CASE PRESENTATION

Löeffler endocarditis due to idiopathic hypereosinophilic syndrome

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Abstract: Hypereosinophilic syndrome encompasses a heterogenous group of non-hematologic and hematologic disorders defined as peripheral blood eosinophilia >1500/mm^3 persisting more than 6 months and eosinophilic end organ complications[1,2]. Löeffler endocarditis (LE) is the most common cardiac manifestation of the hypereosinophilic syndrome (HES) and represents an acute form of primary restrictive cardiomyopathy[3]. We report the case of a 74 years-old woman with symptoms related to congestive heart failure and weight loss. At admission the patient had tachycardia and a grade 2/6 systolic mitral murmur. Laboratory findings revealed eosinophilia, hepatocytolysis syndrome and dyslipidemia. The electrocardiogram (ECG) showed non-specific ST-segment and T wave abnormalities. The echocardiography revealed left ventricular apical thrombus and entrapment of chordae tendineae with restricted motion of mitral leaflets leading to mitral regurgitation. The diagnosis of myocarditis was confirmed by the cardiac magnetic resonance imaging which showed the presence of a left ventricular mass with low signal on steady-state free precession imaging and diffuse circumferential subendocardial late gadolinium enhancement (LGE). When discussing the etiology of the HES the following were taken into consideration: hematologic, reactive or secondary disorders. This case is distinguished by diagnosis in an elderly woman and good response to corticosteroid therapy.
Keywords: Löeffler endocarditis, hypereosinophilic syndrome, cardiac involvement, multimodality imaging.

Abstract: Sindromul hipereozinofilic cuprinde un grup heterogen de manifestări hematologice și non-hematologice, definit prin prezența eozinofiliei >1500/mm^3, care persistă peste 6 luni și afectarea eozinofilică a organelor țintă. Endocardita Löeffler (EL) constituie cea mai frecventă manifestare cardiacă a sindromului hipereozinofilic (SHE) și reprezintă o formă acută de cardiomiopatie restrictivă. Raportăm cazul unei paciente în vârstă de 74 de ani, care se prezintă cu fenomene de insuficiență cardiacă și scădere ponderală. La admisie, aceasta prezenta tahicardie și suflu sistolic gradul 2/6 în focarul mitralei. Biologic asocia eozinofilie, sindrom de hepatocitoliză și dislipidemie. Electrocardiograma (ECG) a arătat modificări nespecifice ale segmentului ST și ale undei T. Ecocardiografia a documentat prezența unui tromb la nivelul apexului ventriculului stâng care îngloba cordajele, cu mișcare restricționată a cuspelor, determinând regurgitare mitrală. Diagnosticul de miocardită a fost confirmat prin rezonanță magnetică cardiacă, demonstrând prezența unei mase cu structură omogenă, cu hiposemnal față de miocardul ventricular și captare tardivă de gadolinium difuză circumferențială subendocardică. Pentru stabilirea etiologiei SHE au fost considerate următoarele: afectare hematologică, reactivă sau afectare secundară. Particularitarea cazului constă în prezența diagnosticului la o pacientă în vârstă, cu răspuns favorabil la corticoterapie.
Cuvinte cheie: endocardita Löeffler, sindromul hipereozinofilic, afectare cardiacă, imagistica multimodală.

INTRODUCTION

Löeffler endocarditis is a restrictive cardiomyopathy caused by eosinophilic infiltration of the heart. It represents the cardiac manifestation of HES and is associated with high mortality and morbidity rates[4]. LE progresses through three stages: acute necrotic stage, thrombotic stage, and fibrotic stage. It is still unclear which is the best imaging method, but both non-invasive and invasive imaging modalities may be useful[5].

CASE REPORT

We report the case of a 74-year-old patient, without family medical history, who addressed to emergency care unit for resting dyspnea, orthopnea, paroxysmal nocturnal dyspnea, atypical chest pain, weight loss, and skin lesion, since two weeks. Her past medical history was remarkable for autoimmune thyroiditis and dyslipidemia. Home medication included Levothyroxine 25 mcg per day.

