Cardiovascular Presentation in Pheochromocytoma: What We Should be Aware

Rizki Amalia,[*,], Ivana Purnama Dewi,[*,**,***], Louisa Fadjri Kusuma Wardhani,[*,**], Budi Susetio Pikir,[*,**]**

**Faculty of Medicine, Airlangga University, Surabaya, Indonesia, **Cardiology and Vascular Medicine Department, Dr. Soetomo General Hospital, Surabaya, Indonesia, ***Faculty of Medicine, Duta Wacana Christian University, Yogyakarta, Indonesia*

ABSTRACT

Pheochromocytoma is a catecholamine-producing tumor that although being a rare disease, it poses diagnostic problems because its clinical presentation often mimics certain diseases, including cardiovascular disorders. The effects of excessive catecholamine secretion cause a variety of cardiovascular presentations ranging from hypertension to life-threatening cases such as hypertensive emergency, shock, supraventricular or ventricular arrhythmias, pulmonary edema, and acute coronary syndromes. The principal medical treatment for pheochromocytoma is a blockade of adrenergic receptors. However, surgical or tumor resection often provides complete resolution of abnormal myocardial dysfunction or arrhythmias, so this approach remains the mainstay of treatment that should be performed as soon as the diagnosis of pheochromocytoma is established. As clinicians, we must be aware of the characteristics of the cardiovascular manifestations of pheochromocytoma to make an earlier diagnosis and more appropriate management.

Keywords: Pheochromocytoma; cardiovascular manifestations; endocrine heart disease (Siriraj Med J 2022; 74: 68-74)

INTRODUCTION

Pheochromocytoma is derived from the Greek "Phios" which means black, "Chroma" which means colour, and "Cytoma" which means tumor. Pheochromocytoma refers to the blackish-brown colour of tumor cells when stained with chromium salts.[1] These tumors usually originate from the adrenal glands, with a triad of clinical symptoms; headache, palpitations, and diaphoresis accompanied by paroxysmal hypertension.[2] Pheochromocytoma is a rare disease, with an estimated prevalence is 0.1-0.6%. The incidence of new cases is 2-8 cases per 1 million people. These tumors are often benign, with a malignancy prevalence of only 10% of all patients with pheochromocytoma.[3] The median age at diagnosis is 40 years.[4]

Pheochromocytoma is a functional tumor derived from chromaffin cells of the adrenal medulla and paragangliomas. Chromaffin cells secrete catecholamines, such as adrenaline (epinephrine), norepinephrine, and dopamine. Most pheochromocytomas secrete mainly norepinephrine, and only about 15% secrete epinephrine.[1] In 20% of cases, chromaffin cells grow outside their normal locations in the adrenal glands, such as in the organs of Zuckerkandl (75%), thorax, mediastinum, abdomen, and pelvis. 70% of pheochromocytomas that grow outside the adrenal glands and 5% inside the adrenal glands are malignant. The dopamine beta-hydroxylase enzyme, which converts dopamine to norepinephrine, is absent in immature tumors. So, this is why dopamine-secreting tumors have

Corresponding author: Rizki Amalia
E-mail: rizkiamalia0291@gmail.com
Received 11 November 2021 Revised 18 November 2021 Accepted 30 November 2021
ORCID ID: https://orcid.org/0000-0001-7311-9908
http://dx.doi.org/10.33192/Smj.2022.9

a higher probability of malignancy.[1] Many other factors can cause pheochromocytoma. In most cases, genetic and environmental factors play a significant role. 25-33% of pheochromocytomas are due to familial factors. Mutations in the VHL, RET, NF1, SDHB, and SDHD genes are all known to cause familial pheochromocytoma or extra-adrenal paraganglioma.[5]

MATERIALS AND METHODS

We conducted an explanatory review to summarize evidence from literatures focusing on cardiovascular presentation and principal management of pheochromocytoma. We included peer-reviewed articles published from 2004 to 2020 on PubMed, EMBASE, The Cochrane Library, and Google Scholar.

