Aortic Valvulitis in Hypereosinophilic Syndrome: A Case Report

Mariano Gaston Bergier,[1] *Rocío Blanco,*[1] *Santiago Decotto,*[1] *Anibal Arias*[1]

Hospital Italiano de Buenos Aires,[1] *Buenos Aires – Argentina*

Introduction

Hypereosinophilic syndromes are characterized by the sustained overproduction of eosinophils, which can infiltrate various organs and release toxins that damage tissues.[1] Causes of increased eosinophils include 1) primary or neoplastic causes (e.g., stem cell, myeloid, or eosinophil neoplasia, and clonal disorders); 2) secondary or reactive causes (e.g., parasitic infections, solid tumors, and T-cell lymphomas); 3) idiopathic causes: part of specific syndromes (e.g., Churg-Strauss); and 4) hypereosinophilia of unknown significance, when there is no organic damage.

When specifically discussing rheumatic syndromes, the most common one is eosinophilic granulomatosis with polyangiitis, formerly known as Churg-Strauss disease. This vasculitis affects small and medium-sized arteries, primarily affecting the skin and lungs. However, it is a multisystem disorder that can affect kidneys, heart, and nervous system as well. This condition is often associated with chronic rhinosinusitis, asthma, and eosinophilia. ANCA antibodies are usually present, except in cases where the heart is involved. In such cases, ANCA antibodies are usually negative, but eosinophil counts remain elevated. Whenever possible, confirmatory diagnosis should be confirmed through an endomyocardial biopsy.[2,3]

Cardiac involvement occurs in approximately 5% of cases and is often associated with eosinophilic myocarditis, the leading cause of morbidity and mortality in hypereosinophilic syndromes. Eosinophilic myocarditis clinically progresses through three stages: 1) acute necrotic stage, characterized by eosinophil infiltration, toxin release, and necrosis, often asymptomatic; 2) intermediate or thrombotic stage, marked by the formation of intracardiac thrombi, with potential detachment and embolization; and 3) fibrotic stage, which involves subendocardial or valvular fibrosis and may lead to valvular insufficiency and heart failure.

While endomyocardial biopsy provides a definitive diagnosis, imaging techniques such as transthoracic Doppler echocardiography and magnetic resonance imaging (MRI) can help identify disease-related effects such as intracardiac thrombi, subendocardial fibrosis, or thickening of the posterior mitral valve or posterior wall. [4,5]

A clinical case of a patient with hypereosinophilia and transient involvement of the aortic valve is presented.

Keywords

Hypereosinophilic Syndrome; Aortic Valve Disease; Stroke

Mailing Address: Mariano Gaston Bergier •
Hospital Italiano de Buenos Aires. Perón 4190. Postal code: C1199ABB. Buenos Aires – Argentina
E-mail: mariano.bergier@hospitalitaliano.org.ar
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Case Report

An 81-year-old female patient with a history of adult-onset asthma, chronic rhinosinusitis, idiopathic sensory neuropathy, and cognitive impairment presented with decreased strength in her left upper limb following a fall five days prior to the consultation.

On physical examination, she was hemodynamically stable but had left brachial (0/5) and left femoral (3/5) paresis. Laboratory results showed a hematocrit of 34.8%, leukocytosis of 16,000/mm^3 with 56% eosinophils, platelets of 153,900/mm^3, serum creatinine of 1.12 mg/dL, and a brain natriuretic peptide (ProBNP) level of over 35,000 pg/mL (normal range up to 750 pg/mL in individuals over 75 years of age). High-sensitivity troponin was elevated to 322 pg/mL (99th percentile < 14 pg/mL). Chest X-ray showed a slight increase in cardiothoracic ratio, with mild evidence of flow redistribution to the upper lung fields. Electrocardiogram showed sinus rhythm, left axis deviation, narrow QRS complex, and poor R wave progression in the precordial leads without ST-T segment abnormalities.

A brain MRI was performed based on physical examination findings. It showed diffusion restriction in several cortical and subcortical regions, including the semioval centers, bilateral occipital cortex, bilateral cerebellum, and border zones in both cerebral hemispheres (Figure 1). These findings were consistent with an ischemic stroke of probable embolic origin. A transthoracic Doppler echocardiogram subsequently revealed diffuse hypokinesis with an anteroseptal defect and mild left ventricular dysfunction, along with mild to moderate mitral regurgitation. Notably, there was significant diffuse and irregular thickening of the right coronary cusp of the aortic valve associated with severe regurgitation, findings not seen in previous studies (Figure 2). Blood cultures were negative.

