Pulmonary edema postcardioversion: A potential calcium signalling problem

Ahmad Hersi MD¹, Paul W Armstrong MD², Jonathan B Choy MD²,
Sajad Gulamhusein MD², Katherine M Kavanagh MD²

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The present report describes an unusual case of pulmonary edema after adenosine cardioversion of a supraventricular tachycardia. Despite a structurally normal heart, a 52-year-old woman presented with pulmonary edema on two separate occasions, having had her atrioventricular nodal re-entrant tachycardia terminated with 12 mg of intravenous adenosine. A third similar episode of tachycardia that was terminated with verapamil was not complicated by pulmonary edema.

Key Words: *Calcium signalling; Cardioversion; Pulmonary edema; Verapamil*

A 52-year-old woman presented to the emergency room with a 10 h history of tachycardia. Immediately before the tachycardia she was healthy and not on any medications. She was hemodynamically stable, with a heart rate of 189 beats/min and blood pressure (BP) of 152/115 mmHg. Her electrocardiogram (Figure 1A) showed a narrow complex tachycardia at a rate of 190 beats/min. She converted to normal sinus rhythm after administration of 12 mg of intravenous adenosine (Figure 1B). Immediately after cardioversion, her sinus rate was 100 beats/min and her BP was 140/85 mmHg. Approximately 1 h after cardioversion, while still in the emergency room, without chest pain, she began complaining of shortness of breath. Over the next 30 min she developed severe shortness of breath, hypoxia (O₂ saturations dropping to 85%) and diffuse bilateral crackles, which were not present before cardioversion. At that time, her BP was 140/90 mmHg and she was in sinus tachycardia at a rate of 140 beats/min. No recurrence of her tachycardia or other arrhythmias was noted. A chest x-ray confirmed the diagnosis of pulmonary edema. She was diuresed 2 L, and symptoms and O₂ saturation improved. Three sets of cardiac enzymes drawn 8 h apart were negative.

Twelve hours after clinical stabilization, a transthoracic echocardiogram showed normal left ventricular (LV) size, an ejection fraction of approximately 50%, anteroseptal akinesis and moderate diastolic LV dysfunction. A transesophageal echocardiogram was arranged in conjunction with an electrophysiological study to assess LV function before and during the tachycardia. The baseline transesophageal echocardiogram at the electrophysiological study demonstrated that the anteroseptal wall had recovered compared with the transthoracic echocardiogram performed 12 h after the tachycardia on initial

Un œdème pulmonaire après une cardioversion : Un problème potentiel de signalisation calcique

Le présent rapport décrit un cas inhabituel d'œdème pulmonaire après une cardioversion d'adénosine d'une tachycardie supraventriculaire. Malgré un cœur de structure normale, une femme de 52 ans a consulté à cause d'un œdème pulmonaire en deux occasions distinctes. La tachycardie nodale auriculoventriculaire de réentrée a été stoppée à l'aide de 12 mg d'adénosine par voie intraveineuse. Un troisième épisode similaire de tachycardie a été stoppé par du verapamil, mais sans complication d'œdème pulmonaire.

presentation, and the rest of the study showed what appears to be a structurally normal heart. Atrioventricular (AV) nodal re-entry tachycardia was induced at a rate of 200 beats/min and it was allowed to persist for 5 min before termination with 12 mg of intravenous adenosine. The patient then underwent successful ablation of the slow AV nodal pathway, after which the arrhythmia could not be reinduced. End-diastolic and end-systolic short-axis views during sinus rhythm, tachycardia, within 1 min of arrhythmia termination by 12 mg of adenosine and at 5 min post-termination are shown in Figures 2 and 3. During AV nodal re-entrant tachycardia, both the end-diastolic and end-systolic LV dimensions were slightly diminished compared with baseline, suggesting underfilling of the left ventricle during tachycardia. Immediately after the termination of tachycardia, the LV dimensions were similar to baseline. However, during the recovery phase (5 min post-tachycardia), there was a marked increase in both end systolic and end diastolic dimensions, along with moderate anteroseptal hypokinesis, suggesting decompensation of the LV. The patient was monitored for 24 h. There were no further arrhythmias, hemodynamic compromise or recurrence of pulmonary edema.

