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AFP-producing Xp11 translocation renal cell carcinoma: Case report and review of the literature

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A B S T R A C T

Alpha-fetoprotein (AFP) is a useful tumor marker for hepatocellular carcinomas and yolk sac tumors. Rare extrahepatic visceral malignancies may be associated with AFP production and those exhibiting a hepatoid differentiation by morphology and immunohistochemical are classified as hepatoid adenocarcinoma. Renal cell carcinoma (RCC) producing AFP is a rare entity. To date, only one case of AFP-producing Xp11 translocation RCC has been reported. We reported another case of Xp11 translocation RCC, in which the tumor cells displayed strong immunostaining for AFP, HepPar1, and GPC-3. Additionally, the other published cases are reviewed.

A R T I C L E I N F O

Keywords: AFP; Renal cell carcinoma; TFE3

Introduction

Alpha-fetoprotein (AFP) is a useful tumor marker for hepatocellular carcinomas (HCC) and yolk sac tumors. Rare extrahepatic visceral malignancies may be associated with AFP production

☆ Conflict of interest: None.

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and those exhibiting a hepatoid differentiation by morphology and immunohistochemical are classified as hepatoid adenocarcinoma (HAC). Renal cell carcinoma (RCC) producing AFP is a rare entity. To date, only one case of AFP-producing Xp11 translocation RCC has been reported.[1] We reported another case of Xp11 translocation RCC, in which the tumor cells displayed strong immunostaining for AFP, HepPar1 and GPC-3. Additionally, the other published cases are reviewed.

Case report

A 41-year-old man who suffered from left lower back pain for 1 week was found to have a renal mass in the lower pole of the left kidney by computed tomography (Fig 1A). Multiple enlarged retroperitoneal lymph nodes were noted. His medical and family histories were unremarkable. Liver function test results were within normal limits. Computed tomography and magnetic resonance imaging showed no tumor in liver and testis. Distant organ metastasis was not identified. Laboratory tests showed markedly increased serum level of AFP (>3000 ng/mL). The remaining tumor markers, including CEA and carbohydrate antigen 199 (CA199) were within the normal range. Radical nephrectomy was performed on March 6th, 2020. Serum AFP level dropped abruptly to 1643.07 ng/mL on the first postoperative day and 735.27 ng/mL on the sixth postoperative day. Serum AFP levels were respectively decreased to 368 ng/mL and 13.54 ng/mL after 1 month and 2 months. Postoperative chemotherapy and radiotherapy was not performed. The patient was alive with bone metastasis (fourth rib and 10 thoracic vertebrae) until his last follow-up on September 4th, 2020.

On gross examination, a relatively circumscribed, 9.0 cm × 7.0 cm × 6.5 cm, solid mass was located in the lower pole of the kidney. The tumor was yellowish white and firm with hemorrhage and necrosis. The tumor was confined to the kidney without involvement perinephric fat. The resection margin was free of tumor. On microscopic examination, the tumor showed various growth patterns: Papillary (Fig 1B), solid, alveolar, and acinar (Fig 1C). The tumor cells mostly contained abundant eosinophilic cytoplasm and a few had clear cytoplasm. The nuclei were large with coarsely granular chromatin and contained distinct nucleoli (Fig 1D). Sarcomatoid change was present (Fig 1E). Desmoplastic stroma had heavy lymphoplasma cell infiltration. Microvascular invasion was frequently noted in the peripheral renal parenchymal (Fig 1F). Mitoses were numerous. On immunohistochemical staining, the tumor cells were diffusely and strongly positive for AFP (Fig 2A), HepPar1, and GPC-3. Moreover, they were positive for cytokeratin, PAX-8, and partly positive for p504s, CD10, vimentin and CA-IX. The tumor cells were negative for CK7, CD117, CEA, CK20, CD34, Melan-A, HMB45, Desmin, and MyoD1. The tumor cells were diffusely strong positive for TFE3 by immunohistochemistry (Fig 2C) and showed TFE3 gene rearrangement (Fig. 2D) by fluorescence in situ hybridization (FISH) using the dual-color break-apart probes. The tumor was diagnosed as AFP-producing Xp11 translocation RCC.

