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A Case Report of Renal Cell Carcinoma Producing Alpha-Fetoprotein

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Summary: We report a rare autopsy case of alpha-fetoprotein producing renal cell carcinoma with multiple metastases to liver, gallbladder, mesenterium, and paraaortic lymphnodes. A 58-year-old male patient was diagnosed as having carcinoma of the right kidney. On admission, the patient showed increased serum level of alpha-fetoprotein (326 ng/ml) which decreased after resection of the renal tumor. The resected tumor was composed mainly of clear cell type of carcinoma cells and partially of granular cells. At autopsy, the main cell type of the metastatic foci was granular type of carcinoma cells. Immunohistochemistry of alpha-fetoprotein by PAP method revealed more positive reaction on granular cell type of carcinoma cells than clear cell type of carcicoma cells in the primary site of the kidney as well as in the metastatic foci.

Key Words: alpha-fetoprotein, granular cell type, renal cell carcinoma,

Introduction

Since Abelev et al. (1) first reported that alpha-fetoprotein is produced in experimentally induced hepatic tumor in a mouse, elevation of serum alpha-fetoprotein has been frequently observed in hepatocellular carcinoma (2) and yolk sac tumor (3). Furthermore, higher level of serum alpha-fetoprotein has been reported to be associated with various tumors such as gastric (4), pancreatic (5), and lung cancers (6). We report a rare case of alpha-fetoprotein-producing renal cell carcinoma.

Case History

Clinical course: A 58-year-old man had a complaint of pain in the right flank and fever for several days. On March 7th in 1987, he visited a physician and was found a mass in the right flank. He was then referred to the Ryukyu University Hospital with suspicion of right renal tumor and was hospitalized. Physical examination: On admission, he had a fever of 39 ℃ . A palm-sized tumor having a smooth surface was palpable. The mobility of the tumor was poor and it was tender on palpation. Several soybean-sized nodules were palpable only in the cervical area.

Laboratory findings: Table 1 shows laboratory data on admission. There was leukocytosis and the ESR was 81 mm/hr. Urinalysis detected occult hematuria. The serum biochemical examination showed slight elevation of GOT and LAP. Serum LDH, total bilirubin, and CEA were within normal limit. Serum level of alpha-fetoprotein (AFP) was 326 ng/ml. The abdominal CT disclosed a markedly swollen right kidney measuring 13x10 cm in diameter. Angiography showed invasion of the tumor to the right renal vein and inferior vena cava which was suggestive of tumor emboli. Tumorous invasion to the transverse colon was also suspected. On the 27th day of admission, the patient underwent radical nephrectomy of the right side, cavotomy, and right hemicolectomy. The serum alpha-fetoprotein level decreased to 37.9 ng/ml on the 6th post-operative day, and it was 0.9 ng/ml on the 22nd post-operative day. During follow-up, serum alpha-feto-protein increased again to 149.3 ng/ml 8 months after operation. Detailed analysis of AFP will be described elsewhere (7). A tumorous mass was found in the duodenum, but not in the liver. The patient was reoperated and ileotransversecolectomy was performed. Anti-cancer drugs and ALK therapy were started. Four months after the second operation, metastatic lesions of the liver were observed by CT and the serum alpha-fetoprotein were gradually increased despite chemotherapy. The patient died of respiratory failure on January 4, 1988.

Table 1. Laboratory findings on admission

WBC 11,500/mm^3	RBC 384 x 10^4/mm^3	Plt 9.7 x 10^4/mm^3
ESR 81mm/hr	TP 5.1 g/dl	Albumin 2.8/dl
BUN 15 mg/dl	Creatinin 1.0 mg/dl	Total bilirubin 0.8 mg/dl
GOT 39 IU/ml	GPT 62IU/ml	ALP 26.8 IU/ml
r-GTP 153 IU/ml	LAP 557 IU/ml	LDH 338 IU/ml

Pathologic findings of the resected tumor: On the first operation, the right kidney and the transverse colon were conglomerated. Tumor emboli were found in the right renal vein and inferior vena cava. The right kidney contained a

hen's-egg-sized tumor, the cut surface of which was mostly yellowish white in color and partially hemorrhagic. Microscopically, major cell type of the primary renal carcinoma was clear cells of alveolar pattern (Fig. 1) and minor cell type of that was granular cells of tubular pattern. Immunohistochemical staining of AFP by PAP method (8) showed slight positive reaction on clear cell subtype of carcinoma cells and moderate positive reaction on granular subtype of carcinoma cells in the primary renal carcinoma. Metastatic foci of the ascending colon were mostly composed of granular subtype of carcinoma cells which showed moderate positive reaction. The resected recurrent tumor of the second operation showed tubular growth of granular cells which intensely reacted with AFP (Fig. 2).

