



Paraneoplastic presentation of cholestatic jaundice in renal cell carcinoma

To the Editor,

Nonmetastatic nephrogenic hepatic dysfunction syndrome (Stauffer's syndrome) is a unique, rare paraneoplastic manifestation of renal cell carcinoma (RCC) that is clinically presented as anicteric cholestasis. Paraneoplastic cholestatic jaundice is rather rare. There are only a few reports of paraneoplastic cholestatic jaundice that is related to the RCC (1-3).

A 46-year-old female was admitted to the hospital with jaundice and pruritus. The patient had no previous history of liver or biliary disease. She had no reported any drug use nor had she any history of cigarette smoking or drinking alcohol. In the physical exam, she had icterus in the sclera of her eyes, and no pathologic exam finding was observed other than mild painless hepatomegaly. There were no palpable lymph nodes, splenomegaly, or ascites. Laboratory findings revealed: hemoglobin 11.6 g/dL, white blood cells 7200/ μ L, platelets 368,000/ μ L, aspartate aminotransferase (AST) 103 IU/L, alanine aminotransferase (ALT) 77 IU/L, gamma-glutamyl transpeptidase (γ -GT) 122 IU/L, alkaline phosphatase (ALP) 183 IU/L, total bilirubin 8.9 mg/dL, conjugated bilirubin 6.3 mg/dL, and albumin 3.3 mg/dL. Thyroid function tests, blood urea nitrogen, and serum creatinine were all within normal limits.

The following investigations showed normal findings: viral serology for hepatotropic viruses (viral hepatitis A, B, and C, CMV, Epstein-Barr virus); hemostasis tests; serology, including rheumatoid factor, antinuclear antibody, anti-smooth muscle antibody, liver kidney microsomal antibody, soluble liver antigen, anti-mitochondrial antibody, anti-extractable nuclear antigens, double-stranded anti-DNA antibody, p-ANCA, c-ANCA (anti-neutrophil cytoplasmic antibody), anti-gliadin IgA and IgG, anti-endomysium antibody, transglutaminase antibody, and seruloplasmin; and copper in 24-hour urine collection.

In the abdominal ultrasound, there was no observation of hepatic metastasis and intrahepatic or extrahepatic biliary dilatation. The spleen was normal, and there was no ascites. The left kidney was normal; the right kidney revealed a solid mass of 5.6 cm. In the computerized tomography, there was a solid mass in the right kidney but without any evidence of liver metastasis, abdominal mass, and lymph node enlargement. There was no pathologic finding in the magnetic resonance cholangiopancreatography (MRCP) and gastroscopy.

The clinical and laboratory finding suggested Stauffer's syndrome and paraneoplastic cholestatic jaundice associated with this syndrome. The patient was referred for radical nephrectomy, and the pathologic findings from the specimen that was collected during the operation revealed clear cell carcinoma. The patient remained stable postoperatively and was discharged home on the tenth postoperative day. One month after operation, liver function tests showed a reduction in AST 64 IU/L, ALT 50 IU/L, ALP 160 IU/L, γ -GT 83 IU/L, total bilirubin 2.3 mg/dL, and conjugated bilirubin 1.1 mg/dL. AST, ALT, ALP, γ -GT, and total bilirubin levels returned to normal levels in the next month. Informed consent was taken from the patient.

Stauffer's syndrome was first identified by Stauffer in 1961 (4). The pathogenesis is unclear. Increased secretion of interleukin-6 by the primary tumor is considered a reason for this paraneoplastic manifestation (5). RCC-related paraneoplastic cholestatic jaundice is very rare (1-3). The pathogenesis of paraneoplastic cholestatic jaundice is also unclear (1).

In our case presentation, the cholestasis was resolved after right nephrectomy operation, which suggests that there was no liver metastasis associated with this presentation and that the cholestasis was secondary to a paraneoplastic manifestation. Postoperatively, liver

Address for Correspondence: Sabiye Akbulut, Department of Gastroenterology, Kartal Koşuyolu High Specialty Education and Research Hospital, İstanbul, Turkey
E-mail: sabiye4@hotmail.com

Received: 27.8.2013 **Accepted:** 25.9.2013

© Copyright 2014 by The Turkish Society of Gastroenterology • Available online at www.turkjgastroenterol.org • DOI: 10.5152/tjg.2014.6048

functions need to be followed to show normalization of the values, and if the values rise again, this should alert the physician of a tumor relapse or metastatic involvement (6). In the early diagnosis of occult renal cell carcinoma, liver function tests may become elevated, and findings of cholestasis may be alerting for a paraneoplastic manifestation of the disease.

In conclusion, patients with unexplained cholestasis should be investigated for malignant diseases, especially renal cell carcinoma.

Ethics Committee Approval: N/A.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - S.A.; Design - S.A.; Supervision - S.A., A.B., F.T.; Resource - S.A., F.T.; Materials - S.A.; Data Collection&/or Processing - S.A., A.B.; Analysis&/or Interpretation - S.A.; Literature Search - S.A.; Writing - S.A., A.B.; Critical Reviews - S.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Akbulut et al. Cholestatic jaundice in renal cell carcinoma

Sabiye Akbulut¹, Ayşe Baysal², Firdevs Topal³

¹Department of Gastroenterology, Kartal Koşuyolu High Specialty Education and Research Hospital, İstanbul, Turkey

²Department of Anesthesiology, Kartal Koşuyolu High Specialty Education and Research Hospital, İstanbul, Turkey

³Department of Gastroenterology, Çankırı State Hospital, Çankırı, Turkey

REFERENCES

1. Giannakos G, Papanicolaou X, Trafalis D, Michaelidis I, Margaritis G, Christofilakis C. Stauffer's syndrome variant associated with renal cell carcinoma. *Int J Urol* 2005; 12: 757-9. [\[CrossRef\]](#)
2. Dourakis SP, Sinani C, Deutsch M, Dimitriadou E, Hadziyannis SJ. Cholestatic jaundice as a paraneoplastic manifestation of renal cell carcinoma. *Eur J Gastroenterol Hepato* 1997; 9: 311-4. [\[CrossRef\]](#)
3. Morla D, Alazemi S, Lichtstein D. Stauffer's syndrome variant with cholestatic jaundice: A case report. *J Gen Intern Med* 2006; 21: C11-3. [\[CrossRef\]](#)
4. Stauffer MH. Nephrogenous hepatosplenomegaly. *Gastroenterology* 1961; 40: 694.
5. Blay JY, Ross JF, Wijdenes J, et al. Role of interleukin-6 in the paraneoplastic inflammatory syndrome associated with renal cell carcinoma. *Int J Cancer* 1997; 72: 424-30. [\[CrossRef\]](#)
6. Chuang YC, Lin AT, Chen KK, Chang YH, Chen MT, Chang LS. Paraneoplastic elevation of serum alkaline phosphatase in renal cell carcinoma: incidence and implication on prognosis. *J Urol* 1997; 158: 1684-7. [\[CrossRef\]](#)