Very delayed pericarditis associated with ethanol ablation of the vein of Marshall for treatment of atrial fibrillation

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Introduction

Catheter ablation of persistent atrial fibrillation has limited success. Procedural strategies beyond pulmonary vein isolation have failed to consistently improve results.

Recently, catheter ablation with vein of Marshall (VOM) ethanol infusion significantly improved the recurrence of atrial tachyarrhythmia in patients with persistent atrial fibrillation. In this report, subacute pericardial effusion/pericarditis occurred in 13 out of 185 patients who underwent ethanol infusion ablation.[1,2] In a recent worldwide survey, the incidence of delayed cardiac tamponade after pulmonary vein isolation, requiring pericardiocentesis, was reported to be 0.2%, with a mortality rate of 5%.[3] The mechanism underlying the development of delayed tamponade remains unclear, but an inflammatory reaction was considered the most frequent mechanism.[3] Mostly delayed-onset cardiac tamponade occurred within a few days.[1–3]

In this case report, we present a patient with very delayed-onset pericarditis after VOM ethanol infusion for treatment of persistent atrial fibrillation.

KEY TEACHING POINTS

- Subacute pericardial effusion/pericarditis rarely occurred in patients with persistent atrial fibrillation who underwent catheter ablation with vein of Marshall (VOM) ethanol infusion.
- We present a case of very delayed (identified at 180 days) pericardial effusion following catheter ablation (extensive radiofrequency pulmonary vein isolation, left atrial dome linear ablation, and endocardial/epicardial (within the coronary sinus) ablation coupled with vein of Marshal ethanol infusion for treatment of persistent atrial fibrillation.
- Physicians should provide careful follow-up for at least 6 months after VOM ethanol ablation.

Case report

A 48-year-old male patient was referred to our institution for persistent atrial fibrillation ablation. He had no remarkable medical history and had no allergies to medication or food. After written informed consent was obtained, the ablation procedure was performed under conscious sedation, with the CARTO 3 (Biosense Webster, Diamond Bar, CA). After extensive pulmonary vein isolation and left atrial dome linear ablation, VOM was cannulated by over-the-wire balloon and a total of 6 mL (2 mL × 3 times) absolute ethanol (95%) was slowly injected every 2 minutes. Selective VOM venography was repeated after each ethanol infusion to confirm balloon stability and contrast staining to the atrial tissue (Figure 1). No contrast extravasation into the pericardial space was observed. After the ethanol infusion, the 12-lead electrocardiogram demonstrated ST-segment elevation in the inferior leads without hemodynamic collapse. Intravenous infusion of isosorbide dinitrate resolved ST elevation immediately. Urgent coronary artery angiography revealed no significant stenosis or occlusion, indicating that coronary vasospasm occurred. Thereafter, mitral isthmus conduction block was achieved by additional endocardial and epicardial (intra–coronary sinus) ablation. During the index procedure, no pericardial effusion or tamponade occurred. The patient was discharged 2 days after the procedure, and routine outpatient visits were performed after 1 and 3 months, where no adverse

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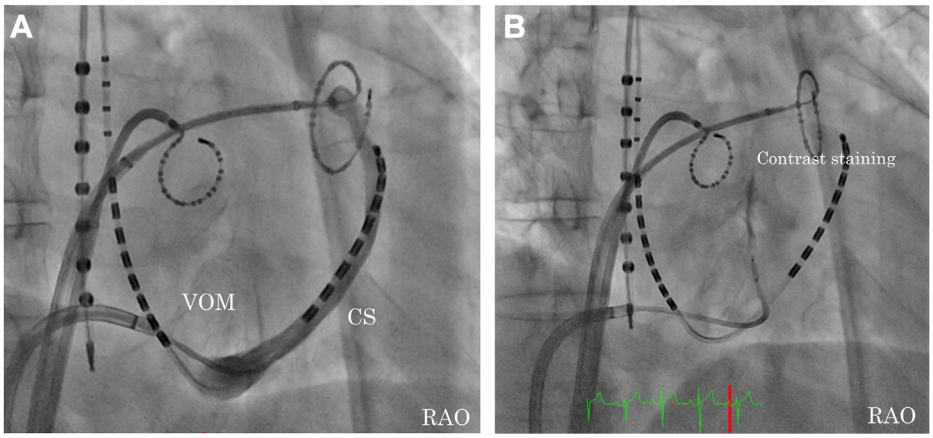

Figure 1 **A:** Coronary sinus venography. **B:** Ethanol infusion to vein of Marshall. CS = coronary sinus; RAO = right anterior oblique; VOM = vein of Marshall.

events were noted. After 6 months, he had sub-fever up to 38°C, accompanied with slight chest pain. Postprocedural routine electrocardiogram and 24-hour Holter electrocardiogram revealed that he still had normal sinus rhythm without any ST-segment change, but a massive pericardial effusion was observed by routine echocardiogram without hemodynamic compromise. Inflammatory markers, such as C-reactive protein, transaminase, and soluble interleukin-2 receptor, were slightly elevated. Contrast-enhanced computed tomography of the chest revealed massive pericardial effusion, significant swelling of the mediastinum lymph nodes, and thickened pericardium (Figure 2).

After admission we decided to perform thoracoscopic pericardiectomy because of the technical difficulty of percutaneous pericardiocentesis. During operation, 600 mL of cloudy yellow pericardial fluid was removed by pericardiectomy, and thoracoscopic mediastinal lymphadenectomy was also performed.

On histological analysis, pericardial effusion and pericardium were normal, and benign lymphocytes and fibrotic tissue were found, respectively. Mediastinal lymph nodes revealed a reactive lymphoid follicle, specifically mantle zone hyperplasia, with no evidence of malignancy (Figure 3). One week after the operation, he was discharged, and no recurrent pericarditis and pericardial effusion occurred thereafter. His physical status was stable and sinus rhythm continued.

