An Unexpected Cause of Severe Hypertension and Bradycardia: The Role of Hemodynamic Assessment by Echocardiography

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Abstract
Severe hypertension has numerous etiologies. When accompanied by bradycardia, the spectrum of differential diagnoses is greatly narrowed and is commonly seen in patients with increased intracranial pressure. However, other etiologies such as bradycardia-induced hypertension are rarely mentioned. Here we report the case of a 73-year-old woman presenting with symptoms of heart failure, severe hypertension, and bradycardia with a 2:1 atrioventricular block. Echocardiography demonstrated increased left ventricular filling secondary to bradycardia and prolonged diastole, leading to greater ventricular stretch, increased contractile force and greater stroke volume (Frank-Starling mechanism), which subsequently caused elevated systolic blood pressure (BP), low diastolic BP and a wide pulse pressure. Treating the bradycardia by pacing led to an immediate and substantial BP reduction, although complete BP normalization had a slower time course and was probably due to the concomitant effect of the antihypertensive treatment initiation. This pathophysiological mechanism has received little attention in the literature. Further, stimulation of sympathetic afferents located in the heart by distension of the cardiac walls as well as the role of vagally innervated cardiopulmonary receptors due to the increased pressure in the heart and the pulmonary artery should also be kept in mind as alternative hypotheses.

Case Presentation
A 73-year-old woman presented to our hospital with a 5-day-history of increasing dyspnea, pitting edema in the legs, severe hypertension, and bradycardia. She was obese (body mass index of 44.6 kg/m²) and had a history of mild (grade I) hypertension, which she had never treated with antihypertensive medications. She did not report any other medical conditions. On admission, her systolic blood pressure (BP) was 249 mm Hg and diastolic BP was 55 mm Hg, yielding a wide pulse pressure. The heart rate was 42 beats/min and the temperature was 38°C. Clinical examination revealed increased jugular venous pressure and a mild systolic murmur but was otherwise unremarkable. An electrocardiogram showed sinus rhythm with a second-degree atrioventricular (A-V) block, left axis deviation, and poor R-wave progression (shown in Fig. 1). She had no history of syncope or presyncope. Laboratory tests showed elevated C-reactive protein at 89 mg/L (ref. <5 mg/L),
Fig. 1. ECG taken on admission showing sinus rhythm with 2:1 atrioventricular block (black arrows indicating p-waves), left axis deviation, and poor R-wave progression.
Fig. 2. Initial echocardiography demonstrating increased LV filling with an E wave >1.5 m/s (a), LV stroke volume of 116 mL (b), systolic tissue Doppler velocity with a medial S’ of 12 cm/s (c), and GLS of −27% (d). Echocardiography after pacemaker implantation (e–h) showing a reduction in LV filling (e) with an E-wave of 0.9 m/s, a smaller stroke volume (f), medial S’ of 8 cm/s (g), and a reduction in GLS to −21% (h) compared with initial echocardiography.
D-dimer 1.15 mg/L (ref. <0.73 mg/L), NT-pro-BNP 2258 ng/L (ref. <338 ng/L), and cardiac Troponin T at 31 ng/L (ref. <15 ng/L). Serum creatinine was normal at 69 μmol/L (ref. 45–90 μmol/L) and eGFR was 76 mL/min/1.73 m². A chest X-ray confirmed pulmonary congestion. CT-angiography of the pulmonary arteries did not reveal any signs of pulmonary embolism but indicated peribronchovascular consolidation suggestive of infection or pulmonary edema. She was started on Penicillin for presumed pneumonia, intravenous diuretics (furosemide 40 mg × 3/day) and received additional doses of a short-acting calcium blocker (nifedipine) if systolic BP exceeded 180 mm Hg. Blood tests revealed no obvious cause of secondary hypertension, including normal urinalysis and kidney function tests. Echocardiography revealed normal systolic function, with a high-normal left ventricular (LV) ejection fraction (73%) and global longitudinal strain (GLS) (−27%), septal S’ (systolic tissue Doppler velocity) 12 cm/s (shown in Fig. 2a–d), greater stroke volume (116 mL), mild mitral regurgitation, mild eccentric LV hypertrophy (LV mass 109 g/m² and relative wall thickness 0.36), and elevated LV filling by transmural flow (E wave >1.5 m/s). Coronary CT angiography did not show obstructive coronary artery disease. The following day, BP was 171/48 mm Hg. A 2-chamber pacemaker was implanted after which BP immediately decreased to 155/77 mm Hg. A further gradual decrease in systolic BP and pulse pressure and an increase in diastolic BP were observed in the following days (shown in Fig. 3). A repeated echocardiography (shown in Fig. 2e–h) the day after pacemaker implantation showed a reduction in systolic LV parameters to more physiological values: LV ejection fraction (65%), GLS −21%, septal S’ 8 cm/s, stroke volume (97 mL), and early transmural filling wave (E 0.9 m/s) compared with the baseline study. The patient was asymptomatic on discharge and received a combination of valsartan, hydrochlorothiazide, and metoprolol, which had been gradually introduced during hospitalization. At 2- and 3-week follow-up visits at her general practitioner, the BP had normalized with an average value of 138/72 mm Hg, confirmed by an ambulatory BP 3 months later with a mean 24-h BP of 98/54 mm Hg.

