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Recurrent Renal Pheochromocytoma in the Retroperitoneum

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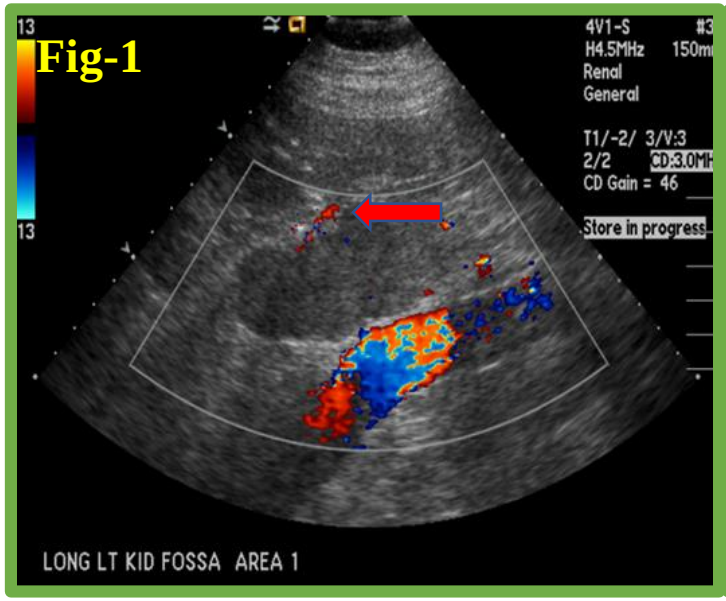
Case presentation: A 58-year-old male with history of left nephrectomy presented with left retroperitoneal mass.



