



Unusual Sites of Rcc Metastasis-Case Series

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Abstract

Clear cell Renal cell carcinoma (RCC) is the most common type of renal cancer. It is potentially a lethal cancer with a high propensity of metastasis. Patients with clear cell RCC have the highest risk of metastasis. The rich vascular proliferation noted in RCC is the cause of increased hematogenous spread. The usual sites of metastasis include lung, liver, bones and adrenals. The present study focuses on cases of clear cell RCC metastasis to few unusual sites as duodenum, sole of foot, submandibular gland and bronchus. It must be considered in the differential diagnosis of clear cell tumours even at rare sites.

Keywords: Clear cell RCC, lethal, rare sites.

Introduction

Renal cell carcinoma (RCC) has a potential to metastasize to almost any site. In descending order of frequency, the most common sites are the lung, lymph nodes, liver, bone, adrenal glands, brain, heart, spleen, intestine, and skin.^[1] It is distinguished by its remarkable metastatic potential, related to the fact that: (i) it receives 25% of the effective circulating volume and (ii) it has a great capacity to adapt to different vascular microenvironments.^[1,2] Here we report renal cell carcinoma metastasis to a few unusual sites.

Case 1

A 53 year old lady was referred to our centre as a case of duodenal mass lesion with intraluminal bleed. She had no history of jaundice/vomiting. There is a history of left nephrectomy for RCC (6years back). Ultrasonography of abdomen showed para-aortic focal lesion at C- loop of duodenum. Differentials included - Metastasis/GIST. Contrast Enhanced computed tomography (CECT) showed 6 cm mass lesion in medial wall of D1 with no dilatation of

common bile duct. Lesion was seen abutting head of pancreas with loss of fat plane. Pancreaticoduodenectomy was done.

Grossly, duodenum on cut section showed a grey white growth measuring 1 cm in greatest diameter in the medial wall; in close proximation to pancreas. On serial section identified a grey white granular growth measuring 3.5 cm x 1.4 cm involving the duodenal wall, abutting the duodenal mucosa with infiltration into the pancreas. Microscopy showed a neoplasm involving and replacing the duodenal wall composed of polygonal cells arranged in sheets and nests. Cells have pale eosinophilic to clear cytoplasm, vesicular nuclei and nucleoli. Neoplasm is seen to infiltrate the pancreatic tissue. (Fig.1). Immunohistochemical analysis showed pan CK, Vimentin, CD10 positivity (Fig 2) and high ki 67. CD34 and CD117 were negative.

Case 2

68 year old gentleman presented to the surgery OPD with complaints of swelling over the sole of the left foot. It was slowly progressing in size and painful.

He had history of clear cell RCC and underwent right nephrectomy 3 years back. Incision biopsy from the foot lesion was taken. Microscopy revealed necrotic tissue with nests of tumour cells with clear cytoplasm and distinct cell borders. (Fig 3) The patient had multiple brain and liver metastasis as well. He succumbed to his disease. Immunohistochemistry showed pan CK, Vimentin, CD10 (Fig4) positivity.

Case 3

58 year old man with history of neck swelling for 6months.He had past history of nephrectomy done 6 years back for RCC (Right nephrectomy). Ultrasonography of neck showed evidence of mass tissue in right submandibular gland with irregular borders measuring 3.8 x 2.7 cm. FNAC showed atypical cells suggestive of malignancy. Right submandibular sialadenectomy was done. Macroscopy revealed a nodular enlarged tan, yellow mass with irregular borders. Microscopy showed sheets of cells with clear cytoplasm and distinct cytoplasmic borders. Network of thin arborizing delicate vessels were present. (Fig5). Cells showed CD10 positivity (Fig6), CEA and S100 negativity.

Case 4

71 year old male patient, known case of COPD (Chronic obstructive pulmonary disease) presented with complaints of cough and breathlessness. He had history of left nephrectomy done 6 years back for RCC. Bronchoscopy revealed small nodule at opening of right lower lobe bronchus. Endobronchial biopsy showed adenocarcinoma with clear cells and distinct cell borders. Delicate thin walled vascular network noted.(Fig7) Immunohistochemistry revealed positive CD10 expression (Fig8) .TTF1, CK7 and CK20 were negative.

Discussion

Renal cell carcinoma (RCC) is one of the most aggressive genitourinary cancers. Distant metastasis years after presumed curative resection are known in RCC. The usual distant spread is hematogenous to lung, liver and bones. Due to the fact that the patterns of metastases from renal cell carcinomas are not clearly defined, there have been several reports of cases of renal cell carcinoma associated with rare metastatic sites and atypical presenting symptoms.

