

Extra-Adrenal Pheochromocytoma Arising From an Accessory Adrenal

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Reported here is a case of pheochromocytoma arising from an accessory adrenal gland. This tumor did not have significant clinical symptoms related to pheochromocytoma. The chief complaint was intermittent left upper quadrant pain. Scintigraphy of the abdomen identified normal bilateral adrenal glands, and a 56×63 mm tumor, adjacent the distal part of pancreas. The resected tumor was located between pancreas and spleen and was composed of normal adrenal cortical tissue and pheochromocytoma. Immunohistochemical staining of tumor for KI67, chromogranin A, NSE, S100 and AE1 was positive. Pheochromocytomas, arising from an accessory adrenal gland, may lack some of the typical characteristics of such tumors and have rarely been reported.

Key Words: Pheochromocytoma, Accessory adrenal, Ectopic pheochromocytoma

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Introduction

Approximately 10-15% of pheochromocytomas show extra-adrenal location^{1,2}. Most extra-adrenal pheochromocytomas arise from chromaffin cells of the paraganglia, and are therefore called paragangliomas. Less

frequently they are found in the ectopic adrenal tissue, and are designated as an accessory adrenal gland³, the origin of which is generally attributed to an embryological developmental defect^{4,5}. Accessory adrenal glands are seen in approximately half of newborns but subsequently disappear⁶.

Approximately all accessory glands contain adrenal tissue, but in some the medulla is less present. In one study, 32 percent of 100 consecutive autopsies revealed accessory adrenal cortical tissue in the area of celiac plexus; of these, in 16 percent the accessory glands contained both cortex and medulla⁷. Most tumors arising from accessory adrenal glands are adrenocortical tumor⁸. Some of the larger accessory cortical nodules contain both cortex and medulla⁹. Although the ectopic pheochromocytoma arising from paraganglia is well recognized, to our knowledge there have been only five reports on pheochromocytoma in an accessory adrenal gland¹⁰⁻¹⁴, two of which were reports on multiple endocrine neoplasia (MEN) 2a^{10, 11}. We report here an unusual case of ectopic pheochromocytoma in an accessory adrenal gland.

Case report:

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A 65 year-old woman was admitted to the gastrointestinal ward, with a history of intermittent left upper quadrant pain and nausea, since the past five months. The patient had a history of pelvic surgery thirty years ago, but without any information about the pathological diagnosis after surgery. Physical examination revealed normal vital signs at baseline and during abdominal pain, a blood pressure of 110/70 mmHg and a pulse rate of 88/minute. Computed tomography (CT) scan of the abdomen revealed a cystic mass, measuring approximately 56×63 mm (Fig. 1) adjacent to the pancreatic tail. Both adrenal glands were normal in size.



Fig.1. Computed tomography scan of the abdomen showing a tumor with mixed density and cystic degeneration between left kidney and distal part of pancreas

Suspected for probable pancreatic tumor, the patient was operated. Anesthesia was premedicated with Midazolam, Fentanyl, morphine, lidocaine, and metochlopramide, induced with penthotal sodium, cisatracurium and maintained with halothane 0.8%, propofol, nitrous oxide 50% in oxygen. During induction of anesthesia and onset of surgery, blood pressure was 100- 125/70-85 mmHg; but manipulation of the tumor induced hypertension (BP: 160/100 mmHg) and ventricular tachycardia. Fentanyl, lidocaine and amiodarone were administered,

and after tumor resection, blood pressure decreased to 80/50 mmHg, resolving the ventricular tachycardia. With decreasing propofol infusion rate, blood pressure returned to 90/60 mmHg. Abdominal exploration revealed normal pancreas and adrenals; the tumor was located between the distal part of pancreas and hilum of the spleen, associated with a branch of splenic artery, but was easily excised without evidence of invasion or splenic involvement. Post operative course was uneventful and the patient was subsequently discharged. Macroscopic examination of the specimen showed an encapsulated yellow-brown tumor, measuring 7 cm in diameter and weighing 70 gr. Its cut surface revealed cystic degeneration and the wall of the cyst contained residual tumor (Fig. 2).



Fig. 2. Gross appearance of ectopic adrenal tumor. Cut surface revealed cystic degeneration and the wall of the cyst contained residual tumor.

Microscopic examination revealed adrenal cortical tissue at the periphery with tumoral lesion in an alveolar and anastomosing trabecular pattern, polygonal cells with vesicular nuclei and mild nuclear pleomorphism; less than 3 mitotic figures were seen in 10 high power field.

Hemorrhage and hemosiderine deposition without necrosis were observed but there was

no invasion of vessels or the surrounding capsule (Fig 3).

