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【 CASE REPORT 】

Cryoballoon Ablation Induced Hyperkalemia due to Possible Cold Agglutinin Disease

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Abstract:
Cryoballoon ablation is a well-established therapeutic tool for paroxysmal atrial fibrillation (PAF). We herein report a rare case of a 69-year-old man with PAF undergoing hemodialysis due to chronic kidney disease who developed hyperkalemia caused by possible cold agglutinin disease during cryoballoon ablation therapy. During the procedure, his electrocardiogram showed wide QRS when we finished cryoablation therapy. We detected hyperkalemia and performed urgent hemodialysis. We should bear in mind that cold agglutinin disease can occur during cryoballoon ablation.

Key words: cryoablation, hyperkalemia, cold agglutinin disease

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Introduction

Atrial fibrillation (AFib) is a major public health burden worldwide, with a prevalence that increases with advancing age (1). AFib is a major cause of stroke and systemic embolism, and anti-coagulation therapy is required in patients with AFib (2, 3). Besides anti-coagulation therapy, pulmonary vein isolation has been well established as a treatment of AFib and is widely accepted (4). In such situations, cryoballoon ablation for paroxysmal AFib (PAF) has been reported to be safe and effective (5).

We herein report a rare case of a patient who developed wide QRS on his electrocardiogram (ECG) during cryoballoon ablation due to hyperkalemia caused by possible cold agglutinin disease. The publication of this case report was approved by the Ethics Committee of Kurume University Hospital, and the patient gave his informed consent.

Case Report

A 69-year-old Japanese man with PAF, undergoing hemodialysis due to chronic kidney disease with no history of hemolytic anemia or hospitalization due to hyperkalemia was admitted to our hospital for catheter ablation. He had complained of PAF since 2015, which gradually became drug-resistant.

On admission, his blood pressure was 90/42 mmHg, and heart rate was 56 beats per minute and regular. No abnormality was detected in the skin or eyes, such as livedo racemosa or jaundice, or in the heart or breath sounds. Chest X-ray showed no significant abnormality. ECG showed sinus rhythm (heart rate 54 beats/min) with left-axis deviation. Echocardiography revealed a mildly enlarged left atrial dimension of 41 mm with a normal left ventricular ejection fraction (60%). Blood tests showed elevated levels of N-terminal pro-brain natriuretic peptide (NTpro-BNP, 1,284.3 pg/mL) and creatinine (Cr, 13.1 mg/dL) (Table 1).

His ECG showed sinus rhythm just before the procedure (Fig. 1), and we performed cryoballoon ablation (Arctic Front Advance Cardiac Cryoablation Catheter; Medtronic, Minneapolis, USA) for PAF at the target for total 240 seconds for each pulmonary vein (PV), in the order of left superior pulmonary vein (LSPV), left inferior pulmonary vein

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Table 1. Blood Tests on Admission.

WBC	3,900 /μL	Na	136 mmol/L	γ-GTP	23 U/L	T.bil	0.29 mg/dL
RBC	423×10⁴ /μL	K	4.5 mmol/L	ALP	148 U/L	CRP	0.14 mg/dL
Hb	13.8 g/dL	Cl	98 mmol/L	LDH	145 U/L	NTpro-BNP	1,284.3 pg/mL
Ht	42.8 %	Ca	8.4 mg/dL	CPK	50 IU/L	PT-INR	1.25
Plt	11.1×10⁴ /μL	P	6.1 mg/dL	TG	79 mg/dL	APTT	34.0
BUN	45.8 mg/dL	AST	14 U/L	HDL-C	35.6 mg/dL		
Crea	13.1 mg/dL	ALT	8 U/L	LDL-C	94.3 mg/dL	Hemolysis	(-)

WBC: white blood cells, RBC: red blood cells, Hb: hemoglobin, Ht: hematocrit, Plt: platelets, BUN: blood urea nitrogen, Cr: creatinine, Na: sodium, K: potassium, Cl: chloride, Ca: calcium, P: phosphorus, AST: aspartate aminotransferaze, ALT: alanine aminotransferaze, γ-GTP: gamma-glutamyl transpeptidase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase, CPK: creatine phosphokinase, TG: triglyceride, HDL-C: high density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, T.bil: total bilirubin, CRP: C-reactive protein, NTpro-BNP: N-terminal pro-B-type natriuretic peptide, PT-INR: prothrombin time-international normalized ratio, APTT: activated partial thromboplastin time

