Apical Hypertrophic Cardiomyopathy

Preliminary Attempt at Palliation with Use of Subselective Alcohol Ablation

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We report a case of severe apical hypertrophic cardiomyopathy in order to discuss the nature of this unusual condition and the possibility of using selective alcohol ablation to effectively treat symptomatic hypertrophic cardiomyopathy that presents with apical aneurysm. A 73-year-old woman with severe, progressive dyspnea and intermittent chest pain was found to have localized left ventricular apical dyskinesia distal to an obstructive mid-distal muscular ring. The ring caused total systolic obliteration of the apical left ventricular cavity. Apical cavity pressure was extremely high, up to 330 mmHg—200 mmHg above that in the main left ventricular cavity. Because of the danger of apical rupture and clot formation, we attempted the experimental use of alcohol ablation for effective palliation. We present our pilot experience, offer a novel interpretation of the nature of this obscure entity, and possibly justify a new catheter treatment. In addition, we discuss the developmental, pathophysiologic, and clinical implications of this unusual form of hypertrophic cardiomyopathy. To our knowledge, ours is the first reported use of subselective, modified-protocol alcohol septal ablation to treat an obstructive mid-apical muscular ring in a patient with apical hypertrophic cardiomyopathy. ***(Tex Heart Inst J 2012;39(5):750-5)***

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Hypertrophic obstructive cardiomyopathy (HOCM) is a congenital heart condition characterized by ventricular hypertrophy and a progressive worsening of symptoms, as related to the worsening of the subaortic gradient.[1,2] Either traditional surgical septal myomectomy[3,4] or alcohol septal ablation (ASA)[2,4,5] can be used to treat HOCM by effectively reducing the subaortic gradient.[1,2] We describe the case of an elderly woman who had the rarer variant of hypertrophic cardiomyopathy (HCM)—that with apical aneurysm and mid-ventricular obstruction. We describe in detail the experimental use of subselective alcohol ablation to treat the obstructive mid-apical muscular ring in this patient, and we revisit the nature of apical HCM.

Case Report

In October 2011, a 73-year-old woman was admitted to our hospital after experiencing electrocardiographic (ECG) changes and the sudden onset of hypotension after anesthesia induction for elective outpatient spinal surgery. Her medical history included hypertension, diabetes mellitus, obstructive sleep apnea, and obesity. The patient had previously reported chronic New York Heart Association (NYHA) functional class II symptoms that had progressed to NYHA functional class III–IV during the months preceding admission. She had dyspnea accompanied by chest pain and heaviness, both at rest and upon exertion, as well as fatigue and general malaise. During investigation of lower-extremity weakness, the patient had been diagnosed with lumbar spinal stenosis. She had not been referred to our cardiology practice for preoperative evaluation. During anesthesia induction before elective surgery, the patient was given a routine dose of fentanyl and midazolam that resulted in hypotension (blood pressure, 80/60 mmHg) and what were thought to be new ECG changes (Fig. 1). The procedure was aborted, and the aggressive administration of intravenous fluids resulted in clinical improvement.

Upon initial cardiovascular evaluation at our hospital, the patient's vital signs were within normal limits. A grade 3/6 mid-systolic murmur at the mid-precordium was heard, as were rales in both lung fields. There was mild bilateral lower-extremity edema. Chest radiography showed new-onset pulmonary edema, bilateral pleural ef-

fusions, and mild cardiomegaly. Cardiac biomarker levels were not elevated. A review of the patient's records revealed that the suspected ECG changes were no different from those observed on prior tracings; nevertheless, because of the possibility of an unstable coronary syndrome, the patient was emergently transferred to the cardiac catheterization laboratory. Coronary angiography showed no significant obstructive coronary artery disease. Left ventriculography revealed normal basal-to-mid left ventricular (LV) systolic function, with localized apical dyskinesia distal to an obstructive mid-distal muscular ring (Fig. 2). The systolic pressure at the apical segment of the LV was 230 to 330 mmHg, and the basal LV pressure was 120 to 130 mmHg, which led to a peak intracavitary pressure gradient of up to 200 mmHg. A clear delay in the early diastolic drop in apical pressure with respect to the basal LV pressure was noted (Fig. 3). Contrast-enhanced echocardiography and magnet-

