Case Reports

Microvascular Permeability Changes Might Explain Cardiac Tamponade

after Alcohol Septal Ablation for Hypertrophic Cardiomyopathy

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Various sequelae of alcohol septal ablation for hypertrophic obstructive cardiomyopathy have been reported. Of note, some cases of cardiac tamponade after alcohol septal ablation cannot be well explained. We describe the case of a 78-year-old woman with hypertrophic obstructive cardiomyopathy in whom cardiac tamponade developed one hour after alcohol septal ablation, probably unrelated to mechanical trauma. At that time, we noted a substantial difference in the red blood cell-to-white blood cell ratio between the pericardial effusion (1,957.4) and the peripheral blood (728.3). In addition to presenting the patient's case, we speculate that a possible mechanism for acute tamponade—alcohol-induced changes in microvascular permeability—is a reasonable explanation for cases of alcohol septal ablation that are complicated by otherwise-unexplainable massive pericardial effusions. ***(Tex Heart Inst J 2014;41(2):217-21)***

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Percutaneous transluminal alcohol septal ablation (ASA), introduced in 1995, mimics surgical myectomy in that it reduces the left ventricular outflow tract (LVOT) gradient.[1] The procedure has become widely used, and it is estimated that ASA therapies exceed myectomy procedures by 9-fold in the treatment of patients with symptomatic hypertrophic obstructive cardiomyopathy.[2] A mean early mortality rate of 1.5% ± 0.03% in ASA has been reported (range, 0–5%).[3] The reported sequelae of ASA include conduction disturbances, ventricular arrhythmias, coronary dissection, alcohol spillover into the left anterior descending coronary artery, post-myocardial infarction ventricular septal defect, right ventricular infarction, and cardiac tamponade.[3,4]

We describe the case of a patient in whom cardiac tamponade rapidly developed one hour after ASA, and we speculate on the cause of that massive pericardial effusion.

Case Report

In February 2010, a 78-year-old woman with type 2 diabetes mellitus and a history of hypertension controlled with diuretics was admitted to our hospital with acute pulmonary edema. Ventilatory support with bilevel positive airway pressure was rapidly implemented. Auscultation revealed an S_4, a grade 3/6 systolic ejection murmur along the left and upper right sternal border, and a grade 3/6 apical pansystolic murmur that radiated to the axilla. Rapid elevation of the patient's cardiac troponin I level was detected, and an electrocardiogram (ECG) showed ST-segment depression in leads V_3 through V_6 (Fig. 1). The presumptive diagnosis was non-ST-elevation myocardial infarction. Emergent coronary angiography yielded patent coronary arteries and normal left ventricular wall motion. A transthoracic echocardiogram showed asymmetric hypertrophic cardiomyopathy (23-mm septal thickness and 8-mm lateral-wall thickness), with a peak instantaneous resting LVOT gradient of 172 mmHg and systolic anterior motion of the mitral leaflet. The resting LVOT gradient decreased to 52 mmHg after normal saline hydration and low-dose β-blocker therapy (Fig. 2A); however, the patient could not be weaned from mechanical ventilation. Substantial mitral regurgitation persisted after the hydration (Fig. 2B).

During left-sided heart catheterization for ASA, the resting peak-to-peak gradient was 40 mmHg. We noted a post-premature ventricular capture beat and a prominent

