Brief Communication

Coexistence of pheochromocytoma/paraganglioma and renal artery stenosis

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ABSTRACT

Renal artery stenosis (RAS) often coexists with pheochromocytoma (Pheo)/paraganglioma (PGL) and often alters the management of patients with Pheo/PGL. We have studied the prevalence of RAS in our Pheo/PGL patients. The study included 70 consecutive, histopathologically proven Pheo/PGL patients from a tertiary health care center. In 60 patients, tumors were limited to adrenal glands (54 unilateral and 6 bilateral) while other 10 patients had extra-adrenal abdominal tumors. Five patients had RAS with an overall prevalence of 14%. Only two out of 60 patients with Pheo had RAS with a low prevalence of 3.3% while three out of 10 patients with extra-adrenal abdominal PGL had RAS with a prevalence of 30%. To conclude, RAS commonly coexists with Pheo/PGL, more often with extra-adrenal PGL.

Key words: Paraganglioma, pheochromocytoma, renal artery stenosis

Introduction

Pheochromocytoma (Pheo)/paraganglioma (PGL) is a neuroendocrine tumor that arises from chromaffin tissue.[1] It is a great masquerador that mimics many disorders. It accounts for 0.1% cases of hypertension. It often coexists with rare vascular abnormalities like renal artery stenosis (RAS). A large study reports RAS in 3.4% patients with Pheo/PGL while another study reports four cases of Pheo/PGL in 500 cases of RAS.[2,3] Hypertension is a manifestation that is common to both RAS and Pheo/PGL. Coexistence of RAS is often missed to get diagnosed only when evaluated for persistent hypertension postoperatively.[4] Coexistence of RAS alters the management and prognosis of Pheo/PGL patients.[2] Hence, identification of their coexistence before surgery is essential for the appropriate management.

Most of the available literature on coexistence of Pheo/PGL and RAS exists as case reports. There are no studies reporting the prevalence of RAS in Indian Pheo/PGL patients. Hence, we have studied the prevalence of RAS in our Pheo/PGL patients.

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Methods

The study included 70 consecutive, histopathologically proven Pheo/PGL patients who were hospitalized in King Edward Memorial Hospital, Mumbai between January 1990 and December 2010. The records were verified for a diagnosis of RAS or evidence of RAS on all available imaging modalities including renal artery Doppler study, contrast enhanced computerized tomography, CT angiogram and MR angiogram.

Results

In 60 patients, tumors were limited to adrenal glands (54 unilateral and 6 bilateral) while other 10 patients

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had extra-adrenal abdominal tumors. Out of the total 70 patients with Pheo/PGL, five had RAS with an overall prevalence of 7%. Among 60 patients with Pheo only two had RAS with a low prevalence of 3.3%. Out of 10 patients with extra-adrenal abdominal PGL three had RAS with a prevalence of 30%. The characteristics of five patients including site of tumor location, age, reason for evaluation, site of RAS, severity of RAS, proximity of tumor to renal arteries, management and postoperative blood pressure status are summarized in Table 1. CT angiogram of patient 4 is shown in Figure 1a which is showing a shrunken left kidney and left RAS involving middle part of the artery. All patients had unilateral RAS on ipsilateral side of the tumor except for one patient (Case 5) who had bilateral renal artery stenoses with a single right renal hilar PGL impinging on both renal arteries [Figure 1b].

Discussion

Our study reports an overall prevalence of RAS in 7% patients with Pheo/PGL with higher prevalence (30%) in extra-adrenal abdominal PGL. A previous large study reports RAS in 3.7% (10/207) patients with Pheo/PGL.[2] Our study presents the second largest data and reports a slightly higher prevalence (7%).

It is very important to identify coexistence of RAS in PHEO/PGL patients since it affects the postoperative outcome. RAS could be a cause of persistent hypertension in the postoperative period.[4] However, none of the patients in our cohort had persistent postoperative hypertension due to RAS alone. The only patient who had persistent hypertension underwent partial excision of PGL and had elevated plasma free metanephrines in the postoperative period. The contribution of RAS for persistent hypertension in this patient could not be assessed.

Pheo/PGL patients with a small kidney, elevated serum creatinine, renal arterial calcification/lesion, delayed nephrogram on routine CECT, tumor impinging on the renal hilum and increased plasma renin activity should be screened for renal artery stenosis.[2] In our cohort, two patients were evaluated for unilateral small kidney, two for tumor impinging on the renal hilum and one for delayed nephrogram on routine CECT.

