Abrupt Onset of Refractory Heart Failure Associated With Light-Chain Amyloidosis in Hypertrophic Cardiomyopathy

Benedetta Tomberli, MD, PhD; Francesco Cappelli, MD; Federico Perfetto, MD, PhD; Iacopo Olivotto, MD

The natural history of hypertrophic cardiomyopathy (HCM) is complex and may include progressive heart failure and severe left ventricular dysfunction. When disease progression is abrupt, however, other coexisting diseases should be ruled out. This may be difficult in the case of amyloidosis, which classically mimics HCM.

RESULTS

We present an example of severe clinical deterioration in a patient with HCM due to superimposed amyloid light-chain amyloidosis. A man in his 70s with a longstanding history of genetically confirmed HCM presented with rapid development of congestive heart failure over 6 months, in sharp contrast to a previously stable, asymptomatic clinical course. He was diagnosed as having the illness in his late 40s after a resuscitated cardiac arrest and regularly followed up on a yearly basis. His most recent electrocardiogram was profoundly changed from previous tracings, with marked and diffuse voltage reduction (QS in V1-V3) and inferolateral T-wave inversion. The echocardiogram showed an abrupt increase in the severity of left ventricular (LV) hypertrophy, with a concentric rather than asymmetric appearance, granular sparkling of the myocardium, bialtrial enlargement, thickening of the mitral valve leaflets, and interatrial septum and mild pericardial effusion. Severe LV dysfunction with a restrictive LV filling pattern was evident, which is associated with LV outflow tract obstruction loss and right ventricle systolic impairment. Following hospital admission, multiple myeloma was diagnosed and confirmed by bone marrow biopsy and aspiration. Furthermore, abdominal fat aspiration showed amyloid deposition and confirmed the diagnosis of amyloid light-chain amyloidosis. Electrocardiograms, echocardiographic images, and videos presented in this report describe the abrupt and marked evolution of a sarcomeric to infiltrative cardiomyopathy, leading to an ominous outcome in which the patient died despite specific treatment.

CONCLUSIONS AND RELEVANCE

While progression to the end-stage phase occurs over several years for patients with HCM and can be detected at relatively early stages, the abrupt onset of congestive heart failure is uncommon and should raise suspicion of other, superimposed cardiac diseases.

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A man in his 70s with HCM presented with recent-onset congestive heart failure. He was diagnosed as having HCM in his late 40s when he was resuscitated from an out-of-hospital cardiac arrest (well before the availability of an implantable defibrillator), discharged, and prescribed β-adrenergic blockers and amiodarone. He was followed up for a number of years with stable findings of LV hypertrophy on electrocardiograms (Figure 1) and moderate hypertrophy of the midbasal interventricular septum on echocardiogram (ECG), which is associated with mild systolic anterior motion of the anterior mitral valve leaflet, mild mitral regurgitation, and moderate dilatation of the left atrium (Figure 2A, B, E, and F and Video 1). Doppler studies showed mild LV diastolic dysfunction (Figure 2I, J, and M) and left ventricular outflow tract (LVOT) obstruction (Figure 2N). Stress echocardiography confirmed the presence of labile LVOT obstruction with good functional
capacity (125 W; 87% predicted heart rate), absence of provo-
cable arrhythmias, and normal blood response to exercise. The
diagnosis was confirmed by genetic analysis, showing the
g.Elu258Lys pathogenic variant in the gene coding for card-
diac myosin binding protein C (MYBPC3).

Regular cardiovascular evaluations, including echocardi-
goaphy and ambulatory 24-hour ECG, were stable over the last
6 years. The patient remained asymptomatic, leading a very
active life—including hiking—without functional limitation, pal-
pitations, lightheadedness, or angina. Despite a history of card-
diac arrest, serial 24-hour ECG recordings were repeatedly
negative for ventricular arrhythmias while the patient was tak-
ing amiodarone and β-blockade. Thus, he never received an
implantable defibrillator.

Years later, he presented with rapid development of con-
gestive heart failure, in sharp contrast to the previously stable,
asymptomatic clinical course. Compared with earlier stud-
ies, his ECG now showed marked and diffuse voltage reduc-
tion, a QS pattern in V1 to V3, and inferolateral T-wave inver-
sion (Figure 1). The echocardiogram showed an abrupt in-
crease in the severity of LV hypertrophy (Figure 2), with a concentric
rather than asymmetric appearance, granular sparkling of the
myocardium, biventricular enlargement, thickening of atrioventric-
ular valve leaflets and interatrial septum, and a mild pericar-
dial effusion (Figure 2C, D, G, and H). Severe LV dysfunction
with a restrictive LV filling pattern was evident, which is as-
sociated with loss of LVOT obstruction and systolic impair-
ment of the right ventricle (Figure 2K, L, O, and P). Notably,
the acoustic window and endocardial border definition had sig-
nificantly improved, and there was a distinct binary appear-
ance of the interventricular septum (Video 1 and Video 2).

Multiple myeloma was diagnosed following hospital ad-
mission. Protein electrophoresis showed hypogammaglobu-
linemia with increased k-free light chains (824 mg/L; normal

Figure 1. Electrocardiograms (ECG) of the Patient in 2012 and 2013, After the Onset of Heart Failure Symptoms

The 2013 ECG showed marked and diffuse voltage reduction (QS in V1-3) and inferolateral T-wave inversion.
range, 3.3-19.4 mg/L), normal λ light chains, and very mild Bence Jones proteinuria. The bone marrow biopsy and aspiration confirmed the diagnosis of multiple myeloma, with a 40% proportion of κ-restricted monoclonal plasmacytosis infiltration. Abdominal fat aspiration showed amyloid deposition and confirmed the diagnosis of light-chain amyloidosis (Figure 3). Genetic testing results for transthyretin mutations were negative. Within 2 months, despite prompt initiation of chemotherapy and support treatment, the patient died of electromechanical dissociation.

Discussion

Abrupt onset of congestive heart failure subtended by biventricular dysfunction is uncommon in patients with HCM, particularly in older patients. Once rare phenocopies (such as Danon or transthyretin-related amyloidosis) have been excluded from consideration, such a clinical course should raise suspicion of superimposed conditions such as coronary artery disease, myocarditis, and infiltrative or systemic
conditions (including autoimmune and malignancy-related disease).1-4 Indeed, while the progression of HCM may lead to end-stage heart failure in approximately 5% to 7% of patients, such a progression generally occurs over several years and can be detected at relatively early stages. Physicians should always consider the presence of an associated disease process in patients with HCM with an atypical disease course to identify conditions amenable to specific treatment, as we attempted to do, unfortunately without success, for this patient.

REFERENCES