Asymmetric Septal Hypertrophy Presenting With Cardiogenic Shock, Complete Heart Block, and Septal Infarction Despite Normal Coronaries

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A 37-year-old man, brought in following a syncopal episode, was found to be in cardiogenic shock with a complete infranodal heart block. A temporary transvenous pacemaker and an intra-aortic balloon pump were inserted emergently. Cardiac catheterization revealed a high left ventricular end-diastolic pressure but normal coronary vasculature. An echocardiogram demonstrated a hyperdynamic left ventricle, severe hypokinesis of the septum, and asymmetric septal hypertrophy. An endomyocardial biopsy showed myofibril hypertrophy and disarray. The patient required implantation of a permanent pacemaker for full recovery. Although arrhythmias are common in asymmetric septal hypertrophy, complete atrioventricular block is rare but can cause syncope and cardiogenic shock. This is the first case, reported in the literature, of asymmetric septal hypertrophy in which the patient presented with cardiogenic shock and complete heart block secondary to a septal infarction, despite normal coronaries, and in whom a myocardial biopsy was performed. The case report is followed by a review of the literature on hypertrophic cardiomyopathy associated with complete heart block.

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Key words: Asymmetric septal hypertrophy • Cardiogenic shock • Syncope • Complete heart block • Septal infarction

Hypertrophic cardiomyopathy (HCM), characterized by ventricular myocardial hypertrophy, is a complex and relatively common genetic cardiac disease with a marked heterogeneity in clinical expression, natural history, and prognosis. In HCM patients, the association of atrioventricular block

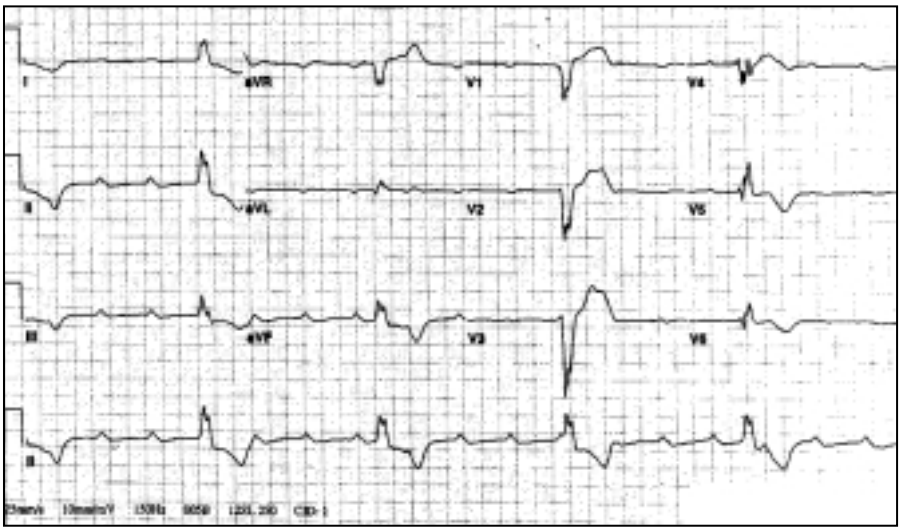

Figure 1. *An electrocardiogram showing complete atrioventricular dissociation, with an atrial rate of 100 beats per minute and a ventricular escape rate of 28 beats per minute.*

and asymmetric septal hypertrophy (ASH) has rarely been described. Arrhythmias are commonly encountered, especially those of ventricular origin. However, the association of atrioventricular block and ASH has rarely been described. In 1965, Luisada[1] first reported this association in a 10-year-old boy with HCM. Only 9 case reports of ASH associated with complete heart block, in adults, have been described in the literature. We report a case of ASH presenting with cardiogenic shock and complete heart block secondary to septal infarction, even though the coronary vasculature was normal. To the best of our knowledge, such a case has never been reported before. Our case is also the first one of this type in which an endomyocardial biopsy was performed.

Case Report

History

A 37-year-old Latin-American male was admitted in cardiogenic shock. The patient complained of substernal chest pain associated with nausea, shortness of breath, diaphoresis, and dizziness on the day of the hospitalization. A brief history was obtained from his family. He was reported to have had at least two similar syncopal episodes, 2–3 years prior to admission. During one of the episodes, a family member noted that the patient's heart rate was in the 20s. The patient did not have any other significant past medical history, including angina, hypertension, or congestive heart failure, and he was not on any medications. His family history was also noncontributory, including the absence of sudden death.

