

The First Patient Clinically Diagnosed With Hypertrophic Cardiomyopathy

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It has now been 50 years since the initial clinical description of hypertrophic cardiomyopathy. In this regard, it is noteworthy that the first patient diagnosed with this disease has survived to date in good health with an active and productive lifestyle—albeit with heart transplantation necessitated by an aggressive disease course with progression to the end-stage phase. © 2008 Elsevier Inc. All rights reserved. (Am J Cardiol 2008;102:1418–1420)

It has been emphasized that hypertrophic cardiomyopathy (HC) is a complex cardiac disease consistent with extended (and often normal) longevity.^{1–4} This outcome may evolve either because the disease itself does not produce major complications (i.e., sudden arrhythmic death, intractable heart failure, or embolic stroke)^{1,5,6} or because disease consequences occur, but are controlled, reversed, or prevented by major treatment interventions such as implantable cardioverter-defibrillators, surgical septal myectomy, or heart transplantation.^{7–9} Recently, we were reminded of this paradigm in HC by an unexpected event. Mr. Claude Brady (of Arlington, Virginia), the first patient clinically identified with HC, emerged on the 50th anniversary of his diagnosis at the recent 11th annual patients' meeting of the Hypertrophic Cardiomyopathy Association in Morristown, New Jersey (Figure 1).

Case Description

The initial suspicion that Mr. Brady had cardiac disease was at 11 years of age, when a local physician heard a precordial murmur, which was attributed at that time to a "family trait" (i.e., the "Brady heart"). Several aunts and uncles had died of heart failure, believed to be due to rheumatic fever. In 1959, at 22 years of age, Mr. Brady presented to the Clinical Center of the National Institutes of Health (Bethesda, Maryland) with exertional dyspnea and fatigue.

His 2 siblings had heart murmurs, and many members of his father's family were said to have heart murmurs. Several of these had died suddenly in childhood or during early adult life. Notably, a grade IV/VI midsystolic murmur was heard at the fourth left intercostal space and apex associated with a prominent left ventricular (LV)

lift. Electrocardiography showed right-axis deviation and incomplete right bundle branch block.

One of the investigators (E.B.) made the clinical diagnosis of idiopathic hypertrophic subaortic stenosis (IHSS), now called HCM. Right and retrograde left-sided cardiac catheterization was performed, and a peak systolic outflow gradient of 40 mm Hg was recorded between the LV cavity and the subaortic area, confirming the precatheterization diagnosis (Figure 2). During a subsequent attempted passage of the catheter into the left ventricle for angiography, ventricular fibrillation occurred. Immediate thoracotomy, cardiac massage, and defibrillation were required to restore sinus rhythm, and the postoperative course was unremarkable.

Comments

Thus, Mr. Brady became the index patient for a new disease, which insofar as we know had not previously been diagnosed clinically^{10–12} and has captured our attention and intense interest over the subsequent 5 decades.¹ In addition, Mr. Brady's brother and sister were also identified with IHSS, underscoring from the onset the familial nature of this disease.^{1,10,12}

Over the next several years, Mr. Brady experienced gradual clinical deterioration, with progressive, unrelenting heart failure and eventually LV systolic dysfunction, recognized as the "burned-out" or "end stage" of HC.⁵ In June 1989, at 52 years of age, he underwent successful heart transplantation at The Johns Hopkins Hospital. He is now 71 years old, with his donor heart of 19 years. Mr. Brady's brother (George) underwent heart transplantation for the same reason 4 years earlier at 45 years of age, making the Bradys, insofar as we know, the only siblings who have received donor hearts in the United States for any condition. It is perhaps odd that the first 2 patients identified clinically with IHSS (Claude and George Brady) ultimately developed a very uncommon clinical profile and course of the disease (i.e., the end-stage phase, which has a prevalence of only 2%), characterized morphologically by widespread myocardial scarring^{5,13} (Figure 3).

Mr. Brady is now healthy and vigorous, and has been particularly active in promoting heart transplantation as the founder of 2 organizations: Transplant Recipients

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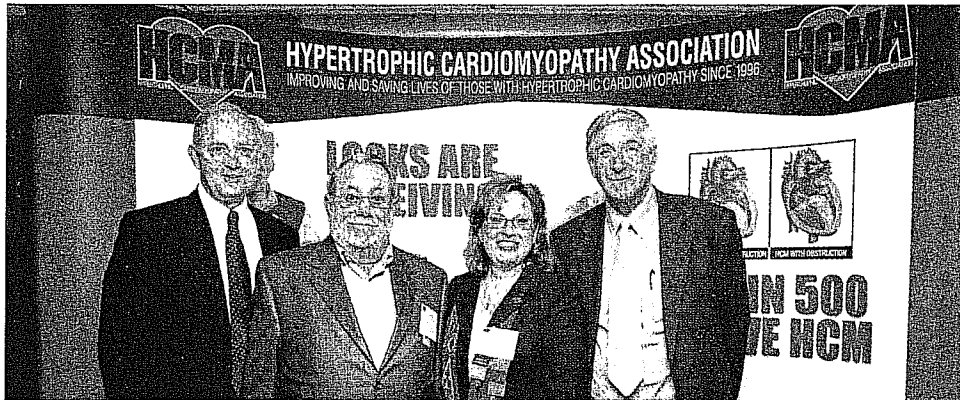


