Received: 20 September 2023 | Revised: 18 October 2023 | Accepted: 28 October 2023

DOI: 10.1002/ccr3.8218

CASE REPORT

Clinical Case Reports Open Access WILEY

# Diagnosis of hypertrophic cardiomyopathy accompanied with primary aldosteronism—Case report

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**Key Clinical Message**

Hypertrophic cardiomyopathy (HCM) is known to be the most prevalent genetic cardiac condition. However, there have been limited reports on the diagnosis of HCM accompanied by secondary hypertension and the subsequent systematic therapy. In this case report, we present the case of a 65-year-old male patient who presented with recurring chest discomfort during physical activity, along with refractory hypertension. Cardiac magnetic resonance imaging (MRI) and transthoracic echocardiogram(TTE) revealed the presence of HCM in this individual. Further investigation revealed hypokalemia, elevated aldosterone levels, decreased plasma renin activity, and an aldosterone-to-renin ratio above 30. These findings strongly indicated primary aldosteronism (PA) as an additional condition affecting this patient. Through the utilization of whole exome sequencing, we successfully identified a suspected pathogenic gene TTN as the underlying cause of the patient's condition. The presence of HCM accompanied by secondary hypertension due to PA resulted in significant enlargement of the left ventricle, particularly the ventricular septum. While certain genetic mutations may suggest a potential link to cardiomyopathy development, they cannot definitively establish a direct association between HCM and PA.

**KEYWORDS**

hypertrophic cardiomyopathy, primary aldosteronism, TTN gene

## 1 | INTRODUCTION

HCM is a prevalent genetic cardiac condition, affecting approximately one in every 200–500 individuals in the general population.[1] It is characterized by left ventricular outflow tract obstruction, observed in up to two-thirds of patients, which can contribute to progressive heart failure symptoms. PA represents the most common form of secondary hypertension and is associated with increased cardiovascular risks. Interestingly, reports suggest that HCM accompanied by hypertension becomes more frequent as individuals age. This combination often results in significant hypertrophy of the ventricular septum and walls. In this case study, we present a patient with a long history of hypertension who experienced accelerated left ventricular hypertrophy during middle to late stages of life. This led to reduced systolic function and hemodynamic changes. Existing literature highlights both an increased occurrence and poor prognosis for this particular complication.[2]

To our knowledge, cases involving HCM accompanied by PA leading to significant hypertrophy of the left ventricle, particularly the ventricular septum, have been rarely reported.

## 2 | CASE PRESENTATION

A 65-year-old male patient was admitted with a chief complaint of recurrent chest distress that had been ongoing for over 10 years, but became aggravated in the past month. The patient's medical history revealed a previous diagnosis of HCM based on findings from a TTE. However, the patient did not receive regular treatment. In the past month, the patient experienced more frequent and severe symptoms during physical activity, specifically while walking. These episodes lasted between 10 min to half an hour and were relieved after rest. Concerned about his cardiovascular health, he measured his systolic blood pressure at 152 mmHg. Further investigations through an electrocardiogram (ECG) revealed sinus bradycardia, first-degree atrioventricular block, left ventricle hypertrophy, and ST-T changes. Additionally, a thoracic computed tomography (CT) scan showed cardiac enlargement and nodules present on both adrenal glands.

The patient has a 30-year history of hypertension, with the highest record reaching 190/110 mmHg. No regular treatment and monitor were received until half a year ago. He took amlodipine, metoprolol, irbesartan, and hydrochlorothiazide until 1 month ago. He changed into valsartan and amlodipine because of hyperuricacidemia and bradycardia. Following monitor showed readings ranging between 130–200 and 80–90 mmHg. The patient also presents with hyperlipidemia. There is a family history of hypertension. During the physical examination, no jugular vein distension or rales were observed in the lungs. The heart rhythm was regular, but an enlargement of the heart border was noted along with an ejective murmur detected in both first and second aortic valve regions as well as the apex region. No edema was present.

