Hypertensive crisis during catheter ablation of atrial fibrillation in a patient with undiagnosed pheochromocytoma: a case report

Kentaro Yoshida1,2*, Kazuhiro Iijima3, Ikuo Yoshida1,4, and Tatsuhide Hiramine5,6

1Department of Cardiology, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba 305-8575, Japan; 2Department of Cardiology, Ibaraki Prefectural Central Hospital, 6528 Koibuchi, Kasama 309-1793, Japan; 3Department of Anesthesiology, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba 305-8575, Japan; 4Department of Cardiology, Moriya Daiichi General Hospital, 1-17 Matsumaeda, Moriya 302-0102, Japan; 5Department of Internal Medicine (Endocrinology and Metabolism), Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba 305-8575, Japan; and 6Hiramine Clinic, 3-24-7 Shimorenjaku, Mitaka 181-0013, Japan

Received 19 September 2017; accepted 5 January 2018; online publish-ahead-of-print 7 February 2018

Introduction
Pheochromocytoma is an unusual cause of hypertension accounting for 0.1% of cases. As the development of atrial fibrillation (AF) is tightly associated with hypertension, patients with pheochromocytoma are at higher risk for AF. Procedure-related external factors, such as prescription of a beta blocker without the preventive administration of an alpha blocker, use of contrast medium, administration of anaesthetics, and emotional and pain-related stress, caused a hypertensive crisis with acute left ventricular dysfunction during ablation procedure. After surgical resection of the adrenal tumour, sinus rhythm was maintained without antiarrhythmic drugs.

Case presentation
A 72-year-old woman with undiagnosed pheochromocytoma underwent catheter ablation of drug-resistant AF. Procedure-related external factors, such as prescription of a beta blocker without the preventive administration of an alpha blocker, use of contrast medium, administration of anaesthetics, and emotional and pain-related stress, caused a hypertensive crisis with acute left ventricular dysfunction during ablation procedure. After surgical resection of the adrenal tumour, sinus rhythm was maintained without antiarrhythmic drugs.

Discussion
Because hypertensive crisis can lead to life-threatening organ damage, electrophysiologists seeing patients with AF should always consider pheochromocytoma as a mechanism of hypertension and AF before proceeding to catheter ablation of the AF.

Keywords
Pheochromocytoma • Hypertensive crisis • Atrial fibrillation • Catheter ablation • Case report

Learning points
• The prevalence of secondary hypertension is reported to be 5–10% among hypertensive patients.
• Patients with secondary hypertension show a highly significant 7- to 12-fold increased risk of atrial fibrillation (AF) when compared with patients with essential hypertension.
• Patients who undergo catheter ablation of AF are at higher risk of periprocedural hypertensive crisis if pheochromocytoma is underdiagnosed.
• Electrophysiologists seeing patients with AF should consider pheochromocytoma as a mechanism of drug-resistant AF before proceeding to catheter ablation.

Introduction
Pheochromocytoma is a catecholamine-producing neoplasm arising from chromaffin cells and is an unusual cause of hypertension accounting for at most 0.1–0.2% of cases. Because of paroxysmal elevation of the blood pressure and the lack of symptoms in these patients, 50% of pheochromocytomas are not diagnosed until autopsy.1,2 As the development of atrial fibrillation (AF) is tightly associated with hypertension and resultant atrial stretch, patients with pheochromocytoma are at higher risk for AF. Particularly in patients undergoing catheter ablation of AF, the periprocedural prescription of beta blockers without the preventive administration of an alpha blocker, use of contrast medium, administration of anaesthetics during the procedure, and emotional and pain-related stress associated with invasive procedures are...
common. Because these external factors can all be causes of a hypertensive crisis associated with pheochromocytoma, patients with undiagnosed pheochromocytoma may be highly susceptible to such crisis during the periprocedural period of catheter ablation of AF.

