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Renal cell carcinoma with t(6:11) (p21;q12). A case report highlighting distinctive immunohistologic features of this rare tumor

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Abbreviations:
RCC, renal cell carcinoma
TFE3, translocation factor E3
TFEB, translocation factor EB

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ABSTRACT

INTRODUCTION: Renal cell carcinoma (RCC) with t(6:11) (p21;q12) are extremely rare, fewer than 30 cases have been reported in literature. These tumors are characterized by specific chromosomal translocation involving TFEB, as against the more commonly known TFE3 (Xp11.2) translocation associated RCCs. The distinctive immnohistologic features are helpful in enabling a diagnosis of this rare tumor, otherwise diagnosed by fluorescence in situ hybridization assay, specific for detecting TFEB gene rearrangement.
PRESENTATION OF CASE: Herein, we report a case of this rare tumor in a 11 years old boy, with the objective of highlighting distinctive light microscopic and immuno-phenotypic features of this rare sub-type of translocation associated renal cell carcinoma, otherwise diagnosed by fluorescence in situ hybridization technique. Morphologically tumor showed distinctive biphasic population of cells, large epitheloid cells with voluminous eosinophillic cytoplasm and smaller cells with much lesser amount of cytoplasm and small rounded nuclei. The smaller cells at places clustered around hyaline pink material forming "pseudorosettes". population. Immunohistochemically both types of tumor cells showed negativity for pan CK (cytokeratin), EMA (epitheleal membrane antigen) and TFE3 (transcription factor E3). HMB 45 (human melanoma black 45) and Melan- A /MART 1 (melanoma antigen recognized by T cells) were moderate to strongly expressed.
DISCUSSION: On review of literature, most RCCs with t(6;11) translocation have been reported to be negative for pan cytokeratins and EMA. Published literature also shows that the most distinctive immunohistochemical feature of t(6;11) translocation RCC is nuclear staining for TFEB protein. Immunostains for TFE3 have always been negative in the reported cases. It is noteworthy that immunoreactivity for melanocytic markers HMB45 and Melan A and immunonegativity for epithelial markers pan CK and EMA may lead to misdiagnosis of angiomyolipoma to the unwary.
CONCLUSION: Knowledge of distinctive morphological and immuno-histochemical features of this tumor can help in establishing a diagnosis of this rare subset of translocation associated RCC on routine hematoxylin and eosin (H and E) staining and immunophenotyping.

1. Introduction

Renal cell carcinoma (RCC) with t(6:11) (p21;q12) are extremely rare, fewer than 30 cases have been reported in literature [1–3]. These tumors are characterized by a specific chromosomal translocation involving the transcription factor EB (TFEB) [4]. This distinctive tumor was first described by Argani et al. [4]. Increasing evidence has shown that these tumors possess unique morphologic and immunohistochemical features. The identification of overexpression of TFEB protein by immunohistochemistry or detecting a t(6:11) (p21;q12) translocation by fluorescence in situ hybridization is necessary for accurate diagnosis [5]. We hereby present a case report of this rare tumor in a 11 year old boy, with the objective of highlighting its distinctive immuno-histologic features.

2. Case report

Patient, a 11 years old boy, presented at our institute with complaints of lump in the right hypochondrium noticed since last 10 days. He also complained of fever since last 10 days. No history of trauma or any other significant past history was reported. An ultrasound study revealed a large heterogeneous appearing mass lesion arising from upper and mid pole of the right kidney with increased vascularity. CT scan showed a large heterogenously enhancing mass lesion arising from the upper pole of right kidney with arterial enhancement and washout on delayed phases, suggestive of neoplastic etiology. A possibilty of Renal Cell Carcinoma or Wilm's Tumor was suggested.

