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Rare association of aortoarteritis and pheochromocytoma: A case report

C. Toutai[a,*], M. Berrajaa[a], H. Aissaoui[a], N. Elouafi[a], R. Jabi[b], M. Bouziane[b], H. Latrech[c], B. Housni[d], N. Ismaili[a]

[a] Department of Cardiology, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Laboratory of Epidemiology and Public Health, Oujda, Morocco
[b] Department of General Surgery, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Oujda, Morocco
[c] Department of Endocrinology, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Oujda, Morocco
[d] Intensive Care Unit, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Oujda, Morocco

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ABSTRACT

INTRODUCTION: Pheochromocytoma is an uncommon but treatable cause of secondary hypertension, it may present with a wide variety of manifestations. The coexistence of pheochromocytoma and vascular abnormalities is described but rarely reported entity.
PRESENTATION OF CASE: A 36-year-old man was admitted to our hospital for severe hypertension, examination revealed absent femoral pulses with notion of intermittent claudication. Abdominal computed tomography revealed the presence of a right adrenal pheochromocytoma. CT angiogram showed thickening of the thoracoabdominal aortic wall and the proximal portions of some of its branches with stenosis of more than 50% of the origin of the celiac trunk, bilateral occlusion of the external iliac arteries and trunk stenosis of the right renal artery. The Pheochromocytoma was surgically removed.
DISCUSSION: Coexistence of pheyochromocytoma and vascular abnormalities especially renal artery stenosis and aortoarteritis seems to be an association rather than a coincidence.
CONCLUSION: To the best of our knowledge, the coexistence of pheochromocytoma along with both aortoarteritis and renal artery stenosis has not been reported thus far. The diagnosis, management and potential mechanisms underlying such an association will be discussed in this case.

1. Introduction

Pheochromocytoma is a rare neuroendocrine tumor that arises from chromaffin cells with annual incidence of approximately 2–8 million persons/year [1]. It is a great masquerador with protean manifestations reasulting from hemodynamic and metabolic effects of high catecholamine levels. It has atypical presentations in 9%–10% cases [1] (organ ischemia, claudication, myocardial infarction, stroke) which often delay diagnosis. Pheochromocytoma is an uncommon but treatable cause of secondary hypertension; it is estimated to occur in 0.1–1% of hypertensive patients [2]. It often coexists with rare but described vascular abnormalities: Cerebral pseudo-vasculitis, coronary vasospasm, aortic aneurysm, inferior vena cava thrombosis, renal artery stenosis and aortoarteritis [3]. We present a case of pheochromocytoma with both aortoarteritis and renal artery stenosis. The subsequent diagnostic evaluation and the possible mechanisms underlying such an association will be discussed in this case report. This work has been reported in line with the SCARE criteria [4].

2. Case presentation

A 36-year-old man, admitted to our hospital for severe hypertension. His past medical history was remarkable. He was hospitalized 3 years ago, for the managementa of a left lenticular cerebral hematoma in the context of hypertensive emergency. He was lost to follow up. Thorough questioning elicited also a history of intermittent headache with sweating and paroxysmal attacks of palpitations with recurrent abdominal pain and severe intermittent claudication of lower limbs (IIB of Leriche and Fontain's classification). On physical examination, the patient had an acute hypertensive crisis with an elevated blood pressure of 240/120 mmHg symmetric in the upper limbs, he had sinus tachycardia with a pulse of 110 beats/minute. The patient was anxious, with facial flushing. The cardiovascular examination showed bilateral abolition of the femoral pulse without signs of acute ischemia. The fundus examination revealed a bilateral papillary edema stage IV.

* Corresponding author at: Department of cardiology, Mohammed VI University Hospital, 60049 Oujda, Morocco.
E-mail address: chaimae.93@hotmail.fr (C. Toutai).

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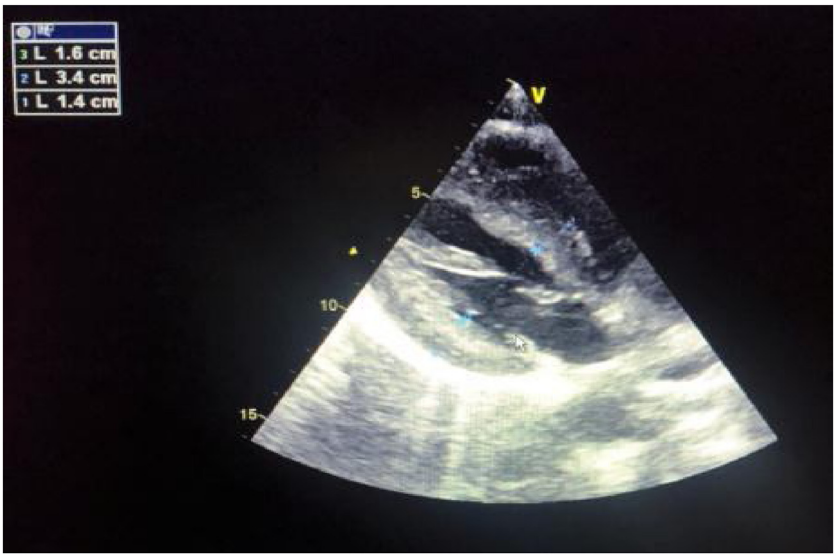

