A. Trevino, M.D.

J. Buerghler, M.D.

THE BROCKENBROUGH – BRAUNWALD – MORROW SIGN

Alejandro R. Trevino, M.D.; John Buerghler, M.D.

Houston Methodist DeBakey Heart & Vascular Center, Houston Methodist, Houston, Texas

Abstract

Hypertrophic cardiomyopathy is a relatively common genetic disorder and usually asymptomatic. However, approximately 25% of patients develop left ventricular outflow obstruction and can develop angina, syncope, or congestive heart failure. Initiation and titration of beta-blockade usually results in symptomatic improvement. Patients with medically refractory symptoms can see further symptomatic improvement and relief of obstruction with either surgical myectomy or alcohol septal ablation (ASA). Although surgical myectomy has been the gold standard, ASA has been shown in nonrandomized studies and a meta-analysis to be comparable. In patients undergoing ASA without a rest obstruction, the Brokenbrough-Braunwald-Morrow sign can be used to accurately determine the degree of left ventricular outflow tract (LVOT) obstruction prior to, during, and after ASA.

Introduction

Hypertrophic cardiomyopathy (HCM) is a relatively common genetic cardiac abnormality, occurring in 1 in 500 patients. The first cases of HCM were first reported in the 1860s in French literature,¹⁻³ but it was not until 1959 that HCM was associated with LVOT obstruction.⁴ This obstruction can result in angina, syncope, or congestive heart failure.^{5,6} Although many patients improve on beta-blockers, some have progressive symptoms and a significant obstruction at rest or with exercise. Interventional options include septal myectomy and ASA. While septal myectomy has been the traditional gold-standard approach for such patients, septal ablation is an alternative shown to be comparable in nonrandomized studies and a meta-analysis.⁷⁻⁹ Both of these procedures improve symptoms and reduce gradients.

In this study we present the dynamics of a patient undergoing ASA for medically refractory symptoms. We illustrate how the Brokenbrough-Braunwald-Morrow sign can be used to determine accurately the degree of LVOT obstruction during and after ASA in a patient without a resting gradient.

Case

A 62-year-old female with a past medical history of hypertension presented to the clinic complaining of dyspnea on exertion and chest discomfort that had been progressing over the last 6 months. The shortness of breath was such that she had to stop her exercise routine. She denied orthopnea or paroxysmal nocturnal dyspnea as well as any syncopal episodes.

On physical examination, her blood pressure was 138/77 mm Hg and pulse was 69 per minute. On neck exam her carotids showed a brisk upstroke without jugular venous distention. On cardiac auscultation, a systolic II/VI murmur at the left sternal border with radiation to the axilla was appreciated. The murmur increased during the strain phase of valsalva. There was no pitting edema in the lower extremities.

Electrocardiogram showed sinus rhythm, possible left atrial enlargement, and small R waves in leads V2 and V3.

Echocardiogram revealed moderate asymmetric left ventricular hypertrophy (LVH) and an interventricular septum diastolic thickness of 1.7 cm. The wall motion was hyperdynamic, with cavity obliteration and an estimated LV ejection fraction (LVEF) of > 70%. There was systolic anterior motion of the mitral valve, and moderate mitral regurgitation with an eccentric jet directed posterolaterally. Agitated contrast resulted in opacification of the basal and mid-septal segments. Left ventricular outflow tract gradient at rest was 100 mm Hg and increased to 131 mm Hg with valsalva. Her left atrium was severely enlarged with a left atrial volume of 96 mL. The Holter monitor was notable for a run of nonsustained ventricular tachycardia. Cardiac magnetic resonance imaging showed similar findings to the echo: a hyperdynamic ventricle (LVEF 75%) with moderate asymmetric LVH (septal 1.5 cm) causing LVOT flow turbulence and chordal systolic anterior motion. It also revealed a patchy midmural septal scar that was in a non-coronary artery disease pattern.

When initially seen, the patient was taking candesartan 32 mg daily and hydrochlorothiazide 12.5 mg daily. Her medications were changed to metoprolol 25 mg extended release daily, as vasodilators and diuretics worsen the LVOT obstruction in patients with hypertrophic obstructive cardiomyopathy (HOCM). Despite these medication changes, after 1 month on the beta blocker she had no improvement with her dyspnea on exertion or chest pain. The patient reported feeling fatigued since she started the metoprolol and felt she would not tolerate an increase in the dose. We discussed septal myectomy and ASA, and she agreed to proceed with ASA.