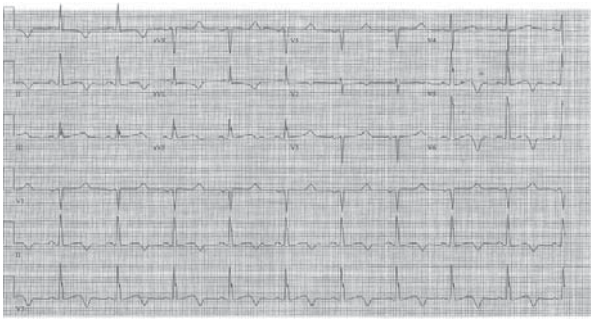

Fig. 1 *Electrocardiographic tracing on admission shows ST-segment changes and deep negative T waves in the anterior leads, with signs of left ventricular hypertrophy.*

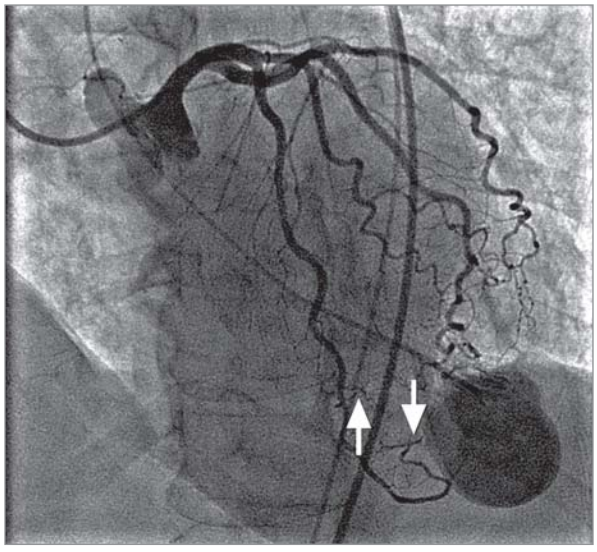

Fig. 2 *Preoperative frame from the simultaneous apical ventricular and coronary imaging used during the alcohol ablation procedure shows the relationship between the obstructive apical hypertrophic ridge and the related coronary branches (arrows). A left ventricular 4F pigtail catheter was used for periodic angiographic testing and for apical pressure monitoring.*