Retrospectively, the patient described two similar episodes of tachycardia. An episode four months previous was also terminated with adenosine and within 2 h she had returned to the emergency room with pulmonary edema. She was admitted to a coronary care unit and investigated with coronary angiography, which was normal. In 1994, postmastectomy, she also had a narrow complex tachycardia at a rate of 190 beats/min that was identical to the tachycardia shown in Figure 1A. This episode was terminated with intravenous verapamil and was not complicated by pulmonary edema.

¹Libin Cardiovascular Institute of Alberta, University of Calgary, Calgary; ²University of Alberta, Edmonton, Alberta
Correspondence and reprints: Dr KM Kavanagh, Health Sciences Centre, 3330 Hospital Drive Northwest, Calgary, Alberta T2N 4N1.
Telephone 403-210-8838, fax 403-283-6151, e-mail kkavanag@ucalgary.ca
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Figure 1) **A** Twelve-lead electrocardiogram at the time of presentation to the emergency room shows a narrow complex tachycardia at a rate of 190 beats/min; **B** Twelve-lead electrocardiogram postcardioversion with adenosine shows sinus rhythm at a rate of 86 beats/min

Figure 2) Transesophageal short-axis (SAX) views acquired at the electrophysiological study showing end-diastolic area at: **A** Baseline sinus rhythm (SR) – end-diastolic area of 10 cm²; **B** Atrioventricular nodal re-entry tachycardia at a rate of 200 beats/min (BPM) – end-diastolic area of 7.5 cm²; **C** Within 1 min of cardioversion with adenosine (ADEN) – end-diastolic area of 11 cm²; **D** Five minutes postcardioversion with ADEN – end-diastolic area of 12 cm². Circ Circumference; HR Heart rate; SVT Supraventricular tachycardia

Figure 3) Transesophageal short-axis (SAX) views acquired at the electrophysiological study showing end-systolic area at: **A** Baseline sinus rhythm (SR) – end-systolic area of 4.1 cm²; **B** Atrioventricular nodal re-entry tachycardia at a rate of 200 beats/min (BPM) – end-systolic area of 3.5 cm²; **C** Within 1 min of cardioversion with adenosine (ADEN) – end-systolic area of 3.8 cm²; **D** Five minutes postcardioversion with ADEN – end-systolic area of 6.6 cm². Circ Circumference; HR Heart rate; SVT Supraventricular tachycardia

The patient has not had any recurrence of her tachycardia or pulmonary edema since her ablation therapy one year ago.

DISCUSSION

Typically, acute pulmonary edema postcardioversion occurs within 3 h of electrical cardioversion of atrial fibrillation in patients with structural heart disease secondary to a variety of etiologies (1). Pulmonary edema postcardioversion has been reported in three patients without structural heart disease (two with lone atrial fibrillation and one with atrial flutter) (1-3).

A review of 712 patients by Upshaw (1) reported that cardiac output may decrease after cardioversion of atrial fibrillation for up to one week in more than one-third of patients. The incidence of acute pulmonary edema is estimated to be between 1% and 3% among patients after electrical cardioversion for ventricular tachycardia, atrial fibrillation and atrial flutter (4,5). The mortality rate in patients that develop pulmonary edema is reported to be 18% (1). A number of mechanisms have been postulated to contribute to postcardioversion pulmonary edema, including shock-induced LV injury/lung injury, anesthesia-induced LV dysfunction, delayed return of left atrial function and coronary/pulmonary emboli (1-3,5-7). Pulmonary edema has also been described after electrical cardioversion in three patients without structural heart disease (2,3,5), as well as in two cases of nonelectrical cardioversion

(structural abnormalities were present in both of these cases) (3,5). The patient in the present report did not have significant structural heart disease or an electrical cardioversion.

