

Catecholamine-induced cardiomyopathy in a patient with pheochromocytoma and polycystic kidney and liver disease: a case report

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Background

Clinical manifestations of pheochromocytoma (PCC) frequently are not specific and can be attributed to other pathologies. The most dreaded manifestation is catecholamine-induced cardiomyopathy. A prompt diagnosis, sometimes extremely problematic due to associated conditions of the patient, is essential for clinical outcomes, because early resection of PCC may prevent progression to irreversible cardiac remodelling.

Case summary

We present a case of 47-year-old woman with suspected acute coronary syndrome but intact coronary vessels. Electrocardiogram examination showed ST depression suggestive for coronary ischaemia. Echocardiography revealed reduced ejection fraction of left ventricle and global hypokinesis. Abdominal ultrasound examination determined multiple cysts in liver and both kidneys. The patient had unclear transient states of sudden sweating, pale skin, nausea, and vomiting accompanied by hypertensive crisis. Fractionated urinary metanephrines were considerably increased. Contrasted computed tomography of abdominal cavity and pelvis revealed in both liver lobes many cysts; both kidneys showed multiple cysts too; in the right adrenal gland was detected a filling defect. Computed tomography findings have established diagnosis of adrenal PCC of right gland associated with liver and kidney polycystic disease.

Discussion

Pheochromocytoma, with primary manifestation as catecholamine-induced cardiomyopathy, in patient with polycystic kidney and liver disease could represent a really challenging diagnosis. Clinical manifestations of PCC frequently are not specific and can be explained by associated pathologies. This is the second case of adrenalectomy due to PCC associated with polycystic kidney and liver disease reported in the medical literature.

Keywords

Pheochromocytoma • Catecholamine-induced cardiomyopathy • Autosomal dominant polycystic kidney disease • Liver cysts • Case report

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Learning points

- Pheochromocytoma (PCC) should be suspected in patients who present with cardiomyopathy and no concomitant valvular or ischaemic pathology even when clinical manifestations are not typical for catecholamine excess.
- Prompt diagnosis of PCC in patients with catecholamine-induced cardiomyopathy is of great importance due to potential reversibility of cardiac remodelling.
- Hypertension and hypertensive crises in a patient with polycystic kidney and liver disease can also be explained by concomitant presence of PCC.

Introduction

Pheochromocytoma (PCC) is an infrequent neuroendocrine tumour, characterized by high catecholamine release.¹ Clinical manifestations include different cardiovascular signs and symptoms, which are related to excessive secretion of catecholamines and may be paroxysmal or sustained.² Catecholamine-induced cardiomyopathy in PCC (CICMPP) is a rare but dreaded complication of PCC and its diagnosis is often delayed because of the atypical presentation.³ Due to potential reversibility of the CICMPP, prompt diagnosis and surgical excision of the PCC are crucial in patient's management, otherwise irreversible cardiac remodelling could appear. We present an interesting (due to variety of clinical manifestations) and rare (due to simultaneous association of another rare disease) case of CICMPP in a patient with polycystic kidney and liver disease.

Timeline

Case presentation

A 47-year-old Caucasian woman presented to local hospital's Emergency Department with retrosternal acute burning pain, diffuse abdominal pain, nausea, vomiting, and fatigue. At physical examination, right hypochondriac tenderness on deep palpation was revealed. Blood pressure was 200/100 mmHg; heart rate was regular at 88 b.p.m., with no heart murmurs, no distension of neck veins or peripheral oedemas. Lung auscultation did not reveal any pathological findings. Respiratory rate was 18 b.p.m., oxygen saturation 94%. Fundoscopy for determination of papillary oedema was not performed. Laboratory tests revealed elevated white blood cell count 18×10^3 units/L (ref. range: $4-9 \times 10^3$ units/L) and elevated erythrocyte sedimentation rate of 46 mm/h (ref. range: 0–20 mm/h).