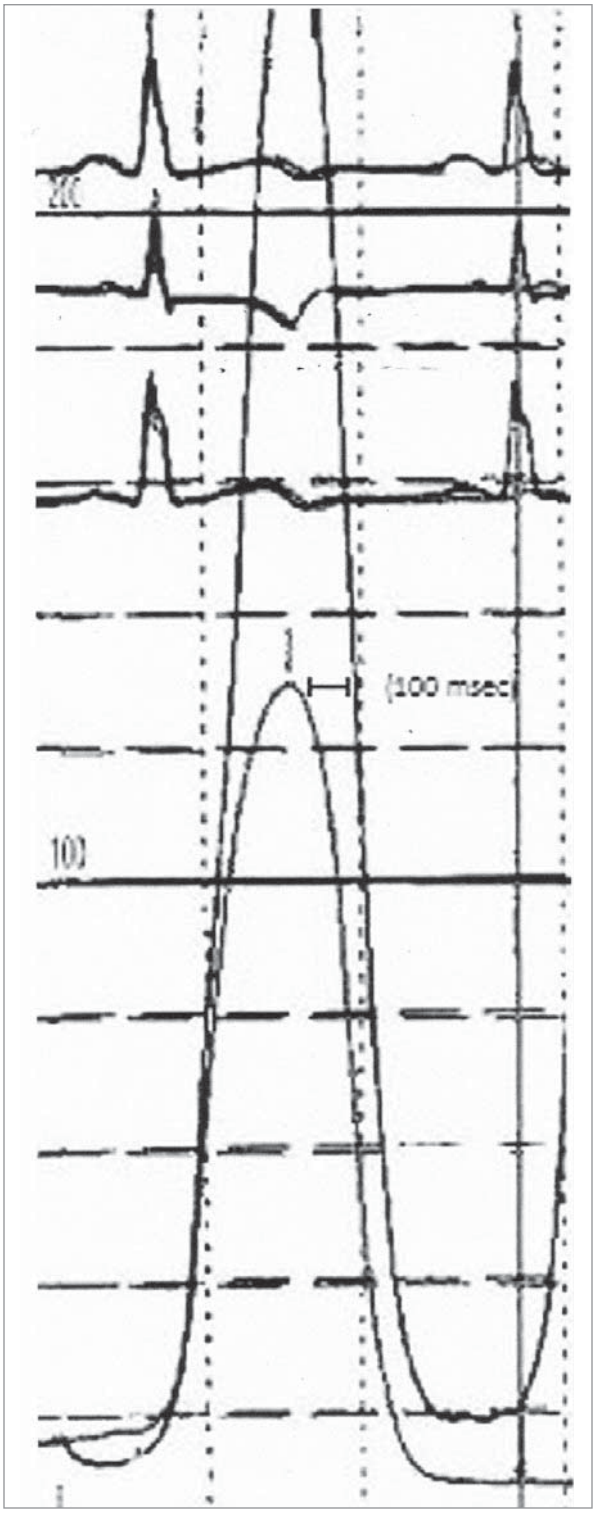

Fig. 3 *Pressure tracings were obtained before alcohol ablation, one at the apex and one at the outflow portion of the left ventricle (and then superimposed by the timing of the QRS interval). The apical systolic pressure was approximately 250 mmHg, whereas the outflow pressure was 125 mmHg. In addition, the drop in end-systolic pressure was delayed in the apical portion by 5 to 10 ms with respect to the outflow chamber, during which time the Doppler signal indicated runoff from this cavity (as shown in Fig. 5).*

ic resonance imaging (MRI) confirmed moderate mid-to-basal concentric LV hypertrophy (thickness, 1.3 cm), with total apical LV cavity systolic obliteration by the obstructive muscular ring (Table I and Figs. 4–6). The patient's global LV ejection fraction was preserved, although the apical portion of the LV appeared dyskinetic, with stasis and minimal effective systolic output (Table I and Fig. 7). Initially, β-blocker and ACE-inhibitor therapy was started.

One month later, the patient's severe dyspnea and intermittent chest pain persisted. Cardiac MRI confirmed the localized severe hypertrophy of the distal third of the LV where the papillary muscles attach, with a thin-walled (3-mm) aneurysmal apical free wall (Fig.

TABLE I. Quantitative Study of Apical Areas and Volumes by Magnetic Resonance Imaging

Variable	Before Procedure	After Procedure
Apical area* (cm^2)		
Systolic	9	8
Diastolic	7	7
Apical volume** (cc)		
Systolic	21	19
Diastolic	16	14
Stroke	5	5

*Obtained by planar measuring of the largest longitudinal area.

