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Letter to Editor

Stauffer's Syndrome With Jaundice Due to The Paraneoplastic Syndrome of Renal Cell Carcinoma

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To The Editor

Cholestasis is the result of stoppage of bile flow by many diseases. Bile is produced in hepatocytes and it is secreted into a network of canaliculi, small bile ducts, interlobular bile ducts, right and left hepatic ducts, common hepatic duct and common bile duct (1). Thus, cholestasis clinically occurs either due to an impairment of bile formation in hepatocytes or an obstruction in the drainage of bile through the biliary tract (2). Cholestasis associated with malignancies are usually secondary to their mass effect on the biliary tract and interrupting the flow of bile or hepatic metastases resulting in an impairment in the bile formation. However, non-metastatic hepatic dysfunction secondary to a paraneoplastic hepatopathy with no evidence of anatomic obstruction of biliary tract, infectious or inflammatory etiology or infiltration of liver is called Stauffer's syndrome, having non-icteric and icteric forms, the icteric form being much rarer (3). It is a clinical presentation of renal cell carcinoma and other malignancies including bronchogenic carcinoma, leiomyosarcoma and prostate adenocarcinoma (4). We report a case a 67-year-old male with a rare of form of icteric Stauffer's syndrome secondary to renal cell carcinoma, which was discovered during an evaluation of cholestatic jaundice.

Case: A 67-year-old male was admitted to hospital with the complaint of jaundice over a time period of one month. He reported a slight right upper quadrant discomfort. His medical history was non-remarkable except from having benign prostate hyperplasia. He did not have any operations. He was a non-smoker and did not have any alcohol use in the past. During physical examination, he had icterus in the sclera of his eyes and a mild hepatomegaly which was painless. Other than these, the examination was non-remarkable.

The laboratory data revealed elevated aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, total and conjugated bilirubin, CRP, prolonged prothrombin time, and decreased serum albumin time (see **Table 1**). Thyroid function tests, blood urea nitrogen, and serum creatinine were all within normal limits. Urinalysis was non-remarkable except for being positive for bilirubin.

Viral serology for hepatotropic viruses (viral hepatitis A, B, and C, delta, CMV, Epstein-Barr virus) was normal; Elisa tests for HIV and leptospirosis were normal; rheumatoid factor, antinuclear antibody, liver kidney microsomal antibody, anti-mitochondrial antibody, anti-smooth muscle antibody, double-stranded anti-DNA antibody, p-ANCA, c-ANCA (anti-neutrophil cytoplasmic antibody) and ceruloplasmin and copper in 24-hour urine collection were in normal limits. Anti-gliadin IgA and IgG, anti-endomysium antibody, transglutaminase antibody were normal. Ferritin was 129 ng/ ml and transferrin saturation was %20. IgM, IgG

Table 1. Laboratory Values

Hemoglobin (g/dl)	10.6
Hematocrit (%)	32
Leukocytes (x10³ U/L)	7.1
• Neutrophil (%)	58.7
• Lymphocyte (%)	24.1
• Basophil (%)	1.3
Platelets (x10³ U/L)	146
Aspartate aminotransferase (AST) (IU/L)	988
Alanine aminotransferase (ALT) (IU/L)	730
Gamma-glutamyl transpeptidase (γ-GT) (IU/L)	121
Alkaline phosphatase (ALP) (IU/L)	141
LDH (U/L)	250
Total bilirubin (mg/dL)	6.9
Conjugated bilirubin (mg/dL)	6.1
Albumin (mg/dL)	2.5
INR	2.13
CRP (mg/L) (normal range 0-5)	11.4
ESR (mm/h)	4

and IgA were in normal limits, IgG sub classification was normal. Alpha-feto protein was in normal limits.

The patient had a fever of 38.4 (°C) and blood and urine cultures were drawn and there were negative.

The abdomen ultrasonography revealed that the liver was larger than normal, 172 mm and increased parenchyma echogenicity. Spleen was in normal size. There was no sign of intra or extra hepatic biliary dilatation, ascites or hepatic metastases. There were also no signs of renal stones, hydronephrosis and renal masses. CT scan showed no signs of biliary obstruction, the gallbladder, pancreas and liver was normal. CT scan report did not mention about any renal pathology.

In MRCP, there were suspected lesions in the vicinity of distal choledocus. Gastroscopy was normal and there were no esophageal varices.

PET-CT was done and it revealed a hyper metabolic lesion approximately 36.5x24x32 mm in size at the level of the left kidney ½ lower pole resembling RCC, metastatic lymph nodes in the abdomen and parenchymal disease in the liver (see **Figure 1**). Nephrectomy was planned at an outer hospital with more experience. However, the patient deceased due to sudden cardiac death during follow-up.