Fig. 1. Doppler echocardiography revealing left ventricular hypertrophy.

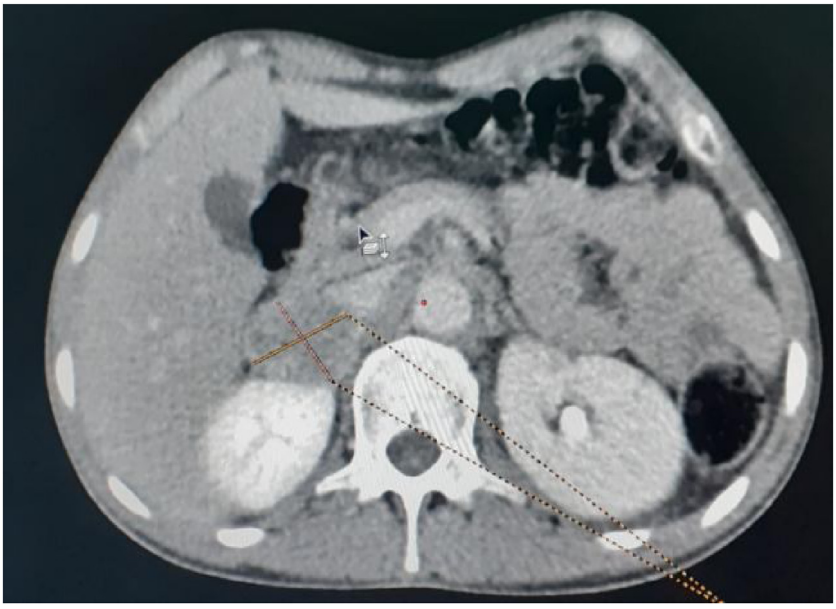

Fig. 2. Abdominal CT demonstrating a right adrenal mass, hypodense, heterogeneously enhancing, enclosing a liquefied area, measuring 42 × 35 mm.

Hypertension was initially managed with nicardipine infusion. The electrocardiogram showed sinus tachycardia and ST and T wave changes consistent with left ventricular hypertrophy. The chest radiograph was within normal limits. Transthoracic echocardiography revealed left ventricular hypertrophy with normal systolic function and without any significant valve disease (Fig. 1). Laboratory evaluation showed a high level of the C-reactive protein of 203 mg/L, with an elevated erythrocyte sedimentation rate of 62 mm/h (<20 mm/h) while procalcitonin was normal. We noted a very disturbed lipid profile, total cholesterol of 4 g/L, LDL of 3, 28 g/L, HDL of 0.46 g/L, TG of 1.32 g/L. Urinalysis showed a positive 24 h urine protein of 1798 mg/day. Computed tomography (CT) from thorax to pelvis revealed a right adrenal mass, hypodense, heterogeneously enhancing, enclosing a liquefied area, measuring 42 × 35 mm (Fig. 2). CT angiogram showed thickening of the thoracoabdominal aortic wall and the proximal portions of some of its branches suggestive of aortoarteritis with stenosis of more than 50% of the origin of the celiac trunk, trunk stenosis of the right renal artery, bilateral occlusion of the external iliac arteries (Figs. 3 and 4). Endocrinological evaluation revealed that urinary metanephrines were increased. Plasma cortisol, 24 h cortisol urine levels were within normal ranges (Table 1). On the other hand dosage of ANCA, rheumatoid factor, tumor markers were negative, antinuclear antibody level was in the upper limit. Thus, the diagnosis of right pheochromocytoma was made, and surgical treatment was recommended. After appropriate preoperative management (blood pressure was 130/80 mmHg on doxazosin 4 mg/day and nicardipine LP 50 mg twice a day), he underwent laparoscopic right adrenalectomy without any comlications (Fig. 5). Light microscopy of the specimen revealed characteristic organoid or zellballen nest of cells confirming the diagnosis of pheochromocytoma without signs of vasculitis. During the postoperative period, the blood pressure was normal without any surgical complication. One month after surgery, the blood pressure remained normal without any antihypertensive therapy, the patient had less invalid intermittent claudication with a walking perimeter >200 m but still have inter-