Conservative management is recommended for RAS smaller than 70% while those having stenosis of more than 70% of the vessel caliber require interventions in the form of angioplasty.[2] In our cohort, case 1-3, had stenosis less than 70% with normal kidney size. All these patients were managed conservatively. Postoperatively their RAS reversed as shown on renal artery Doppler study. Nephrectomy is recommended when there is shrunken or nonfunctional kidney. Although, two of our patients

Table 1: Characteristics of patients with coexisting renal artery stenosis and pheochromocytoma/paraganglioma

Location	Age (yrs)	Reason for evaluation	Renal arteries involved	Region of stenosis	% stenosis	Proximity of tumor to RA	Treatment	Postop
Left adrenal (NE)	32	Delayed nephrogram	Left	Middle	62	Close to LRA	Excision of pheo	Normal
Right adrenal (NE)	38	Impinging on RRA	Right	Middle	68	Impinging on RRA	Excision of pheo+lysis of adhesions	Normal
Left renal hilum (NE)	16	Impinging on LRA	Left	Distal	60	Impinging on LRA	Excision of PGL+lysis of adhesions	Normal
Left renal hilum (NE)	36	Small left kidney	Left	Middle	100	Encased LRA	Excision of PGL+left nephrectomy	Normal
Right renal hilum (NE)	28	Small left kidney	B/L	Middle (Rt) Proximal (Lt)	90 100	Encased RRA, Impinged on LRA Encasing aorta	Preop RRA stenting Partial excision of PGL+left nephrectomy	HTN

B/L: Bilateral, HTN: Hypertension, LRA: Left renal artery, NE: Norepinephrine secreting, NF: Nonfunctional, RRA: Right renal artery

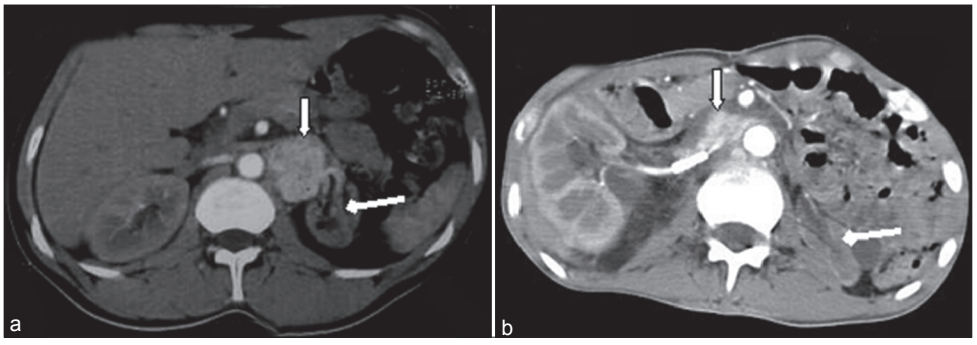

Figure 1: Contrast enhanced computerized tomography of (a) case 4 and (b) case 5 showing tumor (white arrow with black borders) and small left kidney (white arrow with diamond shaped end). Case 5 also had compensatory hypertrophy on right side with stent *in situ* in right renal artery

(4 and 5) qualified for nephrectomy, only case 4 underwent left nephrectomy alone with excision of PGL. In case 5, though nephrectomy was planned, it was deferred since he had severe hemorrhage intra-operatively and only partial excision of the tumor could be done.

In case 1, after excision of Pheo patient was normotensive and renal artery Doppler study was normal. In this case, RAS is likely to be due to vasoconstriction due to high local catecholamines. The most common mechanism of RAS in patients with Pheo/PGL is extrinsic compression of the renal artery which in the long term can lead to myointimal proliferation, reducing the arterial luminal diameter significantly.[2] Fibromuscular dysplasia is often the cause of RAS in Pheo/PGL patients and may result from markedly elevated local catecholamine levels initiating a sustained arterial spasm (spastic phase of fibromuscular dysplasia), culminating in dysplasia-like morphological changes in the muscular elements of the arterial wall (organic phase of fibromuscular dysplasia).[5] In few patients aortorenal atherosclerosis may cause RAS.[2] However, there was no evidence of aortorenal atherosclerosis on CT imaging of any patient or on histopathology of one patient who underwent nephrectomy with excision of the affected renal artery. The simultaneous but independent occurrence of RAS and Pheo/PGL has also been documented. This may be due to inherent risk of developing RAS in these subjects. A long term follow-up to monitor the development of RAS on the contralateral side may identify those with such a risk. However, the follow-up of our patients is limited to address this issue.

Our study found a higher prevalence of RAS in patients with extra-adrenal PGL. This may be due to higher chances of tumor impinging on the artery causing extrinsic compression and predominant norepinephrine secretion by these tumors which is a more potent vasoconstrictor.[2] This study is limited by its retrospective nature and small number of subjects.

To conclude, RAS commonly coexists with Pheo/PGL, more often with extra-adrenal PGL. Coexistence of RAS with Pheo/PGL significantly alters the management, often requiring concurrent nephrectomy or adhesionolysis.

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