Laboratory tests revealed persistent hypokalemia (potassium levels ranging from 3.01 to 3.52 mmol/L; normal range: 3.3–5.3 mmol/L) with extra intake of potassium 3.0–6.0 g daily. High aldosterone (ALD) levels ranged from 456.21 pg/mL (normal range: clinostatism 10–160 pg/mL) to 762.79 pg/mL (upright position normal range: 40–310 pg/mL), low plasma renin activity (PRA) ranged from 0.54 ng/mL/h (upright position normal range: 1.31–3.95 ng/mL/h) to 0.66 ng/mL/h (clinostatism normal range: 0.15–2.33 ng/mL/h), and high aldosterone-to-renin ratio (ARR) ranged from 69.12 to 141.26 (normal range: 0–30).

A CT scan showed nodules on both adrenal glands measuring between 10 mm and 17 mm in diameter. TTE indicated LV wall thickness measuring 15 mm, basal segment of ventricular septum measuring 22 mm, positive SAM sign (Systolic Anterior Motion), Vmax (left ventricular outflow tract velocity measurement) of LVOT measured 2.47 m/s and Peak Pressure Gradient of LVOT was 24 mmHg, and an ejection fraction (EF) of 68% (Figure 1). Cardiac MRI revealed a left atrium measurement of 47 mm, right atrium measurement of 45 mm, left ventricular end-diastolic diameter (LVED) measuring 91 mm, and right ventricular end-diastolic diameter (RVED) measuring 77 mm. The thicknesses of the LV walls ranged from 11 to 23 mm with improper movement noted. Cardiac output(CO) was calculated as 130.52 L/min (Figure 2). Coronary artery CT scan and Holter monitoring both yielded negative results. A comprehensive timeline summarizing the patient's historical information and treatment course is provided in Table 1.

According to the results above, we proposed treatment strategies including: sacubitril/valsartan, nifedipine, bisoprolol, and spironolactone. A 3-month follow-up showed that blood pressure ranging between 120–130 and 70–80 mmHg, and serum potassium level raised to 4.63 mmol/L.

## 3 | DISCUSSION

Initially, we hypothesized that the myocardial hypertrophy observed in this case was primarily attributed to PA. However, the left ventricular wall thickness, ranging from 15 to 22 mm, that is commonly observed in cases of HCM.[1]

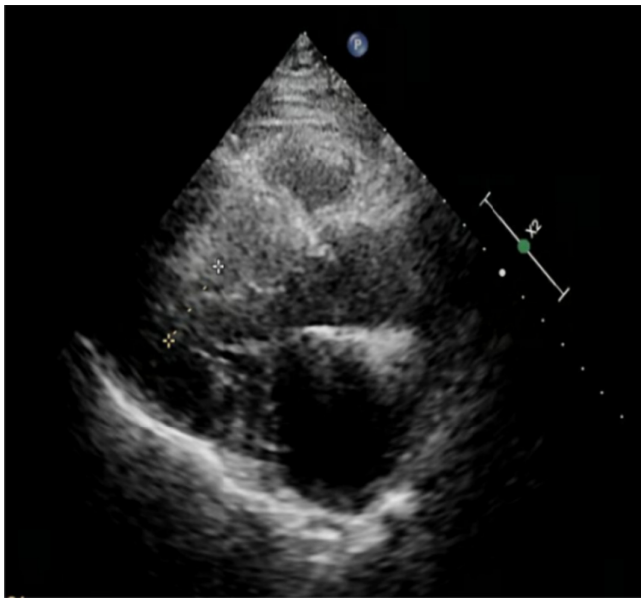

**FIGURE 1** TTE(SAM sign).

Additionally, HCM alone cannot fully explain the presence of left atrial hypertrophy. Therefore, we propose that the changes observed in this particular case are likely a complication resulting from both HCM and PA.

Familial HCM is known to be associated with various gene mutations, including MYH7, MYBPC3, TNNT2, GLA, and TTR. However, the presence of TTN, SLC36A2, and TWNK mutations in this particular case appears to be rare and has not been widely reported.[1,3] We conducted the patient's whole exome sequencing data with the OMIM database. Our assessment revealed suspected variants in TTN, SLC36A2, and TWNK genes. TTN encodes a large protein found abundantly in striated muscle and myocardial cells. Mutations in this gene have been linked to familial hypertrophic cardiomyopathy type 9 (OMIM:613765). SLC36A2 is primarily expressed in renal cells but has no documented reports linking it to the pathogenesis of HCM. TWNK mutations are responsible for infantile onset spinocerebellar ataxia (IOSCA), progressive external ophthalmoplegia (PEO), as well as several mitochondrial depletion syndromes. Considering the patient's clinical history and examination findings mentioned earlier, we identified a suspected pathogenic variation within the TTN gene as being potentially relevant to this case study.

