Melanocytic differentiation in clear cell renal cell carcinoma: a rare case report with review of literature

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Abstract

Renal cell carcinoma has been classified into various subtypes with newer emerging entities. The tumors have different cytogenetic, molecular characteristics and recognizing histologic patterns of Renal cell carcinoma(RCC) is important not only for correct diagnosis, but also for providing insight into the biological behavior of the tumor and subsequent appropriate medical care for the patient. Pigments other than hemosiderin have been described in renal cell carcinoma but a very few case reports are there of melanin deposition. Melanotic tumors, either primary or metastatic, are rare in the kidney. Herein we present a rare case of RCC with melanocytic differentiation, a variant that may lead to diagnostic error and may warrant the classification of this entity separately.

Keywords: Renal cell carcinoma, Melanin, Immunohistochemistry and HMB45.

Introduction

Renal cell carcinoma accounts for approximately 3% of adult malignancies and 90%-95% of neoplasms arising from the kidney.(1) The age-adjusted incidence of renal cell carcinoma is increasing by 3% per year. RCC has been classified into various histologic subtypes: clear cell, multilocular clear cell, papillary, chromophobe, carcinoma of the collecting ducts of Bellini, renal medullary carcinoma, Xp11 translocation carcinomas, carcinoma associated with neuroblastoma, mucinous tubular and spindle cell carcinoma and renal cell carcinoma unclassified. The newer emerging entities include tubulocystic carcinoma, carcinoma associated with end stage renal disease, follicular RCC, clear cell papillary and cystic RCC, oncocytic papillary RCC and leimyomatous RCC.(2) Pigment other than hemosiderin has been documented in different types of RCC(3-9) expanding the spectrum of the histologic features of RCC and increasing the difficulty of diagnosing the tumor. We report a rare case of clear cell RCC exhibiting melanocytic differentiation.

Case Report

A 33-year-old female presented with complaints of abdominal pain. Per-abdominal examination revealed a soft tender mass measuring 4 cm in left lumbar region. Ultrasonography of abdomen showed a mass in lower pole of left kidney. Computed tomography displayed a mass measuring 4x4cm in lower pole of left kidney (Fig. 1A). After presurgical evaluation, patient underwent left partial nephrectomy.

Pathological findings

Gross Features: Partial nephrectomy was done and kidney specimen measured 6×5× 3.5cm. Cut surface showed a circumscribed growth with dark brown tumor area measuring 4x4cm, without any capsular breach(Fig. 1B).

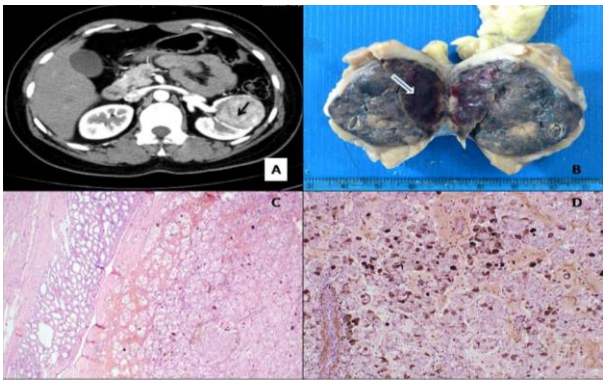

Fig. 1: A: Abdominal Computed Tomography scan showing a mass in the lower pole of the left kidney; B: Gross picture of the mass showing well-defined solid tumor with blackish areas having well defined margin; C: Histolopathology sections showing a well circumscribed tumor with normal kidney (H&E, x200); D: Tumor cells arranged in diffuse sheet and alveolar pattern alongwith abundant amount of intracytoplasmic brown pigment (H&E, x200)

Histopathological examination: Microscopically, tumor cells were disposed in solid, sheets alveolar and acinar growth pattern with intervening rich sinusoidal network of delicate vascular channels. Tumor was composed of cells with abundant clear-to-granular cytoplasm (Fig. 1C) and centrally located nuclei with single prominent nucleoli (Fuhrman nuclear grade-IV). Wide areas of hemorrhage is also seen. In majority of tumor cells, dark brown pigment was observed in cytoplasm (Fig. 1D, 2A). In view of wide areas of hemorrhage it was thought prudent to rule out

hemosiderin laden macrophages with Perls stain (Fig. 2B). The pigment was dark brown, granular, non-refractile and stained black with Masson Fontana stain (Fig. 2C, 2D). The kidney tumor was predominantly composed of clear cells with focal granular cells.