Figure 1. Photograph taken at the 11th annual patients' meeting of the Hypertrophic Cardiomyopathy Association (HCMA) on May 31, 2008. *Left to right:* Dr. Robert O. Bonow (past president, American Heart Association), Claude Brady, Lisa Salberg (president, HCMA), and Dr. Barry Maron.

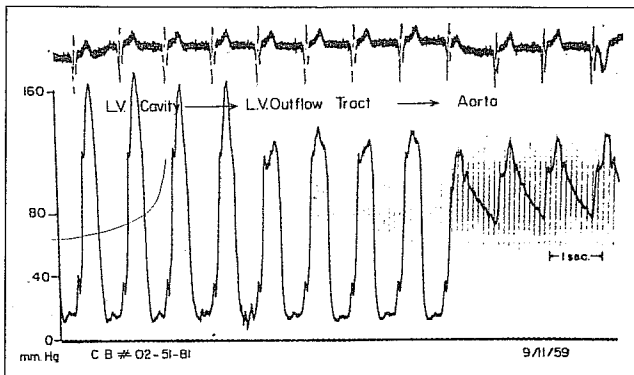


Figure 2. Mr. Brady's continuous pullback pressure tracing, recorded as the catheter was withdrawn from the LV cavity through the outflow tract across the aortic valve and into the aorta. Reproduced with permission from *Am J Med.*¹²

International Organization, Inc. (National Capital Chapter), as well as Transplant Awareness, Inc. As the "IHSS" index case, Claude Brady has taught us a great deal, not only about HC but also the important principle that patients with this sometimes profound hereditary condition can by virtue of their attitudes, perceptions, and fortitude (in conjunction with contemporary management strategies) ultimately prevail against substantial odds.

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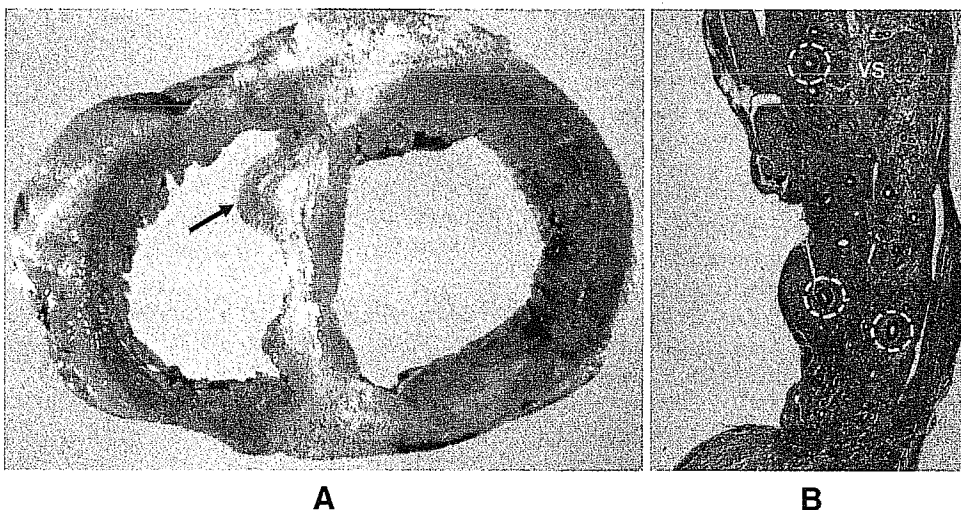


Figure 3. The "Brady heart." (A) Gross and extensive transmural myocardial scarring and thinning of the ventricular septum (yellow areas). A localized area of hypertrophy in the anterior septum persists (arrow). (B) Photomicrograph (elastic van Gieson stain, 3 \times) of septal histopathology showing transmurular fibrosis (stained blue) with small areas of viable myocardium along the endocardial borders (stained red). Abnormal intramural coronary arteries with thickened walls and narrowed lumen ("small-vessel disease"), responsible for bursts of "silent" myocardial ischemia, are present within the area of scarring (broken circles). Reproduced with permission from *Am J Cardiol.*¹³

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