**Obtained by measuring the summation of 1-mm-thick cross-sections.

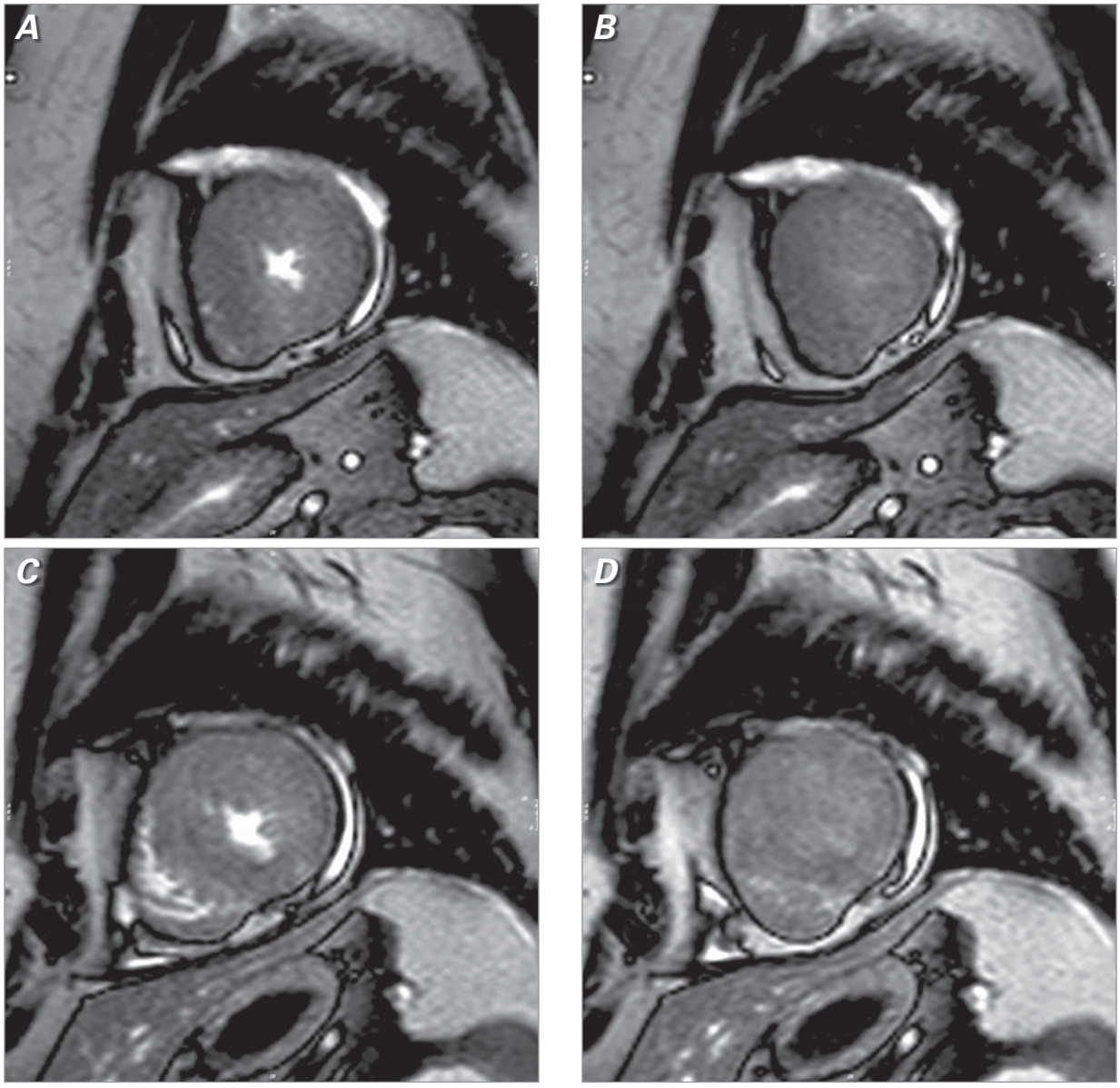

Fig. 4 *Magnetic resonance imaging frames (cross-sectional views at the mid-cavity obstructive ring).* ***A****) Preoperative diastolic,* ***B****) systolic, and* ***C****) postoperative diastolic, and* ***D****) systolic images show that the mid-ventricular ring opening was essentially obliterated in both preoperative and postoperative systolic times.*

7). On viability and ischemia imaging, a small amount of subendocardial scarring was seen in the basal anterior wall; however, the thinned apical wall did not enable proper evaluation of scarring or ischemia at this level.

The patient was told of the risks and the potential (but unproved) benefits of alcohol ablation, and she gave her written informed consent.

To identify the possible target coronary branches for alcohol ablation, subselective angiography was performed with use of a 1.5-mm Apex® balloon catheter (Boston Scientific Corporation; Natick, Mass) inflated to 6 atm of pressure after the guidewire was retracted. The use of echo-contrast subselective infusion with agitated saline solution clearly revealed at least 3 branches that were feeding the obstructive muscular ring (Fig. 2). The branches originated from the distal left anterior descending coronary artery (LAD), which had a wrap-around-the-apex pattern (Fig. 2). Two antero-lateral LAD branches supplied the anterior portion of the mid-apical LV ridge, and a terminal branch of the LAD did the same for the posterior, septal, and lateral sections (Fig. 2). A total of 4.5 cc of alcohol (1.5 cc in each branch) was instilled subselectively at the 3 target branches, with excellent initial response: the peak pressure gradient decreased from 200 to 40 mmHg. The