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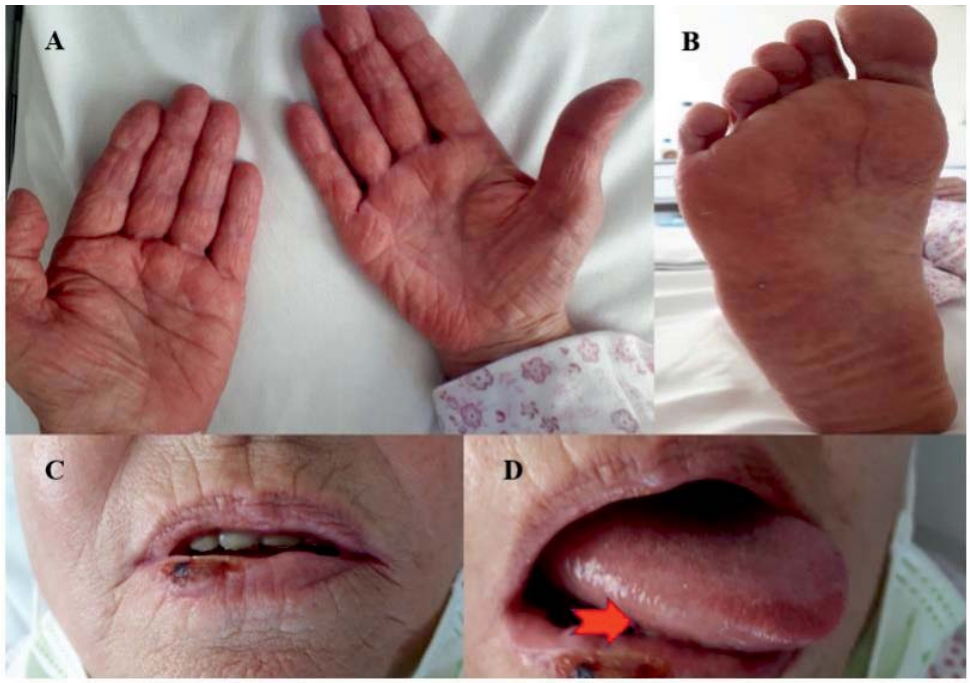

Figure 1. A, B. Palmar and plantar rash. **C, D.** Lower lip and right lateral tongue ulcerations.

On presentation, the patient was afebrile, with a blood pressure of 170/100 mmHg, pulse rate of 100 beats/min, with a grade 2/6 systolic mitral murmur, absent breath sounds on right hemithorax, and peripheral oxygen saturation of 97%. Her physical examination was also notable for palmar and plantar rash (Figure 1 A, B) and lower lip and right lateral tongue ulcerations (Figure 1 C, D).

The biological work up revealed leukocytosis (WBC=18140/mm^3), an eosinophil (Eo) count of 2080/mm^3, representing 11,5% (normal range, 0%-4%), hepatocytolysis syndrome (ALT=45 U/L, AST=86 U/L), electrolyte imbalance (Na=129 mmol/L, Cl=97 mmol/L), and dyslipidemia (Total Cholesterol=226 mg/dL; HDL-Col=34 mg/dL, LDL-Col=166 mg/dL, TGL=181 mg/dL). Her serum NT-pro BNP level was 4070 pg/mL.

The ECG showed sinus rhythm, ST-segment depression in leads V4-V6 and T-wave inversion in inferior leads (Figure 2). She was admitted to the department of cardiology for further evaluation.

Transthoracic echocardiography revealed non-dilated cardiac chambers, good left and right ventricular global systolic function (TAPSE=18 mm and

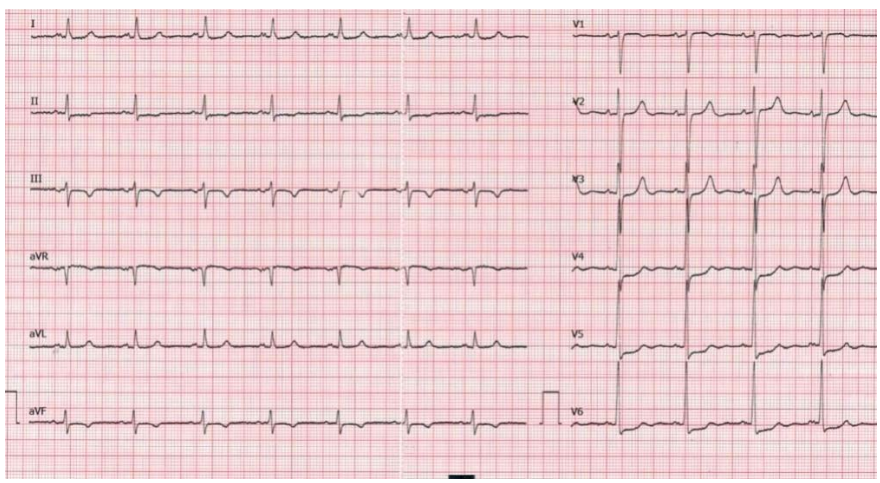

Figure 2. ECG aspect: sinus rhythm, ST-segment depression in V4-V6, T-wave inversion in inferior leads.