Physical Examination

The patient was afebrile (38.6° C), severely bradycardic (heart rate of 30 beats per minute), and hypotensive (systolic blood pressure of 60 mm Hg). He was sedated and intubated. He had equal breath sounds in both lung fields, with bilateral rales. His heart sounds were distant, and the first heart sound was of variable intensity. A grade 1/6 systolic murmur, heard best at the left sternal border, was present. His abdomen was soft; no peripheral edema was observed.

Laboratory Data

The initial laboratory evaluation showed a high white blood cell count of 11,800/mL (reference range, 4000–10,500/mL) with a leftward shift; bicarbonate, 19 mEq/L (reference range, 25–34 mEq/L); potassium, 3.6 mEq/L (reference range, 3.3–4.8 mEq/L); lactate, 2.9 mEq/dL (reference range, 0.7–2.1 mEq/dL); myoglobin, 105 ng/mL (reference range, < 65 ng/mL); total creatine kinase (CK), 787 IU/L, MB fraction = 3.5, and MB index = 0.4 (reference ranges, total CK, 22–269 IU/L, MB fraction < 5). Troponin I was < 0.03 ng/mL (reference level, < 0.15 ng/mL). Serum and urine toxicology screens were negative. A chest radiograph demonstrated congestive heart failure with pulmonary edema, bilateral pleural effusions, and bilateral upper lobe infiltrates. An admission electrocardiogram demonstrated a complete infranodal heart block with a ventricular escape rate of 28 beats per minute (bpm) (Figure 1).

In hypertrophic cardiomyopathy patients the association of atrioventricular block and asymmetric septal hypertrophy has rarely been described.

Hospital Course

The patient was diagnosed with cardiogenic shock. He was intubated and started on fluids and dopamine at 12 µg/kg/min for pressure support. A temporary transvenous pacemaker was inserted and set to a back-up rate of 90 bpm, resulting in minimal improvement in systolic blood pressure to 80 mm Hg. The patient was taken immediately to the cardiac catheterization laboratory, where an

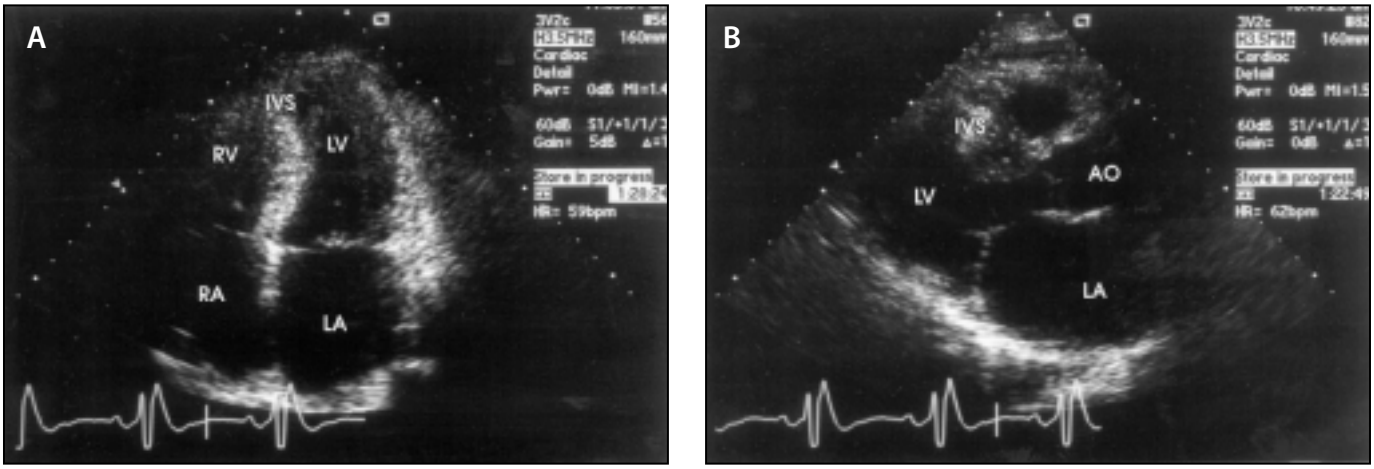

Figure 2. *Echocardiograms demonstrating interventricular septal and posterior wall thicknesses of 30 mm and 14 mm, consistent with asymmetric septal hypertrophy. Left ventricular end-diastolic and end-systolic dimensions were 39 and 30 mm, respectively.* **(A)** *parasternal, long axis view;* **(B)** *apical, four chamber view.*

intra-aortic counterpulsation balloon pump was inserted.