Intravenous adenosine administered for supraventricular tachycardia has been associated with at least two deaths (8). In both cases the arrhythmia was atrial fibrillation and hemodynamic compromise occurred immediately after the administration of the adenosine. The terminal rhythm in both cases was asystole (8). Autopsy findings in one case showed massive bilateral pulmonary emboli. There was no autopsy in the second case, but the patient was known to have severe chronic obstructive pulmonary disease and pulmonary fibrosis (8). A prospective study of adenosine in the emergency room in 160 patients showed a proarrhythmia rate of 13% (9). These arrhythmias included AV block inducing asystole, paroxysmal atrial fibrillation and nonsustained ventricular tachycardia (9). All arrhythmias were transient and subsided spontaneously without intervention (9). Because our patient did not experience any problems immediately after adenosine and no arrhythmia was documented after reversion to sinus rhythm, it is unlikely that adenosine was the cause of the pulmonary edema.

Our patient had neither significant structural heart disease nor atrial fibrillation, yet developed pulmonary edema on reversion to sinus rhythm in the absence of anesthesia and electrical cardioversion. Thus, she does not fit any of the

theories previously proposed to explain postcardioversion pulmonary edema. Although there are no animal studies of postcardioversion pulmonary edema, it is well documented in vitro that tachycardias are accompanied by elevated cytosolic calcium (10,11), and that myocyte contractile dysfunction is not unusual even after brief episodes of tachycardia (12-14). In canine and porcine models, brief episodes of atrial tachycardia resulted in post-tachycardia contractile dysfunction, which appeared to be related to a post-tachycardia Ca^{2+} handling abnormality (12,15). Similarly, in feline ventricular myocytes, Wang et al (14) have also demonstrated that brief episodes of tachycardia result in a transient decrease in myocardial contractility. They proposed that the increased calcium transient during tachycardia is the essential factor for the activation of the signalling mechanism that subsequently depresses myofilament Ca^{2+} responsiveness resulting in depressed myocyte contractile function (14). It has also been shown that contractile dysfunction is enhanced by calcium agonists and inhibited by calcium antagonists (12,15). Although it would be reasonable to suggest that abnormalities of Ca^{2+} handling would result in contractile dysfunction and pulmonary edema during the tachycardia, it is likely that early during the tachycardia, contractile dysfunction is masked by compensatory mechanisms, such as catecholamines and increased heart rate. However, after termination of the tachycardia and compensatory mechanisms, the contractile dysfunction becomes manifest.

These animal studies, the relative infrequency of postcardioversion pulmonary edema and the uniqueness of this patient who developed pulmonary edema after chemical

cardioversion with adenosine but not with verapamil leads us to hypothesize that a small percentage of the population has a genetic or acquired abnormality of calcium signalling. This abnormality results in prolongation or amplification of the contractile dysfunction that is normally transiently seen after episodes of tachycardia.

CONCLUSIONS

Pulmonary edema is a rare complication that manifests after sinus rhythm has been restored. It has been most frequently described in patients with atrial fibrillation and structural heart disease. This is by far the largest group of patients in whom cardioversion is required. However, as highlighted by the present case report, it can occur with tachyarrhythmias other than atrial fibrillation in the setting of a structurally normal heart, no occult coronary disease, no anesthetic drugs and without evidence of pulmonary or coronary emboli. Because the mechanism has eluded us to date, it is difficult to predict who will develop this problem. The frequency of this complication is likely under-reported because it is most likely to occur in the setting of significant structural heart disease; thus, the incidence of this complication is still unknown. The consequences can be devastating, with four deaths reported to date (16). Clinically, it is important to be aware of this entity and vigilant in reporting cases so that new hypotheses regarding mechanisms can be addressed. It may also be reasonable to monitor patients for 2 h to 3 h postcardioversion, regardless of the modality by which it is achieved, and to instruct patients not to delay in returning should they develop symptoms.

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