

Case Report

HOCM/Sigmoid septum: mechanism and management of the obstruction

Walhin N¹, Dulgheru R², Bonnet P³, Petitjean H², Radermecker A^{4*}, Legrand V², Lancellotti P² and Radermecker MA^{1,3}

¹Department of Cardiovascular Surgery, CHU of Liège, Belgium

²Department of Cardiology, CHU of Liège, Belgium

³Department of Human Anatomy, University of Liège, Belgium

⁴Student in medicine, University of Liège, Belgium

Abstract

In Hypertrophic Obstructive Cardiomyopathy Associated to Sigmoid Septum (HOCM/SS), the left ventricular outflow tract obstruction is a complex dynamic phenomenon where the asymmetric hypertrophy of the basal septum and associated anomalies of the mitral valve leaflets and subvalvular apparatus are less likely to explain per se the subaortic obstruction. It is our view that the closure of the aorto-mitral angle in this setting is paramount. It entails, for obvious geometric reasons, a bulging of the basal septum underneath the aortic valve and the misalignment between the LV and outflow/aortic root creates the path for an ejectional flow pattern, which may drag the mitral apparatus and promote obstruction by pushing the subvalvular apparatus and leaflets in the outflow tract. Via the presentation of a complex HOCM/SS case, the pertinent recent literature on this subject is summarized and the recommendations for interventional treatment are discussed. Even with close results, surgery appears to be more efficient in this setting.

Abbreviations

ACCf: American College of Cardiology Foundation; AHA: American Heart Association; AVB: Atrioventricular Block; ED: Emergency Department; ESC: European Society of Cardiology; HCM: Hypertrophic Cardiomyopathy; HOCM: Hypertrophic Obstructive Cardiomyopathy; HOCM/SS: Hypertrophic Obstructive Cardiomyopathy associated to Sigmoid Septum; LV: Left Ventricle; LVOT: Left Ventricular Outflow Tract; MR: Mitral Regurgitation; SAM: Systolic Anterior Motion of mitral valve; SS: Sigmoid Septum

Introduction

Hypertrophic Cardiomyopathy (HCM) is a heterogeneous clinical entity whose etiology is most of the time genetic. HCM is characterized by left ventricular wall hypertrophy not explained by the loading conditions (e.g., systemic hypertension, aortic valve stenosis) [1]. This pathology represents the most common cause of sudden cardiac death among young adults, as well as a significant part of heart failure cases. Amongst the elderly, the hypertrophic myocardium is mostly localized at the base of the interventricular septum and associated changes in local geometry gives a typical morphology named Sigmoid Septum (SS) [2].

We report the case of a patient with hypertrophy of the basal interventricular septum associated to a Systolic Anterior Motion of the mitral valve (SAM).

Clinical case

The patient is a 65 years old Caucasian male. He was admitted in the Emergency Department (ED) in February 2013 after a syncope preceded by rapid palpitations during a moderate effort. His medical records revealed that he was followed at the cardiology clinic for a non-obstructive septal hypertrophy diagnosed 2 years before. He was on chronic therapy with bisoprolol 5mg/day. Rest echocardiography showed thickening of the LV basal septum of 18 mm, a SAM causing a subaortic peak gradient of 135 mmHg at rest and a moderate secondary Mitral Regurgitation (MR). Syncope was considered to be at least partially related to the dynamic subaortic gradient. Therefore, verapamil 240 mg was added to 2.5 mg bisoprolol allowing a reduction of the subaortic peak gradient from 135 to 32 mmHg at rest.

***Corresponding Author:** Dr. Marc Radermecker, PhD, Department of Cardiovascular Surgery in the University Hospital of Liège, Professor of Anatomy at the University of Liège, Belgium. E-mail id: mradermecker@chuliege.be

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Two weeks later, despite treatment adjustment, syncope relapsed. An automated internal defibrillator was implanted, as the patient was considered at high risk of malignant arrhythmias. The new treatment with sotalol 80 mg and verapamil 240 mg allowed a reduction of the gradient to 30 mmHg at rest but still at 72 mmHg during the Valsalva manoeuvre.