General clinical presentation and principal management

The pheochromocytoma clinical presentation is varied, so it is called "The Great Masquerader". The typical classic triad of symptoms are palpitations, headache, and diaphoresis. The presence of these three clinical manifestations accompanied by hypertension often leads to the diagnosis of pheochromocytoma. However, pheochromocytoma can be asymptomatic for many years.[1] In addition to the classic triad, other symptoms that patients with pheochromocytoma often complain of is anxiety, tightness, chest pain, abdominal or low back pain, nausea and vomiting, tremors, flushing, dizziness, blurred eyes, and paresthesias. A catecholamine crisis can also lead to heart failure, pulmonary edema, arrhythmias, and intracranial haemorrhage.[6] When we suspect pheochromocytoma, additional examination such as urine or plasma metanephrine levels and imaging studies such as computed tomography (CT) scan and magnetic resonance imaging (MRI) are needed.

The mainstay of treatment for pheochromocytoma is definitive surgery such as total or partial adrenalectomy. However, specific therapy for each cardiovascular manifestation, especially emergencies, is essential for life-saving efforts while waiting for definitive surgery preparation. Preoperative preparation is crucial, including blood pressure maintained below 160/90 mmHg before surgery. Classically, blood pressure is controlled with alpha-blockers (phenoxybenzamine 0.5-4 mg/kg body weight (BW)). Prazosin, terazosin, and doxazosin can be used as alternatives to short-acting alpha-blockers. Cardio-selective beta-blockers such as metoprolol and atenolol can be used once adequate alpha-blocker effects have been achieved. Antihypertensives such as calcium channel blockers or angiotensin-converting enzyme (ACE) inhibitors can also be used effectively.[1] Minimal invasive techniques (laparoscopy or retroperitoneoscopy) have become the standard approach to pheochromocytoma surgery due to fewer complications and faster healing than open surgery.[6] Compared to open surgery, minimal invasive techniques only need a small incision, which is related to better cosmetic results.[6]

Cardiovascular presentation of pheochromocytoma

Cardiovascular manifestations in pheochromocytoma are range from mild to life-threatening emergencies due to the effects of catecholamine excess[7] (Fig 1).

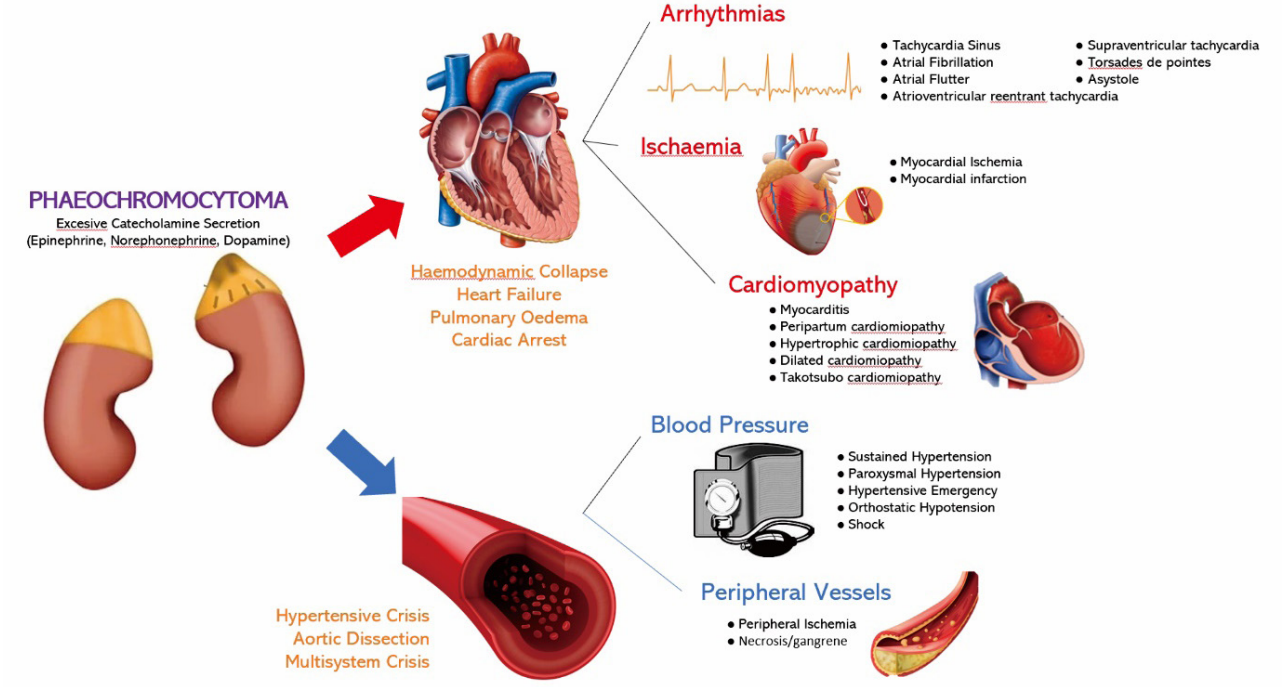

Fig 1. Cardiovascular Presentations of Phaeochromocytoma.

