RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 1 | JANUARY 2016 | ISSN - 2249-555X

Paraganglioma-an Unusual Presentation

KEYWORDS: Paraganglioma, LVF, Serum metanephrines, extraadrenal pheochromcytoma

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ABSTRACT *We report the case of young female presenting with watery diarrhea with febricity for two day and progressive breathlessness for six hours . She had no other significant past history. She was initially treated for left ventricular failure with non invasive ventilation and appropriate drugs. The unexplained cardiovascular compromise in such a senario prompted an evaluation with electrocardiogram (ECG),echocardiography and chestX-ray.An interesting finding on ultrasonography and presence of hypertension related changes in ECG hinted towards a workup to be done for pheochromocytoma.Routine investigation for this tumor in case of secondary hypertension is often missed because of its rare occurence .Renal doppler,blood investigations(serum metanephrines) and computed tomography of abdomen confirmed the diagnosis. Patient was was susequently treated with prazosin,hydration,and betablockers for a week and later underwent surgical excision of the paraganlioma sucessfully. Presently there exists adequate diagnostic tools in suspected cases and when treated suitably results in good prognosis.*

Introduction:

Pheochromocytoma is a rare catecholamine-producing neuroendocrine tumour, derived from the chromaffin cells in the adrenal medulla. [1] This tumor is estimated to occur in 2–8 of one million persons per year and about 0.1% of hypertensive patients.[2] The prevalence ranging from 0.1% to 0.6% in patients undergoing screening for secondary hypertension.[3]The tumor can occur at any age and with equal gender distribution. Typical symptoms include headache, palpitations, excessive sweating, and intermittent or persistent hypertension. Other symptoms such as abdominal pain, shock, respiratory distress syndrome, pulmonary edema, hyperthermia, and cardiogenic shock occur less frequently[4] Cerebral ischemia and stroke symptoms are also one of the infrequent manifestations. The scenario can be worse when dilated cardiomyopathy predisposes patients to mural thrombi and subsequent embolic events.[5] Unfortunately it remains undiagnosed in many patients presenting with atypical symptoms—despite being present in up to 1 : 2,000autopsies.[6]Hereby emphasising the fact that recognition requires a high index of suspicion.

Case History:

A 24 yr old lady had presented to the emergency department with acute onset of breathlessness, altered sensorium and epigastric discomfort. The relatives on quick inquiry gave a history of loose stools, vomiting associated with diffuse and intermittent abdominal discomfort lasting minutes to hours two days prior, for which she had been treated at another nursing home. The patient had to be shifted in the ICU with pertinent positive finding on transfer, temperature - 38.6^{0}C, Heart rate-150/min, blood pressure (B.P) 170/100 mm of Hg, respiratory rate of 44/min, peripheries were cold, and pulse oximetry showed 90% saturation .Pulmonary exam revealed bilateral coarse crepts. On cardiovascular examination the following findings were noted- tachycardia, heartsounds normal no murmur, rub, gallops but JVP was raised. The clinical picture was suggestive of left ventricular failure ,hence the patient was put on non invasive ventilation and administered diuretic after which saturation improved to 100%.Lab studies revealed arterial blood gas analysis (ABG)(on admission)-pH-7.28/ pCo2-39.6/pO2-45.5/HCO3-17.9, WBC-8300cells/cu.mm, Hb-6.4gm%,Serum glucose -45mg%, LFT-AST-222U/l, ALT-95 U/L ,total bilirubin-1.31 mg/dl ,INR-2.4 ,B.N.P-1050pg/ml ,HIV-negative ,HbsAg-negative ,Na-130 meq/l and K-4.0 meq/l.

