Case Report

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Surgery Section

Primary Renal Large Cell Neuroendocrine Carcinoma in a Young Man

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ABSTRACT

Neuroendocrine tumours are usually located in the gastrointestinal or respiratory tract. A 23-year-old man was evaluated for loss of weight and a palpable left loin mass. CECT showed a large heterogeneously enhancing mass with calcification arising from the left kidney. He underwent an open radical nephrectomy. Histopathological examination revealed a large cell neuroendocrine carcinoma (LCNEC). LCNEC of the kidney is extremely rare and portends poor prognosis. It is usually a histopathological surprise and requires immunohistochemistry for confirmation.

Keywords: Cancer, Kidney, Neuroendocrine

CASE REPORT

A 23-year-old man presented with loss of weight and a palpable left loin mass for two months associated with fatigue. He did not have fever, lower urinary tract symptoms or hematuria. He had no history of substance abuse and no comorbid illnesses. A CECT scan revealed a heterogenous, exophytic 10x8x7cm mass in the left kidney with calcification. There was minimal enhancement with contrast [Table/Fig-1]. Considering the age of the patient and presence of calcification in the mass, differentials of neuroblastoma and wilm's were considered.

He underwent a left open transperitoneal radical nephrectomy. Intraoperatively, a large lobulated mass was seen arising from the lower pole of the left kidney [Table/Fig-2], there was no extrarenal extension, no lymph node enlargement.

Microscopic examination revealed that the renal parenchyma was infiltrated by a tumour with gyriform pattern composed of anastomosing trabeculae and papillae lined by tall columnar cells with moderately pleomorphic oval nuclei containing coarse chromatin and scanty to moderate amounts of eosinophilic cytoplasm.In areas foci of necrosis associated with increased mitotic activity are seen, here cells are more atypical, marked with nuclear hyperchromasia and pleomorphism with bizarre cells. The tumour was well demarcated with a thick fibrous stroma around [Table/Fig-3]. Tumour emboli are seen in lymphovascular spaces. There was no infiltration of the renal capsule.

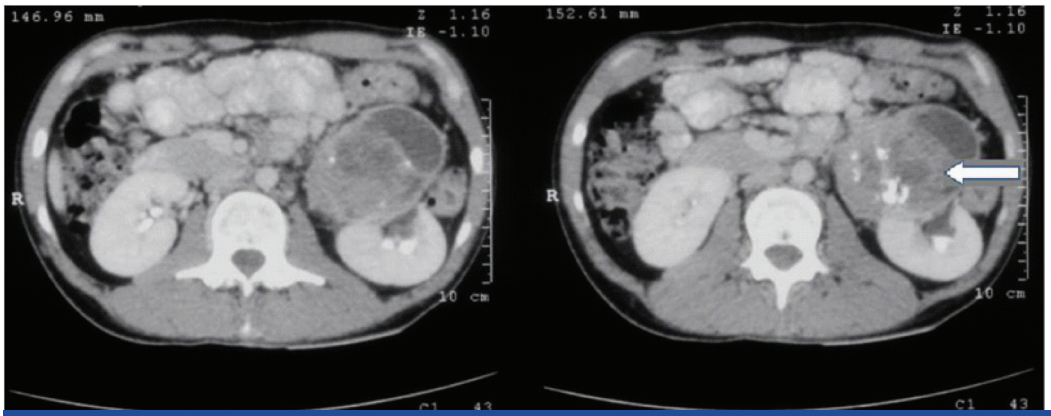
Presence of necrosis, atypia and increase in mitotic activity was more in favour of a large cell neuroendocrine carcinoma. This was confirmed by immunohistochemistry. The tumour cells were positive for vimentin, panCK, synaptophysin [Table/Fig-4] and chromogranin [Table/Fig-5]. They were negative for CD 10, CK7 and Epithelial Membrane Antigen (EMA). This profile was more in favour of a neuroendocrine carcinoma (Large Cell Neuroendocrine carcinoma, LCNEC). The MIB 1 index was over 20% in the poorly differentiated areas.

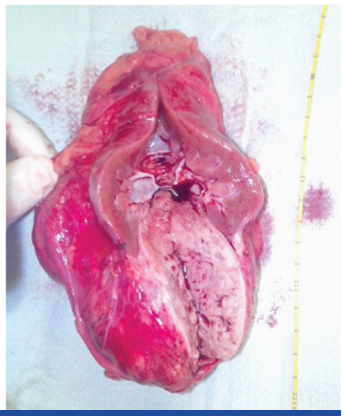
Post operative 24 h urine metanephrine and normetanephrine was within normal range and urine 5-hydroxyindole acetic acid (5-HIAA) was undetectable. A ^{68}Ga-DOTATATE-PET study done postoperatively showed no evidence of metastases or residual functioning neuroendocrine tumour.

Large Cell Neuroendocrine carcinoma portends poor prognosis. Hence, he received adjuvant chemotherapy with Cisplatin and Etoposide. There was no recurrent or residual tumour on follow up at six months.