Discussion

AFP is a fetal serum protein, secreted by the fetal liver and yolk sac. AFP is a useful diagnostic tool for HCC and germ cell tumors, especially yolk sac tumors. However, other malignancies have been reported to produce AFP, such as gastrointestinal, pancreas, ovary, lung, gallbladder, uterus, urological system, peritoneum, and omentum.[2-8] AFP production extrahepatic tumors are classified into two categories: HAC and AFP-producing tumors. HAC requires not only AFP-producing by the tumor but also morphological resemblance to HCC. AFP-producing tumors show serum AFP elevation and AFP immunoreactivity with no histologic characteristics of HCC. HAC is a prognostically unfavorable tumor, due to extensive vascular invasion and frequent distant metastases. Microvascular invasion was frequently noted in the peripheral renal parenchymal in our case and the patient had bone metastasis 6 months after surgery. The mechanisms of aggressiveness and the molecular pathogenesis of HAC are still largely unknown. In gastric carcinoma, elevated-AFP

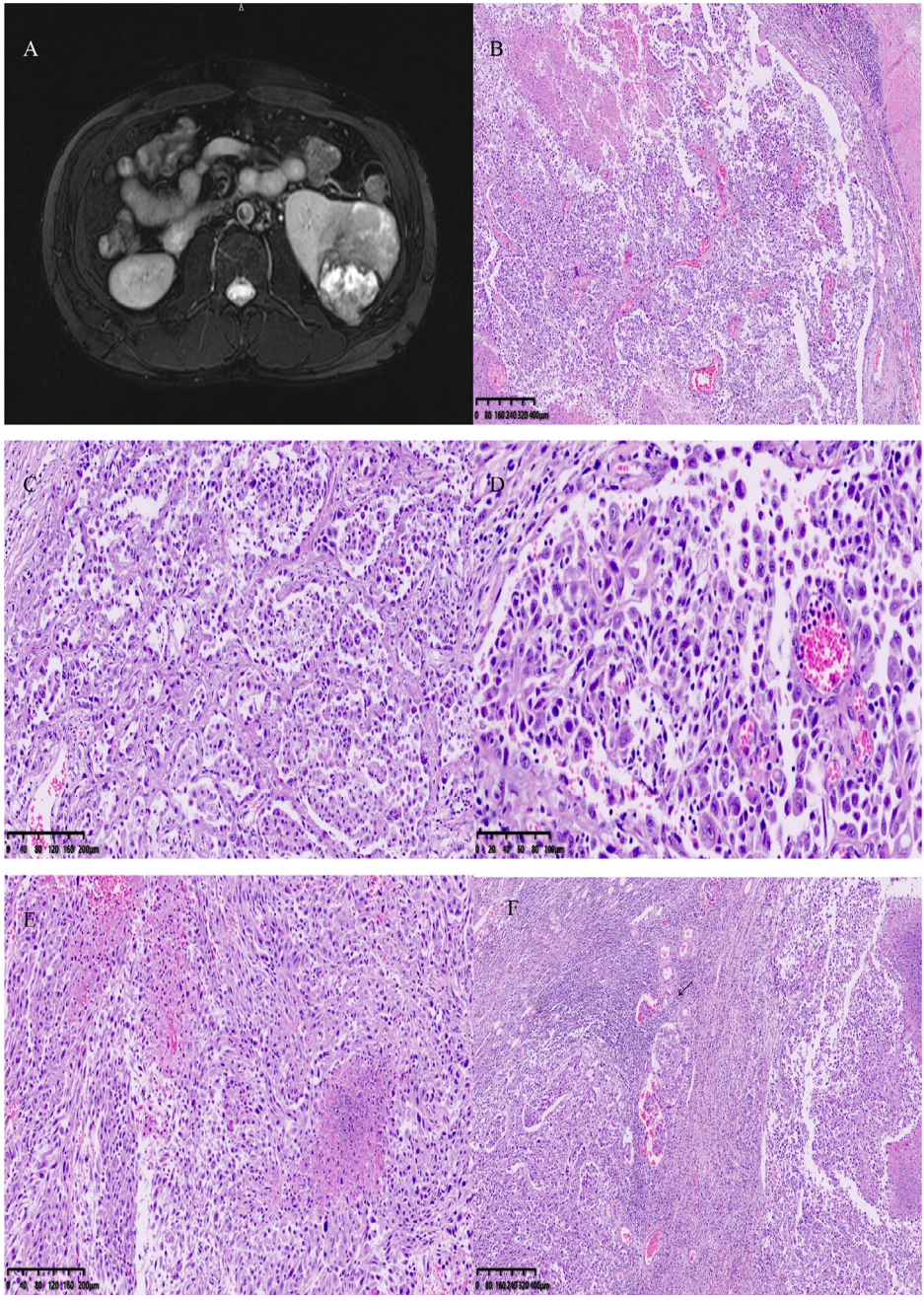

Fig. 1. Radiographic and pathological features of AFP-producing Xp11 translocation renal cell carcinoma showing (A) a 9 cm heterogeneously enhancing mass in the left kidney on CT scan; (B) papillary pattern; (C) alveolar and acinar patterns; (D) abundant eosinophilic cytoplasm of tumor cells and with distinct nucleoli; (E) sarcomatoid area; (F) microvascular invasion (arrowhead) (original magnification: B and F, × 100;C-E, × 200). (Color version of figure is available online.)