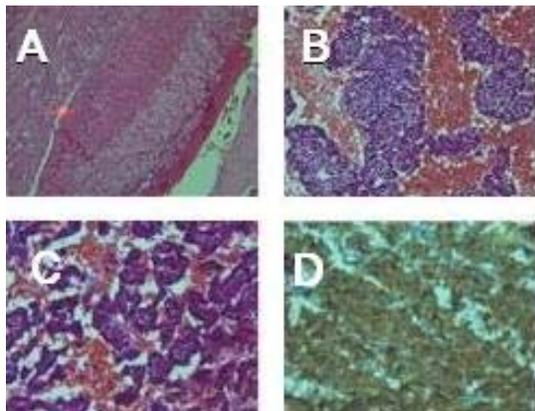


Fig. 3. Histologic features of accessory adrenal pheochromocytoma. A, Adrenal cortical tissue at the periphery with tumoral lesion. There is no true encapsulation at the junction between the tumor and adjacent adrenal cortex (hematoxylin and eosin stain; magnification, $\times 100$). B, Tumoral lesion in trabecular with anastomosing cell cords pattern with hemorrhage (hematoxylin and eosin stain; magnification, $\times 100$). C, Alveolar pattern (Hematoxylin and eosin stain; magnification $\times 400$). D, The brown coloration is due to the presence intracytoplasmic KI67 antigen (stain magnification $\times 400$).

Immuno-histochemical staining of tumor was positive for KI67 (Fig 3D), chromogranin A, NSE, S100 and AE1, but negative with EMA, histo-pathological features usually characteristic of pheochromocytomas.

There was no abdominal pain and nausea after surgery. CT-scan performed 32 days after operation, showed normal pancreas spleen and adrenal glands, and no evidence of tumor. Urinary vanil mandelic acid (VMA), metanephrine and normetanephrine levels measured 17 days after operation, were in the normal range.

Discussion

Although both aberrant adrenal tissue and ectopic pheochromocytoma are not rare findings, occurrence of accessory adrenal involvement with pheochromocytoma is uncommon. In a study, LS Graham reported 32 percent accessory adrenal glands, 16 percent containing both cortex and medulla⁷. Accessory adrenals, usually formed between the 7 to 8th week of development, are composed only of cortical tissue, when formed at a distance removed from the parent gland, while those closer to the adrenal gland may contain medullary substance as well¹⁵; hence the accessory adrenal in our patient, being closer to its origin, contained medullary tissue as well. Pheochromocytomas, constituting 0.3 to 0.95% of neuroendocrine tumors^{16,17}, arise from the chromaffin tissue of the sympathetic nervous system; adrenal tumors are called "pheochromocytomas" and extra adrenal tumors are called "paragangliomas"¹⁶. Ectopic pheochromocytomas were previously said to account for approximately 10% of pheochromocytomas during adulthood and 30% to 40% in children³. However, there is no universal agreement on this opinion^{18,19}. The clinical manifestations of ectopic pheochromocytomas are variable and nonspecific³. The diagnosis therefore is difficult and depends on a high index of suspicion. Biochemical diagnosis remains the diagnostic cornerstone. Commonly used imaging techniques for localization of extra-adrenal pheochromocytomas include CT scan, magnetic resonance imaging and the Metaiodobenzylguanidine scan²⁰. Recently 18F- fluorodopamine positron emission tomography (PET) /CT has been introduced as the preferred technique for localization of the primary paraganglioma²¹. Since there was no suspicion of pheochromocytoma in our case, specific diagnostic studies were not performed before operation. Based on literature available, abdominal symptoms occur in about 7 % of pheochromocytoma

cases²², typical gastrointestinal manifestation of pheochrom-ocytoma including nausea, vomiting and abdominal pain²³; although our patient presented with gastrointestinal symptoms, left upper quadrant pain and nausea, considering the normal adrenals in the CT-scan and lack of typical signs of catecholamine overproduction, the diagnosis of pheochrom-ocytoma was not suspected, because of which, blood and urine catecholamine were not measured before the operation. The paroxysmal triad has been observed in two-thirds of patients with pheochromocytoma²⁴. The uncharacteristic symptoms of pheochromocytoma in our patient may have been due to the lower production and/or release of catecholamine in the pheochromocytoma, occurring in an accessory adrenal gland. Our patient did have hemorrhagic pheochromocytoma but the amount of catecholamines released may not have been great enough to cause severe clinical symptoms. Ventricular tachycardia and hypertension, induced by tumor manipulation during surgery, could be

considered as catecholamine production and release from tumor. We did not measure serum catecholamine levels at the time of the hypertensive crisis that occurred during the operation and would have been helpful for verification of the pheochromocytoma; however, lack of data in this context did not affect the final diagnosis. To conclude, described here is a middle aged woman with intermittent abdominal pain and nausea, who was normotensive. CT scan revealed a mass with cystic change adjacent to pancreatic tail. Ventricular tachycardia and hypertension were induced by tumor manipulation; Surgical excision of tumor showed no relationship with pancreas. Microscopic studies revealed a solid-cystic mass consisting of adrenocortical cells and pheochromocytoma. In differential diagnosis of solid-cystic retroperitoneal masses of unknown origin, it is therefore important to consider pheochromocytoma arising from the ectopic adrenal gland, to decrease/prevent occurrence of any complications during abdominal surgery.

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