**Timeline**

| Event | Description |
|-------|-------------|
| 5 years prior to admission | Hypertension was diagnosed at a medical check-up |
| 12 months prior to admission | Paroxysmal atrial fibrillation was documented by electrocardiogram |
| 5 months prior to admission | Atrial fibrillation was converted to persistent form |
| Admission and catheter ablation for atrial fibrillation (0 days) | Hypertensive crisis occurred during the procedure |
| 4 weeks after catheter ablation | Pheochromocytoma was highly suspected based on blood and urine analyses, magnetic resonance imaging, and 123I-metaiodobenzylguanidine scintigraphy |
| 11 months after catheter ablation | Phased prescriptions of anti-hypertensive drugs were required to control the blood pressure and to increase the circulating plasma volume. Surgical resection of the tumour was performed |
| 35 months after catheter ablation | A 30-day loop recorder did not detect any atrial fibrillation episodes |

**Case presentation**

A 72-year-old woman was referred for catheter ablation of persistent AF. Her chief complaint was mild dyspnoea and palpitations on effort. She had a history of hypertension for 5 years without anti-hypertensive drugs and AF for 12 months. Atrial fibrillation had persisted continuously for 5 months. Cardiac auscultation revealed increased intensity of the second heart sound (S2) but no murmurs or gallops. The remainder of the physical examination was unremarkable. A12-lead electrocardiogram (ECG) showed AF with negative T waves in leads I, aVL, and V3 to V6 (Figure 1A). An echocardiogram revealed normal left ventricular (LV) function with an ejection fraction of 66% and an enlarged left atrium (LA) with a volume of 80 mL. Her blood pressure at the outpatient clinic was 151/80 mmHg, and the beta blocker bisoprolol 2.5 mg was newly prescribed for rate control. A pre-procedural ECG-gated computed tomography (CT) scan using non-ionic contrast medium was performed without adverse events 1 week before catheter ablation to assess the left atrial and pulmonary venous anatomy.

Catheter ablation was performed with conscious sedation using dexmedetomidine (0.7 mcg/kg/h) and fentanyl (20 mcg/kg/h). Throughout the procedure, arterial pressure was invasively measured using a 4Fr sheath inserted in the femoral artery. After coronary angiography and pulmonary venography, anteropulmonary vein isolation was performed under the guidance of a three-dimensional electro-anatomical mapping system (CARTO, Biosense Webster, Diamond Bar, CA, USA). Although her blood pressure at presentation to the laboratory was 120/76 mmHg and the sedation was appropriate with a Ramsay sedation score of 4–5, her systolic blood pressure began to dramatically fluctuate within a range of 80–255 mmHg (Figure 2A). The intravenous injection of nicardipine 0.5 mg was repeated, but its effect was transient, and the BP remained totally uncontrolled. Particularly after the direct cardioversion of AF, her blood pressure was markedly elevated despite the administration of thiamyal sodium 100 mg. This situation fulfilled the definition of a hypertensive crisis. A low-voltage area suggesting advanced structural remodelling was broadly observed in the LA, and pulmonary vein isolation was followed by linear ablation at the mitral isthmus and superior vena cava isolation (Figure 2B). Although the procedure was completed without complications, the LV ejection fraction after ablation was significantly decreased to 48% compared with 66% before ablation. We speculated the presence of secondary hypertension, and her serum catecholamine levels measured 4 weeks after ablation were found to be clearly elevated [adrenalin 0.03 ng/mL (normal range = 0.00–0.10 ng/mL), noradrenalin 3.36 ng/mL (0.10–0.50 ng/mL), and dopamine <0.01 ng/mL (0.00–0.03 ng/mL)]. A 24-hour urine test revealed a normal level of metanephrines of 0.11 mg/day (0.04–0.18) but an increased level of normetanephrine of 1.40 mg/day (0.10–0.28). An enhanced magnetic resonance imaging showed a 2.8-cm right-sided adrenal mass, and 123I-metaiodobenzylguanidine scintigraphy showed high accumulation in association with the tumour (Figure 3). Pheochromocytoma was highly suspected and doxazosin 2 mg was immediately prescribed. To stabilize her blood pressure and increase the circulating plasma volume, additional phased

