Exploring Cardiac Variability in Hypereosinophilia: Clinical Insights and Echocardiographic Findings

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ABSTRACT:

Introduction: The cardiac manifestations of hypereosinophilia include mainly endomyocardial fibrosis, which is the most frequently observed form. However, eosinophilic cardiopathy can manifest itself in different ways, affecting the various layers of the heart and presenting a variety of clinical and echocardiographic presentations.

Aim: The aim of our study is to describe the various aspects of cardiac involvement observed in hypereosinophilia, based on our case series and data from the literature.

Methods: This is a retrospective, descriptive study of five observations illustrating the diversity of eosinophilic cardiopathy, from the cardiology department of the Mohammed VI University Hospital in Marrakech, over a period of 12 months.

Results: Over the period of the study, five patients presented with cardiac damage in the context of hypereosinophilia. The mean age was 53.8 years, with a predominance of women (sex ratio 0.66). In the majority of cases, the discovery of cardiac involvement was incidental to a cardiovascular check-up requested during the course of their medical condition. All cases had high levels of hypereosinophilia, with an average of 5681. These observations illustrate the wide variety of aetiologies of hypereosinophilia, all of which were represented: 3 cases of Churg-Strauss syndrome, 1 case of idiopathic hypereosinophilia syndrome, and 1 case of DRESS syndrome. The cardiac disorders observed were hypokinetic cardiomyopathy at the dilated stage in 60% of cases, acute eosinophilic myocarditis in 20%, and acute pericarditis in the remaining cases. The outcome was marked by an improvement in the FE in 60% of cases, stabilisation in 20%, and a fatal outcome in the remainder. Treatment is based on symptomatic therapy of the CHF and treatment of the underlying aetiology.

Discussion and Conclusion: Eosinophils are cytotoxic through the release of granular proteins that initially attack the endocardium, leading to thrombosis and embolic events. Subsequently, this aggression contributes to fibrosis and valvular complications. Cardiac damage can also manifest itself as potentially serious acute myocarditis or pericarditis, which can progress to cardiac tamponade.These cardiac disorders and the diversity of possible aetiologies serve as a reminder that vital prognosis may be at stake in the acute phase, and to emphasise that functional prognosis depends on early echocardiographic screening and rapid initiation of treatment to limit the risk of thrombo-embolic and fibrosing complications.

KEY WORD: Hypereosinophilia, heart failure, endomyocardial fibrosis, cardiomyopathy

INTRODUCTION:

Hypereosinophilia (HE) is characterised by a persistent increase in the absolute number of eosinophils. Hypereosinophilia is associated with eosinophil-mediated organ damage and can be manifested by involvement of various organs, including the skin, lungs, heart, brain and peripheral nervous system.(1) Cardiac involvement plays a key role in determining morbidity and mortality, with the possibility of the occurrence of cardiac thrombosis and large vessel thrombosis with severe clinical manifestations.

MATERIALS AND METHODS :

This is a retrospective, descriptive study of five observations illustrating the diversity of eosinophylic cardiopathy, from the cardiology department of CHU Mohammed VI of Marrakech, in a period of 12 months in the aim was to describe the different aspects of cardiac involvement observed during hypereosinophilias, through our case series and literature data.

Records of patients hospitalized with the diagnosis of hypereosinophilia with cardiac involvement were catalogued from the department's registers and archives.

A descriptive analysis of the study population was performed. Quantitative variables were presented as medians and extremes, and qualitative variables as numbers and percentages.

RESULTS:

Over the study period, five patients presented with cardiac involvement in the setting of hypereosinophilia. The mean age was 53.8 years, with a female predominance (sex ratio 0.66).
In the majority of cases, the discovery of cardiac involvement was incidental to a cardiovascular check-up requested during the course of the patient's illness.
All cases had high levels of hypereosinophilia, with an average of 5681.
These observations illustrated the wide variety of aetiologies of hypereosinophilia, all of which were represented: 3 cases of Churg-Strauss syndrome, 1 case of idiopathic hypereosinophilia syndrome, and 1 case of DRESS syndrome.
The cardiac disorders observed were hypokinetic dilated cardiomyopathy with moderate to moderate LV dysfunction in 60% of cases, acute eosinophilicmyocarditis in 20%, and acute pericarditis in the remaining case.