The cardiac catheterization demonstrated normal coronary arteries and a left ventricular end-diastolic pressure of 40 mm Hg. Further treatment was initiated, including intravenous fluids and vasopressors (dopamine up to 20 µg/kg/min and norepinephrine at 10 µg/min). An echocardiogram showed normal atria and valves, the pacemaker wire, no pericardial effusion, a left ventricular end-diastolic diameter of 39 mm, a left ventricular end-systolic diameter of 30 mm, with hyperdynamic left ventricular function, and severe hypokinesis of the anterior septum resulting from septal infarction. The most intriguing finding was the disproportionate hypertrophy of the interventricular septum compared to the left ventricular free posterior wall (30 mm vs 14 mm, respectively), consistent with ASH (Figure 2). There was a low-grade dynamic obstruction of the left ventricular outflow tract (15 mm Hg pressure gradient at rest).

Subsequent laboratory data demonstrated a white blood cell count of 23,800/mL, and a thyroid-stimulating hormone level (TSH) of 0.55 IU (reference range, 0.5–5.0 IU). The total CK peaked at 5099 IU/L, with an MB fraction at 413.7 and an MB-index at 8.1. Troponin I peaked at 50.68 ng/mL. The antistreptolysin titer was within normal limits. Blood and sputum cultures, antinuclear antibodies, human immunodeficiency virus (HIV), and Lyme disease serologies were all within normal ranges.

The patient gradually improved clinically with the restoration of his atrioventricular conduction as well as of the first-degree and bifascicular heart blocks by the second day of hospitalization. On the third day of hospitalization, the patient was extubated successfully. A permanent, dual-chamber DDD pacemaker was inserted because the patient continued to have intermittent complete heart block and remained symptomatic, despite receiving drug therapy. Furthermore, efforts to wean him off the temporary pacemaker were unsuccessful. An endomyocardial biopsy was performed and demonstrated interstitial fibrosis, thickening of the subendocardium, and myocardial disarray, as well as hypertrophy. Morphologic evidence of sarcoidosis, amyloidosis, and

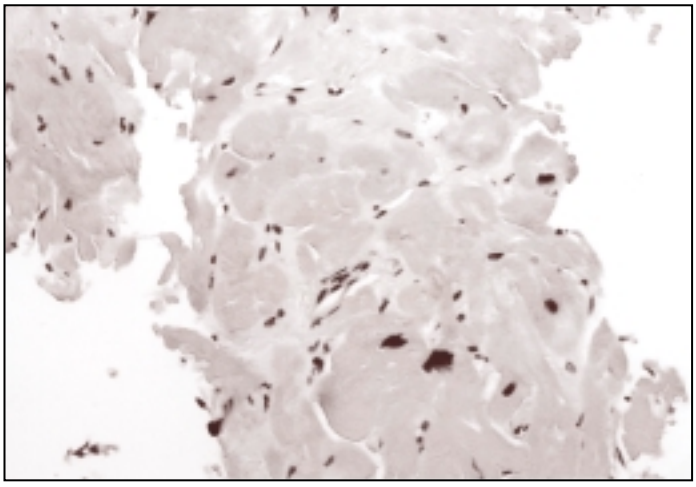

Figure 3. *An endomyocardial biopsy revealing marked myofiber hypertrophy and disarray consistent with the diagnosis of asymmetric myocardial septal hypertrophy. There was no evidence of myocarditis or amyloidosis.*

myocarditis was absent (Figure 3). The patient was discharged home on ß-blocker treatment (atenolol 25 mg daily). A repeat echocardiogram was performed before discharge and demonstrated reduced thickness (24 mm) of the interventricular septum, consistent with septal infarction.

Follow-up

At a 6-month follow-up visit to the clinic, the patient was found to be asymptomatic and in a completely paced rhythm.