![Figure 1](https://academic.oup.com/ehjcr/article-abstract/2/1/1/4841947/1) Twelve-lead electrocardiogram of the atrial tachyarhythmias. (A) Atrial fibrillation before ablation and (B) atrial tachycardia that occurred after ablation. Red arrows indicate discrete P waves in lead V1 (cycle length = 300 ms).
prescriptions of doxazosin 16 mg, prazosin 6 mg, propranolol 30 mg, and nifedipine 80 mg were required. Finally, surgery was performed 11 months after the ablation, and an adrenal mass consistent with pheochromocytoma was successfully resected. Although a slow AT with an atrial cycle length of 300 ms was observed after ablation (Figure 1B), it never recurred after postoperative stabilization of the blood pressure. Her serum noradrenalin and urine normetanephrine levels returned to values within normal limits. During a follow-up period of 35 months, the patient has remained free of any episodes of AF or AT without the need for antiarrhythmic drugs, and her LV function has completely normalized.

Discussion

It is well known that 50–90% of patients with AF have hypertension.1,3 The prevalence of secondary hypertension was reported to be 5–10% among hypertensive patients.4 Because patients with primary aldosteronism showed a highly significant 7- to 12-fold increased risk of AF when compared with patients with essential hypertension,5,6 electrophysiologists performing catheter ablation of AF may have more opportunities to encounter patients with secondary hypertension. Pheochromocytoma is also an important form of secondary hypertension because under-diagnosis can lead to

Figure 2 Blood pressure measurements and CARTO map during the catheter ablation procedure. (A) Uncontrolled blood pressure and hypertensive crisis. (B) Electroanatomical voltage map. The low-voltage area was defined as a voltage of <0.5 mV. CAG, coronary angiography; DC, direct cardioversion; i.v., intravenous; LA, left atrium; LIPV, left inferior pulmonary vein; MV, mitral valve; PVG, pulmonary venography; RA, right atrium; SVC, superior vena cava.
life-threatening organ damage. Catecholamine-induced cardiac remodelling and atrial stretch may facilitate the occurrence and persistence of atrial tachyarrhythmias, and therefore, curing the pheochromocytoma may critically contribute to the restoration of sinus rhythm, similarly to treatment for primary aldosteronism.

Unfortunately, pheochromocytoma was undiagnosed in the present patient until ablation therapy was performed and the following risks for hypertensive crisis were recognized. (i) A beta-blocker was prescribed without the preventive administration of an alpha-adrenoceptor blocking agent. The unopposed stimulation of alpha-adrenoceptors could lead to a rise in blood pressure. (ii) A contrast-enhanced CT scan, coronary angiography, and pulmonary venography were performed without administration of alpha-adrenergic blockade. Although small studies recently reported that non-ionic low osmolar contrast medium had no appreciable effect on catecholamine release in patients with pheochromocytoma, there is still one case report showing the occurrence of hypertensive crisis due to a contrast-enhanced CT scan. (iii) During the procedure, alpha-2 adrenoceptor agonist dexmedetomidine was used for sedation and mild analgesia in combination with fentanyl. Although there are few vascular effects from the activation of alpha-1 receptors during low-dose infusion, higher concentrations of dexmedetomidine cause a biphasic (low, then high) dose–response relation of blood pressure and vascular resistances, which results in systemic hypertension. (iv) The patient was potentially dehydrated due to fasting and experienced emotional and pain-related stress during the periprocedural period.

As a result, the patient suffered from hypertensive crisis (systolic pressure >180 and diastolic pressure >120 mmHg, and the acute presentation of LV dysfunction). The decrease in the ejection fraction may be explained by the increased LV afterload and catecholamine-mediated myocarditis. It was also noteworthy that a recurrent AT resolved with no need for anti-arrhythmic drugs during long-term

**Figure 3** Abdominal magnetic resonance imaging and $^{123}$I-metaiodobenzyguanidine scintigraphy. (A) The white arrow indicates the enhanced (A2 phase) right adrenal tumour. (B) High accumulation of $^{123}$I-metaiodobenzyguanidine observed in the tumour is consistent with pheochromocytoma.
follow-up after cure of the pheochromocytoma by surgical resection. Although it is unclear if AF can be treated only with surgical resection of the tumour and normalization of catecholamine levels, we believe that the maintenance of sinus rhythm by catheter ablation is difficult to achieve without resolution of the pheochromocytoma. The present results suggest that electrophysiologists seeing patients with AF should consider secondary hypertension as a mechanism of hypertension and drug-resistant AF before proceeding to catheter ablation of AF.