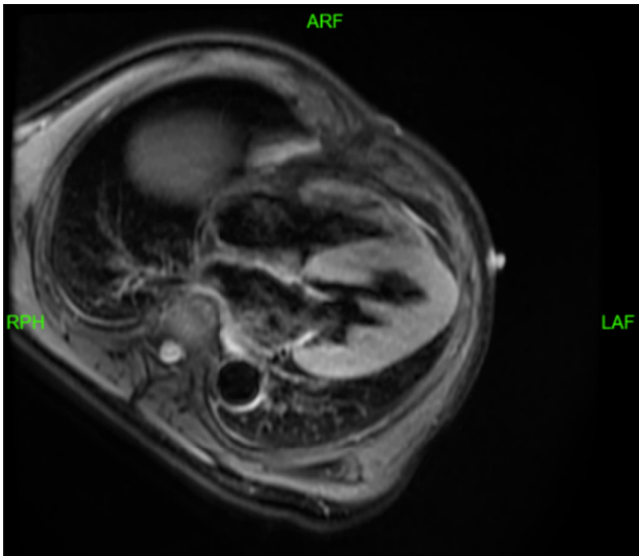


**FIGURE 2** Cardiac MRI (four chamber, T2WI + Black Blood).

Our review of relevant literature and summaries on PA yielded some interesting findings: The exact pathogenesis of PA is not yet fully understood. However, it is believed that somatic mutations occurring in ion channels and pumps within adrenal cells play a role in initiating the development of PA.[4] Studies focusing on three types of familial hyperaldosteronism have identified mutations in genes such as CYP11B1, CYP11B2, CLCN2, GIRK4, and CACNA1D.[5–7] These gene mutations may provide insights into potential pathways involved in the pathogenesis of PA.

Based on the guidelines for hypertrophic cardiomyopathy (HCM) and primary aldosteronism (PA), we have devised a treatment plan as follows: sacubitril/valsartan 100 mg twice daily: this medication combination has been shown to be effective in managing heart failure symptoms and improving outcomes in patients with HCM.[4] Nifedipine 30 mg once daily: nifedipine is a calcium

**TABLE 1** Timeline.

| Time | Events |
|---|---|
| 30 years ago | Hypertension with no regular treatments |
| 10 years ago | Chest distress, TTE revealed HCM and no regular therapy |
| Half a year ago | Hypertension with four types of medical therapy |
| 1 month ago | two types of medical therapy and aggressive symptoms while activities with refractory hypertension |
| Day 0 | Admitted to our department |
| Day 1 | Laboratory test showed persistent hypokalemia and refractory hypertension |
| Day 2 | TTE indicated HCM |
| Day 3 | Coronary CT scan showed negative |
| Day 4 | Laboratory test showed ARR above 30 |
| Day 5 | Adrenal gland CT scan showed bilateral nodes and antisterone applied |
| Day 6–8 | No other abnormal results of adrenal gland found |
| Day 9 | Cardiac MRI showed HCM |

Abbreviations: ARR, aldosterone-to-renin ratio; CT, computed tomography; HCM, hypertrophic cardiomyopathy; MRI, magnetic resonance imaging; TTE, transthoracic echocardiogram.

channel blocker that helps relax blood vessels, reducing blood pressure, and alleviating symptoms associated with PA.[8] Bisoprolol 5 mg once daily: bisoprolol is a beta-blocker that can help control heart rate and reduce cardiac workload, which may be beneficial for patients with both HCM and PA.[4] Spironolactone 40 mg twice daily: spironolactone is a mineralocorticoid receptor antagonist (MRA), which is effective, inexpensive, and widely available treating PA in most patients.[9] At the time of completing this report, our management approach has successfully controlled blood pressure within the range of 120–130/70–80 mmHg and normal serum potassium level at 4.63 mmol/L. Further follow-up will be necessary to monitor any changes in myocardial health.