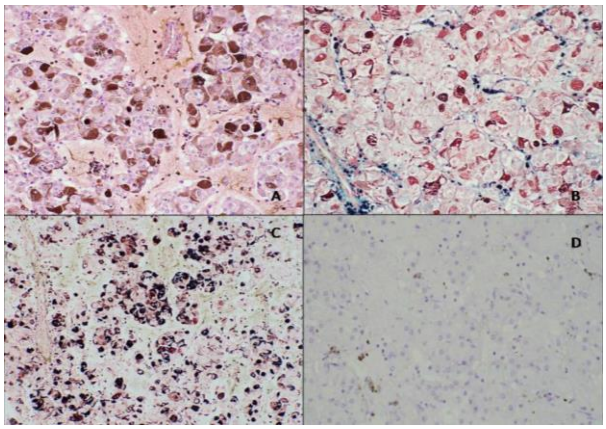

Fig. 2: A: Tumor cells showed moderate amount of clear to granular eosinophillic cytoplasm having moderately pleomorphic nuclei with occasional prominent nucleoli. There are abundant amount of intracytoplasmic brown pigment in most of tumor cells (H&E, x400). B: Perls Stain in tumor cells showing blue color staining of the pigment and negative in black colour pigment. (x400); C: Tumor cells show black color staining of the pigment on Masson Fontana stain (x200); Tumor cells showed brown pigment was negative with Masson Fountan bleach (x200)

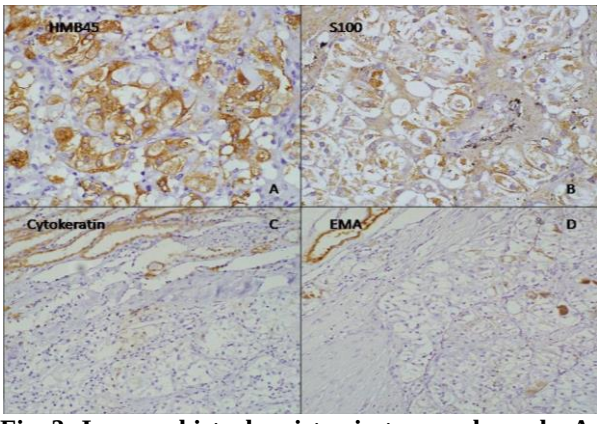

Fig. 3: Immunohistochemistry in tumor showed - A: most of the tumor cells are positive for HMB-45 (peroxidase anti-peroxidase, x400) and B: Positive for S-100 (peroxidase anti-peroxidase, x400); C: Negative for pancytokeratin (peroxidase anti-peroxidase, x100) and D: Negative for Epithelial Membrane Antigen (peroxidase anti-peroxidase, x100). Renal tubular epithelial cells are showing positive staining for Pancytokeratin and Epithelial Membrane Antigen as control

Imunohistochemical Study: Immunohistochemistry (IHC) was performed, tumor cells are strongly positive for HMB45 (3A), S100(3B), and negative for CK(3C), EMA(3D), CD10. A confirmed diagnosis of renal cell carcinoma with melanotic differentiation was made.

Discussion

The pigmented renal cell carcinoma is an uncommon tumor which represents a diagnostic dilemmas and challenge requiring a differential diagnosis with other primary and secondary pigmented neoplasms of the kidney.

