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Recognizing HCM and HF: making the diagnosis

Hello. My name is Mariana Brandão. I'm a cardiology resident from Gaia Hospital Center in Portugal, and I will present on recognizing HCM and heart failure making the diagnosis. I have no disclosures for this presentation.

Hypertrophic cardiomyopathy is characterized by unexplained hypertrophy with a wall thickness of at least 15 millimeters in a non-dilated left ventricle without any other loading conditions to explain this degree of hypertrophy. It can otherwise be defined as unexplained hypertrophy with a wall thickness of 13 millimeters or more. If this is present in a family member of a patient with HCM, or in a carrier of a genetic mutation in a sarcomeric gene. It is the most prevalent cardiomyopathy affecting 1 out of 500 adults, and it is inherited in autosomal dominant pattern due to mutations in sarcomeric genes.

It is characterized by incomplete penetrance and marked phenotypic variability as we can see in these clips, all belonging to patients with HCM, with sarcomeric gene mutations with very different hypertrophy patterns. We can see that the typical HCM pattern with a subtle predominance asymmetrical, however, any degree of hypertrophy and any pattern can be seen.

However, not only left ventricular hypertrophy characterizes HCM. There are multiple phenotypic features that may be present such as myocardial bridging that has been reported to occur in up to 40% of patients with HCM, myocardial crypts that are subclinical markers in genotype-positive patients without overt hypertrophy, and also a hallmark feature of the disease, the submitral apparatus abnormalities with long elongated mitral valve leaflets that predispose to some, and also papillary muscle abnormalities with bifid hypertrophied and apically displaced muscles. However, none of these features are diagnostic of HCM, still in the presence of an unexplained left ventricular hypertrophy, they may suggest a sarcomeric cause for this hypertrophy.

There are many reasons that can lead HCM patient to us. They may be symptomatic. Their family doctor may find an abnormality in their physical examination, most likely a cardiac murmur, or they may be asymptomatic and present due to family screening or due to an abnormal ECG. The initial evaluation of an HCM patient should include a detailed history with a focus on family history and non-invasive testing is paramount to make the diagnosis, identify the phenotype, and for risk stratification. This includes in all patients an electrocardiogram, echocardiography, CMR, and genetic testing.

As I mentioned, patients may present without any symptoms as was the case of this patient, 38-year-old male engaged in high-intensity sports activities that presented with this clearly abnormal ECG with diffuse T-wave inversion in all precordial leads. This patient actually presents with ECG pattern that is typical of apical HCM as we can see in his echo with distal segment hypertrophy and the GLS pattern very typical of apical HCM.

Patients with HCM may also present with chest pain, and microvascular dysfunction is part of the pathophysiology of the disease may cause angina without coronary artery disease. This is actually a prognostic marker in these patients. We can see that stress perfusion CMR is very important to identify this subtype of patients as we can see in these images with an extensive profusion defect affecting all coronary territories.

This has been very recently highlighted by this study from London where they found that apical ischemia is actually a universal feature of hypertrophic cardiomyopathy with apical expression as these authors found 100% of their patients to have perfusion defects on CMR.

Heart failure may be also the first presentation of a patient with HCM, and this may be due to LVOT obstruction, diastolic dysfunction, progression to end-stage heart failure, as was the case of this patient with a troponin gene mutation that presented with a hypokinetic restrictive form of hypertrophic cardiomyopathy, triphasic filling pattern expressing severe diastolic dysfunction, and extensive LGE on our CMR.

This type of presentation of thin filament mutations has been very well elucidated by the group from Professor Olivotto, where they found that patients with thin filament mutations, different from other HCM types, presented with higher degrees of diastolic dysfunction, more frequent fibrosis in their CMR evaluation, and more frequent progression to hypokinetic dilated forms, and end-stage heart failure.

Syncope is also one of the first clinical presentations of patients with HCM as was the case of this patient of ours, 39 years old, recurring syncope on exertion. We can clearly see the mechanism of the syncope on this patient.
Obstructive physiology as we can see from the clear settle contact of the mitral valve during systole, some mid-systolic closure of the aortic valve, a typical MR jet of patients with HCM, eccentric posteriorly directed, and the LVOT gradient that was recorded with the typical continuous wave Doppler envelope plate peaking with a dagger shape.