Malignancy causes cholestasis in many situations. It can be due to the external compression of a lymph node or malignant tumor of pancreatic, ampullary, gallbladder carcinomas on biliary tree or a widespread hepatic involvement by a hepatoma or liver metastases (4). Nonmetastatic nephrogenic hepatic dysfunction (Stauffer's syndrome) is a rare paraneoplastic syndrome in which there is no anatomic compression of the biliary tree or hepatic involvement of a neoplasia. It is a clinical presentation of renal cell carcinoma and other malignancies including bronchogenic carcinoma, leiomyosarcoma and prostate adenocarcinoma (4). The humoral secretions and lysosomal enzymes liberated from the tumor are postulated to have distant effects on hepatocytes. Also, the hepatic hypervascularity seen on angiography, amyloid deposition and nonspecific periportal inflammation in biopsy and an autoimmune process targeting a bilirubin transport protein in liver are speculated to be the reason of this syndrome (5). Moreover, IL-6 has found to be a common theme of some cases in literature (6,7). It can be that pro-inflammatory cytokines could inhibit the expression of hepatobiliary genes and cause an impairment in biliary flow (6). However, the exact pathophysiology is yet to be discovered (8).

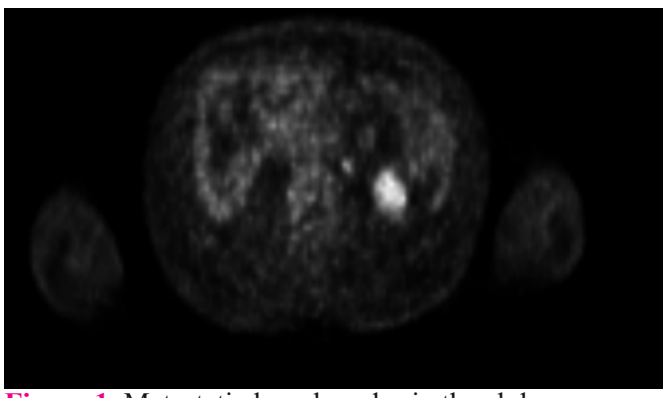

Figure 1. Metastatic lymph nodes in the abdomen mass

In our case, the results were consistent with Stauffer's syndrome with jaundice. There was hepatomegaly with elevated aminotransferases, alkaline phosphatase, decreased albumin, and prolonged prothrombin time, and cholestatic jaundice. No laboratory finding could explain the elevation in liver enzymes. There was no alcohol usage, hepatotoxic agent usage and hepatosteatosis. Viral serology was negative, ceruloplasmin and ferritin was normal. There were no signs of congestive, ischemic hepatitis and sepsis and Budd-Chiari syndrome. There was no cholestatic obstruction and overt autoimmune disease. So there were no hepatocellular or cholestatic cause. In our case, RCC was not seen on USG, as USG does not always show renal tumors (3). There was the finding of renal cell carcinoma in PET-CT and the patient was referred for nephrectomy. However, he deceased before operation and the histopathologic diagnosis could not be made. Nevertheless, there were no other causes clinically and our evidence supports this syndrome.

DECLERATIONS

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REFERENCES

1. Jameson JL. Harrison's Principles of Internal Medicine. 20th ed. New York, NY: McGraw-Hill Education; 2018.
2. Sherlock S, Dooley J. a) Jaundice. b) Cholestasis. In: Sherlock S, Dooley J, eds. *Diseases of the Liver and Biliary System*. 9th ed. Oxford, UK: Blackwell Scientific Publications; 1993:199-213, 214-236.
3. Sharma N, Darr U, Darr A, Sood G. Stauffer Syndrome: A Comprehensive Review of the Icteric Variant of the Syndrome. *Cureus*. 2019;11(10):e6032. Published 2019 Oct 30. doi:10.7759/cureus.6032
4. Morla D, Alazemi S, Lichtstein D. Stauffer's syndrome variant with cholestatic jaundice: a case report. *J Gen Intern Med*. 2006;21(7):C11-C13. doi:10.1111/j.1525-1497.2006.00448.x
5. Sharara AI, Panella TJ, Fitz JG. Paraneoplastic hepatopathy associated with soft tissue sarcoma. *Gastroenterology*. 1992;103(1):330-332. doi:10.1016/0016-5085(92)91131-m
6. Bhangoo MS, Cheng B, Botta GP, Thorson P, Kosty MP. Reversible intrahepatic cholestasis in metastatic prostate cancer: An uncommon paraneoplastic syndrome. *Mol Clin Oncol*. 2018;8(4):609-612. doi:10.3892/mco.2018.1564
7. Karakolios A, Kasapis C, Kallinikidis T, Kalpidis P, Grigoriadis N. Cholestatic jaundice as a paraneoplastic manifestation of prostate adenocarcinoma. *Clin Gastroenterol Hepatol*. 2003;1(6):480-483. doi:10.1016/s1542-3565(03)00227-1
8. Puga M, Gonzalez-Ballina E, Rivas-Moral L. Stauffer's Syndrome Variant as an Unusual Case of Painless Jaundice. *Clin Gastroenterol Hepatol*. 2015;13(9):A25-A26. doi:10.1016/j.cgh.2015.05.011