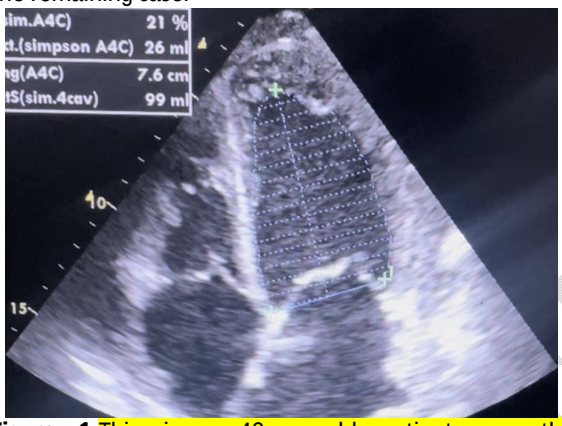

Figure 1: This is a 40-year-old patient, recently diagnosed with Churg strauss disease, who presents with NYHA stage III dyspnea. An echocardiogram was performed as part of the follow-up of her disease, finding an Aspect of hypokinetic cardiomyopathy at the dilated stage with severe LV dysfunction and an estimated LVEF of 21% (SBP).

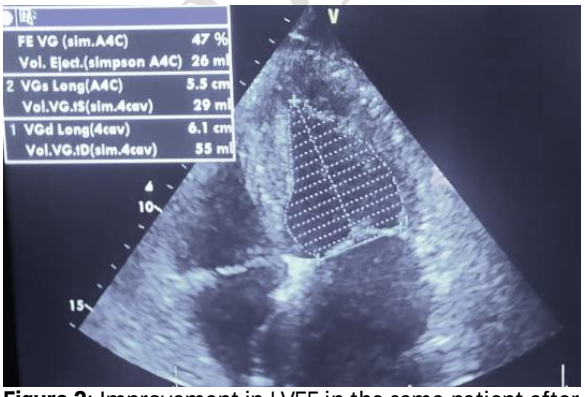

Figure 2: Improvement in LVEF in the same patient after a 12-month follow-up under combined symptomatic and aetiological treatment.

The outcome was marked by an improvement in LVEF in 60% of cases, stabilisation of the disease in 20%, and a fatal outcome in the remainder.
Treatment is based on symptomatic therapy of the heart failure combined with treatment of the underlying aetiology.

DISCUSSION :

The association between blood eosinophilia and cardiac involvement was first noted by Löffler in 1936, when he observed two cases which he termed "fibroplastic parietal endocarditis". Since then, several studies have been carried out on eosinophilic heart disease, which encompasses a variety of cardiac disorders, from acute myocarditis to endomyocardial fibrosis (EMF).
“Several causes can be incriminated, ranging from hypersensitivity or autoimmune diseases to neoplasms and infections. In some cases, the exact cause is not identified, leading to it being classified as an idiopathic HES. This syndrome is a diverse group of haematological disorders marked by unexplained blood eosinophilia caused by secondary clonal proliferation of myeloid cells”(2).