Electrolytes, cardiac biomarkers (Troponin I test strip), renal function (serum creatinine, glomerular filtration rate, blood urea nitrogen), and complete blood count were normal. Brain Natriuretic Peptide blood test was not performed at the Emergency Department at the local hospital. Electrocardiogram (ECG)

| Date | Events |
|-----------------|--|
| 9 November 2017 | Presentation in Emergency Department of local hospital with acute chest pain, fatigue, and uncontrolled high blood pressure values. Due to persistence of chest pain with no response to repeated nitroglycerine administration and insufficient blood control, the patient was redirected to percutaneous coronary intervention (PCI) centre. Coronary angiography revealed no lesions. |
| 5 June 2018 | Patient's presentation to local Emergency Department with complains on acute retrosternal pain, sweating, nausea, and vomiting. Abdominal ultrasound examination showed a large mass in right liver lobe and multiple cysts in both kidneys. The patient was admitted to the Cardiology Department. |
| 6 June 2018 | Transthoracic echocardiography revealed global myocardial hypokinesis. |
| 8 June 2018 | A contrast-enhanced computed tomography scan of the abdomen showed data suggestive for pheochromocytoma of right adrenal gland and kidney and liver cystic disease. |
| 13 June 2018 | Patient discharged. |
| 14–17 June 2018 | Admitted to the General Surgery Department for adrenalectomy associated with right kidney and liver cysts removal. 16 June 2018—adrenalectomy with cystectomy. Morphopathological examination of right adrenal gland, kidney, and liver cysts revealed no evidence of malignancy. |
| 19 June 2018 | Patient discharged. |

