Uncontrolled hypertension, palpitation and sweating in young female - a rare cause

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SUMMARY

Extra-adrenal /retroperitoneal paraganglioma is a rare cause of hypertension in young with increased incidence of metastasis as compared to adrenal pheochromocytoma. We present a case of a young female with history of headache, nausea/vomiting, palpitations, uncontrolled hypertension, heat intolerance and diaphoresis. The 24-hour urine catecholamine levels were elevated. Clinical diagnosis of pheochromocytoma was made and further evaluation with Computed Tomography (CT) scan of the adrenals revealed extradrenal para-aortic retroperitoneal mass in keeping with paraganglioma. Gallium-68 DOTATE positron emission tomography-CT scan (PET-CT) confirmed the diagnosis without evidence of metastatic foci.

INTRODUCTION

A paraganglioma is a rare tumour arising from chemoreceptor cells derived from the neural crest. They generally occur in the head and neck. The adrenal medulla has significant collection of this paraganglionic tissue from which pheochromocytoma arises. About 10% of retroperitoneal paraganglioma are extradrenal. Extra-adrenal retroperitoneal paraganglioma is rare cause of hypertension with increased incidence of metastasis as compared to adrenal pheochromocytoma. The functional tumours secrete catecholamines in the blood, which cause classical symptoms. It can be easily diagnosed with clinical history and biochemical findings including the 24hr urine catecholamine levels. Imaging in such cases is used only to locate the site and detect metastatic foci. Non-functional tumours are clinically not apparent and detected incidentally on imaging or due to pressure effect on adjacent organs. Surgery is completely curative, however lifelong annual follow up is required due to increased risk of recurrence and metastasis.

CASE REPORT

A 36-year-old female presented with on and off headache since two weeks associated with nausea/vomiting, palpitations, heat intolerance and diaphoresis. She had no chest pain, shortness of breath or abdominal pain. Her blood pressure was elevated measuring 160/100 mmHg, not controlled by any antihypertensive medication. The patient had on and off headaches since two years but was not a known hypertensive and not on any antihypertensive medication. Based on the history and clinical presentation, pheochromocytoma was suspected. The 24 hour-urine catecholamine levels were then requested. 24-hour urine catecholamine levels including epinephrine (1991 nmol/day), norephinephrine(325l nmol/day), metanephrine levels(61955 nmol/day) and normetanephrine levels(37248 nmol/day) were significantly elevated.

Clinical diagnosis of pheochromocytoma was made and further investigation with contrast enhanced CT scan of adrenals with low osmolar intravenous contrast agent revealed heterogeneously enhancing mass in right para-aortic retroperitoneal region (Figure 1b) separate from both adrenal glands (Figure 1a). Further evaluation with Gallium-68 DOTATE PET-CT (Figure 2) was done, which detects somatostatin sensitive receptor (SSR) positive lesions to confirm the diagnosis and to detect other metastatic foci. It demonstrated increased uptake corresponding to mass noted on CT scan without evidence of metastatic foci. Imaging diagnosis of extra adrenal phaeochromocytoma/ retroperitoneal paraganglioma was given. The patient was treated with preoperative alpha and beta-blockers to reduce hypertensive crisis during surgery due to release of catecholamines. The imaging findings were confirmed on surgical excision and histology. Immunohistochemically tumour cells stained positive with chromogranin, synaptophysin and focally with S100 stains characteristic of paraganglioma.

DISCUSSION

Retroperitoneal paraganglioma also called as extra-adrenal pheochromocytoma arise from sympathetic ganglia in para-aotic region. It most commonly arises at aortic bifurcation near organ of Zuckerkandl. The malignancy in extra-adrenal paraganglioma is seen in up to 20%[1] as compared to 10% for adrenal pheochromocytoma. The extra-adrenal pheochromocytomas are also associated with increased risk of Carney's triad having gastrointestinal stromal tumour (GIST) and pulmonary chondroma as other components. The classical clinical presentation is in 4th to 5th decades of life without gender predilection and with symptoms related to catecholamine secretion like palpitation, headache, sweating and hypertension. Functional tumours can be diagnosed on the basis of elevated catecholamine and their metabolites in serum and urine (24 hour). More than 50% are functional. The non-functioning tumours are discovered incidentally on imaging or due to mass effect on the surrounding organs. On CT they appear as solid homogenous or heterogeneously enhancing mass depending on size. Care should be taken to use low osmolar intravenous contrast since high osmolar