Review of the Literature

HCM is characterized by myocardial hypertrophy in the absence of an identifiable cause such as hypertension or aortic stenosis. Its prevalence in the adult population is about 0.2% (1:500).[2] Myocardial hypertrophy can be concentric, apical (more common in the Japanese), or asymmetric.[3] ASH can lead to left ventricular outflow obstruction; thus the term "hypertrophic obstructive cardiomyopathy" (HOCM) is used. However, HCM is predominantly a nonobstructive disease; 75% of patients do not have a clinically significant outflow tract gradient at rest.

HCM can be either sporadic or familial. In about 50% of patients, it is hereditary. Thus, screening of family members of the patient is warranted. HCM is inherited as a mendelian autosomal dominant trait. It encompasses a wide array of genetic defects as well as myopathic conditions, primarily involving the cardiac sarcomere.[3] The genetic defects usually involve the structural myocyte proteins such as ß-myosin (the first identified), myosin-binding proteins, α-tropomyosin, and the troponin subunits.[3]

The annual mortality from HCM is approximately 1%. Patients often are asymptomatic. The most common symptoms are a reduction in effort tolerance, shortness of breath, angina, syncope, and sudden death.[2] HCM is the most common cause of sudden death in young people.[3] The physical signs are essentially manifestations of left ventricular hypertrophy and outflow obstruction. The management of HCM includes avoidance of strenuous activity or the use of ß-blockers, dual-chamber pacing, an implantable cardioverter-defibrillator (ICD), alcohol septal-ablation, and surgery (ventricular septal myotomy-myectomy operation).

The 12-lead electrocardiogram is abnormal in the majority (75%–95%) of HCM patients and demonstrates a wide variety of patterns. Arrhythmias are common in these patients, stemming from both the ventricular (> 75% of the patients) and supraventricular (25%–50% of the patients) regions.[3] The most common ventricular arrhythmia is nonsustained ventricular tachycardia. Atrial fibrillation occurs in about 10% of patients and is reportedly the most common sustained arrhythmia in HCM. Although arrhythmias are common in HCM, complete atrioventricular block is unusual. Clinically significant abnormalities of atrioventricular conduction are rare but, if present, can cause syncope.

In our report, we discuss a case of a young male with ASH presenting with cardiogenic shock and complete heart block secondary to septal infarction, despite having angiographically documented normal coronary arteries. The etiology of complete heart block in ASH is unclear. However, histopathologic abnormalities of the conduction system have been described in HCM. In 1974, Gavrilescu and colleagues[4] reported the first case of ASH with spontaneous complete heart block in a 32-year-old male. The patient had a history of angina, dyspnea, and fatigue. A cardiac catheterization confirmed a systolic gradient that worsened with an infusion of isoproterenol. After 1 year on propranolol, the patient presented with syncopal attacks and congestive heart failure, and was found to have a high-degree heart block. The patient became syncopal after developing ventricular fibrillation and died during the implantation of a pacemaker. An autopsy revealed he had concentric left ventricular hypertrophy with a hypertrophied septum and posterior free wall (38 mm and 32 mm, respectively). The coronary arteries and valves were normal, but the histology showed considerably hypertrophied myocardial cells, marked interstitial fibrosis of the interventricular septum, and extensive severe fibrotic and degenerative lesions in the conduction system of the heart. Table 1 gives a brief overview of this case as well as the other cases described in this literature review.

The onset of complete heart block in a patient with HCM may cause significant symptoms resulting from hemodynamic deterioration. Recognition of this condition and management with a pacemaker may prove life-saving. In 1977, Chmielewski and associates[5] described a 35-year-old Portuguese man with ASH who presented with recurrent syncopal attacks secondary to a complete atrioventricular block. The patient had a family history of sudden death in 16 out of his 23 siblings; one brother was diagnosed with ASH. An echocardiogram showed a systolic anterior motion of the mitral valve leaflet and an increase in the ratio of the septal to posterior wall thickness (1.3:1.0). A cardiac catheterization revealed normal coronary vasculature. A 76 mm Hg gradient could be provoked with an infusion of isoproterenol

Table 1
A Review of the Literature on Hypertrophic Cardiomyopathy Associated With Complete Heart Block

