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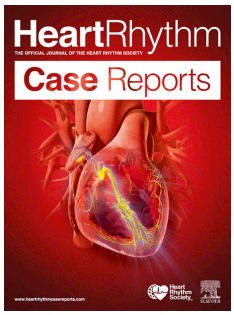

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Acute Kidney Injury Following Pulsed Field Ablation in a Patient with Waldenström's Macroglobulinemia: A Case Report

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Introduction

Pulsed field ablation (PFA) has recently gained prominence as an effective and myocardial-selective energy source for the treatment of atrial fibrillation (AF). Unlike conventional thermal ablation such as radiofrequency and cryoballoon ablation, PFA induces myocardial cell death through electroporation by delivering high-voltage, short-duration electrical fields, while selectively preserving adjacent non-cardiac structures, including the esophagus and phrenic nerve.(1,2) Although PFA is associated with a favorable safety profile, emerging evidence suggests that procedure-related hemolysis may occur, potentially leading to acute kidney injury (AKI).(3,4) The MANIFEST-17K study, a prospective cohort study evaluating the safety of pulsed field ablation (PFA) in 17,642 patients, has identified an increased risk of hemolysis and AKI post-procedure in patients with preexisting renal dysfunction and those undergoing a high number of PFA applications(3). However, hemolysis-induced AKI has also been documented in patients without these traditional predisposing factors, and its pathophysiologic mechanisms remain inadequately elucidated.

Case report

A 58-year-old male with a history of Waldenström’s macroglobulinemia (WM) received PFA due to symptomatic paroxysmal atrial fibrillation (PAF). He had been on treatment with ibrutinib, a Bruton's tyrosine kinase (BTK) inhibitor, for WM. His baseline renal function was within normal limits (serum creatinine: 0.95 mg/dL). The procedure was performed under conscious sedation with

Midazolam. Vascular access was obtained, a single transseptal puncture guided by intra-cardiac ultrasound was performed, and intravenous heparin was administered to maintain an activated clotting time of >350 seconds. Three-dimensional maps of the left atrium and 4 pulmonary veins (PV) were created with CARTO 3 (Biosense Webster). PFA was performed using the FARAPULSE ablation system (Boston Scientific) which consists of a generator (FARASTAR) to induce an electric field with an output between 1.8 and 2.0 kV, a 13.8 Fr (inner diameter) steerable sheath (FARADRIVE), and a 12 Fr over-the-wire catheter (FARAWAVE). The catheter has five splines with four electrodes per spline and its configuration can be changed seamlessly between basket and flower catheter system.(1,5) Each pulmonary vein (PV) received eight applications (four basket and four flower configurations), totaling 32 applications. Two additional applications were delivered to the right PV carina anterior, bringing in the total of 34 applications (Figure). Pulmonary vein isolation (PVI) was successfully achieved without any complications. On postoperative day 1, the patient exhibited an increase in serum creatinine to 2.29 mg/dL. Laboratory findings included decreased hemoglobin (before ablation: 12.6 g/dL, after ablation: 8.9 g/dL), increased LDH (before ablation: 187 U/L, after ablation: 638 U/L), decreased haptoglobin (before ablation: 75 mg/dL, after ablation: 15 mg/dL), and mild increased indirect bilirubin (before ablation: 0.65 mg/dL, after ablation: 0.86 mg/dL). Urinalysis revealed strong positive hemoglobinuria without hematuria. These findings suggested hemolysis-related AKI. The patient was managed with aggressive intravenous fluid resuscitation (2 liters per day). Serum creatinine peaked at 2.76 mg/dL on postoperative day 3 and demonstrated gradual improvement, allowing discharge on postoperative day 6. At the outpatient visit two weeks after discharge, renal function had recovered to baseline.

Discussion

PFA-induced hemolysis and subsequent AKI have been recognized as emerging complications, although the precise mechanisms remain under investigation. The MANIFEST-17K study identified chronic kidney disease and increased application numbers as key risk factors for post-PFA AKI.(3) In this case, despite normal baseline renal function and a moderate number of PFA applications