Because of the patient's history of asthma, chronic rhinosinusitis, and idiopathic sensory neuropathy, along with marked hypereosinophilia, the diagnosis of eosinophilic granulomatosis with polyangiitis was considered. Antinuclear antibody levels were negative, and viral and parasitic infections were excluded. A bone marrow biopsy showed a marked increase in eosinophils with dysplastic changes, but no clonality.

In the presence of a possibly rheumatic hypereosinophilic syndrome, patient was started on empirical treatment with intravenous glucocorticoids, which normalized the eosinophil count within 24 hours (Figure 3). A repeat transthoracic Doppler echocardiogram performed 72 hours after initiation

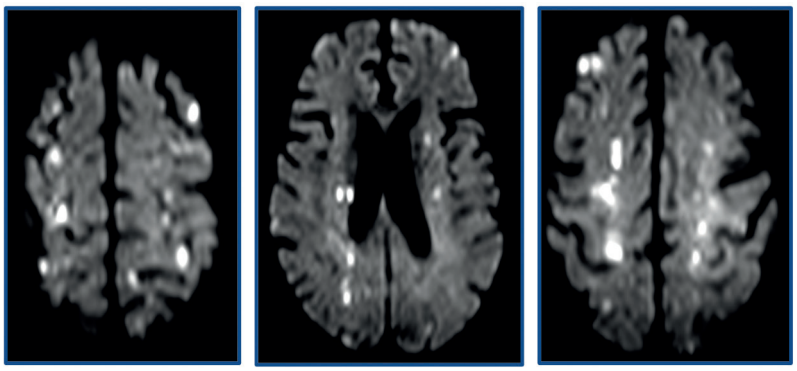

Figure 1 – *Nuclear MRI: Multiple cortico-subcortical hyperintense lesions on T2 and FLAIR sequences, with restricted diffusion, observed in both cerebral hemispheres. These lesions are distributed in border zone or watershed infarct territories.*

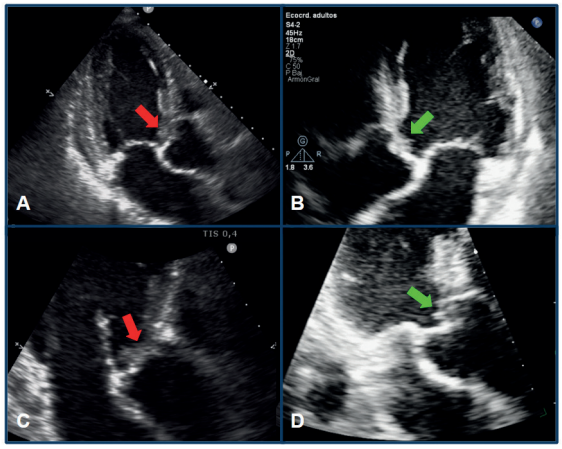

Figure 2 – *Sclerosis and thickening throughout the entire extent of the right coronary cusp of the aortic valve (indicated by arrows). Improvement is observed after treatment with glucocorticoids. Panels A and C show the condition before treatment, while panels B and D show the improvement after the initiation of treatment.*

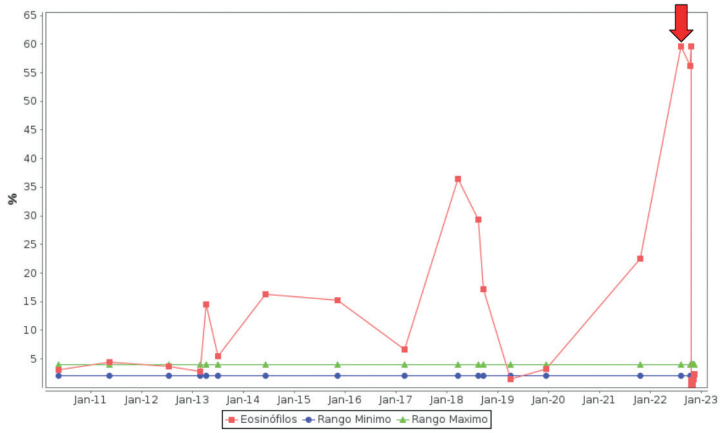

Figure 3 – *Historical trend of eosinophil count over time (in red), with the lowest range indicated in blue and the highest range in green. Figure highlights hypereosinophilia with fluctuations throughout the patient's medical history. Red arrow points to a sharp decrease in eosinophil count following corticosteroid treatment.*

