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PRACTICAL CASE

ASYMMETRICAL HYPERTROPHY OF LEFT VENTRICLE: HYPERTROPHIC CARDIOMYOPATHY OR SECONDARY HYPERTROPHY?

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Abstract

Hypertrophic cardiomyopathy (HCM) is a common genetically transmitted disease, clinically defined by the presence of unexplained left (or right) ventricular hypertrophy. For precise diagnosis of HCM a physician must rule out the secondary causes of left ventricular (LV) hypertrophy, such as aortic stenosis, systemic hypertension or Fabry's disease.

We present three cases of asymmetric hypertrophy of LV with subaortic stenosis associated with aortic stenosis in one case and systemic hypertension in two other cases, but the hemodynamic stress caused by these diseases is not sufficient to account for the degree of LV hypertrophy seen in our patients.

At the same time, aortic calcinosis and systemic hypertension can mimic the clinical pattern of HCM or can be superimposed on the heart with genetic predisposition to HCM, leading to inadequate hypertrophy of LV and acting as initiating factors that lead to phenotypic expression of genotypic abnormality. The differential diagnosis is very hard and almost impossible in these cases.

With this view, only genetic and histological analyses are able to direct a physician to make precise diagnosis without subjective assessment of LV hypertrophy correspondence with aortic stenosis or systemic hypertension.

Nevertheless, the management of such conditions does not depend on the type of genetic defect and degree of cardiomyocyte disorientation, but rather on degree of LV outflow tract (LVOT) gradient, LV hypertrophy, aortic stenosis, systemic hypertension and heart failure. For this aim echocardiography is a gold standard diagnostic procedure and is able to distinguish the degrees of parameters mentioned above.

Keywords: hypertrophic cardiomyopathy, aortic calcinosis, systemic hypertension, cardiomyocite disorientation

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is clinically defined as left (or right) ventricular hypertrophy without a known cardiac or systemic cause, such as systemic hypertension, Fabry's disease or aortic stenosis [*Ker J., 2009*].

HCM is a relatively common genetic disease. It is the most common cause of sudden cardiac death (SCD) in young people, although HCM can affect people at any age. The proportion of individuals inheriting the disease (familial) as opposed to developing a *de novo* mutation (sporadic) remains to be determined [*Maron B. et al., 1995; Roberts R., Sigwart U., 2005*].

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The clinical presentation can range from apical hypertrophy, mid-ventricular hypertrophy, concentric hypertrophy and subaortic hypertrophy of the left and/or right ventricle and may depend on physical activity of the patient [*Fifer M.A., Vlahakes G., 2008; Ramaraj R., 2008*].

A subset of patients with HCM have hypertrophic obstructive cardiomyopathy (HOCM) characterized by asymmetric hypertrophy, systolic anterior motion (SAM) of the anterior leaflet of mitral valve, a left ventricular outflow tract (LVOT) gradient, and varying degrees of mitral regurgitation [*Maron B.J. et al., 2002*].

The echocardiographic examination is the gold standard assessment of ventricular hypertrophy. At the same time, cardiac hypertrophy can be the only expression of the vast array of pathologies with the different prognosis. Almost all clinical symptoms of

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HCM can be mimicked by a broad range of pathologies [*Elliott P., McKenna W., 2004*].

RESULTS

We present three cases, where only genetic analysis can perform the precise differential diagnosis; on the other hand, the prognosis and treatment depends only on clinical expression of asymmetric hypertrophy of left ventricle (LV), LVOT gradient, aortic stenosis, systemic hypertension and heart failure.

Case report 1: Patient 1 (Armenian, male, 53 y.o.) was admitted to our hospital by ambulance. He suffered from compressing chest pain at rest, which was radiating to shoulders; fatigue and dyspnoe. He has had episodic elevation of blood pressure (BP) for 4 years; in 2004 transitory ischemic attack was recorded.

At the presentation he had moderate dispnoe. An ejection systolic murmur (grade 3/6) was heard at the base.

Electrocardiography (ECG) revealed the pattern of LV hypertrophy with ST depression and negative T waves in V_5 and V_6 leads. The preliminary diagnosis was set as "Acute Coronary Syndrome". After antianginal therapy, the blood analysis for assessment cardiac marker (Troponin T) was negative.