Bilateral femoral artery (7-Fr right and 4-Fr left) and femoral vein (6-Fr right) access was obtained. To have continuous monitoring of the arterial waveforms of the LVOT, a 4-Fr pigtail catheter was placed into the left ventricle. A temporary transvenous pacemaker was positioned via the right femoral vein into the right ventricle. Baseline gradients were obtained, which included left ventricular and aortic pressures. The patient had no gradient at rest (Fig 1a), but the beat after a premature

ventricular contraction (PVC) showed a 150 mm Hg gradient (Fig 1b) that is described as the Brockenbrough-Braunwald-Morrow sign, demonstrating the presence of LVOT obstruction with the distinct “spike and dome” waveform pattern. Coronary angiography demonstrated normal coronary arteries. After intravenous bivalirudin was started, a 0.014 Titan™ Soft Support guidewire (Stereotaxis, St. Louis, MO) was maneuvered using the magnetic navigation system. A candidate proximal septal was noted

Figure 1A. Left ventricular and aortic pressures simultaneously measured at rest on a 0 to 200 mm Hg scale show no evidence of a left ventricular outflow tract gradient.

Figure 1B. This is the classical image of the Brockenbrough-Braunwald-Morrow sign. Note the presence of a gradient of 150 mm Hg between the left ventricular (LV) and aortic pressures (Ao) on the beat post-PVC

(Fig 2a), which was cannulated with a 2 x 6 mm Sprinter® Over-the-Wire catheter. A coronary balloon (Medtronic, Minneapolis, MN) was advanced and inflated to occlude the septal branch. The wire was removed, and agitated contrast was injected through the balloon shaft. Transthoracic echo confirmed the potential infarct area as desirable. PVCs were induced using the pigtail catheter, and improvement of the post extrasystolic LVOT gradient was noted. Subsequently, we injected 2.4 mL of dehydrated alcohol through the lumen of the inflated balloon over 3 minutes, after which the balloon was deflated and removed. Coronary angiography after ASA revealed that both branches of the septal artery were occluded (Fig 2b). Hemodynamic measurements after the procedure showed a gradient of 0 mm Hg after a PVC, with resolution of the Brockenbrough-Braunwald-Morrow sign and no evidence of LVOT obstruction (Fig 3). The patient was transferred to the coronary care unit for observation. The patient had an

Figure 2A. A septal branch before ablation.

Figure 2B. Note the absence of the septal branch after alcohol septal ablation.

Figure 3. After alcohol septal ablation, the Brockenbrough-Braunwald-Morrow sign is no longer present.

AICD placed for primary prevention based on the abnormal Holter findings and was discharged uneventfully. Six-month follow-up documented improvement in NYHA class and absence of provoked gradient on echo.

Discussion

In 1961, Brockenbrough et al.¹⁰ noted in HOCM a paradoxical decrease in the arterial pulse pressure and an associated increase in the LV systolic pressure in the beat following a PVC, giving rise to the sign now called Brockenbrough-Braunwald-Morrow. After a PVC, there is a compensatory pause that causes an increase in diastolic filling time and therefore an increase in diastolic volume. The normal physiologic response to increased stretch according to Frank Starling's Law is to increase stroke volume by an increase in contractility, causing the arterial pulse pressure to rise. In patients with HOCM, the increase in contractility after a PVC worsens the LVOT obstruction, causing a decrease in the arterial pulse pressure and the Brockenbrough-Braunwald-Morrow sign.¹¹ This finding was later reproduced in several studies using inotropic agents like isoproterenol and digitalis glycoside, which worsened the LVOT obstruction during their administration.¹²⁻¹³

In 1964, the beta blocker Nethalide (pronethalol) showed a decrease in the LVOT gradient initially produced by isoproterenol.¹⁴ A few years later, propranolol was shown to decrease anginal symptoms in patients with HOCM.¹⁵ Currently, beta blockade is the first-line treatment because of its negative chronotropic and inotropic effects.¹⁶ Additional medications include verapamil and disopyramide as they also have negative inotropic effects.¹⁷⁻¹⁸

Septal myectomy is indicated for severely symptomatic patients who do not respond to maximal medical therapy.¹⁹ The use of ASA has become a widely used alternative interventional treatment strategy. Patients considered for ASA are symptomatic despite optimally titrated medical therapy and have resting gradients of ≥ 30 mm Hg or exercise gradients ≥ 60 mm Hg. As of 2008, more than 5,000 ASA have been performed worldwide, exceeding the total number of septal myectomies, which is considered the gold

standard treatment.²⁰ With ASA rapidly emerging as a treatment option, the Brockenbrough-Braunwald-Morrow sign is a simple and useful maneuver a physician can use in the catheterization laboratory in patients with significant symptoms and an exertional gradient but no resting gradient. While it is said that 75% of the patients with HOCM have no gradient at rest, during the procedure the maneuver can be used to document the degree of dynamic LVOT prior to, during, and after ASA.²¹ Equally important, it serves to document the absence of a gradient after ASA and is also a useful aid on top of contrast echocardiography in targeting which septal branch to ablate.^{22, 23}

Conclusion

As an alternative to septal myectomy, ASA is safe and improves medically refractory symptoms of HOCM. In patients without resting obstruction, use of the Brockenbrough-Braunwald-Morrow sign is a valuable maneuver to confirm an appropriate septal artery for ablation and to document resolution of obstruction after the procedure.

Conflict of Interest Disclosure: The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

Funding/Support: The authors have no funding disclosures.