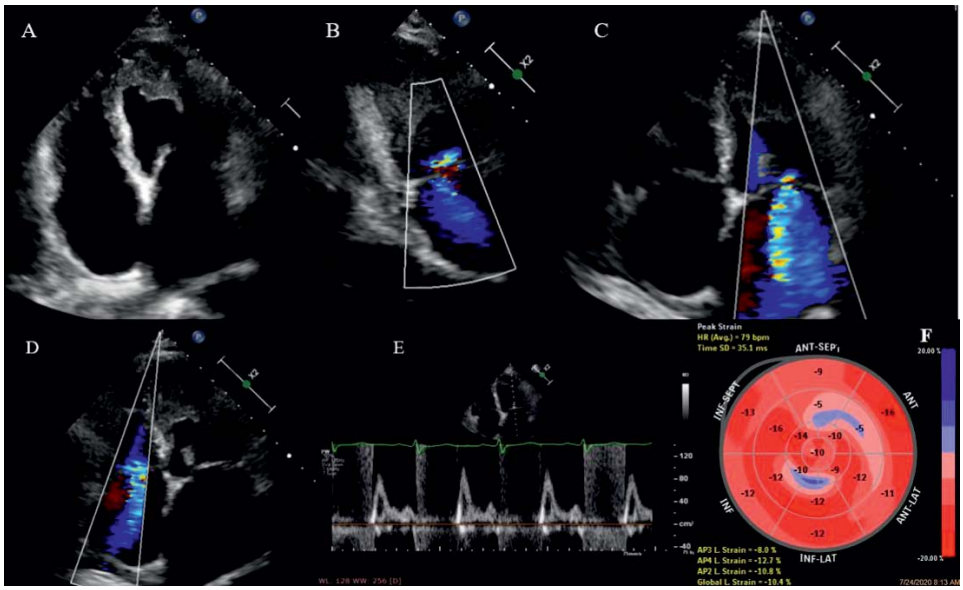

Figure 3. Transthoracic Echocardiography: **A.** Apical four-chamber view- Left ventricular apical obliteration with mural thrombus. **B, C.** Apical four chamber and two chamber view-mitral regurgitation. **D.** Apical four-chamber view-tricuspid valve regurgitation. **E.** Restrictive flow pattern across mitral valve. F. Left ventricular endomyocardial systolic dysfunction.