Renal cell carcinoma metastasis can involve any part of the bowel and accounts for 7.1% of all metastatic tumors to small intestine. Duodenal metastasis from RCC is very uncommon and only few cases have been described in the literature. ^[3,4] Metastatic lesions of the duodenum are most frequently located in the periampullary region or the duodenal bulb. On endoscopy the lesion can be seen as a submucosal mass with ulceration, multiple nodules of varying sizes or raised plaques. ^[3] The majority of patients are found to have metastasis within a year after nephrectomy though it can be seen even after several years. ^[4] Thus, in all patients with a history of RCC, gastrointestinal bleeding should be considered as a possible cause of metastasis. Our patient was referred to a higher centre for further treatment.

The differential diagnosis of clear cell lesions in the duodenopancreatic area should include clear cell variant of Pancreatic Neuroendocrine tumours (Von Hippel Lindau), Pancreatic ductal adenocarcinoma, Perivascular Epithelioid tumours, Intraductal tubulopapillary neoplasm with clear cell phenotype and renal cell carcinoma metastasis.

Metastasis from RCC to the foot is rare (0.01%). It is usually a late manifestation of disseminated disease. Bloodgood reported the first case of metastasis in the foot in 1920. ^[5] Factors related to the low incidence of acrometastasis are the paucity of red marrow in these bones, the lower temperature gradient in the acral areas suboptimal for tumour growth. ^[6] RCC is well known for its unpredictable presentation and tendency to metastasize early. Rarely foot metastasis may be the first manifestation of an occult cancer. This shows the importance and, at the same time, the difficulty of early diagnosis of foot metastases because they are often initially mistaken for more benign processes, such as trauma, infection, abscess etc. ^[6] In our case it was clinically thought of as pyogenic granuloma. But the patient later succumbed to death.

The secondary neoplasms of the salivary gland represent 5% of all salivary gland tumours. The parotid gland is the most commonly compromised gland, whereas it is extremely rare to find metastasis in the submandibular gland. Regarding metastases of RCC to the submandibular gland, there are only seven cases reported in the literature. The critical period in which the metastasis appears is 3 to 5 years

after diagnosis. ^[7] Most close differential is clear cell carcinoma of salivary gland having cells with clear cytoplasm, distinct cell borders, arranged in nests surrounded by sclerotic or hyalinized stroma and variable fibrocellular myxoid stroma. In case of RCC metastasis, cells show CD10 positivity, vimentin and cytokeratin co-expression. The treatment given to each patient depends on the stage of the illness at the moment of diagnosis. ^[8] After the surgical excision our patient was given chemoradiation.

The lung is a common site for metastasis from extrathoracic tumours, but endobronchial metastases are rare. ^[9,10] The most common symptoms are dyspnoea, cough, and hemoptysis as seen in our patient. Endobronchial metastases can involve any airway level but have a predilection for the right lung in up to 80% of cases, although the reason for this is not clear. ^[11] The therapeutic approach to an endobronchial tumour is determined by the characteristics of the primary tumour, biological behaviour, anatomic location of the endobronchial metastasis, and the patient's performance status. ^[11]

Conclusion

RCC, especially clear cell variant is associated with aggressive behaviour and has a greater propensity for metastatic spread. It has been associated with rare metastatic sites. The present study has focussed on these rare distant sites like the sole of foot, submandibular gland, pancreas and duodenum (Table-1). This highlights the importance of considering the same in differential diagnosis of clear cell tumours, even at unusual sites.

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Table 1: Case summary

Case	Age	Sex	Metastatic Site	Years after nephrectomy
Case 1	53	Female	Duodenum	6
Case 2	68	Male	Sole of foot	3
Case 3	58	Male	Submandibular gland	6
Case 4	71	Male	Bronchus	6

Fig1: polygonal cells arranged in sheets with pale eosinophilic to clear cytoplasm, vesicular nuclei and nucleoli.(H&E stain,x400)

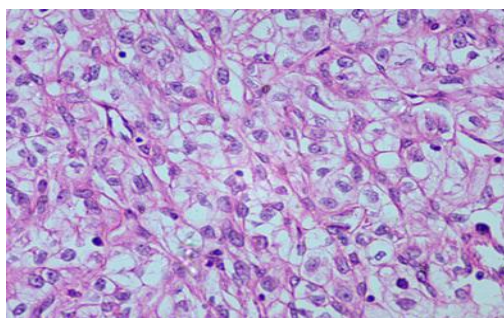


Fig 2: Tumour cells with CD 10 positivity(x400)