This article was accepted: 21 December 2015
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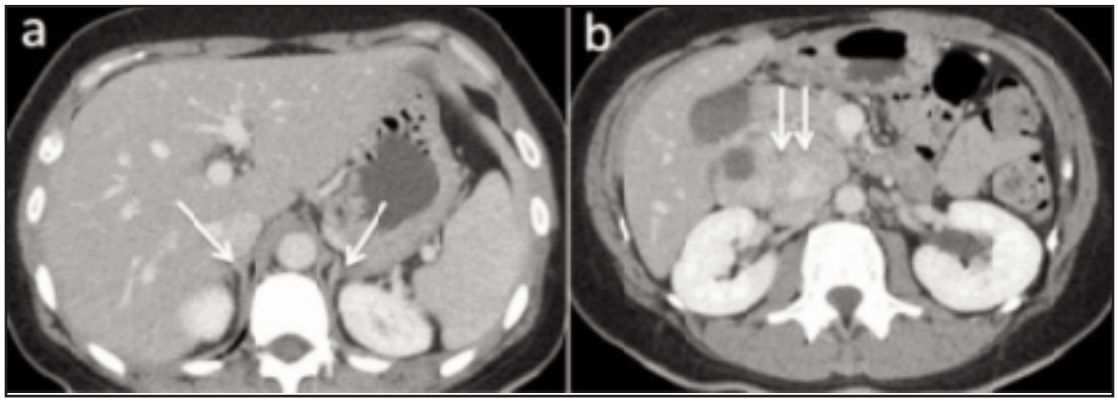

Fig. 1: Axial contrast enhanced CT Scan reveals normal bilateral adrenals (arrows in a) with an extra-adrenal heterogenously enhancing mass in the right para-aortic region(double arrows in b).

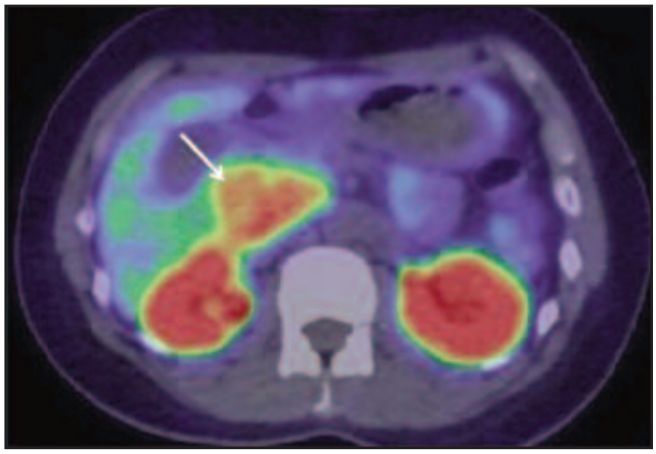

Fig. 2: Ga-DOTATATE PET-CT demonstrates increased uptake in the right para-aortic region (arrow) corresponding to the CT scan in keeping with retroperitoneal paraganglioma.

contrast agents can precipitate hypertensive crisis. On MRI they appear hypointense or isointense on T1 weighted and markedly hyperintense on T2 weighted images. Both modalities cannot however differentiate functioning from non-functioning tumors. Nuclear scintigraphy either with ^{123}I or ^{131}I labelled MIBG a nonepinephrine analogue helps in detecting functioning lesions, multiplicity and metastasis. It is 95-100% specific but sensitivity is about 85%.[2] Scintigraphy with ^{111}Indium and Tc-99m labelled SSR analogues is another alternative. The newer alternative is Ga-68 DOTATATE PET/CT, which binds to somatostatin receptor expressed by paragangliomas. The detection rate is close to 80-100%.[3] The other advantages include better resolution and anatomical localization, faster imaging time and semiquantification of lesions as compared to conventional scintigraphy. [4]

Surgical resection is treatment of choice. Genetic mutation of the succinate dehydrogenase B unit (SDHB) and succinate dehydrogenase D unit (SDHD) are found to have increased risk for extra-adrenal paragangliomas with increased rate of malignancy in patients of SDHB mutation.[5] Hence genetic screening should be offered. Annual lifelong follow up with relevant biochemical investigations including catecholamine and metanephrine levels is recommended because of increased malignant potential and higher recurrence rate in extra-adrenal paragangliomas.[1]

In conclusion, retroperitoneal paraganglioma or extra-adrenal pheochromocytoma is a rare cause of hypertension in young patients. In classic cases with typical history, clinical and biochemical laboratory findings are diagnostic. Imaging with Ga-68 DOTATATE PET/CT is a novel imaging technique, which is One-Stop-Shop imaging modality with high detection rate, better resolution, ability to detect distant metastatic foci and hence can be very useful considering the increased incidence of metastasis as compared to adrenal pheochromocytoma.

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