**Discussion**

Severe hypertension has a multifactorial etiology, and in most instances, the underlying cause or causes cannot be disclosed even by an extensive workup [1, 2]. When combined with bradycardia, the spectrum of differential diagnoses is greatly narrowed because in most hypertensive patients, resetting of the baroreflex prevents the BP increase to be followed by a persistent reduction in heart rate [3]. In practice, the combination of hypertension and bradycardia can be seen in patients with increased intracranial pressure or with the occurrence of irregular breathing known as Cushing’s triad and signaling impending brain stem herniation [4, 5]. Our case report, particularly the echocardiographic findings and the re-
sponse to pacing illustrate the possibility of a heart-BP counter-relationship. Because in the presence of an elevated systolic BP, a markedly elevated LV ejection fraction and an A-V block-dependent bradycardia, removal of the bradycardia by pacing led to an immediate BP reduction, although complete BP normalization had a slower time course and was probably due to the concomitant effect of antihypertensive treatment and a decrease in volume overload. Several possible pathophysiological mechanisms may have been responsible for the association between a marked reduction in heart rate and an increase in BP seen in our patient. First of all, in this patient we observed a marked increase in LV filling (large E-wave) and a prolonged diastolic phase secondary to bradycardia. This led to a greater ventricular stretch, an increased contractile force of the myocardium (Frank-Starling mechanism), and a greater stroke volume, resulting in an elevation of systolic BP, a lower diastolic BP, and a wide pulse pressure. The effect of this mechanical factor, however, may have been enhanced by the heart rate and BP effects of reflexes activated by the increased cardiac and pulmonary pressures and volumes. It is well known that cardiac wall distention can activate sympathetic afferent fibers that reflexively increase sympathetic drive, leading to an elevated BP [6]. Overstimulation of vagally innervated cardiopulmonary receptors has been shown to reduce BP but also to cause, if the stimulation is marked, a reflex bradyarrhythmic effect [7]. Finally, a bradyarrhythmic effect of an arterial baroreceptor stimulation triggered by the marked BP increase can also not be excluded if the marked and probably fast BP increase experienced by the patient was accompanied by a delayed baroreflex resetting. Arterial baroreflexes may also have participated in the impairment of A-V conduction because there is evidence that stimulation of arterial baroreceptors by phenylephrine can markedly lengthen A-V conduction time and even cause an A-V block of the Wenckebach type [8, 9]. The symptoms of clinical heart failure and elevated natriuretic peptides in our patient could be explained by pulmonary congestion/edema induced by severe hypertension, where hypertension per se was a consequence of A-V block/bradycardia and prolonged diastolic filling. Of note, LV ejection fraction, GLS, and systolic and diastolic tissue Doppler velocities were normal and unlikely to explain the patient’s symptoms. Furthermore, the increased heart rate observed after pacemaker implantation led to an increase in cardiac output from 4.872 mL/min to 7.081 mL/min (shown in Fig. 2), and a marked reduction in peripheral resistance would also be necessary to accommodate this increase, suggesting that other pathophysiological mechanisms contributed to the BP reduction. Finally, emotional stress may also transiently cause or accelerate hypertension, although this was unlikely in our patient given the fact that she had a low heart rate and the entire hemodynamic picture represented an exaggerated Frank-Starling mechanism. This pathophysiological mechanism has received little attention in the literature and may explain why BP tends to decrease in hypertensive patients who receive a pacemaker in the setting of acute or chronic bradyarrhythmias [10]. Similarly, suboptimal BP control may be observed in patients with sick sinus syndrome and bradycardia, especially in patients with a low mean daily heart rate and normal cardiac contractility [11]. In our patient, the symptoms improved dramatically after pacemaker implantation, while BP normalization occurred more gradually and required additional optimization of antihypertensive medications. In the literature, there are no original studies on the relationship between hypertension and bradycardia. Whether the exaggerated BP response to bradycardia is evident only in patients with a healthy myocardium, as indicated by similar cases in children [12], or confined to patients with preexisting undertreated hypertension, should be investigated in prospective studies in the future. Furthermore, the importance of vagally innervated cardiopulmonary receptors due to the increased pressure in the heart and the pulmonary artery and stimulation of sympathetic afferents located in the heart (sympathoexcitatory reflexes) stimulated by distension of the cardiac walls should also be kept in mind as an alternative hypothesis. In this regard, our case study is hypothesis generating and may trigger more well-designed prospective studies to explore this interesting research topic.