His clinical condition remained stable until March 2015 when he presented several episodes of true syncope. The subaortic gradient was as high as 125 mmHg at rest (Figure 1). Given the recurrence of symptoms despite optimal treatment, alcohol septal ablation was proposed to relieve the obstruction. Transthoracic echocardiogram with intracoronary contrast was used to assess the suitability of a first septal perforator for this procedure. The intervention was conducted without complications and a part of the basal septum necrotized (max. CK-MB 163 µg/L) after injection of 2 mL of pure ethanol. The echocardiographic control revealed a reduction in the subaortic gradient at 54 mmHg at rest. However, the SAM persisted and the peak subaortic gradient during Valsalva was still as high as 130 mmHg with moderate secondary MR. Furthermore, despite focal mid-septal thinning, the basal septum remained at 18 mm (Figure 2).

Until July 2015, his clinical status did not improve with recurrent syncope complicated by head trauma that resulted in subarachnoid hemorrhage. Given the lack of improvement, a septal myectomy was indicated.

The intervention was performed in September 2015 under extracorporeal circulation. After aortic cross clamping, a transverse aortotomy allowed visualization of the underlying basal septal bulge through a non-calcified and competent aortic valve. A wide, but relatively shallow (8 mm) septal myotomy and myectomy (Morrow procedure) was performed to relieve LVOT obstruction.

Surgery and the postoperative course were uneventful. Rest echocardiography two weeks after the intervention showed absence of subaortic gradient at rest and after Valsalva manoeuvre and the absence

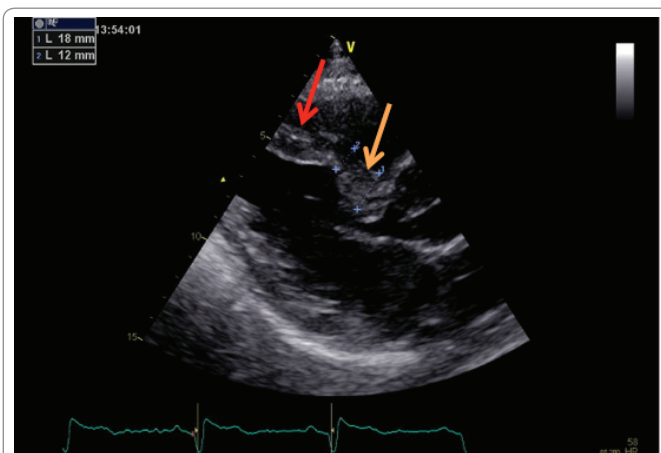


Figure 1.

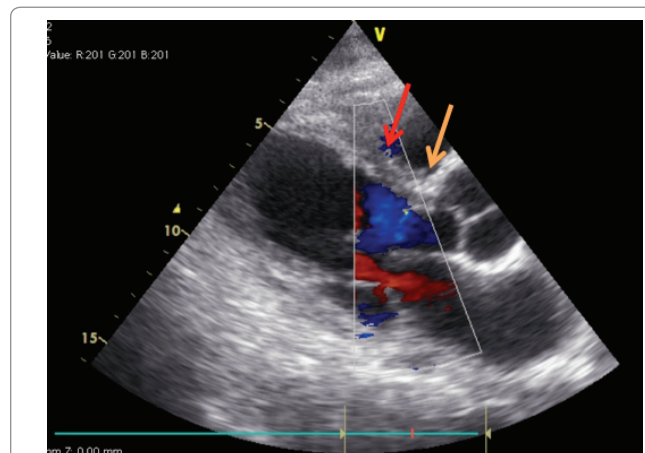


Figure 3.

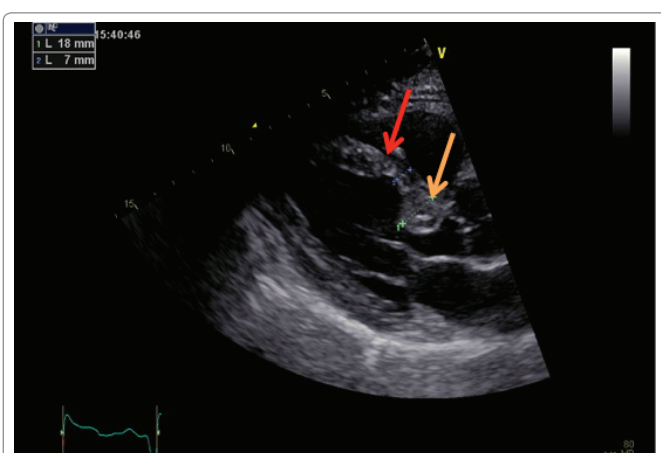


Figure 2.

of SAM, and therefore complete disappearance of the secondary MR (Figure 3). At follow-up, the patient did not report any syncope nor any other symptoms related to his pathology.