“Cardiac involvement generally occurs in three stages. The early necrotic stage is generally asymptomatic and may involve the endocardium and myocardium. In rare cases, it can lead to acute heart failure. This is followed by a stage in which thrombi develop in the damaged endocardium and can cause peripheral embolisms. The final stage is the fibrotic stage, which leads to restrictive cardiomyopathy”(3).
Fever, acute heart failure and cardiogenic shock may occur early in the course of the disease. Embolic phenomena have been well documented in between 4% and 26% of patients. Thrombi typically occur in both ventricles and may extend to ventricular outflow tracts or sub-valvular regions. The atrium is less affected, but when it is, it can lead to stroke. When restrictive cardiomyopathy follows, the prognosis worsens considerably. Arrhythmias such as atrial fibrillation secondary to atrial enlargement are not uncommon. The heart valves may also be affected, leading to regurgitations(4).
Echocardiography plays a key role in the assessment of cardiac damage in HES. It may appear normal at the acute necrotic stage or, on the other hand, reveal a mural hypertrophy related to myocardial oedema secondary to inflammation. (5)
During the thrombotic phase, thrombi may be seen at the apex of the left or right ventricle, or both. This may be confused with LV non-compaction, apical hypertrophic cardiomyopathy (HCM) or even a typical LV apical thrombus caused by abnormal kinetics of the apical wall. The use of contrast agents, aimed at better delineating the apex, may help to distinguish thrombi of

apical HCM and those from LV non-compaction.Furthermore, contrast agents may reveal preserved systolic function at the apex in HES, distinguishing it from an apical infarct with thrombus. The transition from thrombus to fibrosis is not clearly defined, particularly on echocardiography, but it coincides with changes in the clinical presentation, marked by an accentuation of the symptoms of heart failure. The apical regions continue to show obliteration, now characterised more by fibrosis and less by thrombus. The posterior leaflet of the mitral valve may thicken and adhere to the underlying endocardium of the posterobasal wall, limiting its movement. In addition, a pattern of restrictive cardiomyopathy develops, evidenced by characteristic mitral valve Doppler indices reflecting reduced left ventricular compliance and increased filling pressures. At this stage, various abnormalities such as distortion of ventricular geometry, basal hyperkinesis and fibrothrombotic obliteration of the apex can also be identified. (6)

Endomyocardial biopsy is often considered to be the gold standard and can identify whether the infiltrate is eosinophilic, lymphocytic or granulomatous. However, it should be born in mind that eosinophilic myocarditis develops as focal infiltrates surrounded by normal tissue. It is important to note that this is an invasive procedure that cannot be performed in all patients, and no endo-myocardial biopsy was performed in our patients.

As previously mentioned, eosinophilic myocarditis involves focal infiltration of cardiac tissue. Consequently, CMR is a rapidly evolving imaging modality in the field of cardiovascular disease, and is considered the non-invasive gold standard for evaluating such cases of myocardial inflammation and damage with a diagnostic accuracy of 83% (sensitivity of 80% and specificity of 87%) to identify acute myocarditis.

Similar to echocardiographic imaging, CMR can be a useful tool to investigate the acute set- tings, and also the time course of EM . In the acute phase characteristic findings are thickening and edema of ventricular walls ("pseudohypertrophy"), and large or smaller thrombotic lesions (not so easily detectable at the echocardiographic exam). In the chronic phase, during follow-up, it is possible to monitor EF and eventually the reduction of LGE

The main pattern of LGE in EBM is nodular/ patchy (non-ischemic), but there are conflicting reports about prevalent locations, some authors, described a diffuse subendocardial involvement in contrast to viral myocarditis that affects the left ventricular postero-lateral wall. (7;8)