**Conclusion**

The severe isolated systolic hypertension in our patient was probably induced by bradycardia, prolonged diastolic filling, and greater stroke volume with a subsequent increase in systolic BP, lower diastolic BP, and a wide pulse pressure. It is important to recognize that severe bradycardia may be a cause of hypertension and not necessarily a consequence, and may be effectively treated with pacemaker implantation. However, optimization of antihypertensive treatment is equally important. In the setting of severe hypertension and associated pulmonary congestion, patients may have symptoms of heart failure even though systolic and diastolic function is normal by both conventional and deformation echocardiography.
Limitations

The presumed pneumonia might also have contributed to the elevated BP on admission and increased LV contractility. Hence, the initiation of antibiotics with subsequent improvement of infection might have contributed to the gradual decline in BP. However, mild pneumonia infrequently leads to severely elevated BP of this magnitude, and it is unlikely to be the main cause. BP had already dropped from 249/55 mm Hg to 171/48 mm Hg before pacemaker implantation, and the BP lowering effect of pacemaker implantation was relatively small compared to the already observed effect of antihypertensive medications. However, the reversal of hemodynamic changes observed by echocardiography following pacemaker implantation was consistent. Finally, the assessment of LV systolic and diastolic function can be affected by the LV dyssynchrony originating from RV pacing, which should be taken into consideration when interpreting the hemodynamic changes by echocardiography.

Statement of Ethics

The author confirms that the requirement for ethical approval is waived off by the Department of Heart Disease, Haukeland University Hospital, Norway. Written informed consent was obtained from the patient for publication of the details of the medical case and accompanying images.

Conflict of Interest Statement

There are no conflicts of interest for any authors.

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Author Contributions

Gard M.S. Myrmel wrote the first draft and made revisions. Sahrai Saeed conceptualized the manuscript and made revisions. Abukar Ali, Torbjørn Lunde, and Giuseppe Mancia made revisions. All the authors approved the final version for submission.

Data Availability Statement

All data generated or analyzed during this case study are included in this article. Further inquiries can be directed to the corresponding author.

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