Discussion

Septal bulging protruding into the LVOT is not an uncommon echocardiographic finding in elderly patients. It has long been acknowledged that the senescent heart undergoes morphological modifications among which the dilation and the rightward shift of the ascending aorta and the decrease in long-axis dimension of the left ventricular cavity [3]. These geometrical modifications will both cause a leftward shift of the septum giving a sigmoid shape and closing the aorto-mitral angle (Figure 4-D). In elderly patients, this angulation may or may not be associated to basal septal hypertrophy [4]. Therefore, these morphological changes can be observed in the symptom free elderly subjects [2,5].

The prevalence of SS in the general population is estimated between 5,8% and 7% and considerably increases with age: 1,7% < 57 years old and 16,7% > 78 years old [5,6]. The sex ratio seems identical in the different age groups with a 1:1 distribution [5,6].

Its etiology is still a matter of discussion. Several authors consider SS as a true form of HCM. Others consider it as an anatomic variant whose prevalence rises with age-related conditions such as increased impedance to flow during ejection and dilation/elongation of root

vessels [4,5]. Spirito et al., [6] tend to class the SS within primary HCM because it shares common features of HCM (e.g. diastolic dysfunction). In a more recent study, Bos et al., [7] reported the absence of genetic mutation but the presence of this septal bulging in the majority of the patients diagnosed with HCM after the age of 65. They concluded that most of the patients with a late diagnosis are likely to have an acquired, non-genetic subtype of HCM rather than the inherited type. This particular presentation of hypertrophy could also be caused by other unidentified mutations with late penetrance.

Meanwhile, if the cause of the SS is still debated there is no doubt that this subtype of hypertrophy can lead to the obstruction of the LVOT through a physiopathological mechanism similar to that found in the primary Hypertrophic Obstructive Cardiomyopathy (HOCM) but where closure of the aorto-mitral angle and related modifications on LV flow pattern are likely to play a preponderant role [8].

Physiopathology

The LVOT obstruction, defined by an intraventricular gradient ≥ 30 mmHg [9], is a complex and multifactorial phenomenon. Its prevalence into the HCM population is estimated at 20-30% at rest and reaches almost 40% during exercise [10]. In some genetic HOCM, the obstruction occurs at the mid-ventricular level where the hypertrophied septum touches the anterior papillary muscle [10]. However, in most cases, the obstruction is due to the narrowing of the LVOT caused by the bulging of the hypertrophied basal septum inside the LVOT. This could be the consequence of pure myocardial hypertrophy as found in HCM forms of young people or mild/moderate hypertrophy associated to an age-related angulation of the aorto-septal junction defining the SS. Several mechanisms may contribute to the SAM; they are not mutually exclusive.

First the pushing force of flow, called “flow drag” which is probably the predominant mechanism [11], catches the mitral leaflets during ejection and pushes them in the LVOT [12]. Indeed, under physiological conditions the left ventricular systolic flow crosses the ventricle and outflow tract without encountering the mitral valve apparatus owing to the remote postero-lateral coaptation of the mitral leaflets (Figure 4-A&B). This accounts for a lack of interference between the inflow and outflow components of the left ventricular chamber. In HOCM conditions, the septal bulge induces a curvilinear intraventricular flow pattern which may encounter the mitral valvular and subvalvular apparatus especially if anomalies (aberrant cordae, longer mitral valve leaflets, etc.), frequently found in HCM, are present (Figure 4-C). In this situation the pushing force of the flow will bring the anterior mitral

leaflet in contact with the interventricular septum [12]. Accordingly, in HOCM/SS the isolated closure of the aorto-mitral angle can promote on its own this effect of flow drag (Figure 4-D).

Second, the Bernoulli derived flow acceleration at the level of the LVOT narrowing, decreases locally the side-pressure and “aspirates” the mitral leaflet through a Venturi effect [13].

Third, the fibrosis of both fibrous trigones described in HCM has been invoked by Yacoub et al., [14]. Physiologically these trigones have a speculative “hinge” function during systole and allow maximal widening of LVOT through the backward displacement of the subaortic curtain and the anterior leaflet of the mitral valve. The reduction of this “hinge mechanism” may contribute to a reduction of the LVOT surface area and width during systole [14]. This fibrosis of the trigones is present in elderly even in absence of HCM condition [15].