(standard: 32 applications, this case: 34 applications), hemolysis-related AKI developed, suggesting the presence of additional predisposing factors. WM is characterized by elevated serum IgM levels (in this case: 2663 mg/dL), leading to hyperviscosity syndrome, which can impair microcirculatory flow and promote endothelial dysfunction.(6,7) Although a specific IgM threshold predictive of hemolysis during PFA is currently undefined, this case raises the possibility that serum rheological properties, endothelial-modifying therapies (e.g., BTK inhibitors), and baseline laboratory markers may modulate the risk of hemolysis-related complications. These factors warrant further investigation in future studies aimed at improving risk stratification. In addition, although patients with WM rarely develop serious hemolytic anemia, it has been reported that the direct Coombs test is positive in around 10% of cases.(8) Furthermore, ibrutinib, a BTK inhibitor used in the treatment of WM, has been associated with vascular endothelial alterations and platelet dysfunction(9), potentially exacerbating hemolysis under conditions of increased shear stress, such as those induced by PFA. It has been demonstrated that erythrocytes in patients with WM exhibit reduced deformability under high shear stress conditions.(10) In addition to increased plasma viscosity and enhanced erythrocyte aggregation, impaired erythrocyte deformability may contribute to microvascular flow stasis. The interaction between these factors may have heightened the patient's susceptibility to hemolysis and subsequent renal injury, despite a relatively standard FARAPULSE PFA protocol. This case underscores the importance of considering hematologic disorders as additional risk factors for PFA-related hemolysis and AKI. Clinicians should maintain a suspicion in patients with hyperviscosity syndromes or those on BTK inhibitors, even if conventional risk factors such as preexisting renal dysfunction or excessive PFA applications are absent. In patients with hematologic disorders at risk for hyperviscosity syndrome, minimizing procedural risks associated with PFA should be prioritized. To this end. preventive strategies—including preprocedural plasmapheresis, aggressive periprocedural hydration, limiting the number of energy applications, close renal monitoring, and postprocedural surveillance for hemolysis—may reduce the incidence of hemolysis-related complications. While the current evidence base comparing thermal ablation and PFA in hematologic patients is limited, conventional radiofrequency or cryoablation may be

cautiously considered as alternative options in selected high-risk individuals until more robust data become available.

Conclusions

This case highlights a rare but clinically significant occurrence of hemolysis-related AKI following PFA in a patient with WM on BTK inhibitors. The findings suggest that hyperviscosity syndrome and endothelial dysfunction may predispose patients to PFA-induced hemolysis and renal injury. A comprehensive risk assessment, including hematologic conditions, is crucial in optimizing patient safety during PFA procedures.

Figure Legend

(A) and (B) depict the post-PFA voltage map in the AP and PA views, respectively, demonstrating the completion of PVI.

AP; anteroposterior. PA; posteroanterior. PFA; pulsed field ablation. PVI; pulmonary vein isolation.

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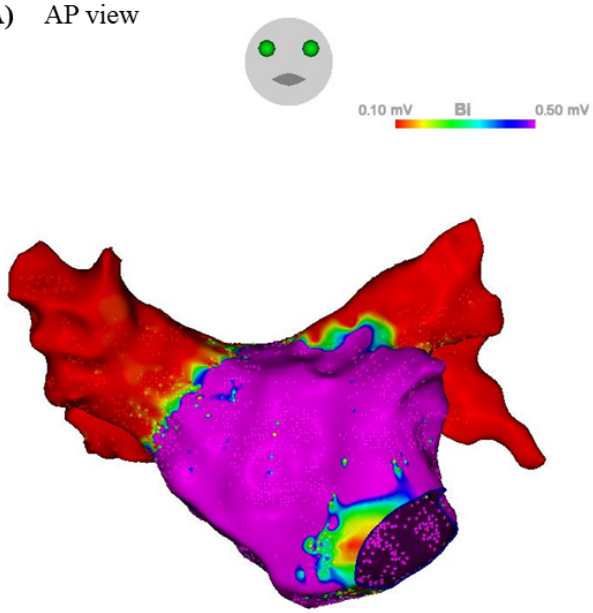
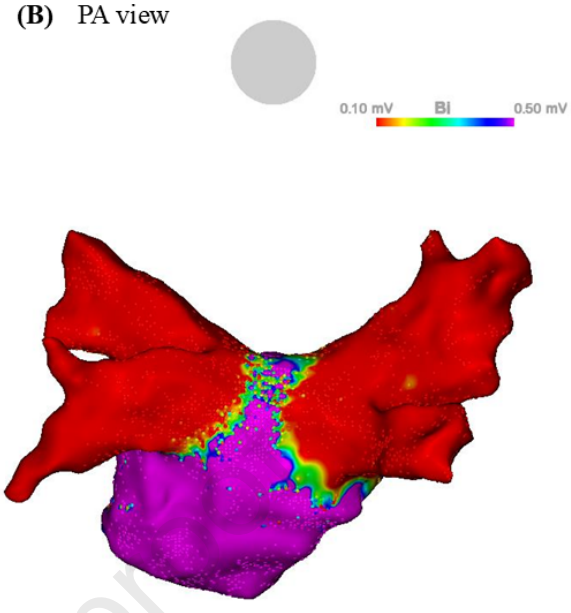
(A) AP view



(B) PA view



Key Teaching Points

- In patients with hematologic disorders undergoing pulsed field ablation (PFA), clinicians should recognize the potential risk of hemolysis-related acute kidney injury (AKI) and ensure appropriate perioperative precautions, including tailored hydration strategies and vigilant postprocedural monitoring.

- Waldenström's macroglobulinemia and treatment with Bruton's tyrosine kinase inhibitors may predispose patients to hemolysis-related complications through mechanisms such as hyperviscosity, endothelial dysfunction, and impaired erythrocyte deformability.

- For patients at high risk of hyperviscosity syndrome, specific preventive strategies—such as preprocedural plasmapheresis, minimizing PFA energy applications, and close renal and hemolysis surveillance—should be considered to mitigate complications. In select high-risk cases, conventional thermal ablation may serve as an alternative until further evidence on PFA safety becomes available.