Two-dimensional echocardiography revealed (Figures 1, 2) asymmetric hypertrophy of LV (thickness of interventricular septum, IVS - 2.38 *cm*; and thickness of posterior wall, PW - 1.27 *cm*; IVS/PW - 1.87 *cm*). The size of chambers and the contractility of the heart were normal (EF - 60%).

Doppler echocardiography showed subaortic stenosis with mean gradient - 34 *mm* Hg (Figure 3).

According to echocardiography, ECG and troponin T data, the patient was diagnosed with asymmetric hypertrophy of LV with LVOT gradient. Drug therapy was administered with β-blocker metoprolol tartrate 25 *mg* daily and Ca-channel blocker amlodipine 5 *mg* a day.

Case report 2: Patient 2 *(*Armenian, female, 69 y.o.) was admitted to our hospital, because of chest pain, which occurred during physical activity; dyspnoe and fatigue. Two days before admission she had an episode of syncope.

Her personal or family history was uncomplicated.

The physical examination revealed systolic murmur (grade 3) at the apex and the base.

Electrocardiography revealed a left atrial and ventricular hypertrophy, the ST segment depression in I, aVL, V_5 and V_6 leads, and the absence of R wave growth from V_1 to V_3 leads (Figure 4).

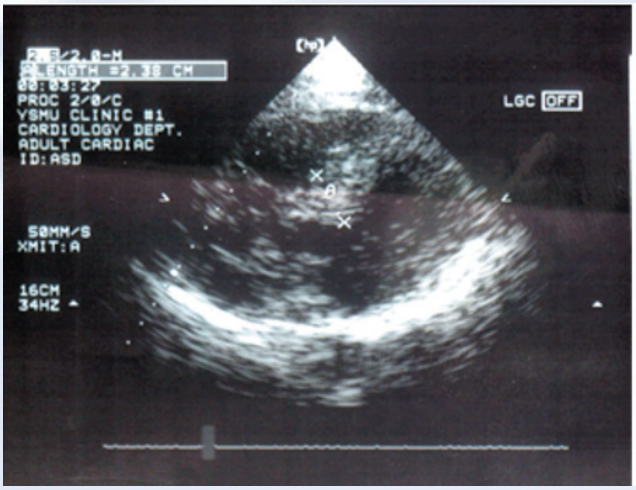

Figure 1. *Parasternal long axis view. Thickness of IVS (A) measured by B-mode echocardiography - 2.38 cm.*

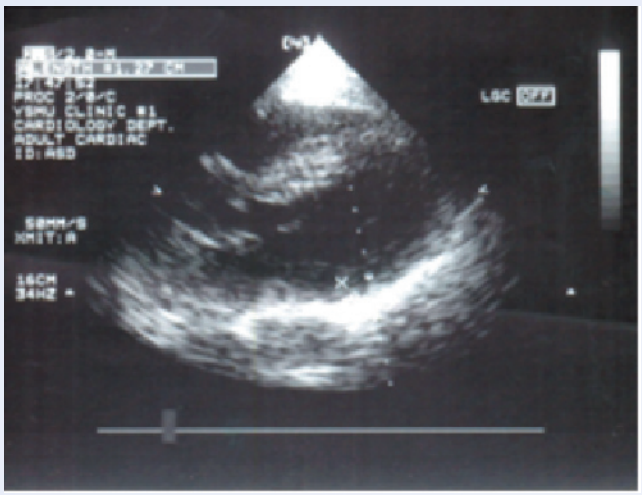

Figure 2. *Parasternal long axis view. LV PW thickness (A) measured by B-mode echocardiography - 1.27 cm.*