These three mechanisms, intermingled at varying degrees, generate the dynamic phenomenon of sub-aortic obstruction and contribute to the development of secondary mitral insufficiency by decreasing the efficiency of leaflets coaptation.

Symptoms and diagnosis

The SS may evolve insidiously and can be diagnosed incidentally in asymptomatic patients [2,5]. In obstructive forms, the patient may develop various symptoms as found in classical HOCM [16].

Exertional dyspnea may appear gradually. It is explained by the associations of diastolic dysfunction and secondary dynamic MR related to SAM, reverberating upstream by pulmonary venous network congestion.

Nearly one in two patients’ develops angina. This is due to increased cardiac work plus microcirculation anomalies exacerbated in genetic forms [10].

Less frequently, patients report fainting or syncopal events provoked by intense exercise. These may be due to the occurrence of reflex bradycardia associated with a peripheral vasodilation known as Bezold-Jarisch reflex [17]. This vagal event occurs when the pressure developed in the LV is abnormally high and results in transient low cardiac output. Malignant ventricular arrhythmia should also be suspected in patients with syncope or fainting.

The SS is defined as an isolated myocardial hypertrophy localized at the proximal third of the interventricular septum and bulging into the LVOT with thickness ≥ 13 mm among males and ≥ 12 mm among females and exceeding of over 50% the septal thickness at mid-

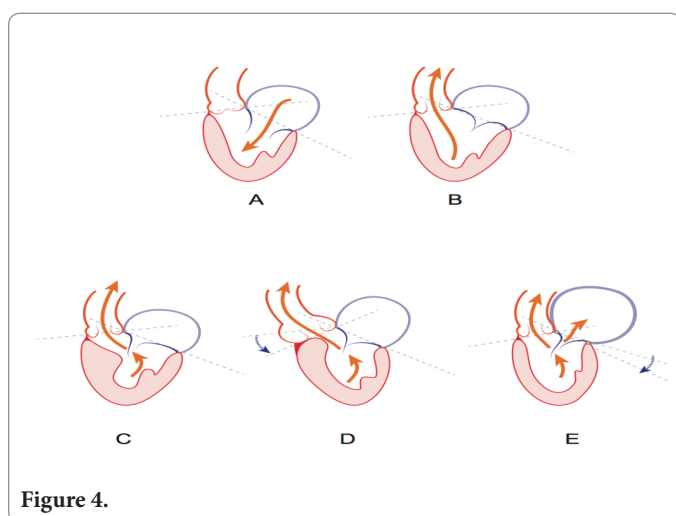


Figure 4.

ventricular level [5]. Once abnormal basal septal geometry is revealed with transthoracic rest echocardiography, the presence/absence of subaortic obstruction at rest as well as during provocative manoeuvres (such as Valsalva) should be systematically assessed, since it holds a key role in the therapeutic management.

Early diagnosis of this particular form of HOCM even at an asymptomatic stage is important, as progression can affect the quality of life. Some surgical teams have also pointed to the importance of describing this unusual septal morphology before mitral valve repair procedures. Indeed mitral surgery also via closure of the aorto mitral angle can herald sub-valvular obstruction and SAM (Figure4-E) [18,19].

Management of HOCM/SS

Usually the above-mentioned symptoms begin to manifest with a gradient superior to 50 mmHg. The initial management of these symptoms will be through medical treatment. If the symptoms become unrelenting and refractory to medications, invasive treatment will be considered.

When the HOCM/SS becomes obstructive and refractory to the drug therapy, (in the absence of specific guidelines for this particular subset), the treatment is based on the HOCM guidelines. In our opinion a case-by-case assessment is necessary considering the absence of obvious septal hypertrophy in some cases (Figure 5).

The latest European guidelines published by the European Society of Cardiology (ESC) [20] and the American guidelines published jointly by the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) [21] for the use of these different treatments can be summarized as follows.

Drug treatment

ESC and ACCF/AHA agree that treatment should be started with a cardio-selective β -blocker upto the maximum tolerated dose. In case of contraindications, Verapamil is an alternative or will be added β -blockers for more efficacy. If symptoms are not adequately controlled by this association, it is recommended to combine the disopyramide to one of these two drugs.