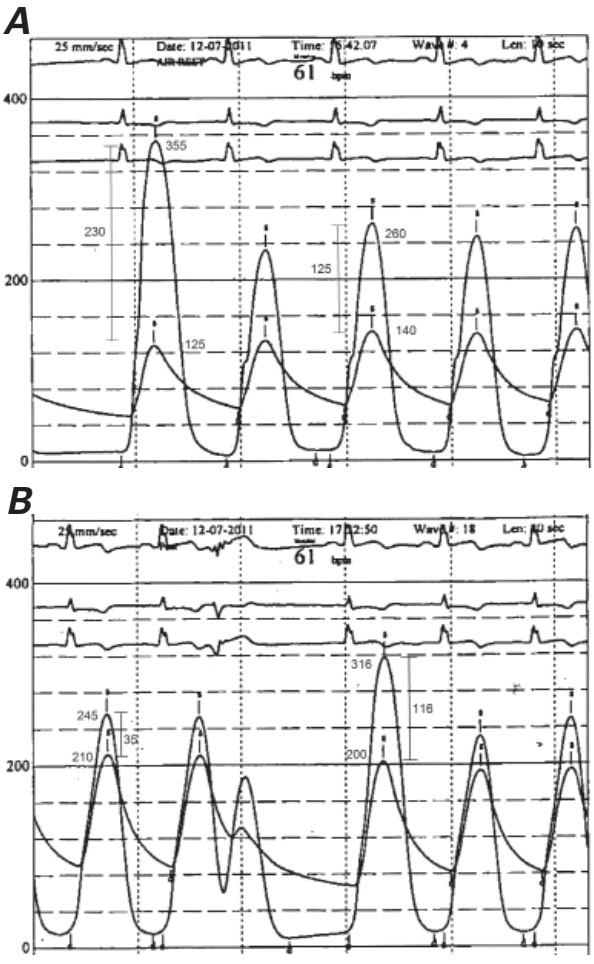

Fig. 5 *Pressure tracings of the patient's states: **A**) preoperative and **B**) postoperative. A 4F pigtail catheter was placed in the apical cavity and a 6F guiding catheter was placed in the aorta. The recorded gradients varied during the procedure. The peak systolic gradient was 230 mmHg after a premature ventricular contraction and 125 mmHg during regular rhythm; postoperatively, they were 116 and 35 mmHg, respectively.*

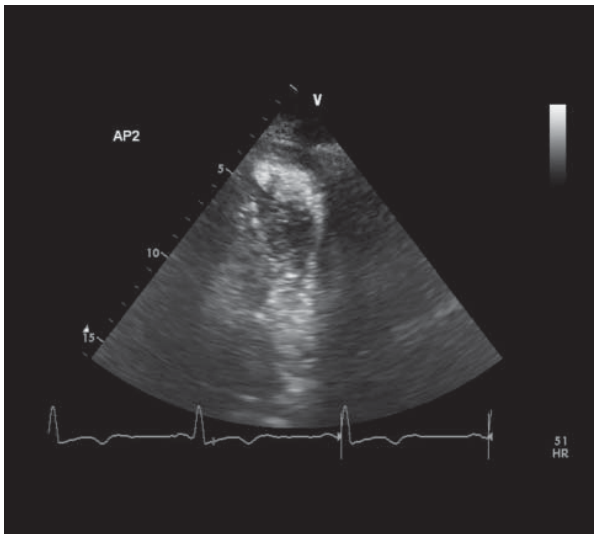

Fig. 6 *Transthoracic contrast echocardiogram shows the protruding, hypertrophic obstructive ring at the mid-apical segment of the left ventricle. The apical aneurysm "filled" in early systole and emptied in early diastole, with no flow during most of systole. The completely occlusive myocardial ring provoked systolic expansion at the apex.*

Click here for real-time motion image: Fig. 6.