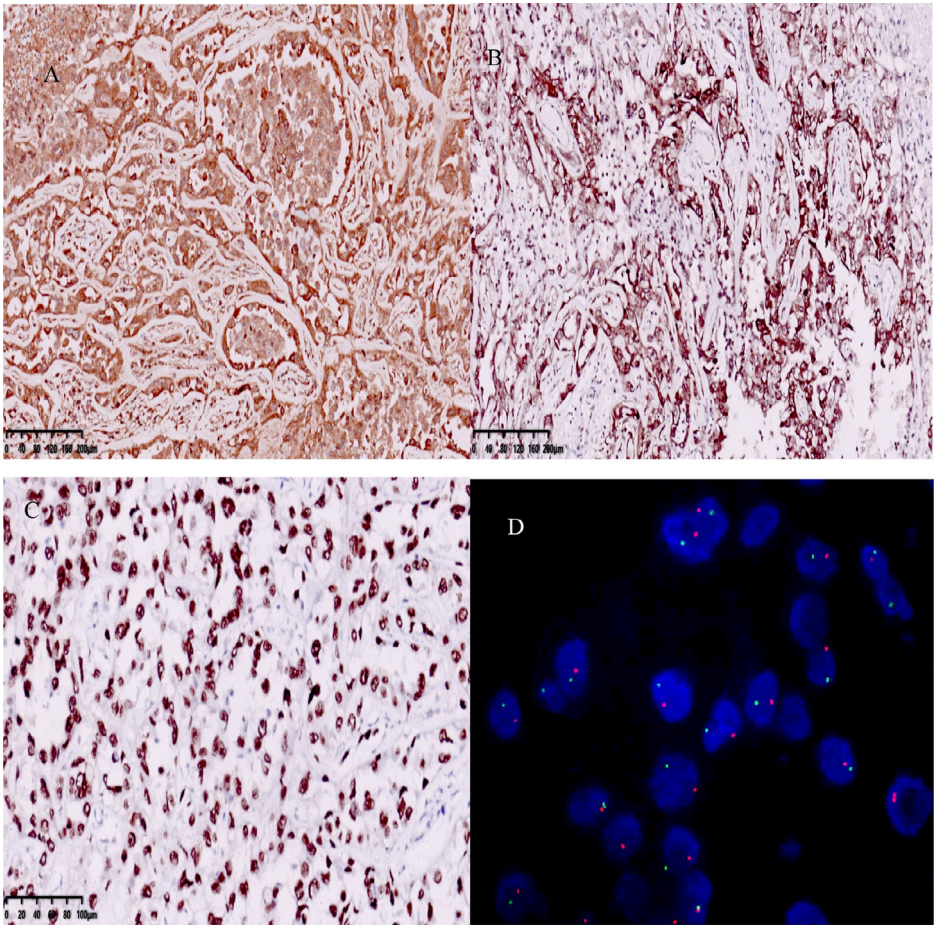

Fig. 2. Immunomolecular features of AFP-producing Xp11 translocation renal cell carcinoma showing (A) diffuse immunopositivity for AFP; (B) diffuse immunopositivity for GPC-3; (C) diffuse nuclear immunopositivity for TFE3; (D) one split (red and green) signal indicative of a translocation on TFE3 break apart FISH (original magnification:A-B, × 200;C, × 400). (Color version of figure is available online.)

cases are categorized as chromosomal instability subtypes with microsatellite instability stable, of which TP53 is one of the most significantly mutated genes.[9] TP53 was also the top mutated genes in HAS cases. Most HAS of the gastric are chromosomal instability, a small number are microsatellite instable (MLH1 loss).[10] Further study is needed in the molecular pathogenesis of AFP production extrahepatic tumors. The knowledge of the presence of AFP-producing renal cell carcinomas will make a new contribution to the study of the oncogenesis of AFP-producing tumors.

RCC–producing AFP is a rare condition with only a few cases reported.[1] There have been reported 14 cases of AFP-producing RCC, of which three showed hepatoid differentiation. The serum AFP level of all cases was elevated, 10 cases were stage IV (all with distant organ metastasis). The histologic subtype was clear cell type (8 cases), mixed types (4 cases), collecting duct carcinoma (1 case), and Xp11 translocation RCC (1 case). Five cases had sarcomatoid areas. The only one case of Xp11 translocation RCC was a 51-year-old woman presented with a multiseptated cystic mass in the right kidney and a raised serum AFP level (313.3 ng/mL). The tumor was pT1a. The tumor was arranged in alveolar, acinar, microcystic pattern, and revealed hepatoid dif-