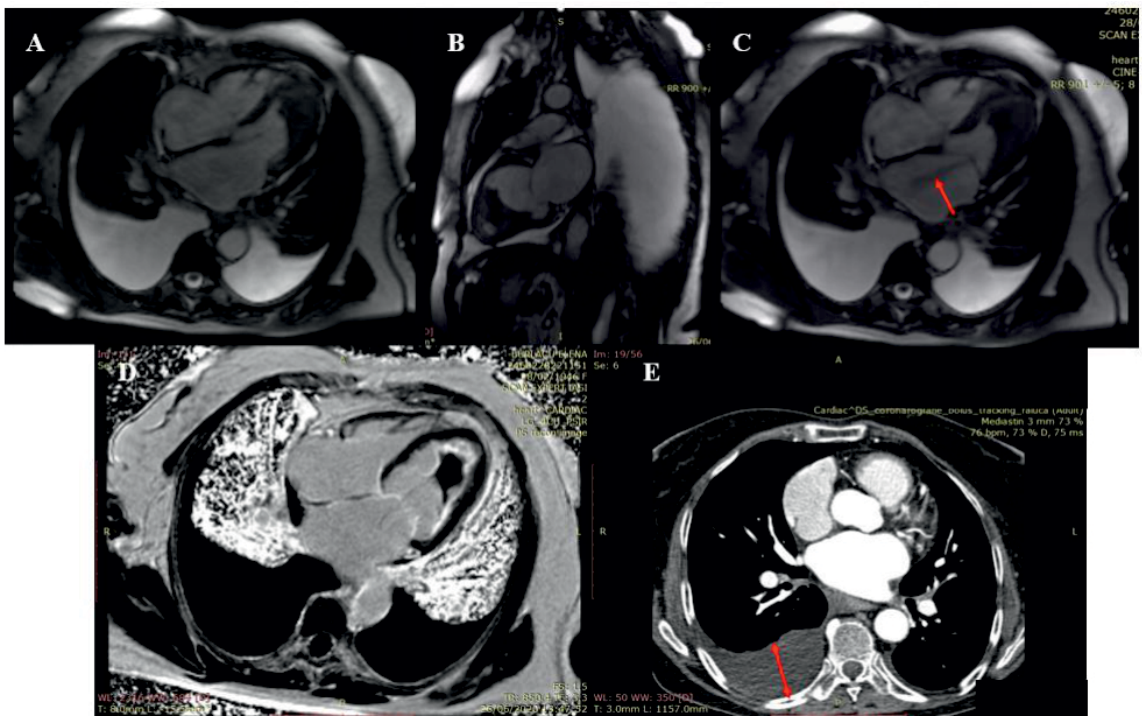

Figure 4. Cardiac magnetic resonance: **A, B.** Left ventricular apical obliteration with mural thrombus. **C.** Moderate mitral regurgitation. **D.** Diffuse circumferential subendocardial LGE, Thrombotic lesion shows no contrast enhancement. **E.** Torax computed tomography-right pleural effusion.

LVEF=53%). Apical four-chamber view showed a large echo density fixed to the left apex (32/31 mm) (Figure 3A) with restriction of the mitral apparatus and moderate-severe mitral regurgitation (Figure 3B,C), and small ventricular cavity due to mural thrombus. Moderate tricuspid valve regurgitation and moderate pulmonary hypertension was also observed (Figure 3 D). Diastolic function was evaluated using a multiparametric approach including: mitral inflow E/A wave (>2.5), E wave deceleration time (<150 msec), incre-

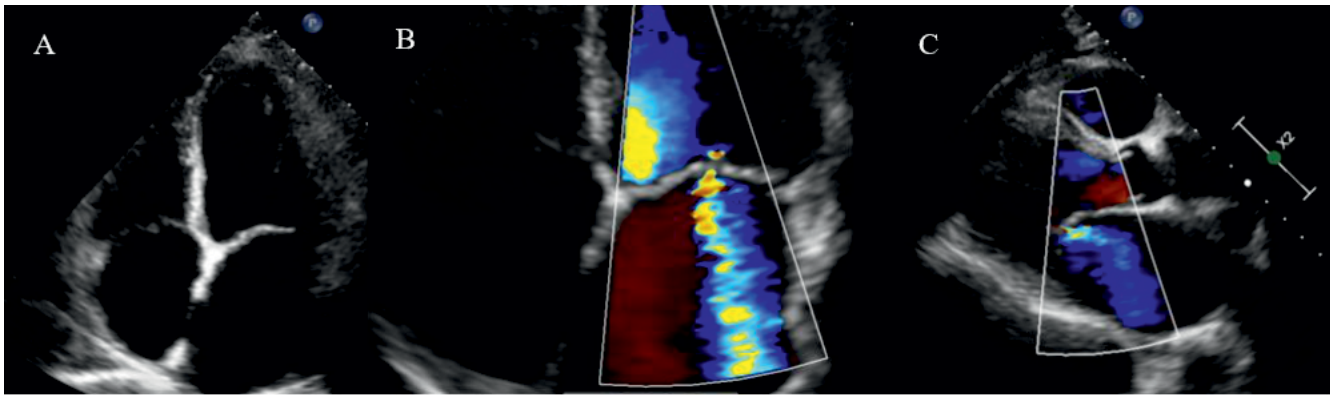

Figure 5. Transthoracic echocardiography: **A.** Four-chamber apical view-complete resolution of the left ventricular apical thrombus. **B.** Four-chamber apical view-Mitral regurgitation. **C.** Parasternal long-axis view-Moderate mitral regurgitation.

ased left atrial volume index (43 ml/m²) (Figure 3-E). Overall left ventricular (LV) global longitudinal strain (GLS) was reduced to -10.4% indicating LV endocardial systolic dysfunction (Figure 3 F).