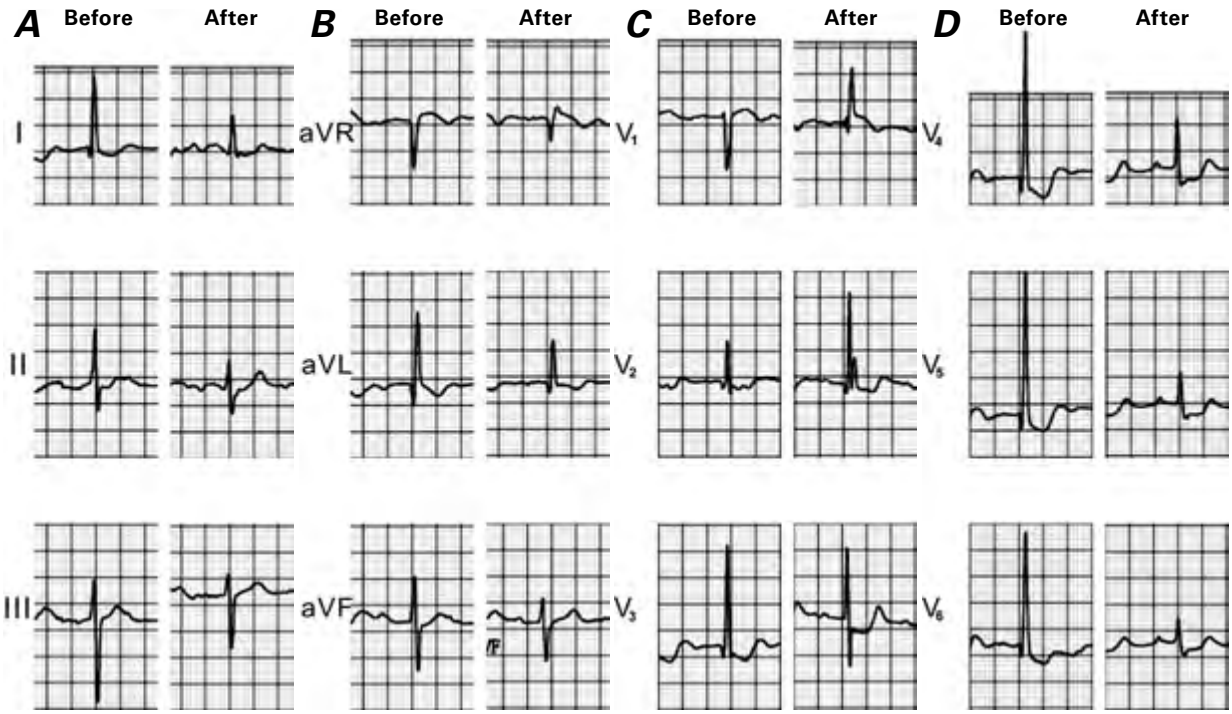


Fig. 1 *Electrocardiograms obtained before and after alcohol septal ablation (ASA).* ***A***, ***B****) The voltage decreased after ASA.* ***C****) After ASA, incomplete right bundle branch block was noted.* ***D****) ST-segment depression from leads V_3 through V_6 was seen before and after ASA. In addition, the high voltage associated with left ventricular hypertrophy reverted to low voltage after ASA.*

Brockenbrough-Braunwald sign. However, there was a provocable peak-to-peak gradient of 159 mmHg at the next sinus beat (Fig. 2C). We placed a temporary pacemaker lead in the right ventricle and injected 2 mL of 99% ethanol into the first septal branch through a 1.5 × 12-mm over-the-wire balloon catheter (Boston Scientific Corporation; Natick, Mass). The first septal branch was successfully ablated, and the resting peak-to-peak gradient decreased from 40 to 0 mmHg. In addition, the provocable peak-to-peak gradient decreased to 9 mmHg at the next sinus beat (Fig. 2D). The entire procedure was completed successfully, and the final angiogram showed no coronary extravasation.

One hour later, cardiac tamponade with shock developed (Fig. 3A). We had no chance for surgical observation of a weeping heart. We performed emergent pericardiocentesis and drained 200 mL of bloody pericardial effusion. Results of fluid analysis showed a red blood cell (RBC) count of 1,840,000 cells/μL and a white blood cell (WBC) count of 940 cells/μL (RBC/WBC ratio, 1,957.4). The peripheral blood was analyzed simultaneously: the RBC count was 3,860,000 cells/μL and the WBC count was 5,300 cells/μL (RBC/WBC ratio, 728.3). Echocardiograms showed little pericardial effusion after the drainage, and the patient's hemodynamic status stabilized. The next day, an additional 30 mL of bloody pericardial effusion was drained. The patient's creatine kinase level was 1,341 U/L, her creatine kinase-MB fraction was 19.2%, and ECG showed a new incomplete right bundle branch block (Fig. 1B).