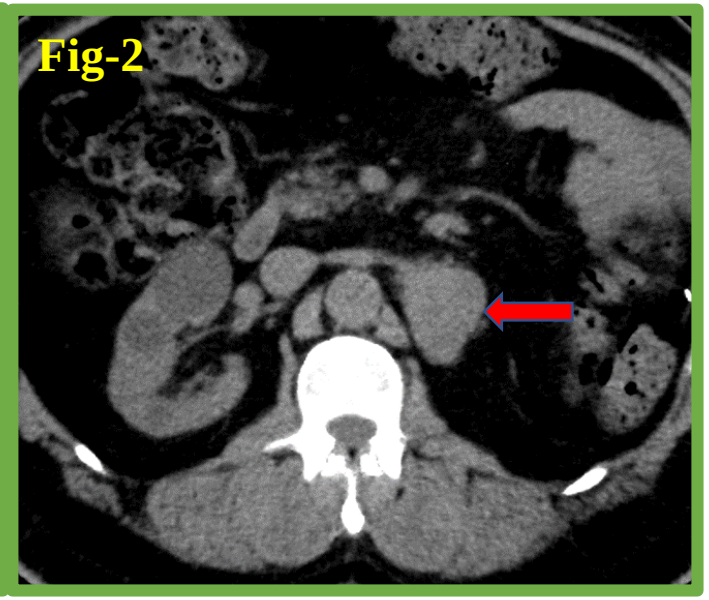
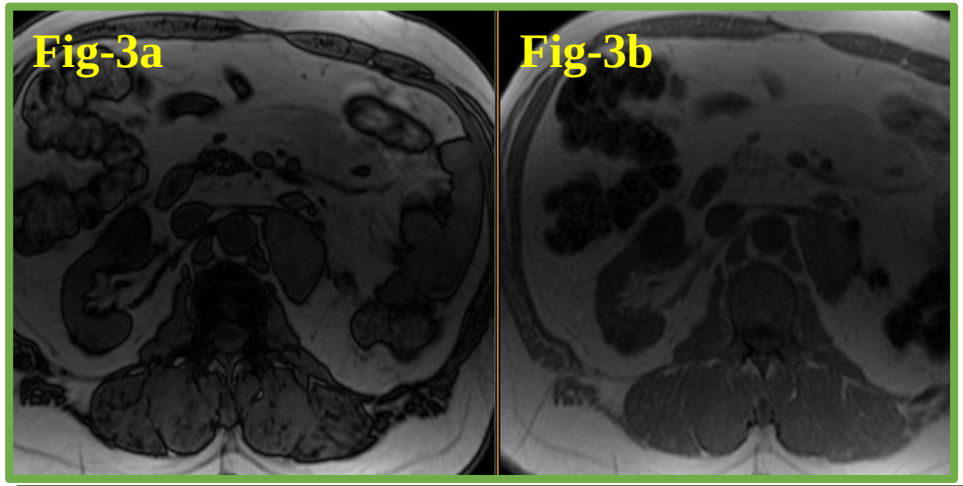
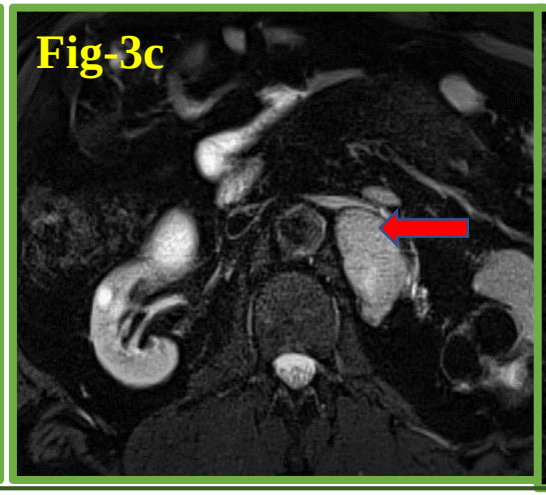
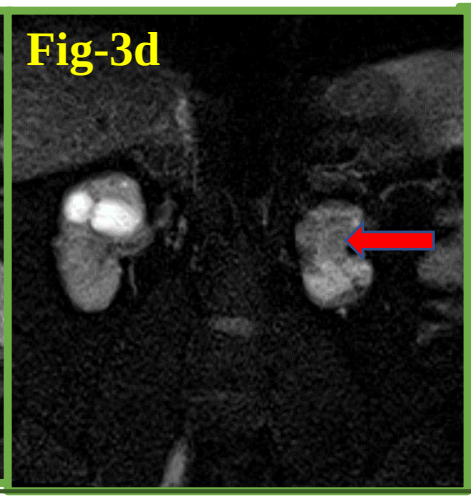


Figure-1: Ultrasound (US): Grey and color Doppler ultrasound demonstrates a lobulated mass in the left renal fossa with peripheral vascularity (arrow). Notice the mass is adjacent to the abdominal aorta.
Figure-2: Computerized Tomography (CT): Non contrast study shows a mass in the left infra renal para aortic region at the level of expected left renal vein.(arrow). Notice absent left kidney from prior nephrectomy for renal pheochromacytoma

- **On US,** pheochromocytomas (PC) tend to be of heterogenous echogenicity. They may exhibit posterior acoustic enhancement and echogenic foci in the cystic mass, representing acute hemorrhage.
- **Non contrast CT:** Usually PC have attenuation values of > 10HU except rare fat-containing PC have an attenuation of <10HU. Calcifications, intralesional hemorrhage, cystic changes and necrosis can give them heterogenous CT density on non-contrast CT.
- **DD:** Adrenal Adenoma.(<10HU- 100% sensitive and 40.5% specific)
- **Contrast enhanced CT:** PC and PGL enhance rapidly due to rich capillary network. Adrenal adenomas usually demonstrate milder enhancement and faster washout than PC.