Invasive treatment

Septal reduction is recommended (myectomy or alcohol ablation) in any patients with an intraventricular gradient ≥ 50 mmHg and severe symptoms refractory to an optimal drug therapy. However, as regards

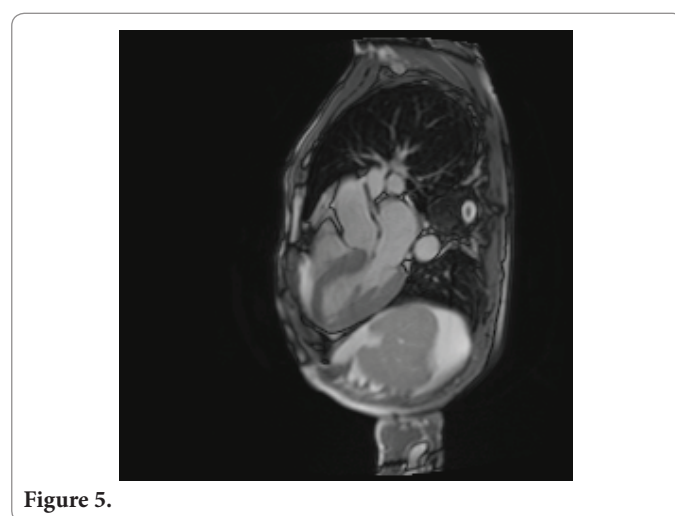


Figure 5.

to the procedure of choice, there are some discrepancies between the American and European guidelines.

Surgery is proposed as a first-line (IIa recommendation) according to the ACCF/AHA. The success of the surgical technique is estimated at 90-95% whereas it is slightly lower after alcohol ablation for an estimated morbidity and mortality less than 1% and up to 4% respectively. The invasiveness of heart surgery is counter balanced by lighter interventional techniques.

The recommendations of the ESC are less in favour of the surgical procedure excepted when magnetic resonance reveals a wide septal fibrosis or for hypertrophied septum greater than 30 mm. The ESC guidelines mention that the overall success rate (about 90%) in terms of improved effort capacity and mortality is quite similar between the two techniques. Therefore, the selection of the procedure should be determined by a multidisciplinary team that will also take into account the operators' experience.

The lack of consensus between these two guidelines led us to review morbidity and mortality data from the literature. Unfortunately, level I recommendation will probably never take place [22].

Sorajja et al., [23] compared the two procedures at four years in terms of survival and sustained improvement of symptoms. The results were quite similar in both age and gender comparable populations. However, complete Atrioventricular Block (AVB) rate requiring definitive pacemaker implantation (20%) was 4 times higher following alcohol ablation than after myectomy. Long-term survival was similar to the general population with nevertheless significantly higher post procedure gradients after percutaneous ablation [24].

Several meta-analyses have demonstrated similar efficacy for both procedures, as much with clinical and echographic improvement with falling of subaortic gradient, as by low mortality rate less than 1 to 2% [25-27]. However, the residual gradient remained significantly higher after septal ablation (15-18 mmHg vs. 9-10 mmHg) as the need to implant permanent pacemaker (18-20,9% vs. 3,4-4,4%).

Of note is that surgical myectomy after an ineffective alcohol ablation, is at higher risk of dysrhythmic complications requiring the implantation of permanent pacemaker in 50% to 85% of the patients [21,28,29]. Moreover, the risk of heart failure and postoperative mortality is also higher than in a first-line myectomy [25].

Conclusions

The HOCM/SS is a real clinical entity and quite frequent in the elderly. While the etiology is imperfectly elucidated, the pathophysiology is well explained by the misalignment of the aortic root associated or not with septal bulging and inducing the closure of the aorto-mitral angle. The echocardiographic identification and follow-up of these patients is important. Indeed, this misalignment may worsen over time as presented here and may cause HOCM symptoms requiring therapeutic support up to septal reduction. It has also surgical implications, as after mitral valve repair with ring annuloplasty, precipitating the LVOT obstruction while the gradient was beforehand non-significant.

Current procedures of septal reduction (i.e. septal alcohol ablation and septal myectomy) which are efficient in the classic genetic HOCM are also relevant for HOCM/SS. However, myectomy seems to us more appropriate in this pathology mainly localised at the level of the basal septum. The resection of the septal bulge is easy in this setting and completely corrects both LVOT obstruction and SAM.

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