Year	Author	Age, y	Sex	Presenting Symptoms	Known HCM	Familial HCM	IVS, mm	PW, mm	Outflow Gradient, mm Hg	Previous Rhythm	Pacemaker	RV Biopsy	Follow-up	Symptoms at F/U
1974	Gavrilescu et al	32	M	Fatigue	+	0	38	32	25/55*	Sinus	0	0	1 year	Died in CHB
1977	Chmielewski et al	35	M	Syncope	0	+	13	10	0/76*	Sinus, then 2° AVB	+ (AVS)	0	6 months	0
1977	Spilkin et al	20	M	CP, DOE	+	+	2:1	Ratio	64	Sinus	+	0	6 months	0
1985	Khair and Bamrah	65	M	Syncope	0	0	18	11	–	Sinus	+ (Demand)	0	16 months	+
1986	Louie and Maron	33	F	Dyspnea	+	+	41	8	75	Sinus, LBBB	+	0	18 months	Paced
1988	Kothari et al	28	F	Syncope	0	+	20	16	–	–	+	0	–	Sudden death (33 years)
1991	Desai et al	22	M	Syncope	0	0	16	9	0	Sinus	+	0	1 year	0
1991	Thongtang et al	20	M	Dyspnea	+	+	30	20	–	Sinus	+	0	0	–
		16	M	Syncope	+	+	27	14	70	Sinus	+	0	0	–
1992	Albanesi Filho et al	19	M	Palpitations, CP	0	+	27	10	NS	SVT	+	0	14 years	0
		33	M	Presyncope	0	+	19	10	NS	–	+	0	14 years	0
		41	F	Palpitations	0	+	20	12	< 10	–	+	0	14 years	0
2004	Bokhari et al	37	M	Cardiogenic shock, syncope	0	0	30	14	15	–	+	+	6 months	0

*Provoked gradient.
HCM, hypertrophic cardiomyopathy; IVS, interventricular septum; PW, posterior wall; RV, right ventricle; F/U, follow-up; +, yes; 0, no; –, unknown/not done/ not applicable; CHB, complete heart block; AVB, atrioventricular block; AVS, atrioventricular sequential pacemaker; CP, chest pain; DOE, dyspnea on exertion; LBBB, left bundle branch block; NS, nonsignificant; SVT, supraventricular tachycardia.

and following premature ventricular contractions. The patient received a sequential atrioventricular pacemaker and was found to be symptom-free at a 6-month follow-up.

In 1977, Spilkin and colleagues[6] reported the case of a 20-year-old male with HCM who developed complete atrioventricular block. The patient had a history of chest pain and dyspnea. His family history included sudden death in his brother at the age of 16 years. An echocardiograph showed the presence of septal hypertrophy and systolic anterior motion of the mitral valve leaflet. A cardiac catheterization revealed "cavity obliteration" of the left ventricle with a 64 mm Hg subaortic gradient. After 6 months, the patient presented with recurrent episodes of dizziness and was found to have complete atrioventricular block with an idioventricular rhythm of 32 bpm. Placement of a permanent, unipolar, ventricular pacemaker resulted in an improvement of his symptoms.

Accessory atrioventricular pathways have been reported in HCM. They are, however, rare.[2] In 1985, Khair and Bamrah[7] described the association of HCM with atrioventricular block in 2 patients, as well as a coexistence of atrioventricular block with Wolff-Parkinson-White syndrome in a patient with HCM. The 65-year-old man with syncope demonstrated ASH and systolic anterior motion of the mitral valve leaflet. A permanent atrioventricular sequential pacemaker was inserted. After 16 months, following the malfunction of the pacemaker, the patient again became symptomatic. The ventricular lead was subsequently replaced, and over the course of a 10-month follow-up the patient did not experience dizziness.

The clinical expression of HCM differs widely among various patients, even if they are close relatives. In 1986, Louie and Maron[8] published a report on two siblings, a female and her brother, with familial HCM, who required the insertion of a permanent pacemaker at similar ages

(29 and 33 years) for the treatment of spontaneous complete heart block. The sister had severe exertional dyspnea, marked left ventricular hypertrophy (interventricular septal thickness of 41 mm), and left ventricular outflow tract obstruction (maximum baseline subaortic gradient of 75 mm Hg). In contrast, the brother was asymptomatic. He had mild left ventricular hypertrophy confined only to the anterior septum (maximum thickness of 16 mm) without any outflow obstruction. At an 18-month follow-up examination, the sister demonstrated a completely paced rhythm. The mother was found to have ASH with a 20 mm thick interventricular septum and a 10 mm posterior wall. The family history was significant because of the sudden death of the maternal uncle and grandmother at the ages of 28 and 38 years, respectively.

