Pheocromocytoma of Adrenal gland - A Rare Tumor: Case Series

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Abstract

Pheochromocytoma is a rare neoplasm arises from adrenal medulla composed of chromaffin cells that produce catecholamines. Most are sporadic tumors that present in the fourth and fifth decade of life. Classic triad of episodic headaches, sweating and tachycardia present in about 30%, while hypertension is present in almost 90 % of cases. Clinical suspicion with laboratory testing and imaging for confirmation. Histopathological examination is gold standard, but no single biomarker or histologic feature predicts malignancy. Pheochromocytoma of the Adrenal Gland Scaled Score (PASS) provides prognosis based on histologic features. Five patients of pheochromocytoma with PASS score are described with the aim to represent a rare neoplasm. They are positive for chromogranin, synaptophysin and S100.

Keywords: Pheochromocytoma, Adrenal gland, PASS

Introduction

Pheochromocytomas are the rare neoplasm of the adrenal chromaffin cells and secrete epinephrine and norepinephrine.[1] The incidence ranges from 0.005% to 0.1% in the general population all over the world.[2] Other literature states the estimated incidence is around 0.3 cases per million per year or even less.[3] The clinical signs and symptoms are due to secretion of catecholamines- Hypertensive episodes or even hypertensive crisis. The triad of sweating, tachycardia, and headache. Paraneoplastic syndrome are also common which are due to other ectopic secretory products: Cushing syndrome (most common), diarrhea/ hypokalemia/ achlorhydria or polycythemia, local tumor symptoms such as abdominal pain or abdominal mass, or are asymptomatic.[1] Diagnosis can be confirmed by testing the evidence of catecholamine production, typically by plasma free metanephrines or urinary fractionated metanephrines, preoperative CT scan and histopathological examination.[1] As it is one of the endocrine emergency with a significant mortality rate of approximately 15%, recognizing the signs and symptoms of pheochromocytoma and performing an appropriate diagnosis is critical.[4] A Pheochromocytoma of the Adrenal gland Scaled Score (PASS) weighted for these specific histologic features can be used to

separate tumors with a potential for a biologically aggressive behavior (PASS ≥ 4) from tumors that behave in a benign fashion (PASS < 4). The pathologic features that are incorporated into the PASS correctly identified tumors with a more aggressive biologic behavior.[5] Application of these criteria will help for grading system in clinical practice. In this case series, five patients with a pheochromocytoma with PASS score are described with the aim of representing one of the rare neoplasm. Pheochromocytoma are immunohistochemically positive for chromogranin, synaptophysin and S100.[1]

Case presentation

We report five patients diagnosed with pheochromocytoma at tertiary care teaching hospital, Ahmedabad over the period of two years and three months (August 2019 to October 2021). Information regarding clinical features, radiological examination, laboratory investigations and histopathological findings were obtained for each patient from LIS. The definitive diagnosis was established based on the histopathological examination through H&E staining.

The age ranges from 21 to 51 years, with majority of cases were in third decade (3 cases). Majority of the patients were female (4 cases) and only single male patient was diagnosed, with female to male ratio is 4:1. Clinical symptoms that were obtained from the patients include lumps (4 cases), headache (2 cases), flank region pain (1 case) and palpitations (1 case).

Hypertension was found in 3 cases with a range of findings of 140-180 / 100-130 mmHg. A hypertensive crisis was found at the initial blood pressure examination in 1 case (female, 23 years old), where the blood pressure was 220/120 mmHg.

The examination of the local status in all cases found a well-demarcated solid mass in the flank region with (2 cases) or without (3 cases) tenderness. No lymph node enlargement was seen in any case.

An abdominal USG and CT examination was performed in all cases. During CT examination, a solid mass with cystic components in suprarenal was found with sizes ranging from 3.0 x 2.5 x 1.2 cm^3 to 9.5 x 8.5 x 7.1 cm^3. All the five cases were unilateral, in 4 cases right adrenal while in a single case left adrenal gland was involved. All masses showed contrast enhancement and hypervascularization without calcification. Necrotic features at the center of the mass were found in three cases.

The five cases of adrenal gland masses were resected and sent for histopathological examination.

