Hypereosinophilic Syndrome: A Case of Fatal Löffler Endocarditis

1. Introduction

Hypereosinophilic syndrome (HES) is a rare disorder with unknown global prevalence, barely reported in Hispanic population [1]. HES is traditionally defined as persistent eosinophilia with more than 1500 cells per microliter for at least six months, which remains unexplained despite a comprehensive evaluation, in association with organ dysfunctions directly attributable to eosinophilic infiltration. Cardiac involvement may be present in 50 to 60% of the patients. This is known as Löffler endocarditis. We present a case of a 36-year-old Hispanic man with signs of heart failure. Laboratory studies showed eosinophilia (23,100/\muL). Thoracic computer tomography showed bilateral pleural effusion and a large left ventricular mass. Transthoracic echocardiography showed left ventricle apical obliteration and a restrictive pattern. Pulmonary angiography demonstrated a thrombus in the lingular and middle lobe. Despite treatment, the patient deceased seven days after admission. Autopsy confirmed the diagnosis of Löffler endocarditis.

2. Case Presentation

A 36-year-old Hispanic male admitted with persistent symptoms of congestive heart failure that began 12 days before admission and persists despite standard medical treatment. During physical examination, he presents atypical chest pain, progressive dyspnea, orthopnea, palpitation, productive cough, and fever. Physical examination revealed normal
blood pressure (110/70 mmHg), tachycardia, tachypnea, ele-
vated jugular vein pressure, and congestive hepatomegaly, in
functional class III according to the New York Heart
Association (NYHA). Cardiac auscultation revealed a third
heart sound as well as mitral and tricuspid holosystolic
murmurs; crackles were heard in both lungs and edema was
observed in both legs.

Chest radiography demonstrated pulmonary congestion
with bilateral pleural effusion and cardiomegaly (Figure 1).
Laboratory test revealed a marked leukocytosis (23,100/µL)
with hypereosinophilia (59%, 13,360/µL). Computed tomog-
raphy of the chest showed bilateral pleural effusion and
a large left ventricular mass (Figure 2). The transthoracic
echocardiogram showed moderate tricuspid and mild mitral
regurgitation with normal left ventricular dimensions and
systolic function; left ventricular filling was reduced because
of endocardial thickening together with a large homogeneous
mass at the apex that occupied 50 to 65% of the
left ventricular cavity (Figure 3). Echocardiographic Doppler
detected restrictive-type diastolic filling an E/A ratio greater
than 2. The echocardiography also revealed another mass in
the right ventricle. A coronary angiography was performed
and found no significant coronary artery disease; pulmonary
angiography demonstrated a thrombus in the lingular and
middle lobe.

An endomyocardial biopsy was performed; however,
pathologic examination of the obtained specimens revealed
mainly thrombus with some necrotic tissue. Despite the
biopsy results, a diagnosis of endomyocardial fibrosis sec-
ondary to HES was made, on the basis of the imaging,
clinical, and laboratory findings, and other secondary causes
of hypereosinophilia were ruled out. Despite the team effort
and adequate treatment, patient deteriorates to NYHA class
IV and died seven days after admission. Then, autopsy was
done which confirms the diagnosis of Löffler endocarditis
(Figure 4).

3. Discussion

Although the real epidemiology of HES is unknown, it is
estimated that 90% of patients are men; the majority of the
cases occur between 20 and 50 years of age, with a peak in
the fourth decade of life [3]. The clinical manifestations of
HES are markedly heterogeneous with a wild clinical spec-
trum from a completely asymptomatic to a life-threatening
condition; this pathology can involve many organs and
systems such as skin, lungs, nervous system, gastrointestinal
tract, kidneys, and heart; therefore the diagnosis could be a
challenge [3, 4]. The major morbidity and mortality in HES
patients are cardiovascular complication, which is found in
40 to 50% of the cases [3].

Löffler endocarditis presents with extensive infiltration of
the ventricular endocardium by eosinophils, with degranula-
tion and arteriolar necrosis with subsequent endomyocardial
fibrosis. The inflammatory changes result in thrombus for-
mation, in this case occupying both ventricular cavities, with
impairment of diastolic filling and a resultant restrictive car-
diomyopathy [8, 9]. The clinical presentation was consistent
with heart failure with NYHA functional class III that rapidly
progressed to functional class IV, despite the treatment. HES
is a potentially fatal disease, with a survival rate of less than
50% after 10-year follow-up. There are several predictors
of early mortality that includes intraventricular conduction
delay, duration of symptoms prior to presentation, NYHA
functional classes III and IV, and the presence of an embolic
event. Our patient had two of these early mortality predictors
(NYHA functional class IV and pulmonary embolism) and
rapid deterioration; finally he deceased [10, 11].

Echocardiographic and radiological studies could be a
useful tool in determining cardiac anatomy and function;
however, Löffler endocarditis requires a pathological diagno-
sis; therefore endocardial biopsy remains the gold standard.
Nevertheless, in some cases the cardiac biopsy could be a
risky procedure; therefore the clinician should assess the
inherent risk of this intervention in each particular clinical
setting. In addition, it is indispensable to rule out Löffler
endocarditis when diagnosis of pulmonary disorders asso-
ciated with hypereosinophilia is considered. Additionally, it
is important to discard the main differential diagnosis of
HES when assessing the possibility of Löffler endocarditis,
which includes hypereosinophilia secondary to hypersensi-
tivity reactions and parasite infections [4].

In this case, despite the endomyocardial biopsy result, the
patient had peripheral hypereosinophilia and typical
echocardiographic findings of restrictive cardiomyopathy;
therefore the diagnosis of Löffler endocarditis was estab-
lished and then was confirmed during autopsy. Pathological
finding in Löffler endocarditis includes fibrous thickening of
the endocardium, leading to apical obliteration, thrombus
formation, and restrictive cardiomyopathy, which clinically
manifest as heart failure, thromboembolic event, and atrial
fibrillation [5–7].

HES treatment primary goals are to reduce eosinophil
level in peripheral blood and tissue, preventing end-organ
damage and avoiding adverse thrombotic events. Heart
failure in Löffler endocarditis is mainly due to diastolic
rather than systolic dysfunction; therefore treatment includes
intravenous diuretics to decrease cardiac preload [4]. In
addition, for the treatment of symptomatic patients, such
as this case, the first-line drug of choice is corticoste-
roids followed by cytotoxic agents such as hydroxyurea or
immunomodulatory agents such as interferon-alpha. Glucocorticoid treatment resulted in clinical and biopsy-proven improvement of eosinophilic and myocardial damage as well as normalization of peripheral hypereosinophilia [12, 13]. Other recent therapeutics includes tyrosinase inhibitors and new types of monoclonal antibodies (Imatinib) [4, 14]. The patient received glucocorticoid treatment without favorable response; his heart failure continued to worsen and led to his death within one week.

4. Conclusion

Löeffler endocarditis is a rare entity probably underdiagnosed and underreported worldwide and, in Hispanic populations, this pathology represents a diagnosis challenge for the attending physician. Therefore, when HES is suspect, an echocardiographic study should be indicated with the intention of determining if there is a restrictive pattern, and if this pattern is present, a biopsy is indicated. When there is a high clinical suspicion of HES and image studies that support the possibility of Löeffler endocarditis and early mortality predictors are present, we consider that treatment should be initiated immediately even in the absence of a definitive pathological diagnosis.

Conflict of Interests

Authors declare no conflict of interests.
References