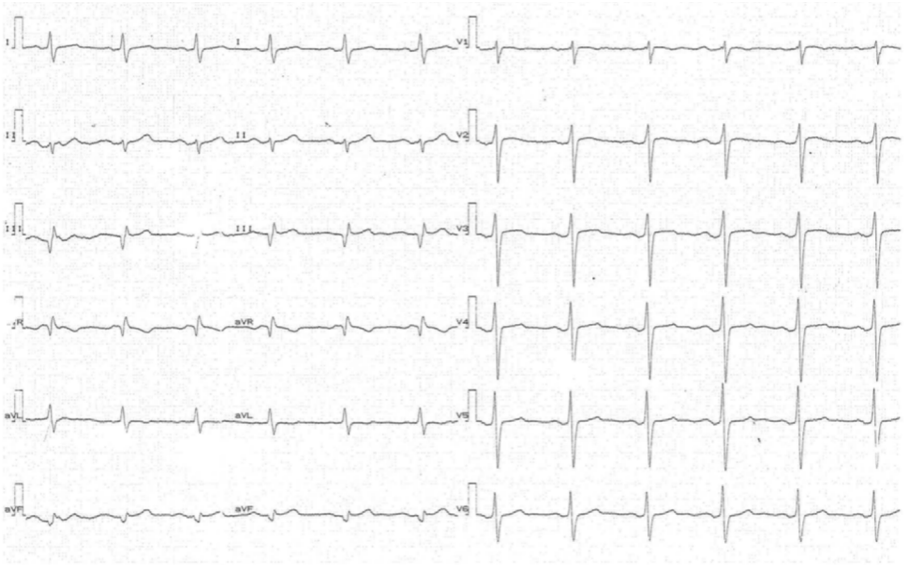

Figure 1. The electrocardiogram before cryoablation.

(LIPV), right inferior pulmonary vein (RIPV) and right superior pulmonary vein (RSPV). We applied minimum temperatures of -52℃ for 240 seconds for the LSPV, -62℃ for 270 seconds for the LIPV, -62℃ for 200 seconds for the RIPV, and -62℃ for 210 seconds for the RSPV. We added further cooling for the LSPV and RIPV because we had confirmed remaining electric potentials. However, they remained even after the additional cryoablation, so we ablated them (30 seconds duration, 30W) using an irrigation catheter (Flex Ability Ablation Catheter, 8F, 2.7 mm; St Jude Medical, St. Paul, USA) and successfully confirmed their disappearance.

The ECG showed wide QRS immediately after we paced the pulmonary veins (Fig. 2). We performed coronary angiography (CAG), which showed no coronary obstruction, but coronary vasospasm in the left anterior descending coronary artery (Fig. 3). We then administered 1 mg of isosorbide dinitrate to the right coronary artery and 2 mg of nicorandil to the left coronary artery, accompanied by the continuous intravenous administration of nicorandil (2 mg/h). Although coronary spasm was improved, wide QRS remained. Because blood tests indicated hyperkalemia (K; 7.1 mmol/L, Table 2), we intravenously administered 850 mg of calcium gluconate and 1.4 g of sodium bicarbonate. The wide QRS was then improved (Fig. 4). After we finished ablation, we performed urgent hemodialysis, and the hyperkalemia was improved (Fig. 5); however, after 6 hours, an ECG showed wide QRS with hyperkalemia (K; 6.4 mmol/L). We again performed urgent hemodialysis, and the ECG and potassium levels were then stabilized (Fig. 5).

To investigate the cause of hyperkalemia, we first considered rhabdomyolysis in malignant syndrome, as we had administered clonazepam. However, he did not have a fever, hyperhidrosis, or extrapyramidal symptoms such as myotonia, which suggested something other than malignant syndrome. A blood test after cryoablation indicated the presence of hemolysis (Table 2), but not before ablation (Table 1). Furthermore, a blood test on the day after cryoablation showed the presence of anemia (hemoglobin: 13.8 on admission to 11.3 g/dL, Fig. 5). We therefore considered hyperkalemia caused by hemolytic anemia. A direct Coomb's test was negative; however, the haptoglobin level was decreased