**Conclusions**

Particularly in patients with AF who are scheduled to undergo catheter ablation, under-diagnosis of pheochromocytoma can lead to a lethal hypertensive crisis due to periprocedural medications, imaging studies using contrast medium, anaesthesia, and emotional and pain-related stress. Electrophysiologists should recognize the possibility that they may more frequently encounter patients with secondary hypertension in association with AF in clinical practice.

**Acknowledgements**

The authors would like to thank Drs E. Fujita, I. Kurata, and A. Takahashi for their endocrinological assessments and therapeutic management in the course of the patient’s care.

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

**Author Contributions:** K.Y. was involved in compilation of data and writing of this report. K.I., I.Y., and T.H. were lead consultants/senior authors involved in the management of the case.

**References**

1. Seccia TM, Caroccia B, Adler GK, Maiolino G, Cesari M, Rossi GP. Arterial hypertension, atrial fibrillation, and hyperaldosteronism: the triple trouble. *Hypertension* 2017;69:545–550.
2. Mazza A, Armigliato M, Marzola MC, Schiavon L, Montemurro D, Vescovo G, Zuin M, Chondrogiani S, Ravelli R, Opocher G, Colletti PM, Rubello D. Anti-hypertensive treatment in pheochromocytoma and paraganglioma: current management and therapeutic features. *Endocrine* 2014;45:469–478.
3. Verdecella P, Reboldi GP, Gattobigio R, Bentivoglio M, Bortolone C, Angel F, Carluccio E, Sardone MG, Porcellati C. Atrial fibrillation in hypertension: predictors and outcome. *Hypertension* 2003;41:218–223.
4. Monticone S, Burrello J, Tizzani D, Bertello C, Viola A, Buffolo F, Gabetta I, Mengozzi G, Williams TA, Rabbia F, Veigio F, Mutatero P. Prevalence and clinical manifestations of primary aldosteronism encountered in primary care practice. *J Am Coll Cardiol* 2017;69:1811–1820.
5. Miliez P, Girerd X, Plouin PF, Blacher J, Safar ME, Mourad JJ. Evidence for an increased rate of cardiovascular events in patients with primary aldosteronism. *J Am Coll Cardiol* 2005;45:1243–1248.
6. Rossi GP, Cesari M, Cuspidi C, Maiolino G, Cicila MV, Bisogni V, Mantero F, Pessina AC. Long-term control of arterial hypertension and regression of left ventricular hypertrophy with treatment of primary aldosteronism. *Hypertension* 2013;62:62–69.
7. Ferrera VM, Marcelino M, Pichnik SK, Marin C, Karamitsos TD, Ntusi NAB, Francis JM, Robson MD, Arnold JR, Mihai R, Thomas JDJ, Herincs M, Hassan-Smith ZK, Greiser A, Aft W, Korbonits M, Karaviatis N, Grossman AB, Wass JAH, Neubauer S. Pheochromocytoma is characterized by catecholamine-mediated myocarditis, focal and diffuse myocardial fibrosis, and myocardial dysfunction. *J Am Coll Cardiol* 2016;67:2364–2374.
8. Bessell-Browne R, O’Malley ME. CT of pheochromocytoma and paraganglioma: risk of adverse events with i.v. administration of nonionic contrast material. *AJR Am J Roentgenol* 2007;188:970–974.
9. Nakano S, Tsushima Y, Taketomi-Takahashi A, Higuchi T, Amanuma M, Oriuchi N, Endo K. Hypertensive crisis due to contrast-enhanced computed tomography in a patient with malignant pheochromocytoma. *Jpn J Radiol* 2011;29:449–451.
10. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colino MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthesiology* 2000;93:382–394.