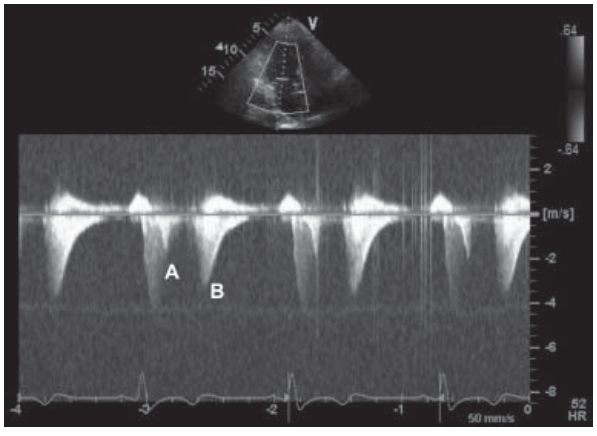

Fig. 7 *Echocardiographic and continuous-wave Doppler images at the obstructive apical ring show a short interval of early systolic blood flow (A), which was interrupted for most of systole and followed by a higher blood-flow velocity peak in early diastole (B), at the time of the delayed diastolic relaxation. See also Figure 3. Therefore, the intraventricular systolic gradient did not seem to be caused by blood flow, but rather by systolic contraction of the obstructive ring in the presence of systolic obliteration of the apical cavity.*

patient's peak creatine kinase levels reached 1,150 U/L, and the peak creatine kinase–MB fraction was 176 ng/mL 12 hours after the procedure. The patient had no chest pain, nor were there conduction abnormalities or arrhythmias during or after the procedure. Her condition remained hemodynamically stable during her hospitalization.

During the next 9 months, the patient's status improved to NYHA functional class I–II for dyspnea and to functional class I for chest pain. At 3 months' follow-up, echocardiography showed persistent dyskinesia of the apical portion of the LV, and the aneurysmal free wall remained thin. The pulmonary systolic pressure had decreased from 50 mmHg preoperatively to 30 mmHg. Continuous-wave Doppler signals showed an early Doppler peak at the apical aneurysm during early systole until the myocardial obstructive ring became totally occlusive. In addition, there was no apparent flow in or out of the apical aneurysm during most of systole, and flow out of the apical aneurysm occurred in early diastole, as indicated by the new Doppler peak (Figs. 6 and 7). Magnetic resonance images obtained at 3 days and 6 months after the procedure showed clear necrotic changes at the obstructive muscular ring, in a circular pattern and with a 2-cm thickness (Fig. 8). The scarring had somewhat decreased at 6 months, but the lumen of the central opening remained essentially obliterated during systole (Table I and Fig. 4). The patient's LV ejection fraction was between 0.45 and 0.50. Medical therapy was continued. Her functional capacity and chest pain were greatly improved over her preoperative state.

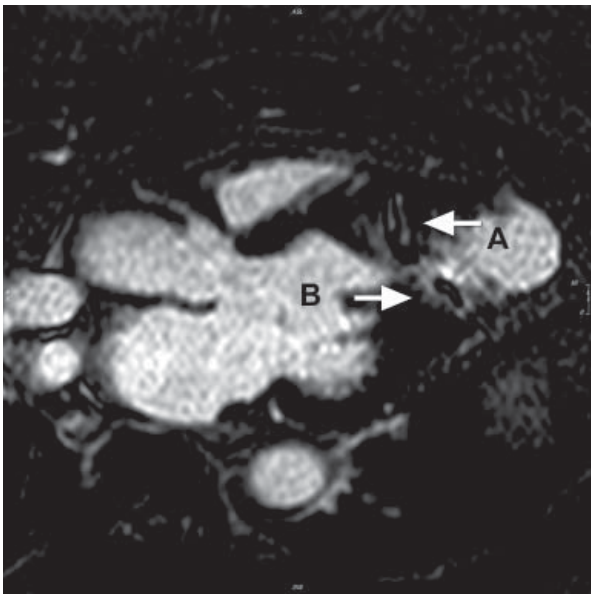

Fig. 8 *Postoperative magnetic resonance sequence shows a 2-cm-thick circumferential scar at the core of the circular obstructive apical ring. The apical cavity (A) was essentially unchanged in size and had a persistently thinned apical free wall.*

B = inflow of the main left ventricular cavity

Discussion

We have described a novel approach to the management of a challenging therapeutic dilemma: symptomatic apical HCM with dangerous pressure gradients and progressive thinning of the distal apical wall. To our knowledge, ours is the first reported use of subselective, modified-protocol ASA to treat an obstructive mid-apical muscular ring in a patient with apical HCM.