ferentiation. The tumor cells were small to large polygonal cells containing clear to eosinophilic cytoplasm and diffusely positive for TFE3 and AFP protein. Other hepatoid markers, such as Hep-Par1and GPC-3, were not expressed. Our case expressed all of the hepatoid markers. The case and our case did not display the most distinctive histological pattern of the Xp11 translocation RCC, a papillary neoplasm composed of epithelioid clear cells with abundant psammoma bodies. The case in the literature resembled clear cell RCC, our case resembled papillary RCC with sarcomatoid change. TFE3 is the most commonly used marker for the diagnosis of Xp11 translocation RCC with strong nuclear TFE3 immunoreactivity. However, a very small minority of clear cell RCC could display TFE3 strong positive immunostaining,[11] which is a potential pitfall in the diagnosis of Xp11 translocation RCC by TFE3 immunohistochemistry. TFE3 break-apart FISH assay is currently the gold standard for the diagnosis of Xp11 translocation RCC.

It is important to be aware of AFP-producing tumors arising in the urological system, which should be considered in the differential diagnosis of tumors in a patient with elevated serum AFP. Due to the rarity, treatment recommendations are limited. Most patients were managed with nephrectomy, a few patients with postoperative chemotherapy, individual patients with postoperative immunochemotherapy and radiotherapy. RCC may be a potential source of serum AFP elevation, we should think of the possibility of RCC when the patient's serum AFP is elevated without liver or germ cell tumors. Pathologists should check the patient's serum AFP level when diagnose RCC, and should have suspicion for hepatoid RCC when cases showed histologic features of HCC, because hepatoid RCC or AFP-producing RCC tend to be very aggressive with poor prognosis.

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