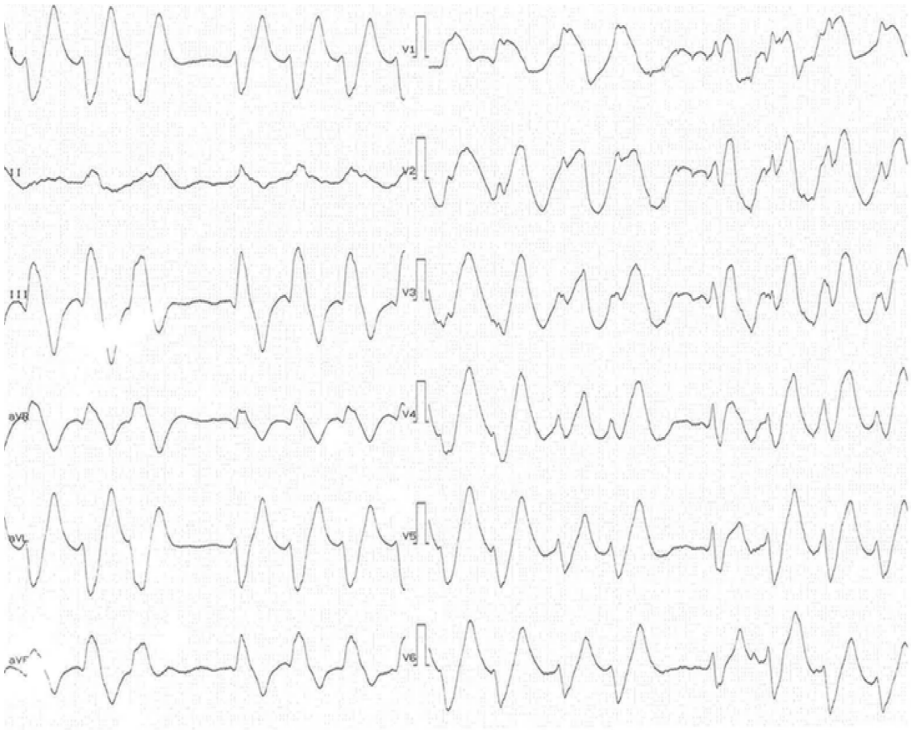

Figure 2. **The electrocardiogram immediately after pulmonary vein isolation.**

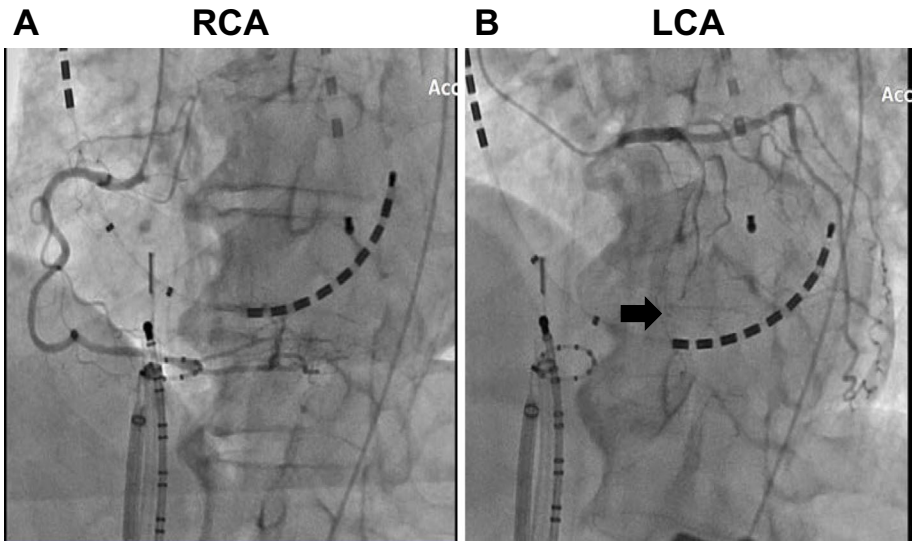

Figure 3. **Coronary angiograms immediately after pulmonary vein isolation. A: Right coronary artery (RCA), B: left coronary artery (LCA). The arrow indicates coronary vasospasm in the left anterior descending coronary artery.**

(<10 mg/dL), and a hemagglutination test was positive (cold agglutinin level 1:128). Therefore, we diagnosed him with possible cold agglutinin disease causing hemolysis and hyperkalemia due to the cold condition induced by cryoablation.

Since the ablation procedure, he has taken his own pulse every day, and his primary care physician monitors his ECG during hemodialysis, but no AFib recurrence has occurred. Furthermore, his blood potassium levels have remained within the normal range, suggesting that no hemolysis occurred after cold cryoablation.

Discussion

This is the first report of hyperkalemia induced by hemolysis (possibly cold agglutinin disease) during cryoballoon ablation. To confirm the rarity of this phenomenon, we performed a hemagglutination test in 20 subsequent patients after this case who had undergone ablation therapy for AFib in our hospital, and none showed "positive" findings. Fur-

Table 2. Blood Tests after Cryoablation.