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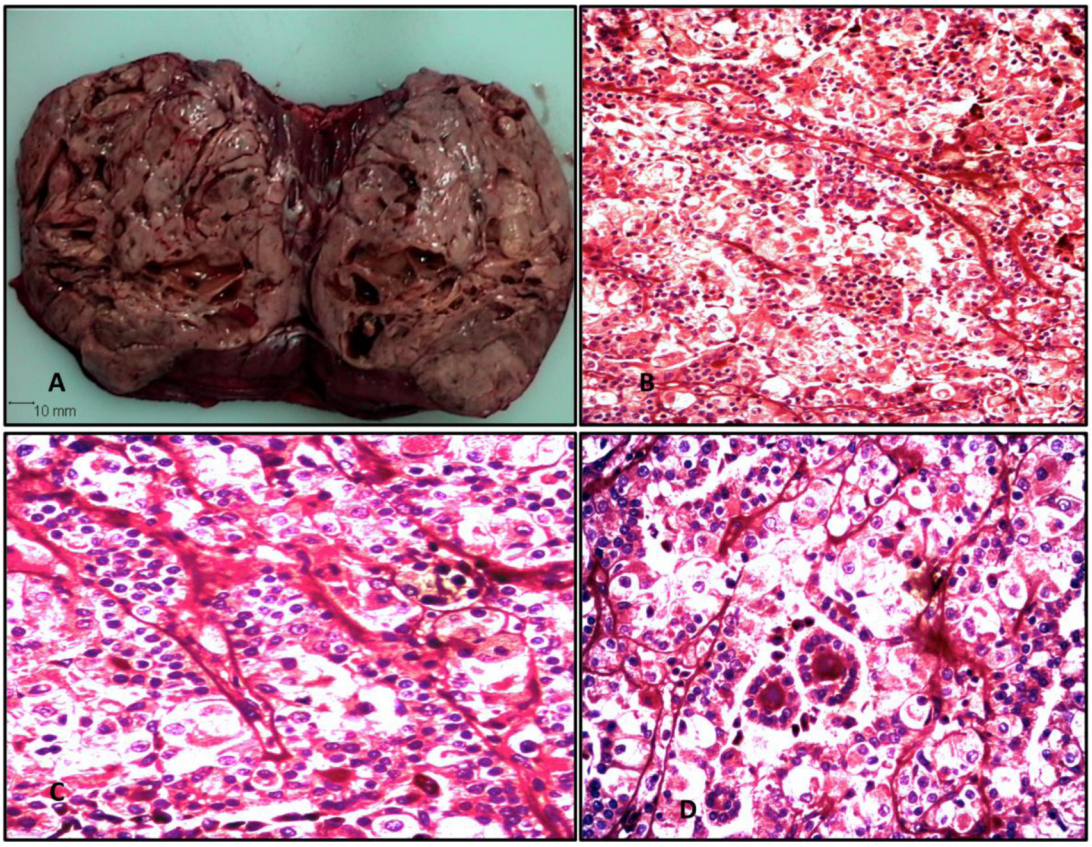

Fig. 1. (A) Gross findings on Nephrectomy specimen: large well-delineated, nodular, tan- brown colored tumor nearly completely replacing the normal renal parenchyma. (B) H and E10× (C) H and E 20×: biphasic population of cells, large epitheloid cells with voluminous eosinophillic cytoplasm and smaller cells with much lesser amount of cytoplasm and small rounded nuclei. (D) The smaller cells at places clustered around hyaline pink material forming "pseudorosettes".

A right radical nephrectomy was performed and sent for histopathological examination. Bisected kidney showed a large well-delineated, nodular, tan- brown colored, soft to firm tumor measuring 13.7 × 11.0 × 8.0 cm, nearly completely replacing the normal renal parenchyma (Fig 1A). No necrosis was identified. Morphology revealed a biphasic population of cells (Fig 1B and C), large epitheloid cells with voluminous eosinophilic cytoplasm and smaller cells with much lesser amount of cytoplasm and small rounded nuclei. The smaller cells at places clustered around hyaline pink material forming "pseudorosettes"(Fig 1D). Dark brown pigmentation was observed in small cell population. Immunohistochemically (Fig 2A–E) both types of tumor cells showed negativity for pan CK (cytokeratin), EMA (epitheleal membrane antigen) and TFE3 (transcription factor E3). HMB 45 (human melanoma black 45) and Melan A/MART 1 (melanoma antigen recognized by T cells) were moderate to strongly expressed. Subsequently, fluorescence in situ hybridization studies done at an outside referral institute showed t(6:11) (p21;q12) renal cell carcinoma.