Additionally, it is worth noting that mavacamten, an investigational therapy for HCM, has shown promising results in reducing obstruction of blood flow, improving symptoms, overall well-being, and enhancing the ability to engage in daily activities.[8] However, there is currently no evidence regarding its use specifically in PA patients.

HCM and PA has been associated with a poor prognosis.[2] Compared to primary hypertension, PA has been shown to cause more damage to end organs and is linked to increased cardiovascular morbidity. This includes conditions such as heart failure, nonfatal myocardial infarction, and atrial fibrillation.[9,10] Additionally, HCM itself can lead to progressive heart failure symptoms due to obstructive physiology and diastolic dysfunction. Therefore, maintaining positive control over blood pressure levels in patients with HCM becomes crucial. By achieving a target blood pressure of 120/80 mmHg in these patients, it may help decrease both preload and afterload on the left ventricle. This approach holds potential for positively impacting the prognosis of this particular complication.

## 4 | CONCLUSION

These findings provide additional support for our hypothesis regarding the involvement of multiple genetic factors in this case, contributing to both HCM and PA. The identification of these specific gene variants adds valuable insights into understanding the underlying mechanisms and potential genetic basis for this rare clinical presentation.

### AUTHOR CONTRIBUTIONS

**Kaiyu Tang:** Data curation; writing – original draft. **Shuaiye Liu:** Data curation. **Sicong Yang:** Data curation. **qinghua Yuan:** Writing – review and editing. **Zhimin Du:** Writing – review and editing.

### ACKNOWLEDGMENTS

The authors thank Yue Tang, Jihua Wang, and Hongwei Zhao of cardiovascular department for supporting this case report.

### FUNDING INFORMATION

This work did not receive any fund from any source.

### CONFLICT OF INTEREST STATEMENT

The authors have no other conflicts of interest to declare.

### DATA AVAILABILITY STATEMENT

There are no data generated from this case report.

### ETHICS STATEMENT

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the Helsinki Declaration (as revised in 2013).

### CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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### REFERENCES

1. Maron BJ. Clinical course and management of hypertrophic cardiomyopathy. *N Engl J Med*. 2018;379:655-668. doi:10.1056/NEJMra1710575
2. Alashi A, Smedira NG, Popovic ZB, et al. Characteristics and outcomes of elderly patients with hypertrophic cardiomyopathy. *J Am Heart Assoc*. 2021;10(3):e018527. doi:10.1161/JAHA.120.018527
3. Cirino AL, Ho C. *Hypertrophic Cardiomyopathy Overview*, GeneReviews®. University of Washington; 2021.
4. Funder JW, Carey RM, Fardella C, et al. Case detection, diagnosis, and treatment of patients with primary aldosteronism:an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2008;93:3266-3281.
5. Fernandes-Rosa FL, Daniil G, Orozco IJ, et al. A gain-of-function mutation in the CLCN2 chloride channel gene causes primary aldosteronism. *Nat Genet*. 2018;50:355-361.
6. Choi M, Scholl UI, Yue P, et al. K+ channel mutations in adrenal aldosterone-producing adenomas and hereditary hypertension. *Science*. 2011;331:768-772.
7. Scholl UI, Goh G, Stolting G, et al. Somatic and germline CACNA1D calcium channel mutations in aldosterone-producing adenomas and primary aldosteronism. *Nat Genet*. 2013;45:1050-1054.

8. Elliott PM, Anastasakis A, Borger MA, et al. ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy. *Eur Heart J*. 2014;35:2733-2779. doi:10.1093/eurheartj/ehu284
9. Byrd JB, Turcu AF, Auchus RJ. Primary aldosteronism: practical approach to diagnosis and management. *Circulation*. 2018;138(8):823-835. doi:10.1161/CIRCULATIONAHA.118.033597
10. Morillas P, Castillo J, Quiles J, et al. Prevalence of primary aldosteronism in hypertensive patients and its effect on the heart. *Rev Esp Cardiol*. 2008;61:418-421.

**How to cite this article:** Tang K, Liu S, Yang S, Yuan Q, Du Z. Diagnosis of hypertrophic cardiomyopathy accompanied with primary aldosteronism—Case report. *Clin Case Rep*. 2023;11:e8218. doi:10.1002/ccr3.8218