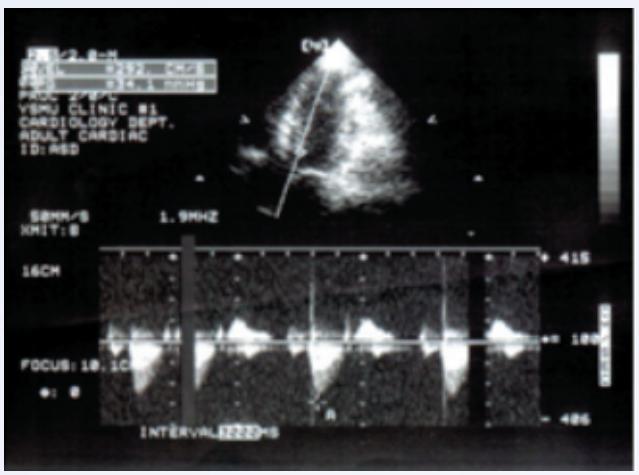

Figure 3. *Continuous wave Doppler echocardiography showing subaortic stenosis.*

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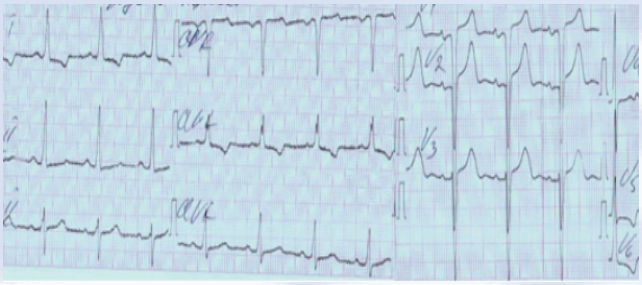

Figure 4. *ECG showing LV hypertrophy.*

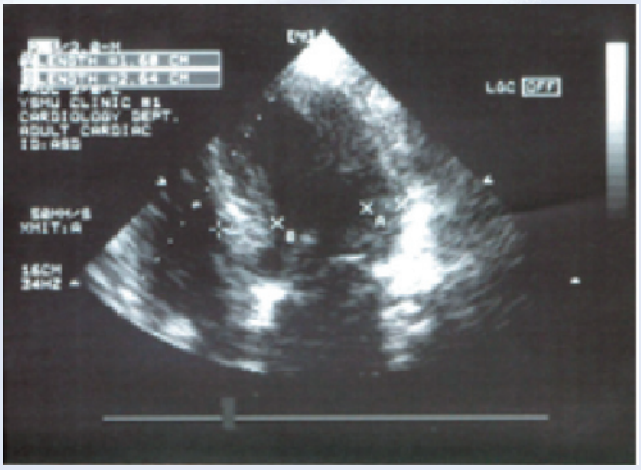

Figure 5. *B-mode echocardiography. Apical four-chamber view showing asymmetric hypertrophy of LV.*

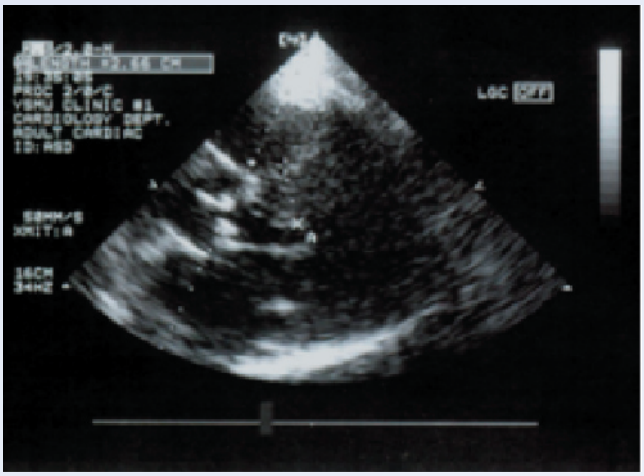

Figure 6. *B-mode echocardiography. Parasternal long axis view showing hypertrophy of IVS (A), and SAM of mitral valve.*

Transthoracic echocardiography was performed (Figures 5, 6). Two-dimensional echocardiography showed left ventricular asymmetric hypertrophy (thickness of lateral wall, LW-1.6 *cm* and IVS - 2.64 *cm*), dilation of left atrium (size of left atrium, LA - 5.5 *cm*), contractility of LV was decreased (end diastolic size, EDS - 5.5 *cm*; end systolic size, ESS - 3.8 *cm*; the ejection fraction, EF - 40%), SAM of the anterior leaflet of mitral valve.

Doppler echocardiography revealed aortic and subaortic stenosis with 26 and 18 mean gradient respectively (Figures 7, 8). It showed also the 2nd degree mitral regurgitation, 2nd degree aortic regurgitation and tricuspid regurgitation. Color Doppler confirmed the results obtained from continuous and pulse wave Doppler.