3. Materials and method

Tissue was fixed in 10% neutral buffered formalin and embedded in paraffin. Immunohistochemical analysis was done using following antibodies: pan CK (AE1 and AE3,Biogenex), EMA (E29, Biogenex), TFE3 (MRQ-37, Cell Marque, 1:100), HMB45 (HMB45, Biogenex), and Melan A (Clone A103, Dako). Immunoreaction was performed using the Horse Radish Peroxidase- conjugated streptavidin (Biogenex Polymer HRP kit). Diaminobenzidine (DAB) was used as chromogen.

4. Discussion

t(6:11) (p21;q12) associated RCCs are rare subsets of the distinctive entity of translocation associated RCCs as described in 2004 WHO classification of renal tumors [6]. These translocations most frequently involve the TFE3 gene on locus Xp11.2 and less frequently involve the TFEB gene on locus 6p21 [7]. Less than 30 cases of t(6:11) (p21;q12) associated RCCs have been reported in literature [1–3]. Recently Rao et al. reported additional 7 cases [8]. The translocation of t(6;11)(p21;q12 or q13) causes fusion of Alpha gene on 11q12 or q13 with the TFEB gene on 6p21, this results in overexpression of native TFEB protein. Review of the published data indicates that RCC with t(6;11) translocation is seen predominantly in children and young adults, minority of patients being older adults [9]. The patient in our case is 11 years old. Microscopically as in our case biphasic pattern of tumor, constituted by large epitheloid cells with voluminous pink cytoplasm and smaller cells centered around hyaline material, so called 'pseudorosette' pattern was the most common pattern. Published literature also shows that the most distinctive immunohistochemical feature of t(6;11) translocation RCC is nuclear staining for TFEB protein [10–12]. Argani et al. [2] detected strong nuclear TFEB labeling in all seven RCCs with t(6;11) translocation studied, in contrast to 1089 other unrelated neoplasms and normal tissues that showed negativity for nuclear labeling of this protein. Noteworthy fact is that melanocytic markers HMB45 and Melan-A are commonly positive in these tumors [4,5]. Moderate to strong expression of HMB45, and Melan-A was seen in our patient case as well. TFEB was however not performed in our case. Most RCCs with t(6;11) translocation are negative for pan cytokeratins and EMA. Only four patient cases have been positive for pan CK [1,3,12] and two have been positive for EMA [5].