Little is known about the natural progression of this condition, especially when it reaches such severity as in the present case. Clinical observations[6-8] have indicated that symptoms such as chest discomfort and dyspnea are probably due to a combination of a suprasystemic-pressure dyskinetic apical cavity, functional ischemia, and the organic coronary obliteration that frequently leads to scar formation. Apical thrombus formation, ventricular arrhythmias, and free-wall rupture can occur.[6-8] No accepted surgical treatment is currently available for this rare condition.

In apical HCM, the hemodynamic behavior of the apical portion of the LV has been discussed in the medical literature for 3 decades.[9,10] In our patient, the unusual hemodynamic conditions appear to have resulted from several factors. First, there was early systolic onset of mid-apical obstruction by the muscular ring, which actively contracted against a severely occluded outlet (the mid-ventricular ring): this was the only portion of the apical chamber that maintained systolic contraction, and it was probably the real cause of the apical systolic hypertension. Suprasystemic systolic pressure at the apex built up in the absence of substantial systolic blood flow into the apical chamber. Second, in early diastole, runoff from the apical segment occurred during relaxation of the muscular ring (Figs. 3, 6, and 7). The accumulated apical pressure was released early after the onset of diastole into the main LV cavity by apparent elastic recoil (Fig. 3), which might explain the unusual Doppler double-peak signals in early systole and early diastole (Fig. 7). Such findings have been reported.[9,10] In our patient, alcohol ablation at the site of the apical myocardial hypertrophy resulted in definite circular scarring, the disappearance of chest pain, and a clear reduction in apical pressure, at least during acute-stage pressure monitoring. Most likely, the decreased apical systolic pressure was the product of decreased contractility of the muscular obstructive ring, induced by ASA. On MRI, the geometry of the muscular ring was not clearly different at 6 months' follow-up (it was still obstructive). It is expected that alcohol ablation in apical HCM will not yield the same dramatic negative remodeling at the obstructive mid-ventricular segment that is seen when the procedure is used for HOCM; however, further follow-up is needed.

Alcohol septal ablation has been gaining popularity as a treatment for HOCM,[2,4,5] and clinicians have noted

that localized infarction of the obstructive hypertrophy (and, eventually, significant ablation) can be effectively carried out by precise subselective ASA.[2] Admittedly, such narrowing is different in apical HCM than in HOCM, wherein a dynamic Venturi effect causes subaortic stenosis between the subaortic ventricular septum and the anterior leaflet of the mitral valve. In evaluation of the effectiveness of alcohol ablation in apical HCM, the crucial technical issues are initially related to the precise identification of the target hypertrophic obstructive muscle and its coronary supply. It remains to be shown whether ASA can or should necessarily result in the widening of the intraventricular narrowing in apical HCM, as it does in HOCM, or whether decreased contractility of the mid-ventricular obstructive ring need be the only minimal targeted change by ASA in order to attain apical-pressure attenuation. We assume that apical hypertension is the essential stimulus to continuous hypertrophy progression and apical dyskinesia.

The delicate nature of this procedure requires a meticulous technique, especially when defining the target myocardial area and its nutrient coronary supply. We appear to have succeeded in causing the desired scarring at the correct location. Transthoracic echocardiographic monitoring, pressure gradient monitoring, and subselective angiography with use of balloon angioplasty catheters are essential during the procedure. Our initial experience suggests that more substantial necrosis (vs surgical resection) could be required to attain more substantial ablation of the obstructive muscular ring (Fig. 9). Clinically, the results in our patient's case appear to support the contention that we effectively alleviated her symptoms and ameliorated the pressure gradient.

