morra ME, et al. Valvular involvement in granulomatosis with polyangiitis: case report and systematic review of literature. Echocardiography. 2018;35(9):1456-1463. doi:10.1111/echo.14094
8. Lacoste C, Mansencal N, M'Rad M Ben, et al. Valvular involvement in ANCA-associated systemic vasculitis: a case report and literature review. BMC Musculoskelet Disord. 2011;12:50. doi:10.1186/1471-2474-12-50
9. Stewart BF, Siscovick D, Lind BK, et al. Clinical factors associated with calcific aortic valve disease. J Am Coll Cardiol. 1997;29(3):630-634. doi:10.1016/S0735-1097(96)00563-3

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