After physical and paraclinical examinations the patient was diagnosed with asymmetric hypertrophy of LV with LVOT obstruction. She was advised to turn to specialized surgery hospital. Drug therapy was administered with metoprolol tartrate 25 *mg* daily, enalapril 5 *mg* twice daily, amlodipine 5 *mg* a day and furosemide 40 *mg* twice a week.

Case report 3: Patient 3 (Armenian, male, 57 y.o.) was referred to our hospital for cardiovascular examination. He suffered from compressing chest pain, which occurred during physical activity. In the past medical history, the patient was diagnosed with the 2nd degree arterial hypertension four years before. In his family history he mentioned that his brother died at 21 years of age from a sudden cardiac death.

A midsystolic murmur (Levine grade 2) was heard at the base on clinical examination.

ECG exhibited the pattern of left atrial and ventricular hypertrophy.

Echocardiography revealed asymmetric hypertrophy of left ventricle (thickness of LW -1.86 *cm* and IVS - 2.57 *cm*), dilation of left atrium (size of left atrium, LA - 4.64 *cm*) and right ventricle (size of right ventricle from apical four-chamber view - 4.2 *cm*) (Figures 9, 10). The contractility was decreased (EF - 40%).

Doppler echocardiography revealed subaortic stenosis 1st degree (mean gradient - 16 *mm* Hg at rest), aortic and mitral regurgitations 1st degree (Figures 11, 12).

The patient has been discharged and administered the following therapy: metoprolol tartrate 25 *mg* daily, enalapril 5 *mg* twice a day and furosemide 40 *mg* twice a week.

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DISCUSSION

Originally described by Brock and Teare, nowadays hypertrophic cardiomyopathy is clinically defined as left (or right) ventricular hypertrophy without a known cardiac or systemic cause, such as systemic hypertension, Fabry's disease or aortic stenosis [*Ker J., 2009*].

Hypertrophic cardiomyopathy (HCM) is a relatively common genetic disease and the most common cause of sudden cardiac death (SCD) in young people. The estimated prevalence is 1 in 500 [*Maron B. et al., 1995; Roberts R., Sigwart U., 2005*].

The primary abnormality responsible for HCM is a genetic defect. The pattern of inheritance is autosomal dominant, which means that only one of the alleles is defective. The mechanism remains somewhat controversial. The main genes, which are responsible for HCM, are: β-myosin heavy chain (β-MYC), cardiac troponin T, myosin-binding protein C, α tropomyosin, cardiac troponin I, myosin light chains 1, 2, etc. [*Marian A., Roberts R., 2001; Seidman J., Seidman C., 2001; Bos J. et al., 2007*].

The clinical presentation can range from apical hypertrophy, mid-ventricular hypertrophy, concentric hypertrophy and subaortic hypertrophy of the left and/or right ventricle [*Fifer M., Vlahakes G., 2008; Ramaraj R., 2008*].

Of all these variants, hypertrophic obstructive cardiomyopathy (HOCM) is the variant that has been mostly studied. In this entity (previously known as idiopathic, hypertrophic, subaortic stenosis), asymmetrical, septal hypertrophy is accompanied by the following three elements: SAM of the anterior leaflet of the mitral valve, a LVOT gradient and mitral regurgitation [*Maron B. et al., 2002*].

The echocardiographic examination is the gold standard for ventricular hypertrophy assessment. At the same time, cardiac hypertrophy can be the only expression of the vast array of pathologies, each one with the different prognosis [*Elliott P., McKenna W., 2004*].

HCM should be differentiated from valvular aortic stenosis, subvalvular aortic membrane and a systemic hypertension [*Ker J., 2009*].