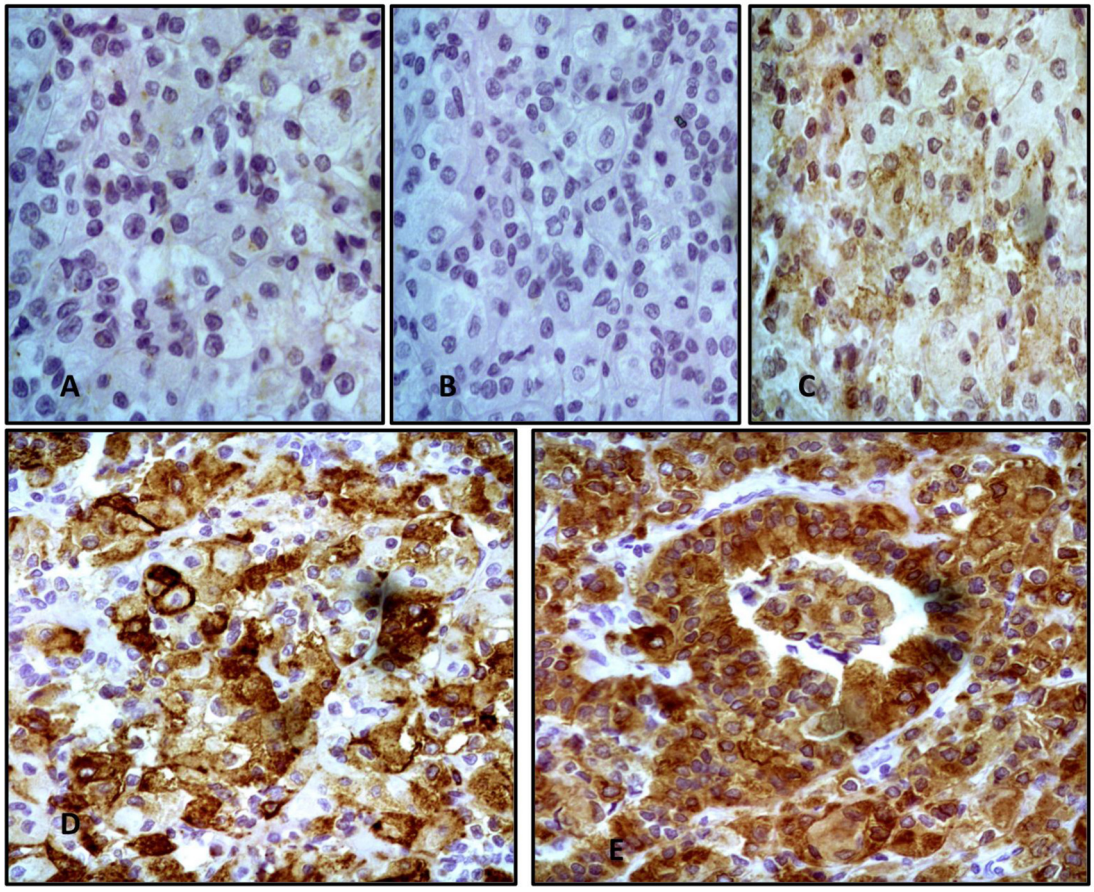

Fig. 2. Immunohistochemistry: (A–C) pan CK, EMA and TFE3, respectively. Immunonegative for pan CK, EMA and TFE3. Note nuclear nonreactivty for TFE3. (D) HMB45 and (E) Melan A. Immunopositivity for HMB45 and Melan A.

Immunostains for TFE3 have always been negative in the reported cases [1,2,4,5,9–11] It is noteworthy that immunoreactivity for melanocytic markers HMB45 and Melan A and immunonegativity for epithelial markers pan CK and EMA may lead to misdiagnosis of Angiomyolipoma to the unwary [9]. This tumor is so far a pathologically and molecularly defined entity. Due to its rarity the clinical behavior of these tumors remains uncertain. One such case study of 7 cases where follow up was available on 6 cases, has shown no evidence of recurrent disease or disease progression after initial surgical resection, indicating thereby that this may represent an indolent tumor [8]. Our case also has been followed up for one year and is free of recurrent disease. However the available data represent a small sample and a short term follow up and may not represent the true nature of these tumors.

In conclusion, knowledge of distinctive morphological and immunohistochemical features of this tumor can help in establishing a diagnosis of this rare subset of translocation associated RCC on routine hematoxylin and eosin (H and E) staining and immunophenotyping.

Conflicts of interest

None whatsoever.

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Ethical approval

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Author contribution

Dr Sarabjeet Kaur Ist Author-Study concept, data analysis or interpretation, writing the paper.Neeraj Gujar-2nd Author, Data collection and writing the paper.

Consent

Patients guardian's consent taken.

Guarantor

Dr Geeta Koppikar, Medical Director Breach Candy Hospital Trust, Mumbai, Maharashtra 26, India.

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