One week later, massive bilateral pleural effusion developed (Fig. 3B). The serosanguineous fluid contained mixed inflammatory cells and reactive mesothelial cells. Right-sided pleural effusion analysis yielded an RBC count of 18,000 cells/μL and a WBC count of 10 cells/μL; left-sided analysis, an RBC count of 8,500 cells/μL and a WBC count of 20 cells/μL. Gram stain and pleural effusion bacterial cultures were negative. After bilateral drainage, the patient was weaned from ventilatory support. Two weeks later, echocardiograms showed mild hypokinesis of the basal septum, a 9.8-mmHg pressure gradient at the LVOT (Fig. 4A), trivial mitral regurgitation (Fig. 4B), and minimal residual pericardial effusion. As of February 2014, the patient exhibited stable clinical signs and normal LV wall motion, mild mitral regurgitation, a pressure gradient of 10 to 12 mmHg at the LVOT, and no obvious pericardial effusion.

Discussion

The approximate prevalence of cardiac tamponade as a sequela of ASA is 0.6%.[3] The reported causes of tamponade include temporary pacemaker leads, transseptal puncture, and progressive heart failure. However, some cases of post-ASA tamponade cannot be readily explained.[4,5]

In our patient, cardiac tamponade developed rapidly and resulted in hemodynamic instability within one hour of ethanol injection. The bloody pericardial effusion had a markedly higher RBC/WBC ratio than did the peripheral blood. In addition, the effusion did not recur after drainage. Lead- or catheter-related trauma could not explain this phenomenon; had the tamponade resulted from vascular and right atrial perforation, the perforation would have bled continuously. In addition, had the tamponade been the result of bleeding, analysis of the pericardial fluid should have yielded results similar to those in the peripheral blood.

Previous pathologic reports have documented the effectiveness of ethanol injection in artificial myocardial infarction, in animal and human studies.[6,7] The transventricular injection of 60% ethanol in dogs produced coagulative necrosis and hemorrhage, with a narrow border zone consisting of myocytes with neutrophilic

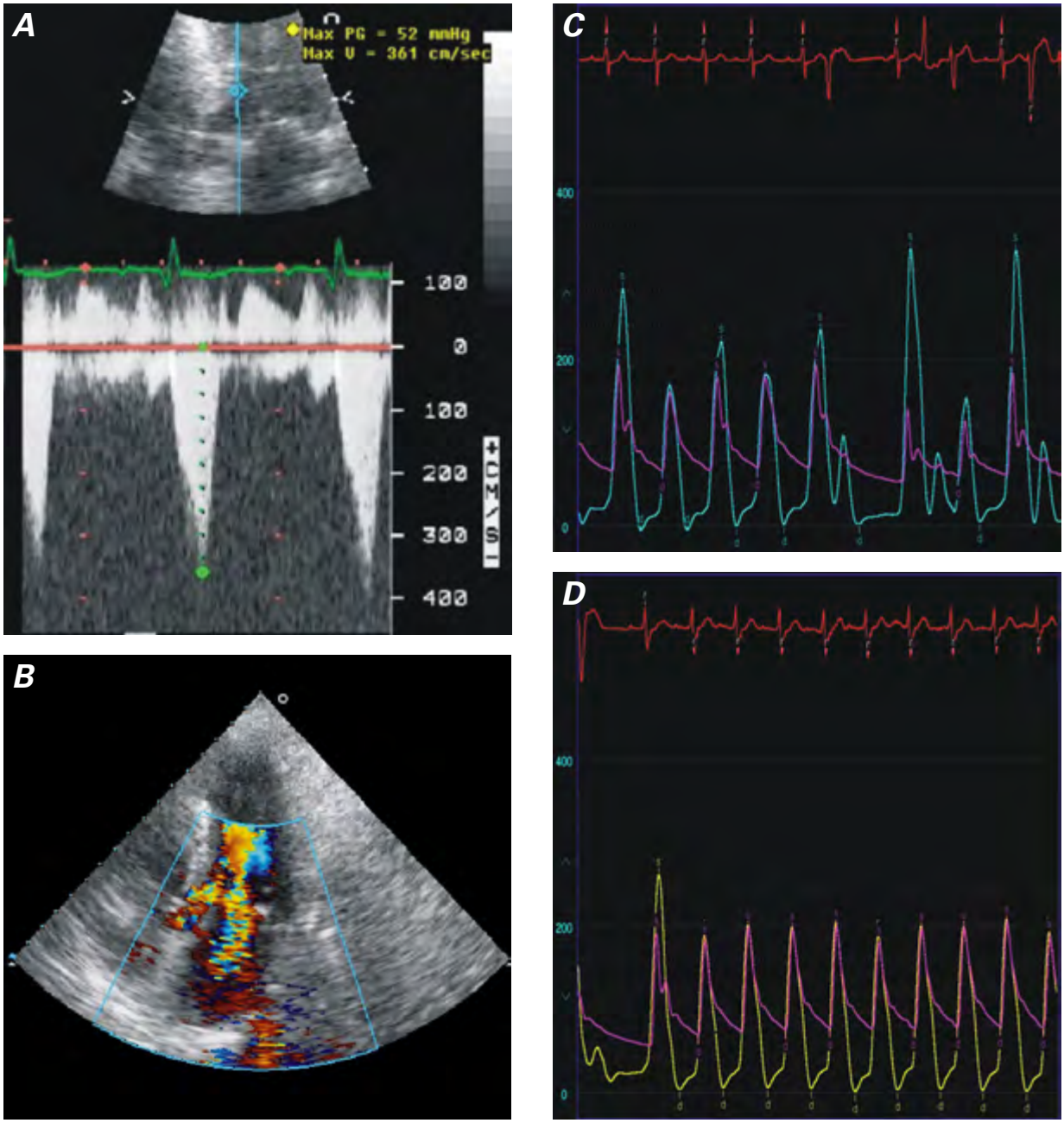
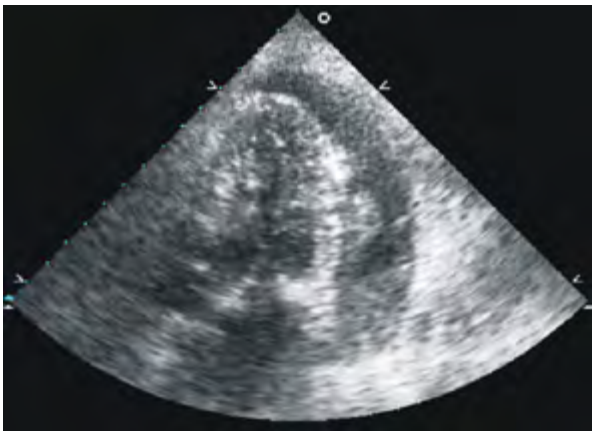