However, despite being present in up to 75% of patients with HCM, LVOT obstruction may be masked during resting echocardiography, hence, the importance of performing stress exercise echo as mentioned in the guidelines as this may unmask LVOT obstruction in up to 50% of patients. We can see in these echos, this patient who was symptomatic, presented with no obstruction in his basal echocardiogram, and when we put him on the bicycle, he added a gradient of 126 on peak exercise.

Obstruction in hypertrophic cardiomyopathy is not limited to the LV outflow tract, and we can see that other forms such as mid-ventricular obstruction are important, and they may be the mechanism for apical aneurysm formation in HCM.

Unfortunately, the presentation of HCM may be dramatic with ventricular arrhythmias and sudden cardiac death. This is the example of a patient of ours that suffered from cardiac arrest while giving birth to her first child. We were able to resuscitate her with ECPR, and after two days on VA-ECMO, we found that she had a severe form of hypertrophic cardiomyopathy that was previously undiagnosed. This is the type of presentation we are now trying to avoid.

Just to mention that not all left ventricular hypertrophy is hypertrophic cardiomyopathy, and there are phenocopies to consider in the differential diagnosis, specifically the ones that have target treatment available for our patients.

I present the case of a 62-year-old male who had a family history of sudden cardiac death, presented to our cardiomyopathy clinic with mild heart failure symptoms. In his initial echocardiogram, we could see left ventricular hypertrophy, a granular sparking appearance of the myocardium, mild systolic dysfunction, a restrictive filling pattern with very low tissue Doppler velocities, and low GLS with an apical-sparing pattern. His CMR evaluation showed high native T1 levels of markedly increased extracellular volume of 62% and diffused late gadolinium enhancement. These multimodality imaging findings were very suggestive of cardiac amyloidosis.

We were able to exclude AL amyloidosis and with a Perugini score of 3, bone scintigraphy, and the negative TTR gene test, we could make the diagnosis of wild-type transthyretin cardiomyopathy. This patient is currently under treatment with tafamidis.

Another case of a 57-year-old male completely asymptomatic. No family history of cardiovascular disease, unremarkable physical examination, and was referred to us by his family doctor only due to this abnormal ECG. His echocardiogram was suggestive of an apical variant of hypertrophic cardiomyopathy.

CMR revealed LGE in the most hypertrophied segments, typical HCM LGE pattern. However, the parametric mapping showed very low native T1 levels that in the presence of LV hypertrophy, should make us suspect of fatty infiltration and Fabry disease.

This was confirmed by his genetic test that revealed the GLA gene variant, and the patient is under treatment with target therapy with migalastat. This may seem like an unexpected diagnosis, however, if you look at the patient ECG, he presents various red flags for Fabry disease according to an Italian score that was recently presented.

That shows that some ECG predictors of Anderson-Fabry disease should be identified in patients with LV hypertrophy such as a short PR or prolonged QRS duration with a right bundle branch pattern or ST segment depression in inferior leads.

CMR and genetics have been very important in the last few years for the differential diagnosis of left ventricular hypertrophy. For sarcomeric HCM, CMR is very important to confirm the diagnosis as it has higher diagnostic accuracy to identify the LV hypertrophy and also different variants such as apical aneurysms and mid-ventricular obstruction. It is also important for risk stratification as the LGE burden has been increasingly included in the algorithms for sudden death stratification. Also, it is very important for the differential diagnosis with phenocopies as we can see that typical LGE patterns such as the inferolateral LGE in Fabry disease, diffuse subendocardial LGE, in amyloidosis are typical of certain phenocopies and the increasing role of parametric mapping in the recent

years. Genetics is also very important to confirm the diagnosis, specifically in patients where the 15-millimeter criteria is not present in HCM, and also, obviously, for family cascade screening and identification of phenotype negative gene carriers. Also, for the identification of phenocopies, even when clinical suspicion is not present as in the two cases that I presented.

To conclude, I would like to reaffirm the importance of family history and physical examination in the workup of patients with HCM. We should pay attention to red flags. Also the importance of the ECG, various clues are present in the ECG, and the devil is frequently in the details. Echocardiography is paramount for the diagnosis, and we should look beyond left ventricular hypertrophy. Also, exercise echocardiography is very important to unmask latent LVOT obstruction, and we should not forego to look for LVOT as this is treatable in our patients. Also, the added value of CMR and genetics for the differential diagnosis and risk stratification of HCM patients, and the importance of recognizing phenocopies, specifically those that have a target treatment that we can make available for our patients. Thank you very much for your attention.