Hypertension in pheochromocytoma

Approximately 90% of patients with pheochromocytoma have paroxysmal hypertension or sustained hypertension. Hypertension in pheochromocytoma is usually characterized by high peripheral resistance and a low cardiac index. Noradrenaline increases peripheral vascular resistance, which increases systolic blood pressure (SBP) and diastolic blood pressure (DBP). While adrenaline increases cardiac output and SBP, it does not affect DBP due to its stimulatory effect on two adrenergic receptors causing peripheral vasodilation. In adrenaline-secreting pheochromocytoma, episodic symptoms often appear as palpitations, headache, syncope, anxiety, and hyperglycemia due to over-stimulation of receptors. Meanwhile, noradrenaline-producing tumors are often characterized by sustained hypertension due to the effects of excess catecholamines that stimulate alpha receptors. Tumors that predominantly secrete dopamine often result in normotension or even hypotension.[7]

Sustained hypertension is usually associated with structural abnormalities of the arteries, but it is still debated whether structural changes in blood vessels cause hypertension or vice versa. An increase in the media-lumen ratio results from vascular remodelling. Endothelial function abnormalities are also found in patients with pheochromocytoma, although this is also present in other causes of secondary hypertension.[7]

Angiotensin receptor blockers, calcium channel blockers, β-blockers, and α blockers have all been used for blood pressure management, even though there is no consensus on preferred medicines. For patients planning to have tumor resection surgery, initial treatment with α-blockers 10-14 days before surgery can be given. After achieving adequate α-blockade, the patient can be treated with β-blockers to achieve heart rate control. Phenoxybenzamine is a preferred α-blocker. It is started with an initial dose of 10mg twice daily and increased by 10-20mg every third day.[8]

Orthostatic hypotension in pheochromocytoma

Orthostatic hypotension often accompanies persistent hypertension, occurring in 70% of patients with pheochromocytoma.[9] Orthostatic hypotension in untreated hypertension individuals should be regarded as a pheochromocytoma diagnostic indication. Most are asymptomatic and rarely lead to syncope. Although hypotension usually occurs only in patients with a dominant adrenaline or dopamine secretion pheochromocytoma, but it can also occur in noradrenaline secretion.[10] Impaired vasoconstrictor response to catecholamines, hypovolemia, desensitization of alpha-adrenergic receptors, and feedback inhibition of sympathetic noradrenaline released by sympathetic inhibition or stimulation of presynaptic alpha-2 adrenergic receptors are all possibilities for orthostatic hypotension.[7]

Management of orthostatic hypotension in patients with pheochromocytoma should focus on efforts to restore volume. Steroid administration is often associated with fatal side effects, so there is no indication for mineralocorticoid administration in patients with orthostatic hypotension.[10] Before surgical therapy, the restoration of blood volume must be maintained so that there is no decrease in blood volume leading to hypotension and shock. Pheochromocytoma should be suspected when the unexplained vascular collapse is associated with significant abdominal pain, pulmonary edema, leukocytosis, mydriasis unresponsive to light stimulation, cyanosis, diaphoresis, and hyperglycemia. Hypotension can occur in patients with an acute myocardial infarction or acute cardiomyopathy. Shock in patients with pheochromocytoma can also be triggered by certain drugs such as steroid hormones, dopamine receptor antagonists, and tricyclics.[10]