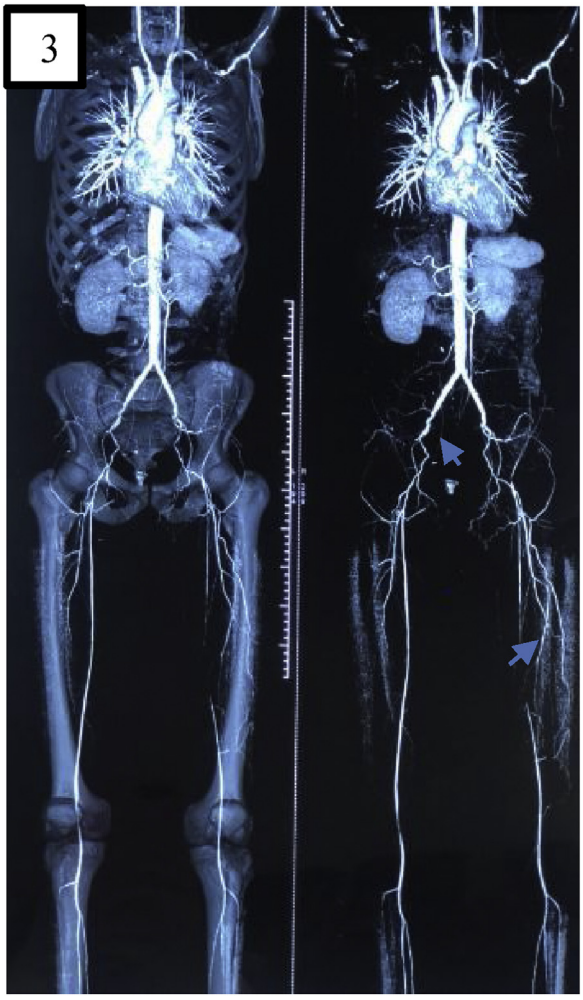

Fig. 3. CT angiogram showed thickening of the thoracoabdominal aortic wall and the proximal portions of some of its branches suggestive of aortoarteritis: stenosis of more than 50% of the origin of the celiac trunk, bilateral occlusion of the external iliac arteries.

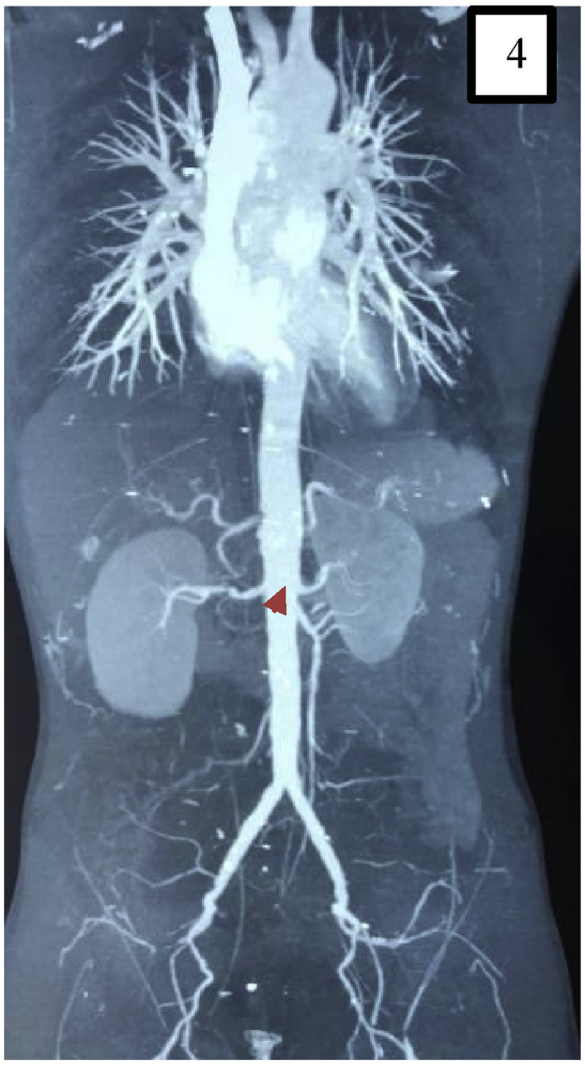

Fig. 4. CT angiogram showed a trunk stenosis of the right renal artery.

Table 1
Baseline biochemical parameters of the patient.