WBC	6,200 /μL	Na	129 mmol/L	γ-GTP	22 U/L	APTT	≥200
RBC	443×10⁴ /μL	K	7.1 mmol/L	ALP	144 U/L		
Hb	14.6 g/dL	Cl	95 mmol/L	LDH	436 U/L		
Ht	42.8 %	Ca	8.2 mg/dL	CPK	639 IU/L	Hemolysis	(2+)
Plt	10.4×10⁴ /μL	P	5.7 mg/dL	CPK-MB	225 IU/L		
BUN	25.9 mg/dL	AST	78 U/L	CRP	0.29 mg/dL		
Crea	11.0 mg/dL	ALT	16 U/L	PT-INR	3.30		

WBC: white blood cells, RBC: red blood cells, Hb: hemoglobin, Ht: hematocrit, Plt: platelets, BUN: blood urea nitrogen, Crea: creatinine, Na: sodium, K: potassium, Cl: chloride, Ca: calcium, P: phosphorus, AST: aspartate aminotransferaze, ALT: alanine aminotransferaze, γ-GTP: gamma-glutamyl transpeptidase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase, CPK: creatine phosphokinase, CPK-MB: creatine phosphokinase-MB, CRP: C-reactive protein, PT-INR: prothrombin time-international normalized ratio, APTT: activated partial thromboplastin time

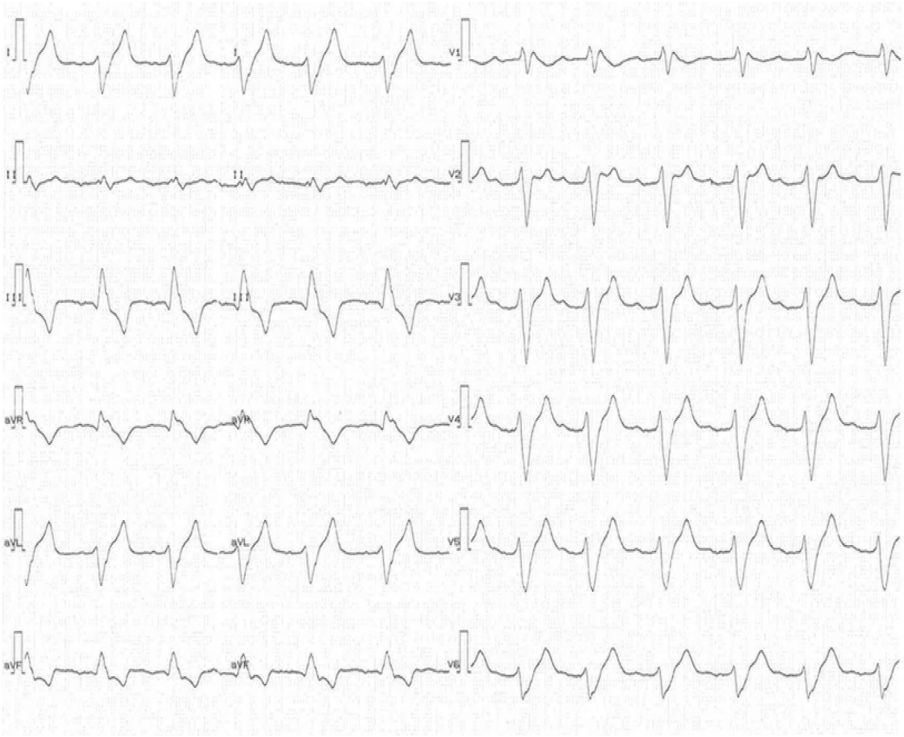

Figure 4. The electrocardiogram after injecting calcium gluconate and sodium bicarbonate.

thermore, in more than 200 patients who have undergone cryoballoon ablation in our hospital, there have been none who have shown obvious hemolysis except for this case. Therefore, we believe that this case is very rare.

Cold agglutinin disease is a form of autoimmune hemolytic anemia (AIHA) (6, 7), which is classified as warm, cold, or mixed type; cold type includes cold agglutinin disease and paroxysmal cold hemoglobinuria (6). AIHA is a rare condition, with a reported incidence of 0.8-3 per 10^5/year in adults, a prevalence of 17:100,000, and a mortality rate of 11% (6). Cold agglutinin disease is typically associated with solid cancer or hematological tumor and is more frequent in aged subjects than in young ones (6). Careful observation in this patient is therefore needed regarding the cancer issue.