RCC originate from the renal proximal tubules, with varied morphologic subtypes based on morphology, histochemistry, clinical behavior, and genetic alterations. Clear cell renal carcinoma (CRCC), papillary renal carcinoma and chromophobe renal carcinoma are most frequently seen and constitute 95% of adult RCC. Clear cell carcinoma alone accounts for 75% of adult RCC.[(1)] Non-hemosiderotic pigmentation in renal cell carcinoma has been described in the clear cell and the chromophobe variant of RCC. Kamishima et al.[(2)] reported the first case of pigmented RCC and it was attributed to abnormal lysosomes, with histochemical features consistent with neuromelanin. This was followed by more cases from the same group of authors. Fukuda et al.[(4)] reported neuromelanin in 3 out of 5 cases; a finding that suggested the lysosomal origin of granules in those three cases. One of these three cases, the diagnosis was chromophobe RCC. A total of 8 cases (including current case) of pigmented clear cell RCC with intracytoplasmic pigment deposition have been reported in English literature,[(3-10)] (Table 1).

Recognition of melanin pigment is essential to differentiate from metastatic malignant melanoma and others tumors comprising of neuroendocrine neoplasm, neuroectodermal tumors, pigmented perivascular epithelioid clear cell tumor (PEComa), and pigmented pheochromocytoma. With the emergence of various newer entities like tubulocystic carcinoma, carcinoma associated with end stage renal disease, follicular RCC, clear cell papillary and cystic RCC, oncocytic papillary RCC, leimyomatous RCC, it is also prudent to think whether a separate classification is needed for the said entity. It has been proposed that pigmented renal cell carcinoma may be a unique variant of renal cell carcinoma.[(1,6)] Pigment in our case is composed of dark brown nonrefractile fine granules which stained black with Masson Fontana, consistent with melanin. It was further confirmed by immunhistochemistry when the cells were for found immunoreactive for HMB-45 and S100.

Dark brown endogenous pigments other than melanin found in renal cell carcinoma are hemosiderin, homogentisic acid and lipofuschin. Hemosiderin granules are variably sized, refractive and golden brown and can be confirmed with Perl's stain. Lipofuschin

shows perinuclear location. Homogentisic acid is a brown black pigment with alkaptonuria, a rare metabolic disease. Which presents in the skin, connective tissue, and cartilage of patients with alkaptonuria, a rare metabolic disease. Our patient did not have alkaptonuria, and the pigment existed only in the tumor cells.

Conclusion

In summary, we report a rare case of pigmented clear cell RCC with melanocytic differentiation which expands the spectrum of morphological changes of RCC. The behavior of pigmented clear cell RCC is yet to be ascertained given rarity of the condition. Further molecular and cytogenetic studies are needed on these types of pigmented clear cell Renal cell carcinoma.

Table 1: Reported cases of pigmented clear cell renal cell carcinoma and review of literature[10]

Authors	Age/ Sex	Diagnosis	Type of pigment	Special stains	IHC	Electron microscope	Follow up
Kamishima et al. 1995	38/F	CRCC	Neuromelanin	PAS/PASD + MF+,PB-Schmorl-	HMB 45-S100-	No melanosome	A/W-8 mon
Fukuda et al. 1997	61/M	CRCC	Neuromelanin	PAS/PASD + MF+,PB-	HMB 45-S100-	No melanosome	A/W-52mon
Hirokawa et al. 1998	40/F	CRCC	Neuromelanin	PAS/PASD + MF+,PB-Schmorl-	HMB 45-S100-	N/A	N/A
Lei et al. 2001	26/F	CRCC	Melanin	MF+	HMB 45+ S100+ CK-	N/A	A/M-15mon
Rossi et al. 2009	48/M	CRCC	Neuromelanin	PAS/PASD + MF+,PB-	HMB 45-S100-	No melanosome	A/W-4mon
Matalka et al. 2013	27/F	CRCC	Neuromelanin	PAS/PASD + MF+,PB-	HMB 45-S100-	No melanosome	A/W-120mon
Kiran krishne Gowda 2014	12/F	CRCC	Melanin	PAS/PASD + MF+,PB-Schmorl+	HMB 45+ S100+, CK-, EMA-	N/A	A/W-7mon
Current case Rao et al 2016	30/f	CRCC	Melanin	MF+ Perl Stain-	HMB 45+ S100+, CK-, EMA- and CD-	N/A	A/W till date

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