Parameters	Values	Normal range
Urinary Normetanephrin	18,04 umol /l (46,9 umol/24 h)	0,4–2,50 umol/24 h
Urinary Metanephrin	7,82 umol /l (7,33 umol/24 h)	0,20–1,50 umol/24 h
Aldosterone/renin ratio	Upright: 5 Supine : 3	<64 <64
8 AM plasma cortisol (ug/dl)	17,9	3,7–19,4
24 h cortisol urine (ug/24 h)	32	4,3–176

mittent abdominal pain. Dosage of 24 h urinary metanephrines returned normal.

3. Discussion

We report a case of aortoarteritis and renal artery stenosis in a patient with pheochromocytoma. Coexistence of these conditions seems to be an association rather than a coincidence. Aortoarteritis is a nonspecific inflammation of the artery walls [3]. Several pathophysiological mechanisms leading to aortoarteritis in pheochromocytoma have been proposed. First of all, Aortoarteritis may occur because of the mechanical trauma to the artery wall due to significant rise in blood pressure, moreover, persistently high levels of catecholamines may damage the vascular endothelium, leading in intimal fibrosis and destruction of the elastic lamellae. It may also induce medial necrosis due to the constriction of the vasa vasorum resulting to aortoarteritis in large and medium vessels [5]. The Involvement of an autoimmune phenomenon has also been advanced. Kim et al. and Bethea et al. concluded of a definitive rule for catecholamine excess in the pathogenesis of Behcet's disease after resolution of Behcet's symptoms rapidly after excision of pheochromocytoma [6,7]. This observation was supported by the report of Antony et al. where serological levels of several autoantibodies of systemic lupus erythematosus were normalized on follow up after resection of pheochromocytoma [8]. Elenkov et al. also demonstrated the role of catecholamines especially norepinephrine in modulation of lymphoid organs with dominance of humoral immunity [9]. Our patient didn't have any symptoms of Behcet's disease with initial laboratory evaluation concerning vasculitis returned in normal ranges allowing to eliminate the other differential diagnoses which are summarized in Table 2. We think that similar mechanisms might have occurred in our patient, leading to vascular nonspecific abnormalities.

The coexistence of pheochromocytoma and renal artery stenosis is very rare with 87 cases reported in the literature [3]. The patho-

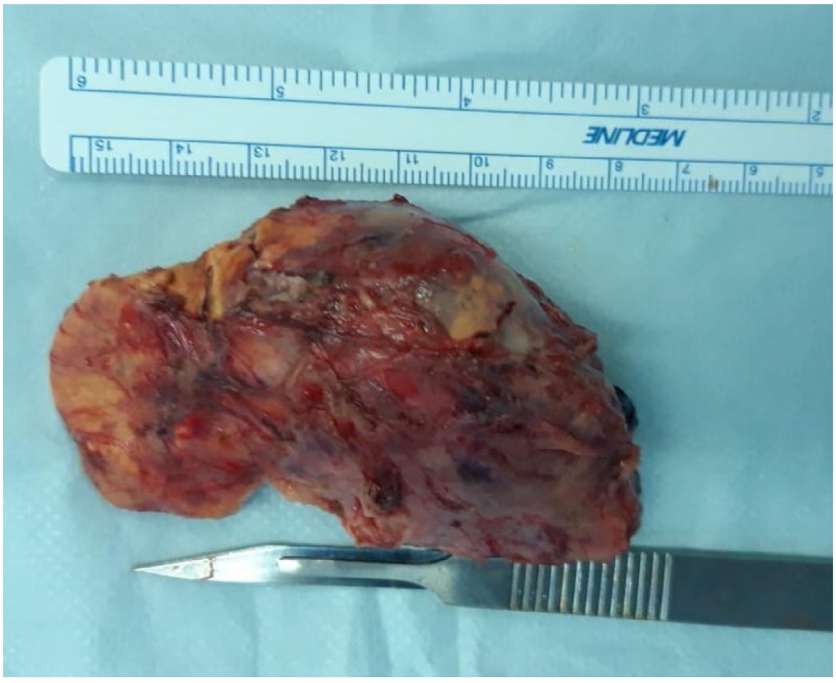

Fig. 5. Macroscopic aspect of the right adrenalectomy with 90 × 70 × 40 mm.

Table 2
Differential diagnosis of aortoarteritis.