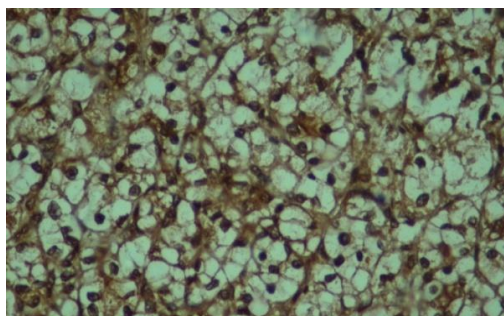


Fig 3: Necrotic tissue with nests of tumour cells with clear cytoplasm and distinct cell borders.(x100)

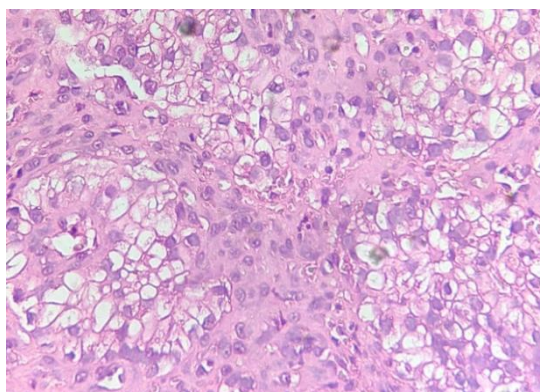


Fig4: Tumour cells with CD 10 positivity (x400)

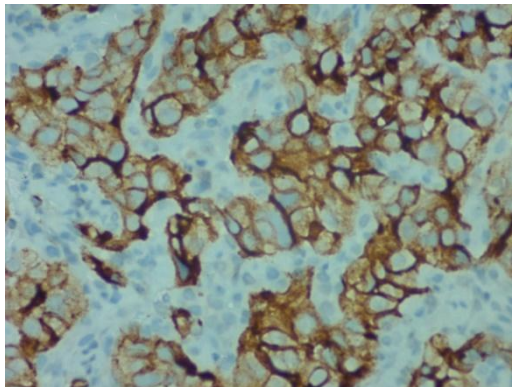


Fig5: Sheets of cells with clear cytoplasm and distinct cytoplasmic borders. Network of thin arborizing delicate vessels were present.(H&E stain,x100)

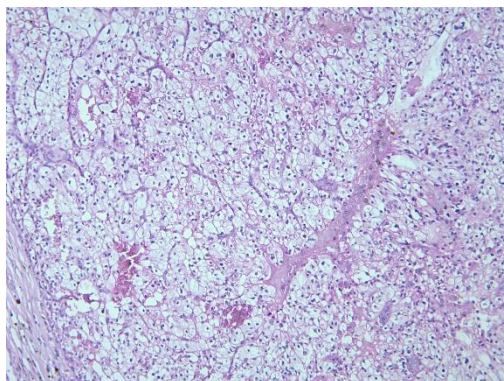


Fig 6: Tumour cells with CD 10 positivity(x400)

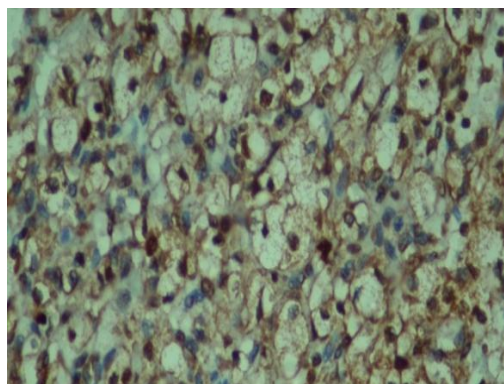


Fig 7: Adenocarcinoma with clear cells and distinct cell borders. Delicate thin-walled vascular network noted.(H&E stain, x400)

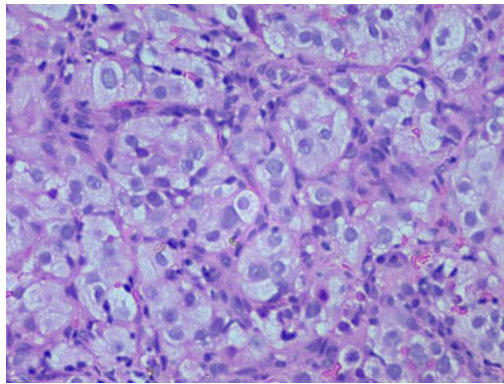


Fig 8: Tumour cells with CD 10 positivity(x400)