On gross examination the tumor (in each case) was well encapsulated, size ranging from 3.5x 2.5. 2 cm^3 to 9.8 x 8.5 x7.5 cm^3. The outer surface was grey brown. On cut surface solid to cystic, tan colour, multiple small cystic areas identified and were filled with haemorrhagic material. At places necrotic and haemorrhagic areas were also identified. Representative sections were taken and after routine tissue processing and H & E staining the diagnosis was confirmed for each case through the histopathological examination; which shows histology of pheochromocytoma. Microscopic images of tumors showed adrenal tissues containing well-defined tumor masses. Tumors consisted of the proliferation of chromaffin cells forming an alveolar (Zellballen) pattern and solid nests separated by capillaries. The cells were polygonal in shape with clear cytoplasm, round nucleus and markedly pleomorphic. Mitosis was <3/10hpf. No capsular, vascular or periadrenal fatty tissue invasion was found in any case. The mass was categorized using PASS score, which was more than 4 in all cases. In our 2 cases PASS score was 6 while in another 2 cases PASS score was 9 and in a single case PASS score was 5. IHC was performed in each case and shows Positivity for synaptophysin, chromogranin and S100.

Discussion

Pheochromocytoma is a neuroendocrine tumor which can produce excessive amounts of catecholamines, especially epinephrine and norepinephrine, and release them continuously or intermittently.[5] The incidence ranges from 0.005% to 0.1% in the general population.[2] Even though paediatric cases are identified, this condition is more common during 40–50 years of the age.[2] Present case series showed a age ranges from 21 to 51 years. More number of cases in 3rd decade (3 cases), this suggests that increasing number of cases in young adults. Literature states the same frequency for both sexes[2], we

found female predominance with F:M ratio is 4:1.

Symptoms and signs of pheochromocytoma often resemble other clinical conditions. The classic triad of diaphoresis, palpitations and headaches, is reported to have a sensitivity of 67%. This number may even reach 91–94% if accompanied by hypertension. We reported hypertension in 3 cases. Other complaints are generally related to the effect of the tumor mass (e.g. local pain).

The incidence of pheochromocytoma ranges from 0.1% to 0.2% of the hypertensive adult population; however, this figure may only represent 50% of all pheochromocytoma patients because some patients have paroxysmal hypertension or even normotension.[2] Hypertension was found in 3 patients of the reported cases; the range of findings was 140–180/100–130 mmHg. One case (23 year old female) even came with hypertensive crisis status, with BP was 220/120 mm Hg. Thus our 4 (80 %) patients had complaint of hypertension.

The radiological examination needs to be done to identify the location of the tumor. Computed Tomography (CT) scanning is the first choice of modality because of its superior spatial resolution compared to Magnetic Resonance Imaging (MRI). CT scan has a sensitivity of 90-100% and a specificity of 70-80% for detecting pheochromocytoma.[2] Pheochromocytoma on imaging often contains necrotic, cystic and/or hemorrhagic areas. Smaller lesions tend to be solid, whereas larger lesions tend to be cystic or hemorrhagic. Macroscopic radiology features of pheochromocytoma include cystic, calcified, fibrotic and necrotic regions with internal hemorrhage.

The main treatment modality for pheochromocytoma is through surgical resection. Minimally invasive adrenalectomy with laparoscopy is recommended over open resection. Open resection is preferred in cases of large mass (>9 cm).[2] During the present study open resection was performed in all cases.

Pheochromocytoma tumor cells microscopically consist of polygonal cells that form alveolar, trabecular, or solid patterns. Alveolar patterns are formed from cells surrounded by structures that are rich in capillary vessels, which resemble well-demarcated nests or often referred to as Zellballen and are bound by amyloid containing fibrovascular stroma. The size and shape of these tumor cells vary and have smooth granular basophilic or amphophilic cytoplasm. Nuclei are usually round or oval in shape with prominent nucleoli and may contain inclusion structures resulting from deep cytoplasmic invagination.[1]

Recently phochromocytoma of Adrenal gland scaled Score (PASS) is a tool used to predict the behavior of a tumor. A score of < 4, suggests the tumor is likely to behave in a noncancerous manner and is cured by surgery alone. In contrast, the score of ≥ 4 means that the tumor is more likely to behave like cancer and spread to other parts of body. All our cases were reported using PASS score. In all our cases the score was > 4, this suggests that all cases have potentially aggressive behavior. According to the ROC curve analysis, malignant pheochromocytoma can be identified by PASS score ≥ 4 with sensitivity of 50% and a specificity of 45%.[6]

Chromogranin and S100 are positive in pheochromocytoma and are important to differentiate from adrenal cortical carcinoma.[1]

The prognosis of pheochromocytoma also depends on the resectability and genetic profile. The 5-year survival rate in pheochromocytoma patients, if present with metastasis, is 34-60%. Survival becomes <5 years when metastases occur in the liver or lungs and longer if there is bone metastasis. Local invasion can provide a long survival rate if complete excision is carried out.

Conclusion

Pheochromocytoma is a rare tumor with prognosis depends upon PASS score, despite its low sensitivity, may help to reserve the more aggressive treatment and narrow follow up for potentially malignant tumors.

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