Primary inflammatory vasculitides	Giant cell arteritis Kawasaki disease Polyarteritis nodosa Wegener's granulomatosis Takayasu arteritis Systemic lupus erythematosus
Secondary inflammatory vasculitides	Rheumatic fever Sarcoidosis Behcet's disease Spondyloarthropathies Fibromuscular dysplasia
Non-inflammatory vascular disease	Congenital aortic abnormalities Ehlers-Danlos and Marfan syndrome Neurofibromatosis
Other	Infections (endocarditis, tuberculosis, syphylis, boreliosis, HIV) Malignancy Post radiation fibrosis

physiologic mechanisms involved in this combination include the compression of the renal artery by ipsilateral tumor, persistent arterial vasospasm due to catecholamines excess, atherosclerosis secondary to high blood pressure and disturbed lipid profile resulting from catecholamines excess, generalized neuroectodermal dysplasia and finally a periarterial adhesion complicating tumoral resection. In some cases, this association may be a chance phenomenon where renal artery stenosis is secondary to an independent etiology like fibromuscular dysplasia [10]. Importance of preoperative diagnosis of the pheochromocytoma and renal artery stenosis is clear. On the one hand, a missed diagnosis of pheochromocytoma in a patient with renal artery stenosis may expose the patient to the risks of catecholamine excess during the surgical intervention. On the other hand, irrecognition of renal artery stenosis in a patient with pheochromocytoma may lead to persistent hypertension after tumoral resection [11]. However, vascular stenosis and abnormalities do not interfere with the laboratory diagnosis of a pheochromocytoma [3].

Management of vascular abnormalities associated with pheochromocytoma is obviously based on the control of catecholamine release. Definitive treatment of pheochromocytoma is surgical removal, which is curative in approximately 90% of cases [12], after control of blood pressure and intravascular fluid volume optimization to avoid lethal complications (hypertensive crises, arrhythmias and organ failure). Pre-operative medical management is based on initial alpha antagonism followed by beta antagonism [13,14]. Calcium channel blockers can be used with α-adrenergic blockers to control blood pressure. However, the Endocrine Society's Clinical Practice Guidelines (2014) do not recommend the use of calcium channel blockers as monotherapy [15]. Laparoscopic adrenalectomy is indicated for all small pheochromocytomas (<6 cm) without malignant radiological features, while open surgery is recommended for large (>6 cm) or invasive pheochromocytomas to ensure complete tumor removal and to avoid local recurrence or if a malignant disease is found [15]. Partial adrenalectomy may be an interesting option in the case of small tumors.

Ischemic symptoms and arterial stenosis may reverse after removal of pheochromocytoma especially in early cases. However, once fibrosis has formed, the vascular stenosis may persist. Razavi et al. reported a case of 34-year-old woman with phochromocytoma which, on cerebral imaging, had Central nervous system vessel caliber variation resembling vasculitis. The patient had a complete resolution of the angiographic findings after adrenalectomy without any immunosuppressive therapy [16]. However, in the study of Kumar et al., no angiographic improvement was observed (persistence of the aortic arch arteries occlusion even under long term steroids) after pheochromocytoma removal [17]. CT or MRI can be used to follow the vascular response after adrenalectomy [18]. In the case of persistent arterial stenosis and ischemic symptoms intervention may be considered [19].

The renal artery stenosis coexisting with pheochromocytoma may be transient "pseudostenosis" due to the reversible vasospasm induced by catecholamines, or permanent. In this case, the aims of operation include tumor removal, preservation of renal function

and correction of significant renal artery stenosis (more than 70% of the vessel caliber) [3].

For our patient, after one month of surgery, there is no indication for renal angioplasty because blood pressure is normal and there is no renal insufficiency. For visceral and low extremity arteries stenosis, we plan to follow up by CT scan after 6 months.

4. Conclusion

In the light of our case report we think that coexistence of pheyochromocytoma and vascular abnormalities especially renal artery stenosis and aortoarteritis seems to be an association rather than a coincidence. The early diagnosis and treatment of pheochromocytoma may lead to total resolution and correction of vascular abnormalities. We think that pheochromocytoma should be included as differential diagnosis and reversible etiology of aortoarteritis.

Conflicts of interest

There are no conflicts of interest.

Funding

None.

Ethical approval

Not required for this case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Author contribution

All the authors approved the final draft of the manuscript.

Dr. Chaimae Toutai wrote the manuscript and conducted the literature review. Dr. Mehdi Berrajaa and Dr. Hanane Aissaoui helped in data collection and analysis. Professor Mohammed Bouziane and Dr. Rachid Jabi operated in the patient and provided imaging data. Professors Hanane Latrech and Ibrahim Housni conducted the preoperative medical management. Professors Nabila Ismaili and Noha Elouafi supervised the writing and reviewing of the manuscript.

Registration of research studies

Not required.

Guarantor

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