In aortic stenosis, the aortic valve is calcified and has restricted mobility. In HCM, the obstruction occurs below the aortic valve, and the valve structure and functions are preserved. However,

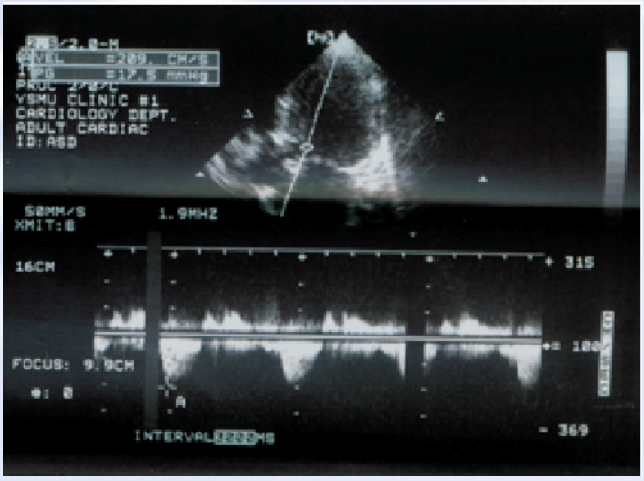

Figure 7. *Continuous wave Doppler showing subaortic stenosis with mean gradient (A) - 17.5 mm Hg.*

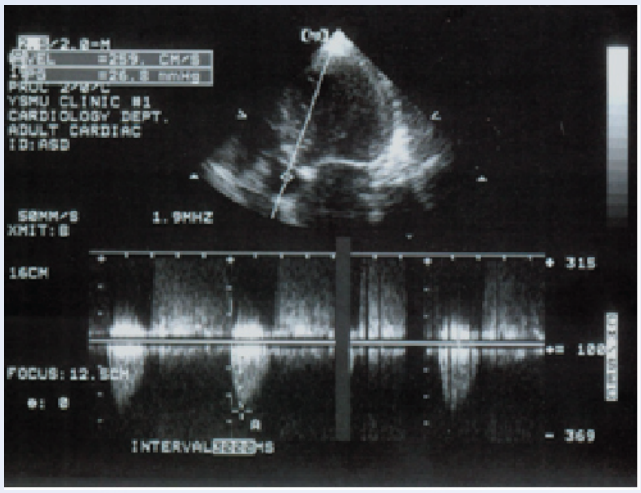

Figure 8. *Continuous wave Doppler showing transaortic gradient (A)- 26 mm Hg.*

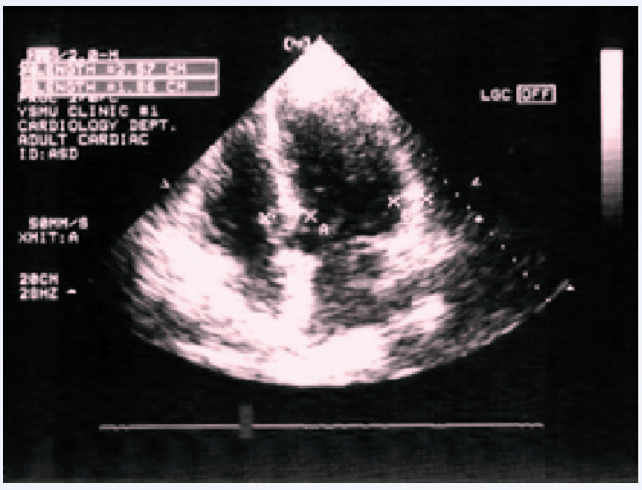

Figure 9. *B-mode echocardiography. Apical four-chamber view showing asymmetric hypertrophy of the left ventricle. A - thickness of IVS, B - thickness of LW.*

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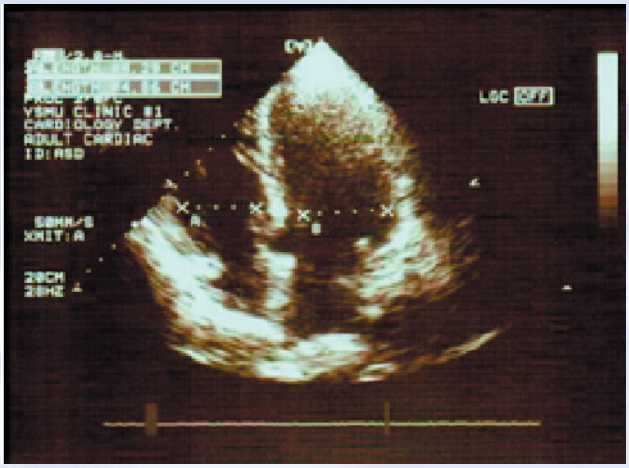

Figure 10. *B-mode echocardiography. Apical four-chamber view showing dilation of right ventricle (A).*