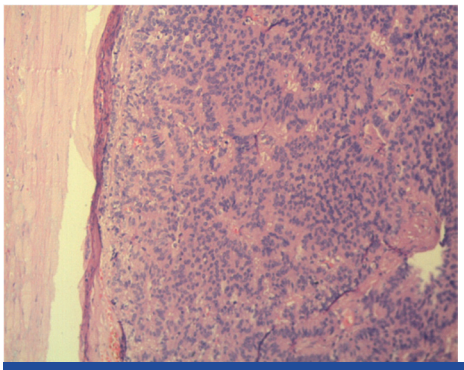
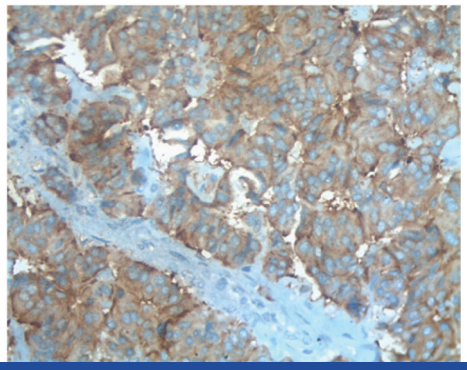
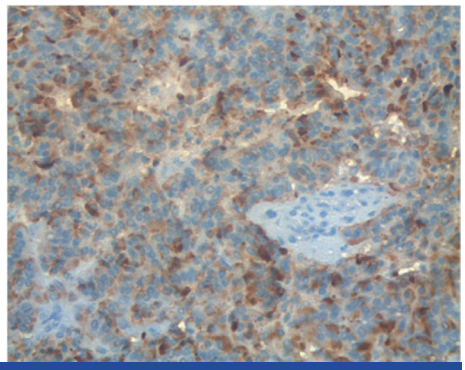
DISCUSSION

Primary renal neuroendocrine tumour is rarely diagnosed preoperatively, and is usually a pathological surprise. Most well differentiated neuroendocrine tumour (Carcinoid tumour) are located in the gastrointestinal tract or respiratory tract but unlike these, renal carcinoid rarely present with carcinoidsyndrome (<10%). The mean age at presentation is 59 years with no sex predeliction [1]. Renal carcinoid present like any other renal neoplasm, most are incidentally diagnosed and non specific in presentation, few present





[Table/Fig-1]: CECT scan revealed a heterogenous, exophytic 10x8x7cm mass in the left kidney with calcification **[Table/Fig-2]:** Cut section of the gross specimen showing lobulated mass arising from the lower pole of the kidney

[Table/Fig-3]: H&E x20 showing tumour composed of tall columnar cells with nuclear hyperchromasia, pleomorphism and surrounding thick fibrous stroma **[Table/Fig-4]:** Tumour cells positive for synaptophysin on immunohistochemistry **[Table/Fig-5]:** Tumour cells positive for chromogranin on immunohistochemistry

with abdominal pain and hematuria. With about 90 cases of renal NET reported in English literature, the classification and behaviour of these tumours still remains uncertain [2].

Interestingly, Horseshoe kidneys have a higher incidence of carcinoid tumours (17.6% of all renal carcinoid), located mostly in the isthmus. It is postulated that hyperplasia of interspersed neuroendocrine cells within the metaplastic or teratomatous epithelium or nest of misplaced progenitor cells in the isthmus can be the origin of renal carcinoids [1].

Neuroendocrine tumours originate from the neural crest cells and are divided into neural type (which include paraganglioma and neuroblastoma) and epithelial type [3]. Epithelial type includes well-differentiated NE tumour (Carcinoid), well-differentiated NE carcinoma (NEC), and poorly differentiated (large cell NEC and small cell carcinoma (SCC). The most common characteristic findings on CT are calcification, poor enhancement on contrast study and rarely, a cystic neoplasm [2]. Octreotide scintigraphy has a high sensitivity (85%) in detecting functioning neuroendocrine tumour but during preoperative imaging, the normal renal parenchymal uptake may obscure small NET [4].

The diagnosis is made on histopathological examination aided by immunohistochemistry. Histologically, carcinoid are polygonal tumour cells with indistinct cell borders, round, regular nuclei, 'salt and pepper' chromatin and infrequent mitosis and atypical cells. They are positive for neuroendocrine markers including chromogranin A, synaptophysin, CD56 (NCam) and neurone specific enolase; hormonal polypeptides (serotonin, calcitonin, adrenocorticotropic hormone) may be detected. As in the small cell carcinoma (SCC) variant, large cell NEC also display malignant characteristics which are increased mitosis, vascular emboli, tumour necrosis and perivascular DNA deposits (Azzopardi phenomenon) [5].

Well differentiated carcinoid has a variable prognosis, whereas neuroendocrine carcinoma (large cell neuroendocrine carcinoma (LCNEC) and small cell carcinoma (SCC) has a poor prognosis [3]. Older patients (>40years), large tumour (>4cm), pure tumour on cut surface, mitosis higher than 1/10 high power fields, metastasis and tumour extending through the capsule are considered poor prognostic factors [4].

Surgical resection is the mainstay of treatment with curative potential even when regional lymph nodes were involved [4]. Metastatic disease has the worst prognosis. Poorly differentiated NEC has been treated with platin-based therapy but the outcome is not known. Somatostatin analogs (Octreotide) [6] has benefitted patients with or without chemotherapy in symptomatic pulmonary and intestinal carcinoid but their effect in renal carcinoid and neuroendocrine carcinoma is not known. Radionucleotide therapy90Y/177Lu-DOTATATE has shown promising results in neuroendocrine carcinoma of other origin [7,8], but long term effect is not known. Everolimus (An m-TOR kinase inhibitor) and sunitinib has been used in advanced pancreatic carcinoid after failure of chemotherapy and its use in renal carcinoid is promising [8,9]. LCNEC is a rare primary renal malignancy and this case is the youngest patient reported so far [1,3,4,10].

CONCLUSION

The diagnosis of renal LCNEC though rare, demands cognizance on the part of both the urologist and pathologist in order to ensure appropriate management of this entity.

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