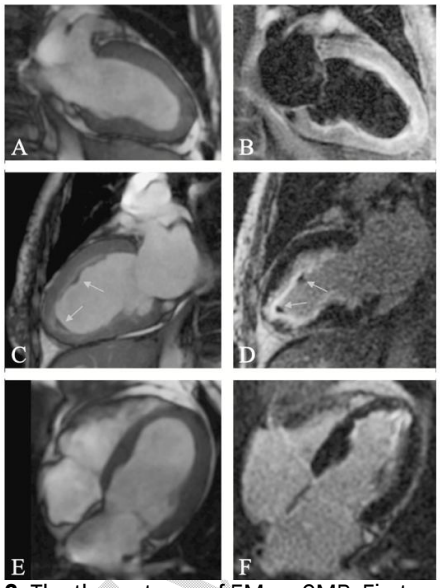

Figure 3: The three stages of EM on CMR. First acute "ne- crotic stage" with pseudohypertrophy (2c SSFP, A) due to myocardial inflammation (subendocardial/transmural hyper- intensity in 2c STIR, B). Second acute "thrombotic stage" with endomyocardial thrombi (hypointense lesions indicated by arrows in 2c SSFP and 2c GRE, C, D, with diffuse suben- docardial late gadolinium enhancement, d). Chronic phase with normal segmental kinesis without thrombotic lesion (4c SSFP, E) and endomyocardial fibrosis (4c GRE, F). 2c: 2-chamber; SSFP: steady-state free precession sequence; STir: short tau inversion recovery sequence; gre: gradi- ent echo sequence; lge: late gadolinium enhancement; 4c: 4-chamber.(7)

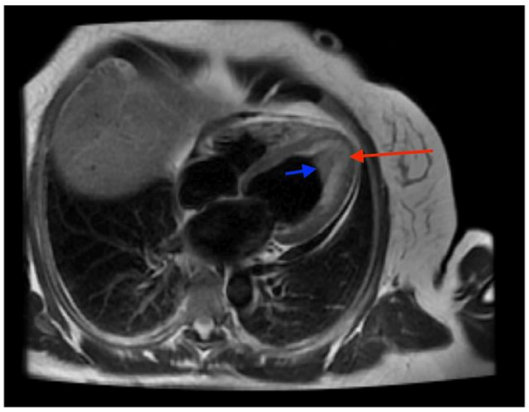

Figure 4 : Cardiac MRI (T2 imaging, 4-chamber view).T2 weighted image demonstrates areas of hyperintensity in the left ventricular apex suggestive of underlying edema and inflammation (red arrow) resulting in complete obliteration of the apex. The overlying area of hypointensity was suspicious for an organized apical thrombus (blue arrow). T1 weighted image demonstrated significant late gadolinium enhancement of the left ventricular apical cavity consistent with a

background of myocardial fibrosis and scarring (not depicted).(8,9)

"The main aim of treatment is to reduce the absolute number of eosinophils, improve signs and symptoms and prevent disease progression.
The timing of treatment depends on the severity of the hypereosinophilia and the presence of signs and symptoms.
If patients develop symptoms of hyperleukocytosis due to extremely high levels of eosinophils, even if these are rare, the hypercellularity should be rapidly reduced.
Most patients are asymptomatic and have lower eosinophil counts. Pharmacological treatment is aimed at reducing the signs and symptoms of eosinophilic disease and keeping levels below 1.5 x 109/L (1500 cells/μL) to help prevent the development of organ damage(11;12).
Corticosteroid therapy is the most common treatment modality, with anticoagulant therapy in cases of intracardiac thrombosis"(13).

In the complete absence of information about whether anticoagulationcould prevent the progression of hyper eosinophilic cardiac disease from the thrombotic to the fibrotic stage, prophylactic treatment for this indication cannot be recommended; however, patients who have HES with evidence of intracardiac thrombosis by echocardiography or CMR should be treated with anticoagulant therapy because of reports, limited though they are, that approximately 25% of these patients develop emboli (14,15).

In severe clinical forms, combined treatment with corticosteroids and immunosuppressive therapy is recommended.
In addition to medical treatment,in patients with reduced cardiac function, conventional HF treatment is recommended (16), while cases with hemodynamic instability may require mechanical circulatory support or intra- aortic balloon counterpulsation along with inotropic agents,some patients benefit from surgical removal of intracardiac thrombi, endomyocardial fibrosis or valve replacement.

CONCLUSION :

Cardiac involvement in hypereosinophilia is a diagnostic challenge given the wide variability of these clinical and echocardiographic forms, but at the same time it is a major prognostic factor, underlining the importance of early echocardiographic screening and rapid initiation of treatment to limit the risk of thromboembolic and, above all, fibrosis complications, which can be irreversible.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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