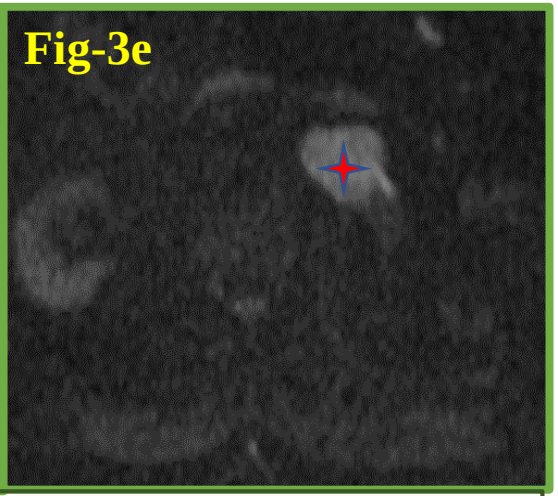


Figure-3: Magnetic Resonance (MR): Axial out and in phase images do not demonstrate drop of signal suggesting no intra voxel fat (3 a,b). Axial and coronal T2 Fat saturation images shows marked high T2 signal with in the soft tissue mass (3 c,d) arrows. Axial DWI high B value demonstrates marked restricted diffusion in the soft tissue mass (3 e) star.

- On T1W- imaging PC is isointense to muscle and hypointense to liver. On T2W-imaging, PC appears as a classic "light-bulb" bright lesion with similar intensity to CSF and can be noticed in 11-65% of cases. Another classical sign of paragangliomas, seen both on T1 and on T2 weighted images, is "salt and- pepper" appearance. Signal heterogeneity within the tumor due to hemorrhage, cystic transformation, and calcifications, remains a helpful feature in differentiating pheochromocytomas from benign adenomas.
- Signal loss on chemical shift MR imaging can be seen in rare occasions of PC with microscopic fat.

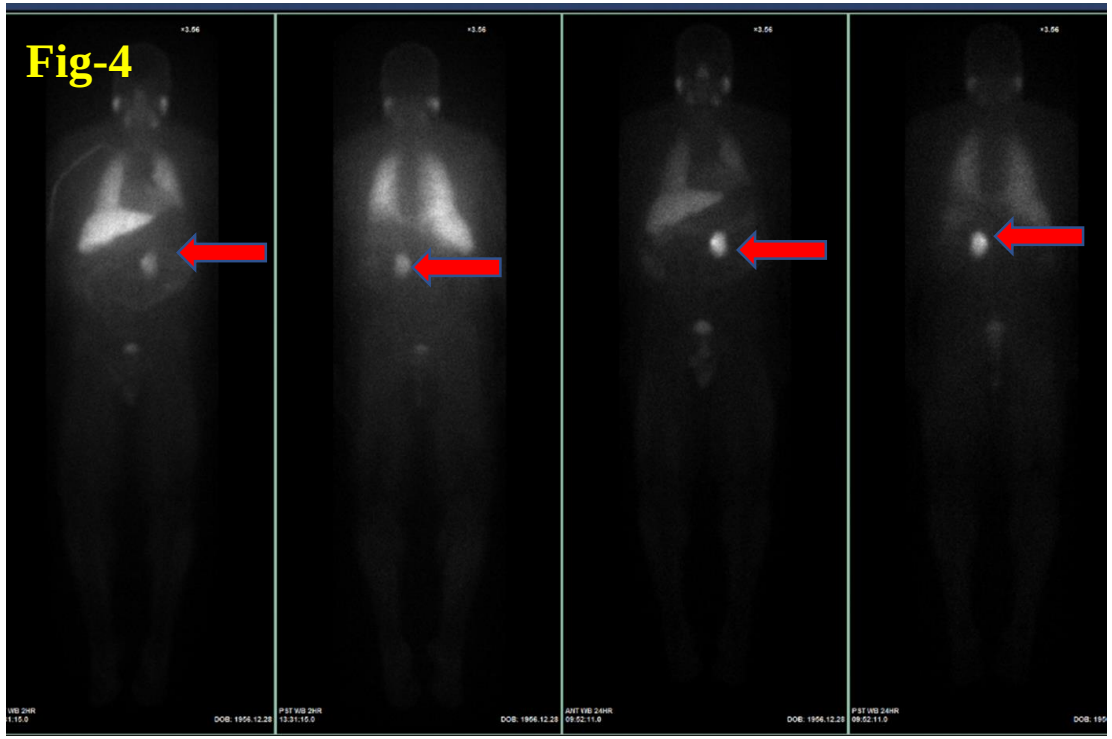


Figure-4: I-123 Meta-iodobenzylguanidine (MIBG) Scan planar images including delayed 24 hr images demonstrate uptake in the left retroperitoneal soft tissue mass (arrows).