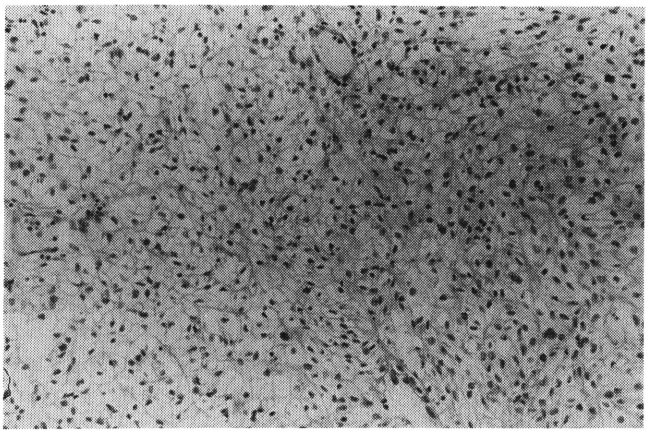

Fig. 1. Almost all of the primary renal cell carcinoma is composed of clear cell subtype of carcinoma cells (H. E. x 150).

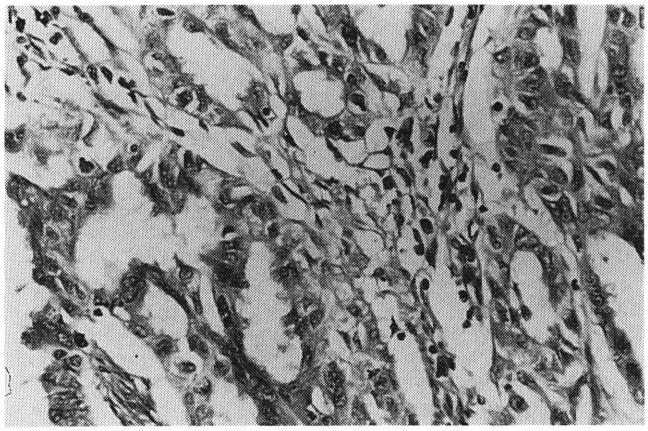

Fig. 2. Strongly positive reaction of AFP is demonstrated in granular cell subtype of carcinoma cells in the metastatic foci of the transverse colon (PAP stain x 300)

Autopsy findings: After opening the abdominal cavity 350ml of hemorrhagic ascitic fluid was found. Tumor embolism of the superior mesenteric vein was seen, which resulted in suture insufficiency of the anastomotic site between jejunum and transverse colon. Multiple metastatic foci were seen in the liver, gallbladder, mesenterium, and paraaortic lymphnodes. Most carcinoma cells in the metastatic foci were granular cell type and presented various histologic growth patterns such as alveolar, tubular, and papillary. Carcinoma cells in the metastatic foci showed marked necrotic change probably due to chemotherapy, but viable carcinoma cells were still frequently observed. Slightly positive reaction of AFP was seen on granular type of carcinoma cells showing tubular pattern in the liver (Fig. 3). The retroperitoneum contained numerous granular cell type of carinoma cells which showed papillary pattern. These carcinoma cells showed strongly positive reaction of AFP (Fig. 4). Final pathological diagnoses were summarized in Table 2.

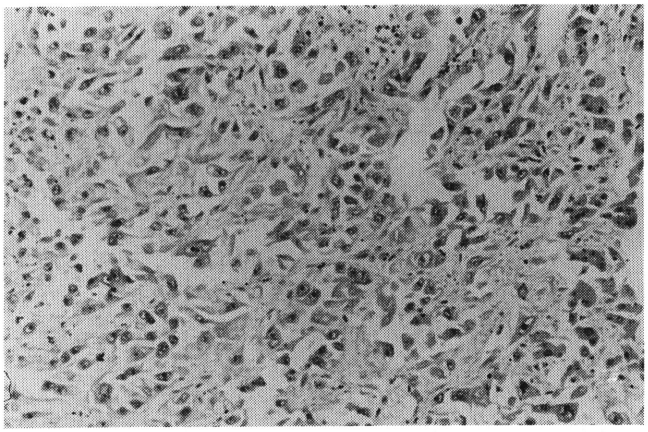

Fig. 3. AFP is slightly positive in the cytoplasm of granular cell subtype of carcinoma cells in the liver (PAP stain x 150).