Fig. 2 *Transthoracic echocardiogram reveals* ***A****) a decrease in the resting left ventricular outflow tract gradient to 52 mmHg after normal saline hydration and low-dose β-blocker therapy, and* ***B****) persistent substantial mitral regurgitation after hydration (color-flow Doppler mode). During left-sided heart catheterization, continuous-wave Doppler pressure recordings show* ***C****) a provocable peak-to-peak gradient of 159 mmHg before alcohol septal ablation and* ***D****) a decrease to 9 mmHg after ethanol was injected into the first septal branch.*



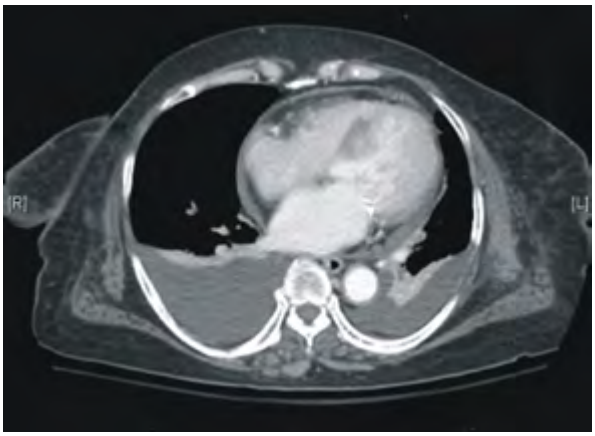


Fig. 3 ***A****) Transthoracic echocardiogram shows cardiac tamponade one hour after ethanol injection.* ***B****) Computed tomogram shows a massive bilateral pleural effusion one week after alcohol septal ablation.*

infiltration.[6] Pathologic examination early after ASA revealed coagulative necrosis of the myocardium and the septal perforator arteries.[7] Creatine kinase-MB fraction is elevated in accordance with the size of the necrotic area. However, initial vascular damage would be accompanied by changes in endothelial permeability.[8]