In 1988, Kothari and associates[9] reported a case of a 33-year-old man with familial HCM presenting with syncope, complete heart block, and Stokes-Adams seizures. The patient's 28-year-old sister also had ASH associated with complete heart block and syncope, necessitating the placement of a VVI permanent pacemaker. She died suddenly at 33 years of age.

Most, but not all, reported patients with ASH and complete heart block had familial HCM. In 1991, Desai and colleagues[10] reported the case of a 22-year-old male with recurrent syncopal attacks who was found to be in complete atrioventricular block, with atrial and ventricular rates of 116 bpm and 48 bpm, respectively. An echocardiogram demonstrated ASH with a septal-to-posterior wall ratio of 1.6:0.9. A cardiac catheterization revealed normal coronary arteries and a hyperdynamic left ventricle without a gradient. An electrophysiological study suggested an infra-Hisian atrioventricular block. A VVI permanent pacemaker was implanted, and the patient improved. He remained asymptomatic during the 1-year follow-up.

The review of the literature shows that although arrhythmias are common in hypertrophic cardiomyopathy patients, complete atrioventricular block is rare but can cause syncope in these patients.

Thongtang and associates[11] published a report on two brothers, aged 16 and 20 years, with familial HCM, who developed syncope and complete atrioventricular block. An echocardiogram revealed ASH. Both patients recovered after the placement of a permanent pacemaker. Albanesi Filho and colleagues[12] described 3 patients in the same family, aged 33, 41, and 19 years, with HCM and complete heart block. All of the patients were treated with permanent pacemakers and were reported symptom-free after 13–14.5 years of follow-up.

Cardiogenic shock is characterized by an inadequate tissue perfusion despite adequate intravascular volume. The management of cardiogenic shock in ASH patients is not well-established, mainly because of a lack of literature. Early recognition of shock, along with its underlying etiology, and the definition of coronary anatomy, are extremely crucial in the setting of pump failure. The current American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend the insertion of an intra-aortic balloon pump (IABP) in cardiogenic-shock patients who are candidates for aggressive therapy. The goal is to achieve an early reversal of hypotension and the maintenance of mean arterial pressure (MAP) to prevent devastating neurological and renal sequelae. Pharmacological suppressors like dopamine and norepinephrine should be instituted promptly and maintained at the minimum doses required to achieve adequate MAP. However, dynamic left ventricular outflow tract (LVOT) obstruction, a hallmark of HCM, may actually worsen with inotrope and/or IABP therapy. Treatment of LVOT obstruction includes ß-blockers and α-1 agonists as well as the avoidance of agents that could aggravate

Main Points

- A case of asymmetric septal hypertrophy (ASH) is reported here for the first time in which a man presented with cardiogenic shock and complete heart block secondary to a septal infarction, even though the coronary vasculature was normal. The case is also the first one of this type in which an endomyocardial biopsy was performed.
- The management of cardiogenic shock in ASH patients is not well-established, mainly because of a lack of literature.
- The awareness and recognition of complete heart block in ASH patients is important with respect to their appropriate treatment, which frequently includes the implantation of a permanent pacemaker.

the gradient (eg, nitrates, inotropic agents, and afterload reducers). Volume loading and the use of negative inotropes such as ß-blockers, calcium channel blockers, and disopyramide can reduce the LVOT gradient and improve cardiac output. However, in our patient with isolated ASH without any significant gradient, septal infarction, and complete heart block, the therapy would be the same as that for cardiogenic shock from any other cause of pump failure. Therefore, our patient was treated with volume loading, pharmacological pressors, IABP, and the insertion of a pacemaker, for his hemodynamic recovery.

Conclusion

This review of the literature shows that although arrhythmias are common in hypertrophic cardiomyopathy patients, complete atrioventricular block is rare but can cause syncope in these patients. Although the exact mechanism of high-degree heart block remains unclear, most patients can be treated adequately with the implantation of a pacemaker. In the current case report, we describe a young male who presented with syncope and cardiogenic shock and was found to be in complete atrioventricular block, caused by septal infarction despite having normal coronary arteries. The patient was found, however, to have ASH. We hypothesize that in this case the septal infarction caused complete heart block that led to a cardiogenic shock. The awareness and recognition of complete heart block in ASH patients is important with respect to their appropriate treatment, which frequently includes the implantation of a permanent pacemaker. ■

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