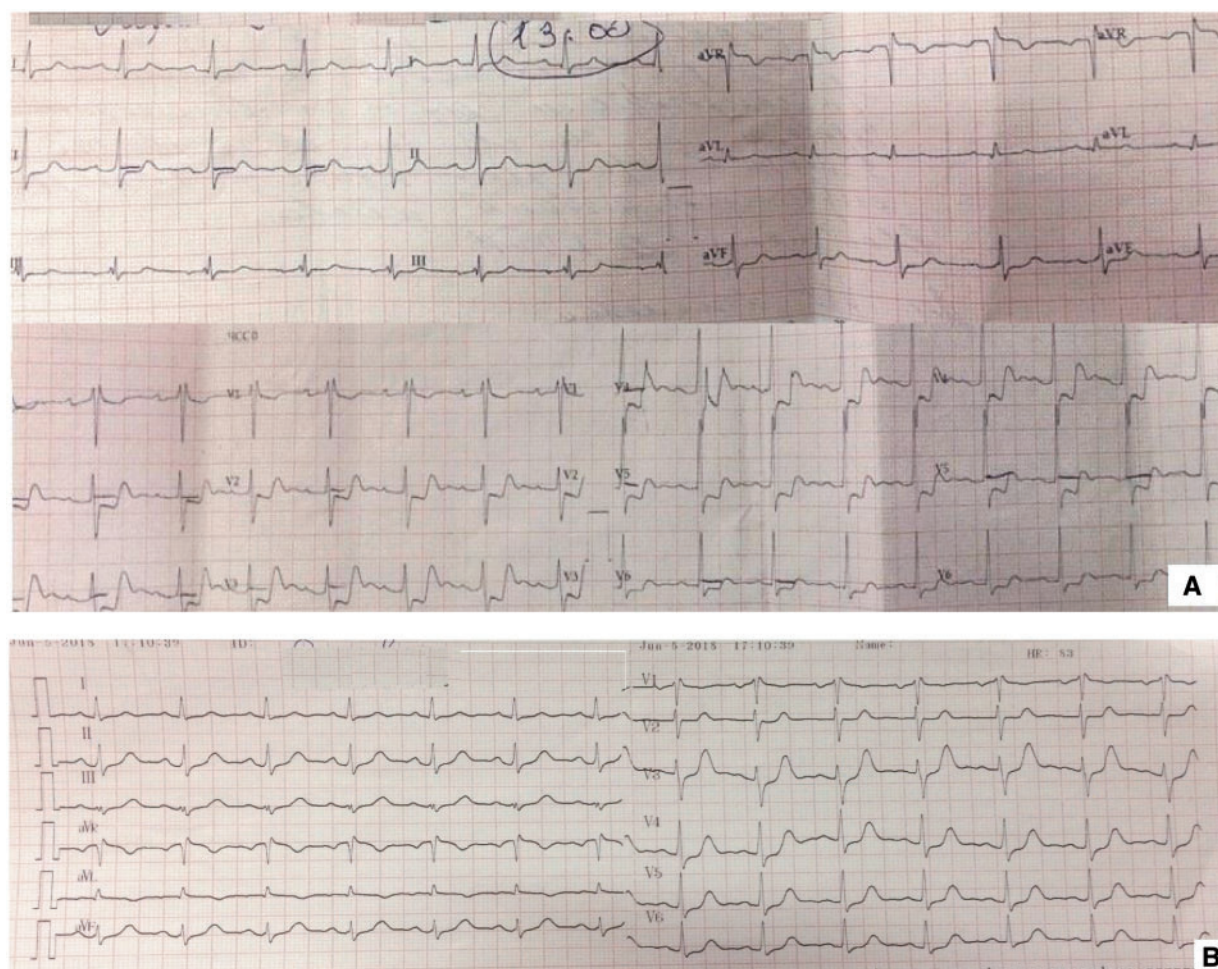


Figure 1 Electrocardiogram of the patient. (A) On admission, suggestive ST depression about 1.0–2.5 mm in lead II, V2–V6; ST elevation >0.5 mm in aVR lead. (B) Electrocardiogram after 3 h of index presentation.

examination showed ST depression about 1.0–2.5 mm in lead II, V2–V6; ST elevation >0.5 mm in aVR lead (Figure 1). The patient's chest X-ray was normal with clear lung fields and no other abnormality detected. Abdominal ultrasound exam detected cystic masses in right liver lobe and multiple cysts within the both kidneys; adrenal glands were not visualized.

When detailed history was taken, the patient mentioned often episodes of headache that she linked to her daily job as a teacher. The patient did not mention any history of haematuria or prominent flank pain. Detailed analysis of patient's family history did not reveal information about neuroendocrine tumours. The patient said that her mother had suffered from polycystic kidney disease (without liver cysts) and that she had an aunt with polycystic kidney disease who, unfortunately, had died at the age of 40 years because of renal insufficiency.

The patient's prior treatment plan included amlodipine 10 mg po qd, indapamide 1.5 mg po qd, but she was not perfectly adherent to treatment.

Half a year before, the patient was admitted to percutaneous coronary intervention (PCI) centre, due to similar acute burning chest pain, sweating, and fatigue. Blood pressure was 210/105 mmHg, heart rate was regular 93 b.p.m. Then, her ECG showed ST depression <2 mm in leads II, V2–V5. Her laboratory results included: Troponin T HS 1200 ng/mL (ref. range: 0–50 ng/mL), creatine-kinase MB 44 IU/L (ref. range: 0–24 IU/L), D-dimers 1600 ng/mL (ref. range: <500 ng/mL), C-reactive protein 12.2 U/L (ref. range: 0–5 U/L), creatinine 64.66 μmol/L (ref. range: 53–97 μmol/L). Echocardiography showed moderately reduced ejection fraction (EF) of the left ventricle (~36%) due to global hypokinesia, tricuspid valve regurgitation was moderate-to-severe; pulmonary artery systolic pressure was 42 mmHg. Coronary angiography was performed immediately and revealed no atherosclerotic lesions. Due to detection of fall of cardiac enzymes values, positive dynamic on ECG and clinical amelioration the patient was discharged after a couple of hours. The final diagnosis at that moment was: acute myocarditis, simple form (probably of viral aetiology).