Keywords: hypertrophic cardiomyopathy; alcohol septal ablation; Brockenbrough-Braunwald-Morrow sign

References

1. Hallopeau M. Rétrécissement ventriculo-aortique. *Gazette Medicine Paris*. 1869;24:683-4.
2. Vulpian A. Contribution à l'étude des rétrécissements de l'orifice ventriculo-aortique. *Archives de Physiologie*. 1868;3:456-7.
3. Liouville H. Rétrécissement cardiaque sous aortique. *Gazette Medecine Paris*. 1869;24:161-3.
4. Brock R. Functional obstruction of the left ventricle (acquired aortic subvalvar stenosis). *Guy's Hospital Reports*. 1959;108:126-43.
5. Maron MS, Olivetto I, Betocchi S, Casey SA, Lesser JR, Losi MA, et al. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. *N Engl J Med*. 2003 Jan 23;348(4):295-303.
6. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. *JAMA*. 2002 Mar 13;287(10):1308-20.
7. Qin JX, Shiota T, Lever HM, Kapadia SR, Sitges M, Rubin DN, et al. Outcome of patients with hypertrophic obstructive cardiomyopathy after percutaneous transluminal septal myocardial ablation and septal myectomy surgery. *J Am Coll Cardiol*. 2001 Dec;38(7):1994-2000.
8. Nagueh SF, Ommen SR, Lakkis NMM, Killip D, Zoghbi WA, Schaff HV, et al. Comparison of ethanol septal reduction therapy with surgical myectomy for the treatment of hypertrophic obstructive cardiomyopathy. *J Am Coll Cardiol*. 2001 Nov 15;38(6):1701-6.

9. Leonardi RA, Kransdorf EP, Simel DL, Wang A. Meta-analyses of septal reduction therapies for obstructive hypertrophic cardiomyopathy: comparative rates of overall mortality and sudden cardiac death after treatment. *Circ Cardiovasc Interv.* 2010 Apr;3(2):97-104.
10. Brockenbrough EC, Braunwald E, Morrow AG. A hemodynamic technique or the detection of hypertrophic subaortic stenosis. *Circulation.* 1961;23:189-94.
11. Pollock SG. Pressure tracings in obstructive cardiomyopathy. *N Engl J Med.* 1994 Jul 28;331:238.
12. Braunwald E, Brockenbrough EC, Frye RL. Studies on digitalis. V. Comparison of the effects of ouabain on left ventricular dynamics in valvular aortic stenosis and hypertrophic subaortic stenosis. *Circulation.* 1962 Aug;26:166-73.
13. Braunwald E, Ebert PA. Hemodynamic alterations in idiopathic subaortic stenosis induced by sympathomimetic drugs. *Am J Cardiol.* 1962;10:489-95.
14. Harrison DC, Braunwald E, Glick G, Manson DT, Chidsey CA, Ross J. Effects of beta adrenergic blockade on the circulation, with particular reference to observations in patients with hypertrophic subaortic stenosis. *Circulation.* 1964;29:84.
15. Cherian G, Brockington IF, Shah PM, Oakley CM, Goodwin JF. Beta-adrenergic blockade in hypertrophic obstructive cardiomyopathy. *Br Med J.* 1966 Apr 9;1(5492):895-8.
16. Wigle ED, Rakowski H, Kimball BP, Williams WG. Hypertrophic cardiomyopathy: clinical spectrum and treatment. *Circulation.* 1995 Oct 1;92(7):1680-92.
17. Rosing DR, Idanpaan-Heikkila U, Maron BJ, Bonow RO, Epstein SE. Use of calcium-channel blocking drugs in hypertrophic cardiomyopathy. *Am J Cardiol.* 1985 Jan 25;55(3):185B-195B.
18. Sherrid MV, Barac I, McKenna WJ, Elliott PM, Dickie S, Chojnowska L, et al. Multicenter study of the efficacy and safety of disopyramide in obstructive hypertrophic cardiomyopathy. *J Am Coll Cardiol.* 2005 Apr 19;45(8):1251-8.
19. Brown ML, Schaff HV. Surgical management of obstructive hypertrophic cardiomyopathy: the gold standard. *Expert Rev Cardiovasc Ther.* 2008 Jun;6(5):715-22.
20. Sigwart U. Catheter treatment for hypertrophic obstructive cardiomyopathy: for seniors only? *Circulation.* 2008 Jul 8;118(2):107-8.
21. Maron BJ. Hypertrophic cardiomyopathy. *Lancet.* 1997 Jul 12;350(9071):127-33.
22. Kern MJ, Rajjoub H, Bach R. Hemodynamic rounds series II: hemodynamic effects of alcohol-induced septal infarction for hypertrophic obstructive cardiomyopathy. *Catheter Cardiovasc Interv.* 1999 Jun;47(2):221-8.
23. Soon CY, Buerigler JM. Alcohol septal ablation and the Brockenbrough-Braunwald phenomenon. *Catheter Cardiovasc Interv.* 2008 Dec 1;72(7):1016-24.