Note: MIBG uptake after 24 h is normally seen in the myocardium, spleen, liver, urinary bladder, lungs, and salivary glands (which are rich in sympathetic innervation)

- The sensitivity of I-123 MIBG has been reported to range from 77 to 95%, with a specificity of 95–100%.
- MIBG has a reported false negative rate of 13% mainly due to the lack of sufficient tracer uptake in the lesion.
- Scenarios where MIBG has lower sensitivity for PPGL include tumors above the diaphragm, small tumors, or those that are necrotic and/or dopamine secreting and sometimes metastatic disease.
- The lower sensitivity has also been attributed to the variable affinity of MIBG to amine transport system, variable amount of cytoplasmic storage granules and loss of the amine transport system in dedifferentiated tumors.
- Nuclear medicine also provides targeted molecular therapy with MIBG, and somatostatin-targeted radioactive lutetium or yttrium.

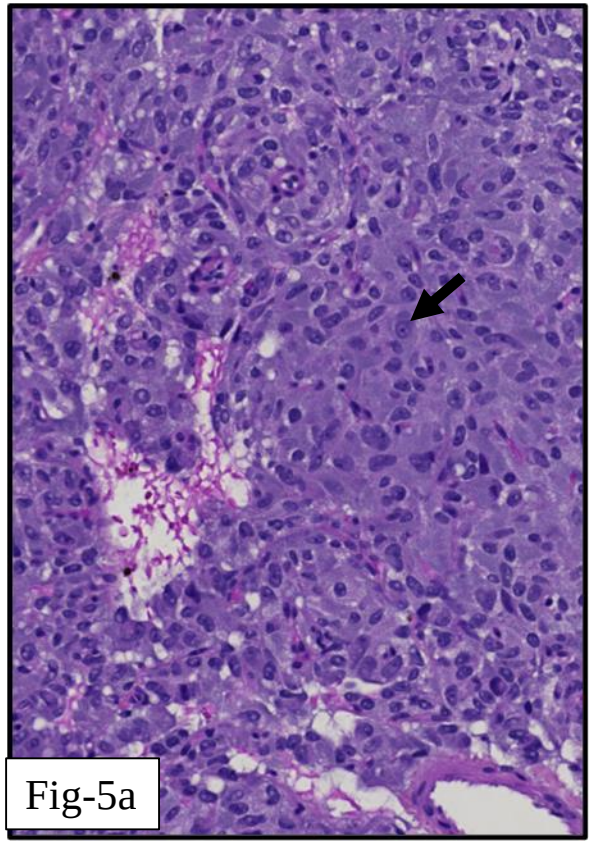


Fig-5a

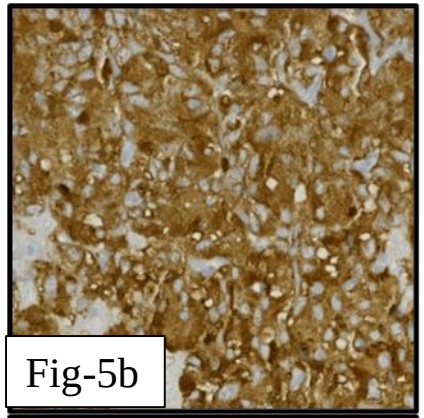


Fig-5b

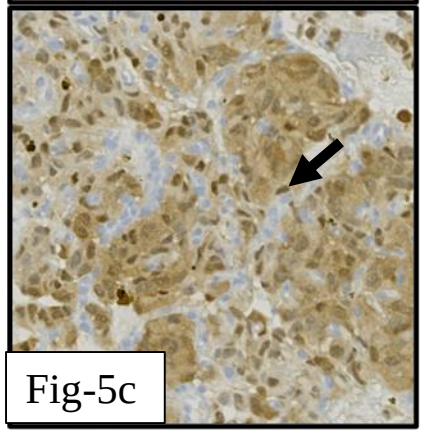


Fig-5c

Figure-5a Epithelioid tumor cells with amphophilic and finely granular cytoplasm, centralized nuclei ± nucleoli (arrow); (5b) Diffuse cytoplasmic staining of synaptophysin; (5c) S100 highlighting sustentacular cells (arrow).