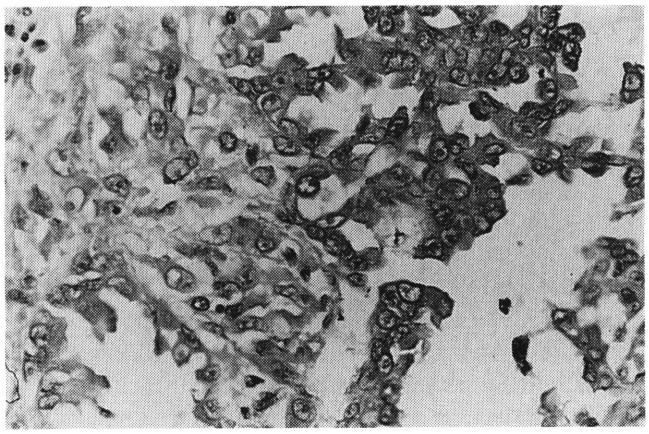

Fig. 4. PAP staining of AFP shows strong positive reaction in granular subtype of carcinoma cells in the retroperitoneum (PAP x 300).

Table 2. Final pathological diagnosis

1. Renal cell carcinoma, right kidney (alveolar type, mixed subtype, production of alpha-fetoprotein)
2. Carcinoma metastasis and invasion to; liver, gallbladder, ductus choledocus and mesenterium, and paraaortic lymphnodes.
3. Status after right nephrectomy and hemicolectomy
4. Thrombosis, superior mesenteric vein
5. Suture insufficiency caused due to #3
6. Suppurative peritonitis
7. Marked jaundice; entire skin, liver, kidney
8. Terminal endocarditis
9. Shock kidney

Discussion

Mori et al. (9) reviewed AFP-producing malignant tumors originated from tissues other than hepatocellular carcinoma and yolk sac tumors, and they reported that 78.8% of them was gastric carcinoma and 5.85% pancreatic cancer. We presented a case of AFP producing-renal cell carcinoma with the following findings; 1) high level of serum AFP, 2) decreased level of serum AFP post-operatively, 3) immunohistochemically demonstrated AFP positivity in carcinoma cells, 4) no other foci of AFP production than kidney.

With regard to the cell types and sites of AFP production in cases of AFP-producing renal cell carcinoma, various hypothesis have been proposed. Ishida et al. (10) speculated that AFP was mainly produced in the metastatic foci of the vertebrae from the finding that serum level of AFP decreased after resection and irradiation of the metastatic vertebral lesions, but serum AFP level was not decreased by nephrectomy of the affected kidney. In case of AFP-producing renal cell carcinoma reported by Takai et al. (11), serum AFP level was markedly decreased by removal of mediastinal lymphnodes, which were immunohistochemically demonstrated to have AFP. Therefore, they speculated that the production site of AFP was the mediastinal lymphnodes. We decided that major sites of AFP production in the present case were the metastatic foci such as the transverse colon and retroperitoneum, because positive reaction of AFP was more intensely observed in the metastatic lesions than the affected primary renal lesion.

Histology of the AFP-producing tumors except for hepatoma and yolk sac tumor has been often reported to show hepatic differentiation (4). However, this case did not show hepatic differentiation. Concerning the cell types of AFP-producing renal cell carcinomas, clear or granular cell subtypes of carcinomas (11, 12, 13) have been described. In the present case, primary tumor which was mainly composed of clear cell type of carcinoma cells show weak positive reaction, while metastatic lesions which were mainly composed of granular cell subtypes of carcinoma cells had immunohistochemically moderate to marked reaction of AFP.

Kato et al. (14) reported that most cases of AFP-producing malignant tumors originate from the foregut of endodermal tissues and mesodermal tissues, and a few cases of AFP producing-malignant tumor originate from the meso- and hind-gut and ectodermal tissue. Furthermore, they stated that AFP coding genes are easily activated in the process of tumorogenesis as in hepatocellular carcinoma. In reviewing 114 cases of AFP producing gastric cancer, Murakami et al. (15) reported that AFP-producing gastric cancer possesses multidifferential potentiality, and medullary structure is essential for the production of AFP, and grading of histological differentiation of gastric cancer has no correlation with the ability of AFP production. Furthermore, several cases have been reported in which AFP is produced in carcinoid of Kulchitsky cell of neuroectoderm (16) and epithelial cell tumor of Bowens (17). We also previously experienced AFP producing-mature teratoma showing no hepatic differentiation in which AFP was immunohistochemically demonstrated in epidermis (18). Therefore, we speculate that AFP production is not specific for tumor with hepatic differentiation and tumor originating from yolk sac and liver. On the other hand, the presence of heterogeneity of AFP has been also reported that AFP being produced in the fetal liver was Con A-reactive and AFP being produced in yolk sac tumor was Con A-non-reactive (19). Ishikura et al. (4) reported that 7 cases of gastric carcinoma showed hepatic differentiation by means of both histology and the ConA binding affinity. However, the present case has been reported to show Con-A non-reactive type of AFP (7).

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