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Paraneoplastic cholestasis associated with prostate carcinoma

Prostat karsinomu ve paraneoplastik kolestaz birlikteliği

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Paraneoplastic syndromes associated with prostate carcinoma are very rare. We report a patient with prostate carcinoma and cholestatic jaundice without biliary obstruction, hepatic involvement or infectious etiology. In the literature, only one case of idiopathic cholestatic jaundice with prostate carcinoma has been reported and a paraneoplastic etiology was suggested. In our case, cholestasis rapidly regressed with chemotherapy and the patient is well at six months of follow-up. Paraneoplastic cholestasis should be kept in mind in the absence of biliary tract obstruction, hepatic involvement or infectious etiology.

Key words: Paraneoplastic syndromes, prostate carcinoma, obstructive jaundice

Paraneoplastik sendrom ile prostat kanseri birlikteliği nadir görülen bir durumdur. Bu olgu sunumunda sarılık etyolojisini açıklayacak enfeksiyöz ajan, karaciğer tutulumu, biliyer obstruksiyon olmaksızın kolestazla seyreden prostat kanserli bir vaka sunuldu. Literatürde idiyopatik kolestazla seyreden paraneoplastik olduğu düşünülen sadece bir prostat kanser vakası rapor edilmiştir. Bizim vakamızda; kemoterapiyi takiben kolestaz hızla gerilemiş ve 6 aylık takipte hastanın iyi olduğu izlenmiştir. Biliyer obstruksiyon, karaciğer tutulumu, enfeksiyöz ajan olmaksızın kolestazla seyreden prostat kanserli vakalarda paraneoplastik kolestaz olabileceği akılda tutulmalıdır.

Anahtar kelimeler: Paraneoplastik sendrom, prostat karsinoma, obstrüktif sarılık

INTRODUCTION

Cholestasis in patients with malignant tumors may be due to various causes, including mechanical bile duct obstruction by the primary tumor, compression by enlarged lymph nodes or liver metastasis and/or infiltration (1). In a minority of patients, when metastatic hepatic involvement, bile duct obstruction and other causes were ruled out, cholestasis was attributed to the remote effect of the tumor, called paraneoplastic syndrome (2). Cholestasis as a paraneoplastic syndrome has been well described in patients with non-metastatic renal cell carcinoma (Stauffer's syndrome), soft tissue sarcomas and lympho-proliferative diseases, in particular Hodgkin's disease (3-5). Cancer of the prostate presenting as cholestatic jaundice is very unusual. Only one prostate carcinoma case of paraneoplastic cholestatic jaundice has been reported in the literature, to our knowledge (2). In this case report, we present a second case with paraneoplastic cholestasis of prostate carcinoma and we discuss its possible pathophysiological mechanisms.

CASE REPORT

A 77-year-old man was admitted to the Gastroenterology Department of University Research Hospital with the complaints of low back pain, pruritis and jaundice in September 2002. The patient had a three-month history of lumbar bone pain and history of jaundice with pruritis in the last week. There was no history of melena or acolic feces. The patient did not smoke and had not taken any toxic substance, such a mushrooms. There was no history of toxic drug use, organic toxin exposure or history of blood transfusion. There was no personal or family history of diabetes mellitus, renal disease or hypertension. Physical examination revealed an oriented, thin, jaundiced man.

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Head and neck examination revealed icteric sclera and no lymphadenopathy. The liver and spleen were not palpable, and ascites was not detected. No Dupuytren contracture, spider angioma or palmar erythema was noted. In laboratory evaluation, hemoglobin was 8.7 g/dl, white blood cell was 8500/mm^3 and thrombocyte count was 170,000/mm^3. Aspartate aminotransferase (AST) was 67 U/L (normal range:30-40 U/L) and serum alanine aminotransferase (ALT) was 108 U/L (normal range: 40-50 U/L). Total bilirubin was 10.0 mg/dl (normal range: 0-lmg/dl), and direct bilirubin 7.04 mg/dl (normal range 0-0.5 mg/dl). Alkaline phosphate (ALP) was 5631 U/L (normal range: 50-140 U/L). Gamma-glutamyl transpeptidase (GGT) was 1748 U/L (normal range: 50-125 U/L). Total protein was 5.4 g/dl (normal range: 5-7 g/dl) with an albumin of 3.2 g/dl (normal range: 3.4-5 g/dl). Blood urea nitrogen, serum creatinine, sodium, potassium, chloride and glucose were normal. Urine analysis was positive for bilirubin but otherwise normal. Prostate specific antigen (PSA) was 100 ng/ml (normal range: 0-4 ng/ml). Anti-mitochondrial antibodies (AMA) and antinuclear antibodies (ANA) were negative. The bone marrow biopsy was normal. The examination of abdomen by ultrasound and computed tomography was normal. The bones scan with technetium-99m revealed that the pelvis and vertebral column had bilateral multiple foci of abnormal increased uptake. Endoscopic retrograde cholangio-pancreatography revealed a normal biliary tree (Figure 1). The liver was normal at histological examination. Histological examination of a prostate biopsy was determined to be adenocarcinoma (Gleason score: 3+3) (Figure 2).