- The precise pathogenesis of renal paraganglioma is unknown. Postulated theories include ectopic adrenal tissue, adrenal rests in kidney and aberrant migration of neuroendocrine progenitor cells from the neural crest during embryogenesis.
- PGL can be identified by presence of S-100 sustentacular cells, basophilic or amphophilic cytoplasm, salt- and-pepper chromatin, diffusely positive neuroendocrine markers (synaptophysin, CD56 and chromogranin), GATA3 (A transcription factor, seen in 80% of cases), and weakly positive keratin.
- Histologic scoring system, Pheochromocytoma of the Adrenal gland Scaled Score (PASS) ≥4 is considered to be predictive of clinically aggressive malignancy.
- The presence of sustentacular cells in the primary tumors could not be used as an absolute indicator of tumor metastatic potential.
- No definitive histological features such as mitotic rate, tumor size, vascular invasion and capsular invasion can discriminate benign from malignant PC.

Discussion

- Pheochromocytomas are catecholamine secreting tumors originating from adrenal chromaffin cells. They are termed as paragangliomas (PGL) when originate at extra-adrenal sites.
- PGL comprise 10% of PC. Estimated prevalence of 1 in 2000 to 1 in 6500.
- Most common site of PGL- Organ of Zuckerkandl (between the origin of the inferior mesenteric artery and the aortic bifurcation)
- Unusual extra-adrenal sites of origin include kidney, uterus and prostate.
- Associated with familial syndromes:

    Multiple endocrine neoplasia type 2 (MEN2)

    Neurofibromatosis type 1 or von Recklinghausen's disease

    Von Hippel–Lindau (VHL) disease

    Hereditary pheochromocytoma– PGLs syndrome (succinate dehydrogenase (SDH) mutations)

- Although CT and MRI have greater sensitivity than MIBG in detecting PGL, they are limited by lower specificity.

AJCC 8th staging system for pheochromocytoma/paraganglioma

Stage	Definition
I	T1 N0 M0
II	T2 N0 M0
III	T1-2 N1 M0 or T3 any N M0
IV	Any T any N M1

T1: Pheochromocytoma (i.e., within adrenal gland) <5 cm, no extra-adrenal invasion, T2: Pheochromocytoma (i.e., within adrenal gland) ≥5 cm OR paraganglioma-sympathetic, no extra-adrenal invasion, T3: Tumor of any size with local extension to surrounding organs.

M1a: bone-only metastases; M1b: distant lymph nodes, liver, or lung metastases; M1c: bone plus multiple other sites.

N0 No lymph node metastasis; N1 Regional lymph node metastasis

- Renal paraganglioma is rare and is difficult to distinguish from renal cell carcinoma, clinically and pathologically. To date, <20 cases of renal PGL are reported in the literature.
- PGL are usually benign and up to 10% of patients encounter malignant transformation.
- Due to difficulty in characterizing benign, and malignant tumors on imaging and histopathology, all PGL are considered malignant and treated by surgical resection.
- Recurrence rate of PGL ranges from 6.5- 16.5%, with large tumor size (>5 cm), age, tumor location (right-sided and extra-adrenal), and familial disease pattern (MEN2, VHL, NF1) being the critical risk factors.
- Treatment of recurrent tumor is unlikely to result in cure and hence MIBG can be considered as a palliative management. MIBG have shown symptom response in 75-90% and tumor response in 30-47% of patients.

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THANK YOU