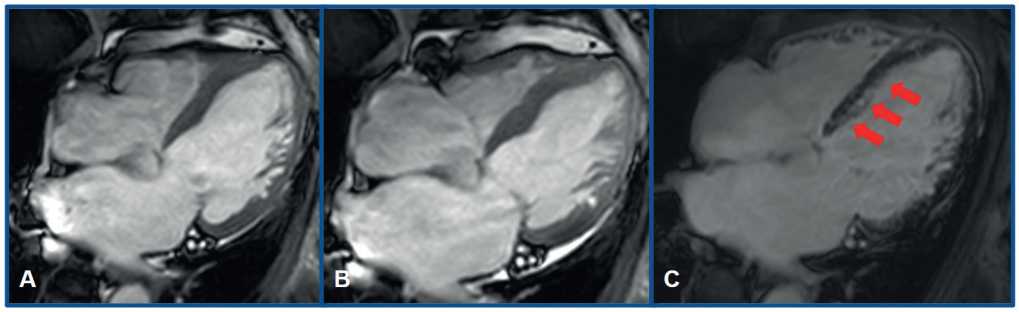

Figure 4 – *Nuclear MRI: Severe impairment of left ventricular systolic function (LV ejection fraction 25%) due to global hypokinesis. Panel 4A shows the heart at the end of diastole, and panel 4B shows it at the end of systole. Late gadolinium enhancement sequences (panel 4C) reveal subendocardial enhancement in the basal and medial septal segments, consistent with myocardial fibrosis, indicated by the three red arrows. Fibrosis is likely related to hypereosinophilia, although an ischemic origin cannot be entirely ruled out.*

of treatment showed a significant reduction in aortic valve involvement (Figure 2).

Further evaluation with contrast-enhanced cardiac MRI showed late gadolinium enhancement with a subendocardial pattern, predominantly in septal segments, suggesting fibrosis probably related to hypereosinophilic syndrome. However, the possibility of subendocardial injury from another cause could not be completely excluded. Left ventricular systolic function was severely impaired, with an ejection fraction of 25% due to global hypokinesia. Fat-suppressed T2-weighted images suggested a slight prolongation of relaxation times, but this was not confirmed by mapping techniques (Figure 4). Because of the patient's age and frailty, coronary angiography and endomyocardial biopsy were not performed.

The patient showed clinical improvement and was discharged with prescriptions for oral glucocorticoids and anti-remodeling medications (angiotensin-converting enzyme inhibitors and beta-blockers). She continues to be followed on an outpatient basis by cardiology, neurology, and rheumatology with good progress and no relapses.

Discussion

While there are reports in the literature of myocardial and mitral valve involvement associated with this hematological syndrome, valvular involvement generally results from changes in ventricular remodeling and subsequent tenting of the posterior mitral valve leaflet. In this case, the involvement occurred on the aortic valve, and the thickening and restriction of valve mobility were reversible with medical treatment with corticosteroids. The response to this empirical treatment raised suspicion of an inflammatory-prothrombotic process occurring on the valvular endocardial surface. Although we lack pathological confirmation of this mechanism, the reduction in eosinophil counts in response to treatment, and its timing with the administration of corticosteroids, support a dose-response phenomenon. While we cannot rule out the presence of thrombosis by another mechanism, we believe this differential diagnosis should be considered due to the therapeutic implications.[4,5]

Regarding the patient's acute cerebral event, strokes in border zone or watershed territories are typically hemodynamic in origin, often following cardiac arrest. However, the patient did not exhibit any hemodynamic disturbances that could justify such an event. Other potential causes of ischemic stroke in this context include intracardiac embolism secondary to endomyocardial fibrosis or toxic endothelitis caused by the release of eosinophil-derived cytokines.[6,7]

Although the subendocardial enhancement pattern on imaging could suggest ischemic necrosis, the extent of ventricular dysfunction and the limited area affected by focal fibrosis argue against this hypothesis. Because of the patient's frailty, coronary angiography was not performed, leaving some uncertainty.

The significant elevation of biomarkers such as ProBNP and high-sensitivity troponin, together with global ventricular dysfunction, raised the suspicion of eosinophilic myocarditis. However, this diagnosis was not confirmed by endomyocardial biopsy. Similarly, fat-suppressed T2-weighted imaging suggested a slight prolongation of relaxation times, although mapping techniques could not confirm this finding.

Conclusion

This case presents a patient with a history of asthma, chronic rhinosinusitis, and sensory neuropathy who developed hypereosinophilia and ischemic stroke in border zone territories. Notably, thickening and dysfunction of the aortic valve were observed, an uncommon manifestation of hypereosinophilic myocarditis. The clinical symptoms and imaging findings improved with glucocorticoid treatment, suggesting a rheumatologic origin for the valvular and cerebrovascular involvement in this patient.

Author Contributions

Conception and design of the research, acquisition of data, analysis and interpretation of the data, writing of the manuscript and critical revision of the manuscript for intellectual content: Bergier MG, Blanco R, Decotto S, Arias A.

Potential Conflict of Interest

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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