Arrhythmia in pheochromocytoma

In patients with pheochromocytoma, excessive amounts of catecholamines can stimulate beta-adrenergic receptors and trigger mild or severe arrhythmias. However, many factors will trigger this condition. In humans and mice with pheochromocytoma, prolonged catecholamine stimulation decreased receptor density and induced cardiovascular adrenergic receptor desensitization. Reflex bradycardia and nodal escape rhythms have been reported during hypertensive emergencies and episodes of increased vagal tone.[7] Palpitations are reported in 50-70% of pheochromocytoma patients. Pheochromocytoma can cause various arrhythmias, including supraventricular tachycardia, atrial fibrillation or flutter, ventricular fibrillation, atrioventricular reentrant tachycardia, torsades de pointes, and sinus arrest.[9] Patients with paroxysmal or recurrent arrhythmias accompanied by diaphoresis, hypertension, anxiety or pallor, should be suspected of having a diagnosis of pheochromocytoma.[10]

Intravenous esmolol, a short-acting cardio-selective beta-blocker, can be used to control the rate of atrial fibrillation or atrial flutter at a dose of 0.5 mg/kg intravenously over 1 minute followed by an intravenous infusion of 0.1-0.3 mg/kg per minute. However, it is necessary to give an alpha-blocking agent before using a beta-blocker so that there is no excessive stimulation of alpha receptors resulting in a hypertensive emergency.[7]

Myocardial ischemia and myocardial infarction in pheochromocytoma

Only a minority of patients with pheochromocytoma have symptoms related to myocardial ischemia or myocardial infarction. Recent clinical studies have found an association between pheochromocytoma and myocardial infarction. In some cases, myocardial damage is documented on electrocardiogram (ECG), echocardiography, and angiography. In cases for which angiographic data were obtained, less than half of patients had significant coronary atherosclerosis and classic coronary risk factors. In these patients, the excess amount of catecholamines secreted by the tumor exacerbates the course of myocardial infarction. Meanwhile, in cases without significant coronary atherosclerosis, myocardial infarction is caused by catecholamines' direct toxic effects, which cause necrosis and fibrosis of myocardial cells. High catecholamine levels cause ischemia by increasing myocardial oxygen consumption, disrupting the hemodynamic balance of myocardial supply and demand, and rising afterload.[5]

Patients can present with chest pain, tachycardia, diaphoresis, anxiety accompanied by an ECG appearance of T waves, hyperacute T, diffuse low voltage, and other nonspecific ECG changes. One essential ECG change in pheochromocytoma is repolarization ECG changes associated with QT interval prolongation.[11] It happened due to the effects of catecholamines that stimulate coronary artery vasoconstriction and simultaneously increase myocardial oxygen demand through stimulation of heart rate and cardiac contractility, resulting in ECG abnormalities without coronary atherosclerosis. However, the clinician could find cardiac marker elevation.[9,12]

Patients with symptoms and indications of an acute myocardial infarction will often be treated with β-adrenergic blockade. However, suppression of β-adrenergic mediated vasodilation in skeletal muscle causes paradoxically higher blood pressure owing to unopposed α-adrenergic receptor activation, exacerbating the patient's condition.[9] Combination of these two drugs is recommended

Cardiomyopathy and myocardial hypertrophy in pheochromocytoma

Phaeochromocytoma can cause cardiomyopathies, such as hypertrophic, dilated, takotsubo, and peripartum cardiomyopathy. Several mechanisms may explain myocardial damage associated with catecholamines. Catecholamines can directly affect the myocardium by increasing sarcolemmal permeability, lipid mobility, free radical production, or calcium overload. Myocardial damage can occur secondary to a persistent increase in cardiac oxygen demand along with decreased oxygen availability due to the effects of catecholamines that trigger coronary vasoconstriction and platelet aggregation.[7]

High levels of catecholamines in the blood released by tumors can trigger myocarditis and cardiomyopathy. Myocarditis has previously been reported in patients with pheochromocytoma. In a case report of 26 patients at the Mayo Clinic who died of pheochromocytoma complications, 58% were diagnosed with active myocarditis. The pathological changes of active myocarditis are similar to the lesions found in the myocardium of animals treated with catecholamine injections in several laboratories.[9]

High levels of catecholamines in the blood can cause dilated or hypertrophic cardiomyopathy. Patients with pheochromocytoma and heart failure have atypical symptoms that are difficult to distinguish from idiopathic dilated cardiomyopathy. Patients with advanced dilated cardiomyopathy who will undergo heart transplantation should be excluded from causes of reversible cardiomyopathy, including pheochromocytoma. Several patients who had undergone successful heart transplantation then later diagnosed with pheochromocytoma have indistinguishable clinical symptoms compared to dilated cardiomyopathy.[13]