Szabo and colleagues[9] reported early vascular injury and increased vascular permeability in a rat model after gastric mucosal injury caused by ethanol. The intragastric instillation of 75% and 100% ethanol increased vascular permeability within one to 3 minutes. After one hour of 100% ethanol exposure, the grossly visible hemorrhagic region was strikingly larger in area, and it approximated that of vessel-staining with India ink and monastral blue that labeled damaged blood vessels. Trier and colleagues,[10] also using a rat model of gastric injury, showed a gradient of damage in the endothelial cell structure. The most severe disruption was in the capillaries close to the luminal surface; however, some morphologic damage was evident in the capillary walls at an average depth of 256 μ.

On the basis of the aforementioned animal studies and pathologic reports, we can conclude that vessel permeability changes immediately after exposure to ethanol. This can result in hemorrhage, with a different RBC/WBC ratio because of the substantially different sizes of RBCs and WBCs. This pathologic mechanism can reasonably explain the results of the pericardial effusion analysis in our patient.

Several approaches might prevent this sequela of ASA. First, to decrease the area of necrosis and the number of damaged microvessels, a smaller volume of ethanol might be injected, thus evoking less pericardial effusion and diminishing the possibility of tamponade.[11,12] Ultra-low-dose ethanol (1 mL) has evoked an effect similar to that of higher-dose ethanol (>2 mL).[12] Second, other embolic material, such as glue (cyanoacrylate), might be used to ablate the occluded first septal branch.[13] The use of a covered stent has been reported for ablating the first septal branch.[14] In our patient, the delayed formation of the bilateral pleural effusion might have been the result of post-cardiac-injury syndrome.[15]

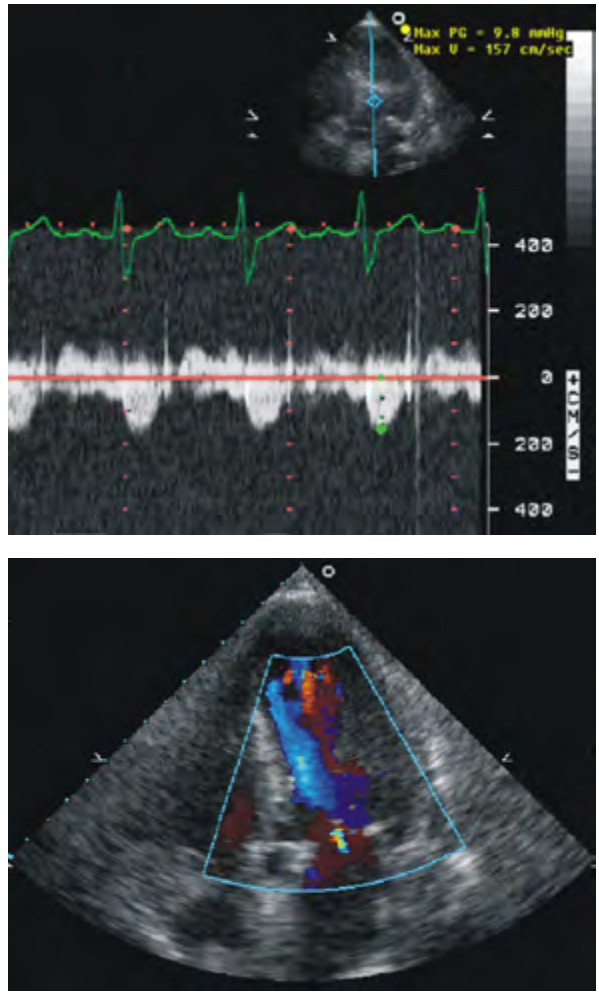


Fig. 4 *Transthoracic echocardiograms 2 weeks after alcohol septal ablation show* ***A****) a low peak instantaneous resting left ventricular outflow tract gradient of 9.8 mmHg, and* ***B****) trivial mitral regurgitation (color-flow Doppler mode).*

In summary, the data from this case offer an alternative, and we think reasonable, explanation for acute cardiac tamponade after ASA. Although the mechanism of altered microvascular permeability is speculative and needs to be verified through further clinical observations, it should be kept in mind in those rare cases that are complicated with otherwise-unexplainable massive pericardial effusion.

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