Figure-1

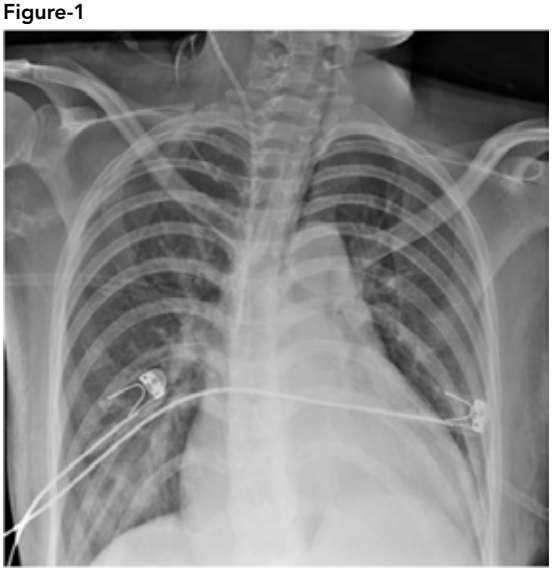
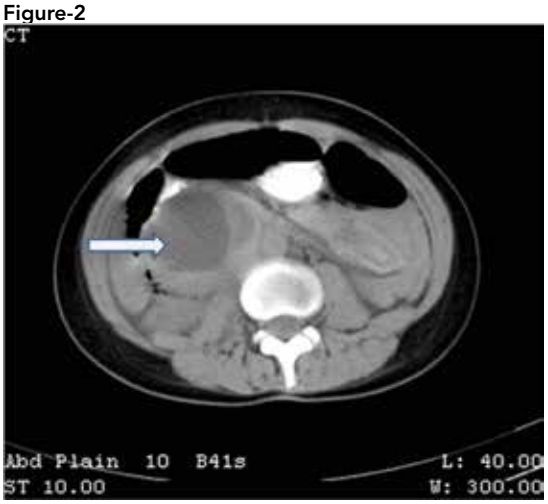


Figure-2



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Interestingly ECG showed left ventricular hypertrophy (LVH) and chest X-ray revealed cardiomegaly with basal infiltrate (Figure no. 1).Both these findings along with the present clinical picture pointed to incidental long-standing hypertension. Transthoracic Echocardiography showed global hypokinesia, ejection fraction -20% and dilated chambers. There were no signs of takasubo cadiomyopathy.As the patient gradually improved, she was weaned off non invasive ventilator, although blood pressure remained on higher side. Under the working diagnosis of young hypertensive heart disease with LVF, she was further evaluated with fundoscopy, ultrasound (USG)abdomen, renal doppler, urinary vinyl mandellic acid (VMA) and serum metanephrines.

Renal doppler was normal .Fundoscopy showed grade one/two hypertensive changes. USG showed well defined heterogeneous lesion with iso-echoic solid and cystic component adjacent to the head of pancreas approximately measuring 9x5.4cm, that was further evaluated with CT scan abdomen (Figure no..-2) which confirmed a heterogeneously enhancing mass at retroperitoneal region measuring 12x7x5.5cm.Given the clinical and radiological finding it revealed the possibility of paraganglioma. Follow up serum metanephrines were 376 nmol/l (reference range< 90 nmol/l) and urinary VMA- 5.43 mg/24 hrs which reinforced the diagnosis of extra adrenal pheochromocytoma. Patient was pre-treated with alpha blocker prazosin and subsequently beta-blocker was added. As the patient was posted for surgical excision of the tumor, INR was corrected with fresh frozen plasma (FFP), packed cell transfusion was given gradually .She underwent uncomplicated excision on day eight of admission .After resection and pathological confirmation of paraganglioma was done. Patient clinically improved and was stabilized as B.P was 100/70 mm of Hg. Repeat echocardiography showed improvement in ejection fraction of 55%.Patient was discharged on day fourteen after near full recovery with follow up in the hospital.

Discussion:

The mean age at diagnosis of pheochromocytomas or paragangliomas is about 40 years, although the tumors can occur from early childhood until late in life. The "rule of tens" for pheochromocytomas states that about 10% are bilateral, 10% are extraadrenal, and 10% are malignant.[2] The diverse manifestations of this tumor reflect variations in the hormones it releases, their patterns of release, and in the individual-to-individual differences in catecholamine sensitivities.[7] Typical symptoms include headache, palpitations, excessive sweating, and intermittent or persistent hypertension. Other symptoms such as abdominal pain, shock, respiratory distress syndrome ,pulmonary edema, hyperthermia, and cardiogenic shock occur less frequently. [8,9] The timely and accurate diagnosis of pheochromocytoma is quite challenging because their clinical manifestations are highly varied ,frequently nonspecific and coupled with a low prevalence. Hence early diagnosis remains difficult in patients with atypical presentations as mentioned previously. In these patients, a high index of suspicion is vital to arrive at a timely diagnosis.In our case, the patient presented with acute left ventricular failure and hypoglycaemia were quite unusual ; on the contrary hyperglycaemia is a common symptom of pheochromocytoma .However an unexplained transient hyperinsulinemia with reactive hypoglycaemia has been reported in literature.[10] She had undetected hypertension which was evident on ECG changes .As the patient was young hypertensive,she was evaluated for the same and a high index of suspicion for pheochromocytoma was included in the differential diagnosis . As the patient also gave a history of intermittent abdominal pain ,a USG was done which led to the incidental finding of a lesion that was further evaluated with CT scan and confirmation of the incidental extra adrenal mass.[3] 24 hour urine VMA levels were done and were reported normal (5mg/24 hrs). Urinary VMA at least 11.0 mg/24 h makes the diagnosis highly probable. As Neumann et al reported that although urinary vanillylmandelic acid (VMA) have been employed extensively in clinical practice, the sensitivity of this test used to detect pheochromocytoma is 64% . Therefore no biochemical test is completely diagnostic in pheochromocytoma and lab testing should complement clinical judgement and not replace it.[11] We pursued our suspicion of paraganglioma and sent for more specific test i.e serum metanephrine test which was found to be high. Plasma metanephrine has been advocated as the best marker for pheochromocytoma ,as metanephrine in patients with tumor are produced independently of catecholamine release and some tumor do not secrete catecholamine but metabolize them to plasma metanephrine,hereby making it a specific test for phaeochromocytomas. Lenders et al in a study of 52 patients with benign and malignant pheochromocytomas reported test sensitivity and negative predictive value of serum metanephrine as 100% each.[12]

Once the diagnosis of pheochromocytoma has been established the main stay of therapy is complete surgical resection. However it is utmost important to optimize patient condition prior to surgery and careful pharmacological treatment is essential. Treatment can be challenging in cases of unusual presentations initially .As in our case in which treatment was initially focused on hemodynamic stabilization of the patient with dobutamine and diuretics for left ventricular failure which is contrary to treatment of pheochromocytoma where fluid intake is encouraged to counteract both catecholamine induced volume contraction and orthostasis. Central venous line and arterial line were established in this patient, for better hemodynamic monitoring and fluid management. In patients with congestive heart failure and renal insufficiency, clinical judgment is prudent in monitoring the degree of volume expansion to avoid complications. Once the patient recovered from LVF , then medical treatment with an alpha blocker was initiated. The most common alpha-adrenergic antagonist utilized for blood pressure control and arrhythmia prevention during the preoperative period is phenoxybenzamine. It is an irreversible, long-acting, nonspecific, oral, alpha-adrenergic antagonist and is typically started seven to twenty-one days prior to surgery at a dose of 10 mg once or twice daily and increased by 10–20 mg every two to three days for optimal blood pressure and symptom control. The average required dose is between 20 and 100 mg daily, but may be as high as 400 mg a day.[3] As per the local availability patient was started on an effective alternative alpha-adrenergic antagonist - Prazosin .A low dose of Prazosin was initiated and up titrated before initiation of beta-blocker therapy .Beta-Blockers must never be used alone, because unopposed alpha-stimulated vasoconstriction may result in hypertensive crisis.[13]This medical therapy reduced the risk of intraoperative hemodynamic changes during tumor resection and patient had stable perioperative course. Hypotension and hypoglycemia are the most common immediate postoperative complications after adrenalectomy. The patient was monitored in the intensive care unit and had stable post operative course and was managed successfully. Unfortunately, pheochromocytoma remains undiagnosed in many patients presenting with atypical symptoms despite adequate diagnostic tools, potentially leading to lethal outcomes. Given the ample treat-

Volume : 6 | Issue : 1 | JANUARY 2016 | ISSN - 2249-555X

ment options that greatly improve survival, it is essential to sustain a high index of suspicion to entertain the diagnosis early in patients with atypical presentations such as unexplained acute heart failure to improve the outcome for the individual patient.

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