Clinical impression and differential diagnosis

Given the patient's presentation and prior investigations, the few top diagnoses included apical thrombus, apical hypertrophic cardiomyopathy, left ventricular non-compaction cardiomyopathy, or Löeffler endocarditis.

Cardiac magnetic resonance (CMR) demonstrated left ventricular apical obliteration with mural thrombus with a low signal on steady-state free precession imaging, first-pass perfusion and postcontrast late enhancement images (Figure 4-A, B, D), moderate mitral regurgitation (Figure 4-C), and diffuse circumferential subendocardial late gadolinium enhancement (LGE) (Figure 4-D). However, since subendocardial LGE is a hallmark of ischemic heart disease, coronary heart disease was excluded using computed tomography angiography.

In addition, her hyper eosinophilia and skin rash prompted evaluation for others etiologies. Hematology was consulted and BCR-ABL (for chronic myeloid leukemia), CALR (for myeloproliferative neoplasms), and JAK-2 (for essential thrombocythemia, polycythemia vera, or myelofibrosis) mutation were all negative. Test results for parasitic infection were also negative. The patient's immunoglobulin E level was normal (40.5 UI/mL, the upper normal limit is 100.0 UI/mL). The work up for cytoplasmic antineutrophil cytoplasmic antibody and perinuclear antineutrophil cytoplasmic antibody was negative. A complete computed tomography scan including thorax, abdomen and pelvis was performed in order to exclude the presence of a malignant mass. Right pleural effusion was observed (Figure 4 E) and laboratory analyses after transthoracic puncture revealed transudate. Thyroid function was in normal range. There were not enough criteria for Churg-Strauss syndrome.

Therefore, the final diagnosis was Idiopathic Hypereosinophilic syndrome with Löeffler endocarditis. Management of this patient included gradual tapering of methylprednisolone guided by echocardiogram and biological work up, acenocumarol and heart failure treatment according to current guidelines[6] with Furosemide 40 mg od, Spironolactone 25 mg od, Candesartan 16 mg od, and Bisoprolol 2.5 mg od.

At seven-months follow-up, she was asymptomatic with no skin lesions, normal hemogram (Eo=360/mm³) and resolution of left ventricular thrombus, but persisting mitral valve regurgitation and restrictive pattern diastolic dysfunction (Figure 5).

DISCUSSION

HES is a disorder characterized by persistent eosinophilia with damage to the multiple organs. After activation, eosinophils express several proteins including eosinophil major basic proteins (MBP1 and MBP2), eosinophil peroxidase (EPO) and eosinophil-derived neurotoxin (EDN) with numerous biological properties including direct cell toxicity[7]. Dermatologic involvement followed by pulmonary, gastrointestinal, and cardiac manifestations are the most common clinical implications reported[2]. Cardiac involvement usually follows 3 stages: the first stage, frequently asymptomatic, with acute necrosis, the second stage characterized by mural thrombi formation, and third stage with fibrosis and restrictive cardiomyopathy ensues[4,8].

Our patient presented with symptoms of heart failure and demonstrated a moderately elevated eosinophil count. The underlying causes of HES are various. The patient received an almost complete workup to find the underlying etiologies, and the negative results led to the diagnosis of idiopathic HES.

Transthoracic echocardiography plays an important role in both diagnosis and follow-up[5]. The most common echocardiographic findings are endomyocardial thickening, left or right mural thrombus, frequently in apex, small ventricular cavity due to endocardial thickening and mural thrombus, atrioventricular valves implication with mitral or tricuspid regurgitation, biatrial enlargement, and pericardial effusion[5]. Cardiac magnetic resonance is crucial for LE diagnosis due to detection and characterization of ventricular thrombi and early detection of subendocardial thickening associated with myocardial tissue abnormalities. Due to the focal nature of the disease, the endomyocardial biopsy has a low sensitivity[4].

Given the limited indication of endomyocardial biopsy for the diagnosis of LE because of numerous false-negative results, cardiac involvement was observed in transthoracic echocardiography and confirmed by CMR.

CONCLUSIONS

The presented case highlights a Löeffler endocarditis which was diagnosed in an elderly patient in the thrombo-fibrotic stage with restrictive cardiomyopathy and it is distinguished by no specific cause for HES and good response to corticosteroid therapy. Every imaging tool has advantages and limitations. A multimodality imaging stepwise approach is the most rational way for precise characterization of LE

Conflict of interest: none declared.

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