Takotsubo cardiomyopathy is a condition of patients with signs and symptoms of acute myocardial infarction without coronary artery stenosis or spasm with the appearance of the heart in the form of a Japanese octopus fishing pot, called "Takotsubo". The rounded apex of the heart indicates the effect of local toxic concentrations of catecholamines in the absence of coronary artery disease. High concentrations of noradrenaline stimulate basal hyperkinesis, increase mechanical stress on the apex wall and end-diastolic pressure. Another patient with pheochromocytoma-induced cardiomyopathy has severe left ventricular dysfunction, basal segment akinetic, midventricular, and apical hyperkinetic. This percentage is called "Inverted Takotsubo Cardiomyopathy". Therefore, there is no definite pattern of ventricular dysfunction in patients with pheochromocytoma-induced Takotsubo cardiomyopathy.[7] Treatment of pheochromocytoma-induced-cardiomyopathy is primarily supportive care until definitive surgical therapy can be performed.[9]

Peripheral ischemia in pheochromocytoma

Although very rare, pheochromocytoma can result in peripheral ischemia and vasculopathy that results in necrosis or gangrene. This complication occurs as a result of severe vasoconstriction or diffuse arterial vasospasm induced by hypercatecholaminemia. Ischemia can also occur due to arterial occlusion of cardiac thrombus embolism in patients with catecholamine-induced arrhythmias,

but this is extremely rare.[6] The patient can have a similar presentation with peripheral artery disease, complaining about claudication or limb pallor.[9]

Early detection of these situations is critical to prevent vasoconstrictive medicine, which can exacerbate distal ischemia in both the upper and lower limbs. In the case of pheochromocytoma induced acute limb ischemia (ALI), treatment of choice includes an open surgical or using catheter direct thrombectomy (CDT). Early trials show successful CDT in 70% of cases.[14]

Life-threatening cardiac manifestations

In some cases of pheochromocytoma, the cardiac presentation that appears can be life-threatening and cause death. The most common life-threatening cardiac manifestation of pheochromocytoma is a hypertensive emergency due to the rapid and excessive release of catecholamines from the tumor. Malignant arrhythmias, shock, aortic dissection, and acute heart failure due to myocardial dysfunction are less common.[15]

Hypertensive emergency in pheochromocytoma

An increase in systolic blood pressure in patients with pheochromocytoma can reach a very high and dangerous value above 200 mmHg. This situation becomes a life-threatening hypertensive emergency when accompanied by acute target organ damage. Hypertensive emergencies can also result from using certain drugs in patients with pheochromocytoma, such as beta-blockers that are not accompanied by adequate use of alpha-blockers. Hypertensive crises can happen in 75% of patients with pheochromocytoma as often as once weekly. Symptoms of a hypertensive crisis may vary, such as headache, confusion, visual disturbances, or tachycardia. This condition can cause organ damage, such as acute myocardial infarction, congestive heart failure, or cerebrovascular disorders.[9] Intravenous phentolamine is the treatment choice for a hypertensive emergency in patients with pheochromocytoma. The drug is usually given in an intravenous bolus dose of 2.5-5 mg at a 1 mg/min rate. This dose should be repeated every 3-5 minutes until hypertension is controlled because of the short half-life of phentolamine. Phentolamine can also be given by continuous infusion. However, due to the availability of other drugs with safer pharmacokinetic profiles, phentolamine is no longer used as a hypertensive emergency treatment during surgical anaesthesia. Intravenous vasodilators such as nicardipine, sodium nitroprusside, nitroglycerin, and fenoldopam provide more effective short-term control in intraoperative hypertension. It is easier to titrate, has a shorter duration of action, and can be used alone or with other vasodilators. Another alternative therapy is urapidil, a selective alpha1 adrenergic receptor antagonist that can be given as an intravenous bolus dose (25-50 mg) or accompanied by an infusion (50-100 mg/kg per minute).[7]

Malignant arrhythmia in pheochromocytoma

Although rare, pheochromocytoma can result in QT prolongation, even malignant arrhythmias such as ventricular tachycardia.[16] Several recent case reports have described cases of ventricular tachycardia accompanying a patient with suspected acute myocardial infarction but no coronary artery stenosis on angiography. The more common arrhythmias in pheochromocytoma are sinus tachycardia, atrial fibrillation, and atrial flutter.[7]