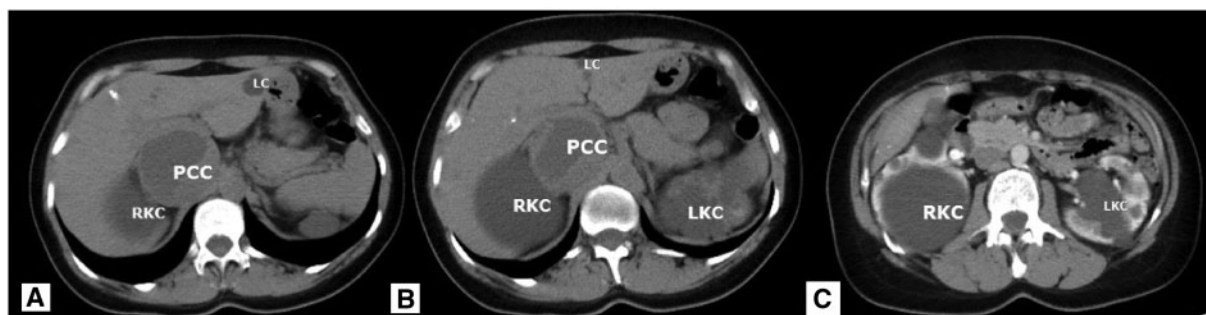


Figure 2 Abdominal computed tomography scan. (A–C, multiple cross sections) Axial C + arterial phase, showing: LC, well-defined round, low-density mass (liver cyst in left lobe), with peripheral calcifications and no contrast enhancement; LKC, multiple different sized cysts in the left kidney; PCC, pheochromocytoma of right adrenal gland; RKC, right kidney cysts.



Figure 3 Abdominal computed tomography scan. (A) Coronal view. LC, giant liver cyst in left lobe; LKC, multiple cysts in left kidney; PCC, pheochromocytoma of right adrenal gland; RKC, right kidney cysts. (B) Sagittal view. LC, liver cysts; PCC, pheochromocytoma of right adrenal gland; RKC, right kidney cysts.

From the local hospital Emergency Room (first-level hospital), the patient was redirected for the admission to the Institute of Cardiology (third-level hospital). Echocardiography revealed global hypokinesia with severely reduced left ventricular EF (~28%), mild aortic, mitral and pulmonary regurgitation, and moderate-to-severe tricuspid regurgitation. Pulmonary artery systolic pressure was 49 mmHg. Cardiac magnetic resonance imaging was not performed. Repeated abdominal ultrasound examination determined a vascularized semiliquid mass (7.0 × 6.7 cm) with multiple membranes in the right lobe of the liver (segment 8 by Couinaud's classification). Moreover, another avascularized semiliquid mass (8.9 × 8.3 cm) was found in the right liver lobe (segment 7 by Couinaud's classification). Kidney ultrasound exam showed multiple bilateral cysts with average diameter of 4–5 cm. However, the adrenal glands were not visualized. The patient's treatment plan was lisinopril 10 mg po qd, indapamide 1.5 mg po qd, and bisoprolol 2.5 mg po qd. During the whole period of admission to the Institute of Cardiology, the patient had several

transient states of sudden sweating, pale skin, nausea, and vomiting, accompanied by hypertensive crisis with blood pressure values above 200/100 mmHg. Based on specific clinical features of the patient and her previous instrumental examinations we decided to evaluate urinary fractionated metanephrines. These biochemical markers were collected according to the Endocrine Society Clinical Practice Guideline on PCC⁴ in order to avoid misdiagnosis. The results were: 397 µg/24 h/L (ref. range: 0.0–350 µg/24 h). The aldosterone level was normal. Contrasted computed tomography of abdominal cavity and pelvis was performed immediately. It revealed in both hepatic lobes multiple cysts, the biggest one being of 21 mm. Both kidneys showed multiple cysts, the biggest one of 90 mm in the upper pole of right kidney. Also, in the right adrenal gland was determined a filling defect of 71 × 89 × 20 mm. Computed tomography findings (Figures 2 and 3) in common with urinary fractionated metanephrines, helped to establish the diagnosis of PCC of right adrenal gland associated with liver and kidney polycystic disease. The final diagnosis was:

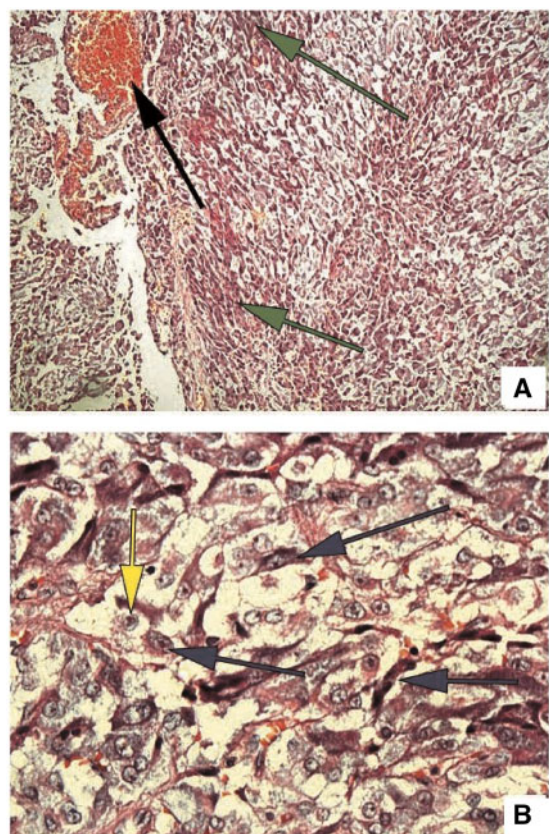


Figure 4 Histopathology of post-resectional mass, haematoxylin and eosin stain. (A) 10× magnification. Tumoural cells are organized in pseudoglandular or trabecular structures (green arrows), covered by well vascularized stroma, note the diffuse necrosis areas (black arrows); (B) haematoxylin and eosin stain, 40× magnification tumour cell with granular basophilic cytoplasm and round or oval nuclei with prominent nucleolus, frequently found giant nuclei with degenerated chromatin within (yellow arrows). Also is well seen marked cellular pleomorphism, represented by fusiform and polygonal cells (blue arrows).

Catecholamine-induced cardiomyopathy due to the presence of PCC, secondary arterial hypertension, polycystic kidney and liver disease.

The treatment plan was changed to: terazosin 2 mg po qd, amlodipine 5 mg po qd, high-sodium diet, and surgery for PCC and cysts.

Four days following discharge the patient underwent adrenal mass, kidney and liver cysts removal.

Firstly, minimally invasive laparoscopic approach for the surgery was selected. The persistent bleeding occurred during the surgery that determined transition to xifo-umbilical median laparotomy. No reactive tachycardia or sustained postoperative hypotension were observed.

Histopathology (Figure 4) revealed PCC with predisposition to growing in diffuse pattern, tumoural necrosis, and marked pleomorphism (LVI-0); T1, Nx, Mx. Due to suggested potential malignancy because of remarkable pleomorphism and tumoural necrosis,

it was decided to perform complex morphohistopathological examination at the National Cancer Centre. This did not reveal any evidence of malignancy.

After discharge, the patient displayed good control of blood pressure. Her treatment plan included lisinopril 20 mg po qd and indapamid 1.5 mg po qd. During outpatient follow-up 1 month post-operative, clinical improvement was substantial. Transthoracic echocardiogram showed prominent increase in left ventricular EF (up to 58%) and resolution of all wall motion abnormalities with mild mitral and tricuspid regurgitation; pulmonary artery systolic pressure was 24 mmHg. No hypertensive crises or unexplained sweating were reported. The quality of patient's life was much better. Because of concomitant polycystic kidney and liver disease, the patient remains at risk for renal insufficiency and poor control of blood pressure. At 6-month follow-up, visit an abdominal ultrasound exam with blood control for renal function are planned at the local medical centre.