In this patient, hemolysis occurred during the cryoablation procedure; however, it has not occurred during hemodialysis therapy since then, suggesting that daily clinical procedures have been performed safely, even in winter. If a patient has symptomatic anemia, transfusion dependence, or disabling circulatory symptoms, the treatment of cold agglutinin disease is required (8). In cold agglutinin disease secondary to malignant or infectious diseases, there is no evidence-based therapy, and the treatment of the underlying disease is generally accompanied by resolution of the hemolysis, particularly in cases of lymphoproliferative disease and mycoplasma pneumonia (8).

However, we should also consider the possibility of warm-type hemolytic anemia during radiofrequency catheter or hot balloon ablation, although warm AIHA is also rare. The first-line therapy for warm AIHA is corticosteroids, which is effective in 70-80% of patients and should be

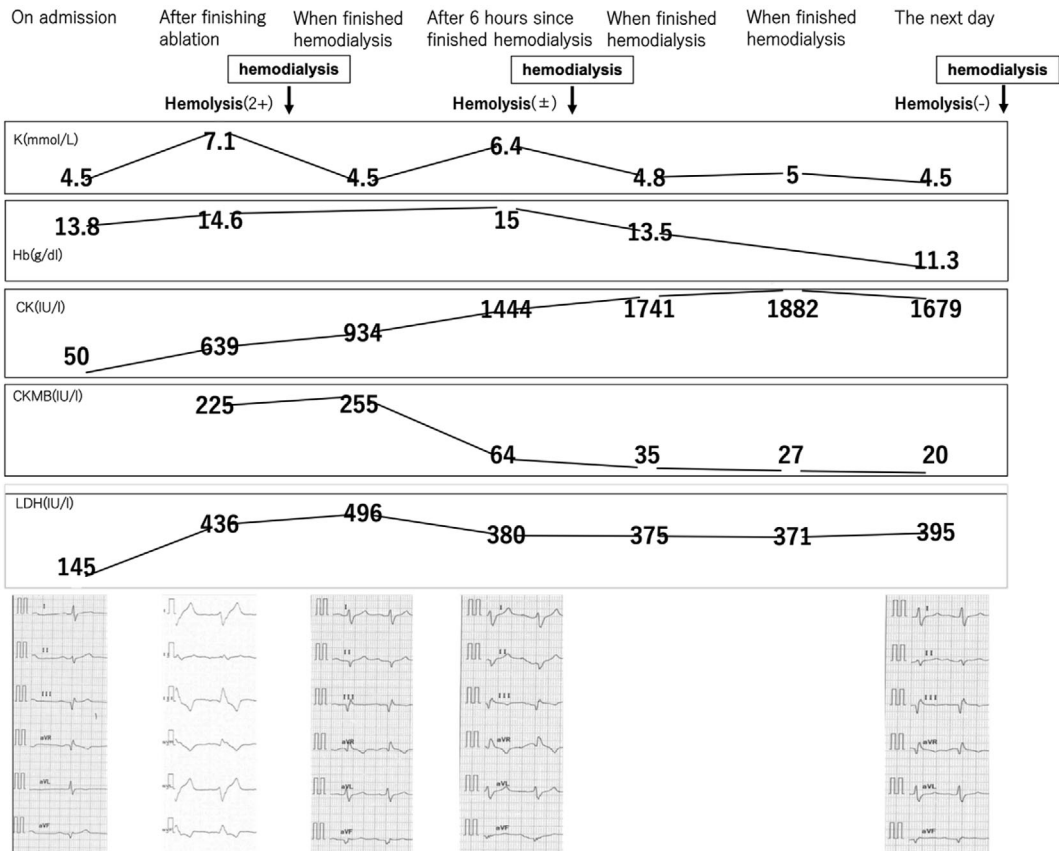

Figure 5. **Clinical time course.**

slowly tapered over a period of 6-12 months (8). The second lines are splenectomy, rituximab, and immunosuppressive drugs thereafter (8). Because AIHA can develop gradually and have a fulminating onset with life-threatening anemia (8), careful observation is needed.

Conclusion

We encountered a rare case of a 69-year-old man with PAF who developed hyperkalemia caused by possible cold agglutinin disease during cryoablation therapy. In hemodialysis patients in particular, the association between ECG findings and serum potassium levels should be carefully considered during cold or warm procedures.

The authors state that they have no Conflict of Interest (COI).

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