After treatment with 3.6 mg goserelin (Zoladex) (first intramuscular injection) and 50 mg/day bicalutamide (Casodex) (oral) and 4 mg zolendronate (Zometa) (first intravenous infusion), obstructive jaundice disappeared within 15 days. His total bilirubin, AST and ALT levels decreased to 0.9 mg/dl, 25 U/L and 32 U/L, respectively. Likewise, his ALP and GGT levels also decreased to 542 U/L and 432 U/L, respectively, within three weeks after beginning the treatment. The patient was markedly recovered and discharged on the 21st post-treatment day. Three months after hormonal therapy (before third doses of monthly Zoladex 3.6 mg and Zometa 4 mg), his PSA level decreased to 24 ng/dl. Because of the good response of bone pain to treatment he has not received any palliative radiotherapy for bone lesions. The patient is in remission at the end of six months and is being followed up at monthly intervals.

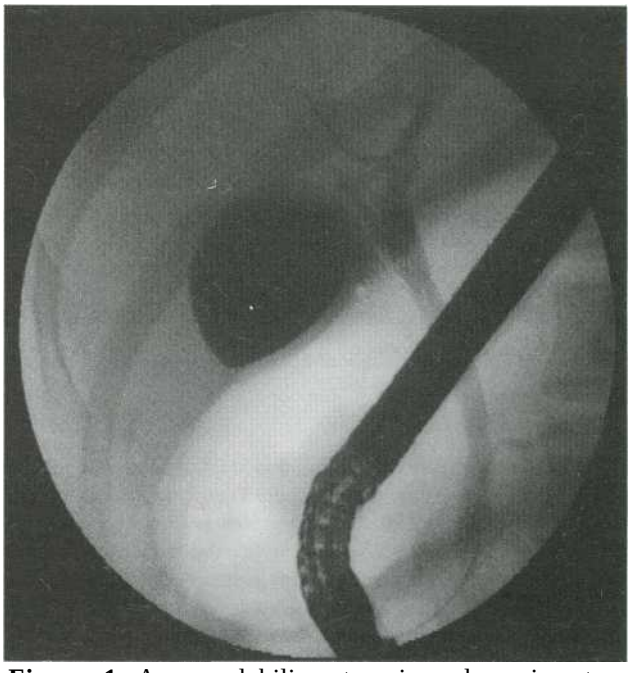

Figure 1. A normal biliary tree in endoscopic retrograde cholangro-pancreatography

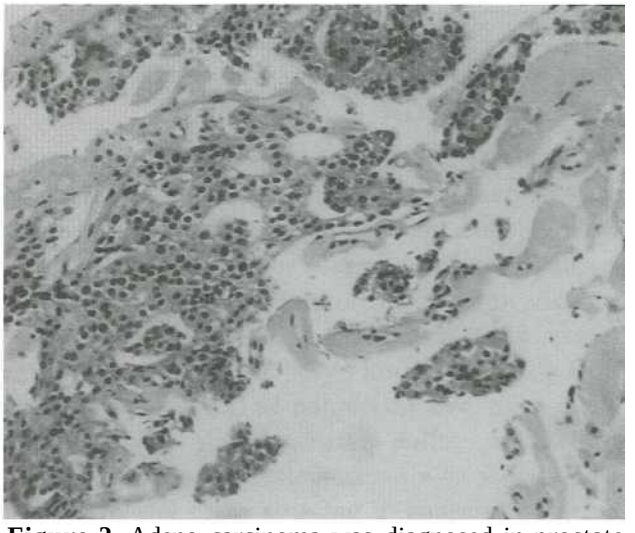

Figure 2. Adeno carcinoma was diagnosed in prostate biopsy (Gleason score: 3+3)

DISCUSSION

Patients with metastatic prostate carcinoma usually present with bone metastasis and/or lymphadenopathy. Liver metastasis is a very rare complication of newly diagnosed prostate carcinoma. Malignant diseases may cause cholestatic jaundice

through either main bile duct obstruction or widespread hepatic metastasis. Literature reveals a few cases of prostate cancer causing obstructive jaundice by metastasis or infiltration to the liver or by compression by enlarged lymph nodes to the common bile duct or head of the pancreas (1, 6). A paraneoplastic cholestasis is postulated in the absence of anatomic obstruction of the bile duct, evidence of an infectious etiology, or metastatic hepatic involvement. Paraneoplastic cholestasis associated with prostate carcinoma is very unusual. Previously, only one prostate carcinoma case of paraneoplastic cholestasis has been reported in the literature (2).

Cholestasis may result either from a functional defect in bile formation at the level of the hepatocyte or from an impairment of bile secretion into bile ductules or ducts. Inflammation-induced cholestasis arises from activation of the inflammatory cytokine system by infectious or non-infectious injuries. Inflammation-induced cholestasis also occurs in the non-metastatic malignant tumors. The common part is that pathophysiologically cholestasis generally results from systemic and intrahepatic release of proinflammatory cytokines, which are potent inhibitors of hepatocellular bile secretion. These cytokine effects are reversible and bile secretory function is restored upon disappearance of the inflammatory injury (1). Blay et al (7). also reported that interleukin-6 is involved in the physiopathology of paraneoplastic cholestasis in renal cell carcinoma.

It is also important to remember that jaundice may be due to the treatment of prostate cancer. Cyproterone acetate, flutamide and bicalutamide, used in treatment of prostate cancer, have been associated with fulminant hepatitis and jaundice (8, 9).

In conclusion, a paraneoplastic cholestasis should be kept in mind in the absence of biliary tract obstruction, hepatic involvement or infectious etiology in prostate carcinoma.

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