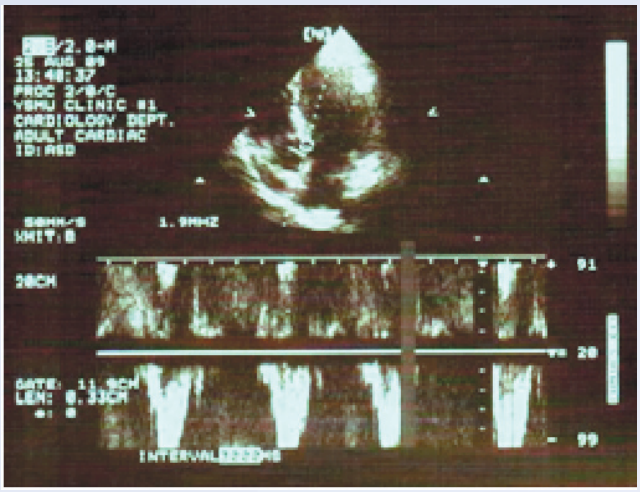

Figure 11. *Doppler echocardiography showing aortic stenosis and regurgitation.*

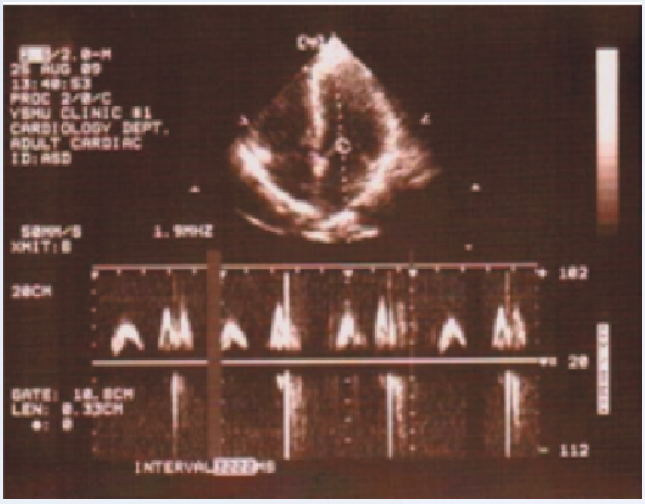

Figure 12. *Doppler echocardiography showing mitral regurgitation.*

with aging, degenerative calcific disease of the aortic valve may make it difficult to distinguish between two entities. Left venrticular asymmetric hypertrophy can also occur due to systemic hypertension [*Maron B. et al., 2002*]. Thus, despite affecting people at any age, HCM is responsible for at least one third of all sudden deaths seen among competitive athletes [*Maron B. et al., 1996; 2002; Shirley K., Adirim T., 2005*]. A minority of people HCM develops for the first time in later life. This phenomenon is sometimes called "late-onset" HCM. The symptoms and treatment of patients with late-onset disease are the same as patients, who develop the disease at a younger age (β-blockers, calcium antagonists, anti-arrhythmic drugs, anticoagulants, diuretics, pacing, cardiac operation. etc.). In some circumstances, the relatives of patients with late-onset disease may be advised to undergo repeated screening after their early twenties [*Maron B. et al., 2002; Elliott P., McKenna W., 2004*].

CONCLUSION

It becomes clear that in cases with assymetric hypertrophy of left ventricle associated with secondary causes, such as aortic stenosis, systemic hypertension or Fabrye's disease, the precise diagnosis of HCM requires genetic and histological analyses, but there are many genes involved in the pathogenesis of HCM, which makes the clinical diagnosis more complicated.

At the same time, aortic calcinosis and systemic hypertension can mimic the clinical pattern of HCM or can be superimposed on the heart with genetic predisposition to HCM, leading to inadequate hypertrophy of left ventricle and acting as initiating factors that lead to phenotypic expression of genotypic abnormality. In these cases the clinical diagnosis is very hard and almost impossible.

On the other hand, the treatment of left ventricular asymmetric hypertrophy depends on clinical expression of LVOT gradient, LV hypertrophy, presence of aortic stenosis, systemic hypertension, or heart failure.

Thus, presented cases show the importance of complex assessment of echocardiographic parameters, particularly LV hypertrophy, possible origin of hypertrophy, presence of aortic calcification for clear differentiation and confirmation of HCM diagnosis.

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