Bradycardia has been reported in 10% of patients with pheochromocytoma due to noradrenaline secretion. Episodes of nodal rhythm, altering sinus intervals, giving rise to ectopic heartbeats, both atrial and ventricular. Other mechanisms, such as vagal increase by the baroreceptor reflex due to a sudden increase in arterial pressure and desensitization of adrenergic receptors, can also cause bradycardia, mainly found in adrenaline-secreting pheochromocytoma.[12]

Sinus arrest due to catecholamine release, often accompanied by nodal escape rhythms, has been reported in several case reports. On the other hand, atrioventricular dissociation associated with pheochromocytoma only occurred in a few cases.[17] Unfortunately, the diagnosis of pheochromocytoma leading to sinus arrest, AV dissociation, supraventricular and ventricular arrhythmias are often delayed. The patient has had a pacemaker inserted and even ablated his bundle. Tumor resection therapy can solve all cases without the need for a pacemaker or ablation.[12]

Several cases of pheochromocytoma have complications of malignant arrhythmias, namely life-threatening ventricular tachycardia, such as a young woman from Beijing who complained of the classic triad of pheochromocytoma with recurrent ventricular tachycardia in the course of the disease.[18] Paulin et al., suggested that the sudden release of catecholamines from pheochromocytoma is related to ventricular tachycardia (VT) mechanism.[19] Excess catecholamines cause abnormal electrical activity of the myocardium, such as the excessive opening of ion channels and the increased function of the ion exchange pump, which causes large amounts of sodium, potassium, and calcium to enter through the membrane in automatic, intensive myocardial conductivity. In addition, excess catecholamines can reduce the threshold for ventricular fibrillation, resulting in sudden death or

abnormal repolarization that underlies various types of rapid arrhythmias.[12]

Sustained ventricular tachycardia in pheochromocytoma can be treated by ablation. However, such therapy cannot stop the systemic arrhythmogenic mechanisms due to the effects of catecholamines, so tachyarrhythmias will often recur. A Pheochromocytoma should be considered a diagnosis in a hypertensive patient with a typical clinical presentation of palpitations and headaches with an ECG showing VT or other tachyarrhythmias. Biochemical and imaging tests will guide the diagnosis, and symptoms often have a complete resolution after tumor surgery.[20] Preoperative use of phentolamine may be considered. Beta-blockers, such as propranolol, can be used in catecholamine-induced tachyarrhythmias but should be started after adequate doses of alpha-blockers administration to prevent hypertensive emergencies.[12]

Shock in pheochromocytoma

Sudden cessation of catecholamine secretion in patients with inadequate circulating volume, and desensitization of adrenoreceptors due to prolonged exposure to catecholamine-induced hypertension, are the main mechanisms that explain shock in patients pheochromocytoma.[10] Hemorrhagic necrosis of catecholamine-producing tumors are also associated with severe shock. Another less well-known mechanism is shock due to the negative inotropic effect of hypocalcemia. Shock in patients with pheochromocytoma is often responsive to volume addition.[7]

CONCLUSION

Cardiovascular presentation of pheochromocytoma varies widely, ranging from mild to life-threatening abnormalities requiring immediate action, such as hypertensive emergencies, malignant arrhythmias including VT and ventricular fibrillation, shock, and acute heart failure or pulmonary edema. Therefore, it is necessary to consider pheochromocytoma diagnosis in patients with cardiovascular presentations accompanied by unstable blood pressure and/or the classic triad of symptoms, namely headache, palpitations, and diaphoresis.

Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Funding

The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

Authors' contributions

RA has given substantial contributions to the conception of the design of the manuscript. RA and IPD were major contributors in writing the manuscript. IPD and LFKW are editing the manuscript for publications. All authors have participated in drafting the manuscript, BSP revised it critically. All authors read and approved the final version of the manuscript.

ACKNOWLEDGMENTS

Not applicable.

Consent for publication

Written informed consent was taken from the patient to use medical data for academic and research purposes, including publication.