Discussion

To our knowledge, this is the first report of very delayed pericarditis associated with ethanol ablation of VOM, with presentation almost 6 months after the procedure. Owing to this lengthy time between the catheter ablation procedure and presentation, we initially speculated the etiology of this pericarditis and pericardial effusion as malignant pathogenesis. However, histological findings revealed no malignancy and possibly autoimmune pathogenesis, with inflammatory pericardial reaction following ethanol damage to the myocardium or pericardium, indicating the terms of post–cardiac injury syndrome (PCIS).[4] PCIS occurs by initial myocardial damage caused by myocardial infarction (Dressler syndrome), cardiac surgery, thoracic trauma, or catheter ablation. According to a report by Li and colleagues,[4] more

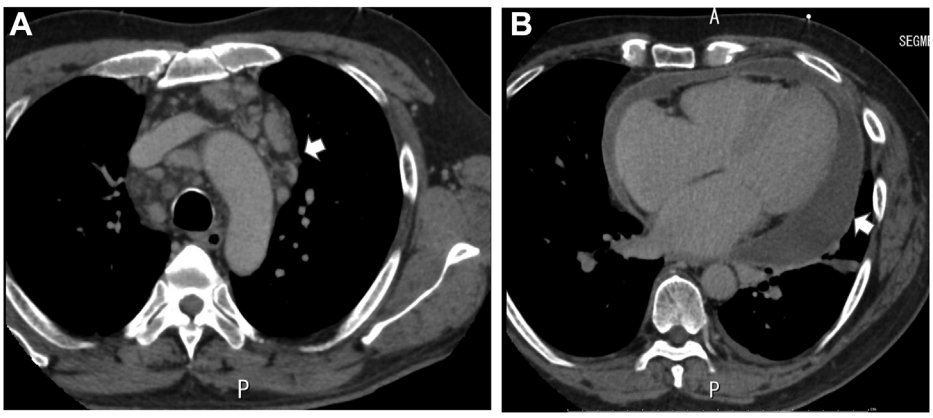

Figure 2 Contrast-enhanced computed tomography of the chest. **A:** Swelling of the mediastinum lymph nodes. **B:** Thickened pericardium and massive pericardial effusion.

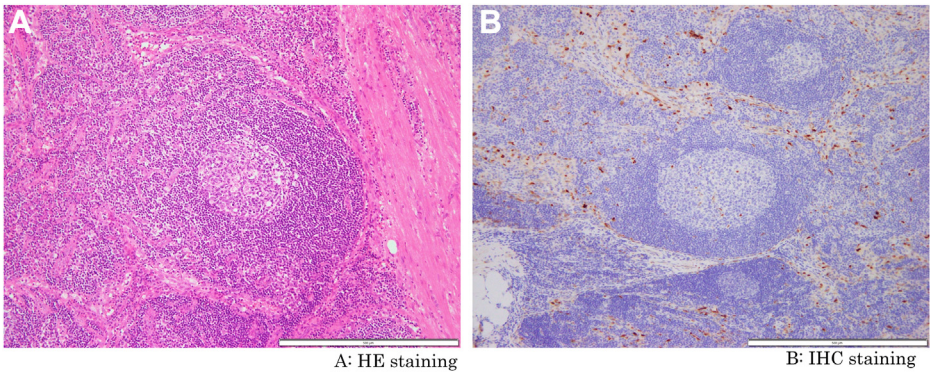

Figure 3 Representative images of hematoxylin-eosin (HE) and immunohistochemical (IHC) staining showing the reactive lymphoid follicle. **A:** HE staining. **B:** IHC staining. The samples show positive staining for CD5 and negative for CyclinD1, indicating absence of mantle cell lymphoma.

than 70% of pericardial effusion cases due to catheter ablation were caused by left atrial ablation for atrial fibrillation and right atrial flutter ablation.

In response to catheter ablation, PCIS most frequently occurs after extensive radiofrequency application. The pathophysiology of PCIS after ablation is poorly understood. Putative triggers are considered, including the release of autoantigens from necrotic myocardial tissue from radiofrequency burn. This immune-mediated syndrome generally occurs a few weeks prior to the appearance of the clinical manifestation.[5]

Delayed cardiac tamponade after atrial fibrillation ablation was previously recognized by Cappato and colleagues,[3] who reported 45 cases among 27,921 sessions (0.2%). Delayed tamponade occurred a median of 12 days (range: 0.2–45 days) after ablation. In a recent report of ethanol ablation of VOM, delayed serious cardiac tamponade occurred in 5 out of 713 patients who underwent catheter ablation (0.7%) at least 14 days after the procedure.[2] In this report, the number of days before onset of tamponade had a very wide range of 14–106 days compared with Cappato's report. Our case also had significant delayed onset of pericarditis, almost 180 days after the procedure, indicating that different inflammatory mechanisms may have occurred owing to the ethanol itself on the myocardium and pericardium injury compared with radiofrequency alone.

This case had accompanying coronary vasospasm during the procedure. Coronary vasospasm might be caused by parasympathetic activity, owing to stimulation of left inferior ganglionated plexi by ethanol infusion, resulting in transient right coronary artery vasospasm.[6] We have no hypotheses on the association between coronary vasospasm and very delayed pericarditis. Vasospasm is the acute response, but pericarditis is subacute and progressive in nature. This case indicates that widespread injury of cardiac tissue by ethanol infusion might cause these various phenomena.

Conclusion

Our case is the first clinical report to describe very delayed occurrence of pericarditis caused by PCIS associated with ethanol ablation of VOM. Although very delayed PCIS is a rare case, physicians should provide careful follow-up for at least 6 months after ablation.

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