Discussion

Pheochromocytomas are rare mostly benign neuroendocrine tumours with an annual incidence of three to eight cases per 1 million per year in the general population.⁵ The prevalence of CICMPP is about 8–11% in patients with PCC.^{6,7} Excessive catecholamine-induced stimulation of cardiac myocytes leads to remodelling which generally manifests in three types of cardiomyopathies that can be present in patients with PCC: dilated cardiomyopathy (DCM), takotsubo cardiomyopathy (TCM), and hypertrophic cardiomyopathy (HCM).² Different types of CMP are formed by means of heart adaptation to catecholamine excess.² According to the results obtained by Zhang *et al.*,³ many patients lack classic signs or symptoms of PCC with hypertension as a presenting symptom in 65% and the triad of headache, palpitations, and diaphoresis only in 4%. More of that, hypertension is more common in patients with PCC and HCM (80%) or DCM (83%) than classic TCM.³ Wide variety of clinical manifestations of PCC, especially when it is associated with one of types of CICMPP, makes the diagnosis a real challenge. Differential diagnosis in most cases includes acute coronary syndrome and myocarditis. Coronary angiography with left ventricular angiogram usually are sufficient for confirming or refuting coronary artery disease pathology, except rare cases, such as myocardial infarction with non-obstructive coronary arteries.⁸ Myocarditis presents in many different ways, ranging from mild symptoms of chest pain and palpitations associated with transient ECG changes to life-threatening cardiogenic shock and ventricular arrhythmia.⁹ Unfortunately, only endomyocardial biopsy (the diagnostic gold standard) confirms the diagnosis of myocarditis and identifies the underlying aetiology and the type of inflammation, and it is used infrequently.⁹ For the diagnosis of PCC fractionated metanephrines in plasma, urine or both are useful, followed by radiological imaging for tumour localization.⁴

Due to paucity of cases, there is still no specific therapeutic approach regarding the management of CICMPP.² All the present data is based on retrospective studies or case reports. The main idea in management of CICMPP involves the stabilization of blood pressure by α -adrenoceptor blockers followed by β -adrenoceptor blockers and surgical resection of PCC when the patient is clinically stable.² Myocardial changes in CICMPP are improved in most cases after the

administration of appropriate pharmacologic treatment and resection of PCC.² Time for improvement of heart changes due to CICMPP may take as short as 1–2 weeks or may be up to several months.¹⁰

We present the second case reported in the medical literature of adrenalectomy due to PCC in a patient with polycystic kidney and liver disease; one other group described similar clinical case, where PCC was responsible for hypertension in a patient with autosomal dominant polycystic kidney disease (ADPKD).¹¹ The most frequent cause of genetic kidney disease represents ADPKD that is responsible for up to 15% of patients on renal replacement therapy. Due to the fact that ADPKD is a systematic disorder, cysts can occur not only in the kidneys, but also in other organs, such as liver, pancreas, arachnoid membrane, and seminal vesicles.¹² Arterial hypertension is the most common clinical manifestation in these patients and occur even before there is an important renal insufficiency due to cystic compression of renal microvasculature, resulting in activation of the renin–angiotensin–aldosterone system.^{11,12} That is why suspicion of PCC in patients with ADPKD seems to be doubtful, because ‘When we here hoofbeats, we always think of horses not zebras’.

Conclusions

Catecholamine-induced cardiomyopathy in PCC is a rare and difficult to manage complication that can resemble acute coronary syndrome or myocarditis. Unfortunately, the diagnosis is often delayed due to the atypical presentation. Our case demonstrates that the diagnosis is a real challenge if PCC is associated with another rare clinical condition. Early diagnosis and resection of PCC are of great importance due to potential reversibility of cardiac remodelling.

Lead author biography



Dr. Ecaterina Sedaia began her medical career at State University of Medicine and Pharmacy “Nicolae Testemitanu”, the Republic of Moldova in 2005. Ecaterina decided to dedicate her professional future to Cardiology, worked as a resident at the Department of Internal Medicine, Cardiology and graduated in 2015. In 2015 Ecaterina continued her medical career also as an Assistant Professor at the same

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Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

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.

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