REFERENCES

1. Pourian M, Mostafazadeh D, Soltani A. Does this Patient Have Pheochromocytoma? A Systematic Review of Clinical Signs and Symptoms. Journal of Diabetes and Metabolic Disorders. 2016; 15 (11): 1-12.
2. Delekta J, Riadhi S, Eschen O. Rare cause of ventricular tachycardia: Pheochromocytoma. Journal of Cardiology Cases. 2015; 11(2): 62-5.
3. Vilcant V. Pheochromocytoma-induced Cardiomyopathy Mimicking Acute Coronary Syndrome. The Journal of The American Osteopathic Association. 2017; 17: 537-40.
4. Shawa H, Elsayes KM, Javadi S, Sircar K, Jimenez C, Habra MA. Clinical and radiologic features of pheochromocytoma/ganglioneuroma composite tumors: a case series with comparative analysis. Endocrine Practice. 2014; 20(9): 864-9.
5. Gimm O, Koch CA, Januszewicz A, Opocher G, Neumann HP. The genetic basis of pheochromocytoma. Frontiers of Hormone Research. 2004; 31: 45-60.
6. Fu SQ, Wang SY, Chen Q, Liu YT, Li ZL, Sun T. Laparoscopic versus open surgery for pheochromocytoma: a meta-analysis. BMC Surgery. 2020; 20(1): 167.
7. Prejbisz A, Lenders J, Eisenhofer G, Januszewicz A. Cardiovascular Manifestations of Pheochromocytoma. Journal of Hypertension. 2011; 29(11): 2049-60.
8. Garg MK, Kharb S, Brar KS, Gundgurthi A, Mittal R. Medical management of pheochromocytoma: Role of the endocrinologist. Indian Journal of Endocrinology Metabolism. 2011; 15 (Suppl4): S329-36.
9. Gu YW, Poste J, Kunal M, Schwarcz M, Weiss I. Cardiovascular Manifestations of Pheochromocytoma. Cardiology in Review. 2017; 25(5): 215-22.
10. Shawa H, Bajaj M, Cunningham G. Pheochromocytoma-induced Atrial Tachycardia Leading to Cardiogenic Shock and Cardiac Arrest. Texas Heart Institute Journal. 2014; 41(6): 660-3.
11. Hassan SY, Falhammar H. Cardiovascular Manifestations and Complications of Pheochromocytomas and Paragangliomas. Journal of Clinical Medicine. 2020; 9(2435): 1-19.
12. Zhang M, Mao W, Wu D, Liu P. Pheochromocytoma with Ventricular Tachycardia as The Presenting Symptoms. Chinese Medical Journal. 2016; 129(12): 1505-6.

13. Bernard M, Gold M, Cuoco F. Pheochromocytoma Presenting as Recurrent Stress Cardiomyopathy with Multiple Monomorphic Ventricular Tachycardias. The Journal of Innovations in Cardiac Rhythm Management. 2012; 3: 803-8.
14. Mederos MA, Orr LE, Livhits MJ, Rigberg DA. Management of acute limb ischemia related to underlying pheochromocytoma. Journal of Vascular Surgery Cases, Innovation and Techniques. 2020; 6(2): 272-6.
15. Leite L, Macedo P, Santos S, Quaglia L, Mesaz C, Paola A. Life-Threatening Cardiac Manifestations of Pheochromocytoma. Case Reports in Medicine. 2010; 1-4.
16. Yamada Y, Fujiwara H, Banno H, et al. Complete atrioventricular dissociation and sinus arrest after pheochromocytoma resection. IJU Case Report. 2020; 3(3): 108-11.
17. Choi SY, Cho KI, Han YJ, et al. Impact of Pheochromocytoma on Left Ventricular Hypertrophy and QTc Prolongation: Comparison with Takotsubo Cardiomyopathy. Korean Circ J. 2014; 44(2): 89-96.
18. Li S, Wang T, Wang L, et al. Ventricular Tachycardia and Resembling Acute Coronary Syndrome during Pheochromocytoma Crisis. Medicine. 2016; 95(14): 3297-301.
19. Paulin F, Klein G, Gula L, Skanes A, Yee R, Krahn A. QT Prolongation and Monomorphic VT Caused by Pheochromocytoma. Journal of Cardiovascular Electrophysiology. 2009; 20(8): 931-34.
20. Čtvrtlík F, Koranda P, Schovánek J, Škarda J, Hartmann I, Tüdös Z. Current diagnostic imaging of pheochromocytomas and implications for therapeutic strategy. Experimental and Therapeutic Medicine. 2018; 15(4): 3151-60.