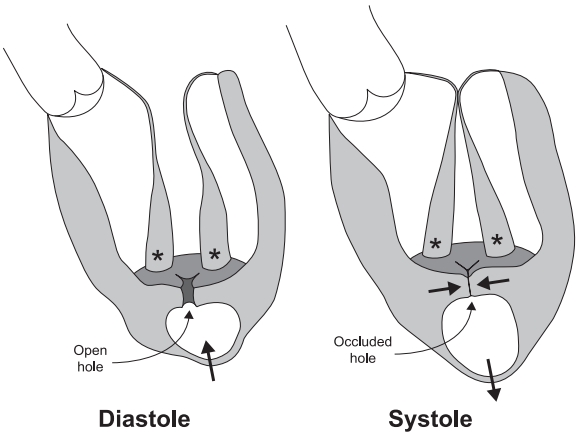

Fig. 9 *Schematic representation of the essential features of obstructive apical hypertrophic cardiomyopathy. The inflow/outflow/main cavity and the apical cavity are separated by a hypertrophic obstructive ring in diastole, which causes total obliteration of this segment during early systole. The asterisks indicate the papillary muscles that in this condition are found implanted on the obstructive ring. The obstructive mid-apical ventricular ring can be thought of as an abnormal, hypertrophic apical plane made of dense, coalescent trabeculations, which results in an intrinsic mechanism of progressive apical cavity enlargement and thinning of the apical free wall. Alleviation of the apical hypertension can be obtained by eliminating the mid-ventricular obstruction, by impairing the contractility of (or ablating) the myocardial hypertrophic ring, or both of these.*

References

1. Maron MS, Olivotto I, Zenovich AG, Link MS, Pandian NG, Kuvin JT, et al. Hypertrophic cardiomyopathy is predominantly a disease of left ventricular outflow tract obstruction. Circulation 2006;114(21):2232-9.
2. Angelini P. The "1st septal unit" in hypertrophic obstructive cardiomyopathy: a newly recognized anatomo-functional entity, identified during recent alcohol septal ablation experience. Tex Heart Inst J 2007;34(3):336-46.
3. Maron BJ. Controversies in cardiovascular medicine. Surgical myectomy remains the primary treatment option for severely symptomatic patients with obstructive hypertrophic cardiomyopathy. Circulation 2007;116(2):196-206.
4. Sigwart U. Non-surgical myocardial reduction for hypertrophic obstructive cardiomyopathy. Lancet 1995;346(8969):211-4.
5. Lakkis NM, Nagueh SF, Kleiman NS, Killip D, He ZX, Verani MS, et al. Echocardiography-guided ethanol septal reduction for hypertrophic obstructive cardiomyopathy. Circulation 1998;98(17):1750-5.
6. Sato Y, Matsumoto N, Matsuo S, Yoda S, Tani S, Kasamaki Y, et al. Mid-ventricular obstructive hypertrophic cardiomyopathy associated with an apical aneurysm: evaluation of possible causes of aneurysm formation. Yonsei Med J 2007;48(5):879-82.
7. Maron MS, Finley JJ, Bos JM, Hauser TH, Manning WJ, Haas TS, et al. Prevalence, clinical significance, and natural history of left ventricular apical aneurysms in hypertrophic cardiomyopathy. Circulation 2008;118(15):1541-9.
8. Gao XJ, Kang LM, Zhang J, Dou KF, Yuan JS, Yang YJ. Mid-ventricular obstructive hypertrophic cardiomyopathy with apical aneurysm and sustained ventricular tachycardia: a case report and literature review. Chin Med J (Engl) 2011;124(11):1754-7.
9. Nakamura T, Matsubara K, Furukawa K, Azuma A, Sugihara H, Katsume H, Nakagawa M. Diastolic paradoxic jet flow in patients with hypertrophic cardiomyopathy: evidence of concealed apical asynergy with cavity obliteration. J Am Coll Cardiol 1992;19(3):516-24.
10. Hanaoka Y, Misumi I, Rokutanda T, Akahoshi R, Matsumoto M, Sakamoto T, et al. Simultaneous pressure recording in mid-ventricular obstructive hypertrophic cardiomyopathy. Intern Med 2012;51(4):387-90.