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Cholestatic Jaundice as a Revealing Manifestation of a Metastatic Prostate Cancer: A Case Report

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Abstract

Cholestatic jaundice as the initial symptom in patients with metastatic prostate cancer is extremely rare. Few cases only of paraneoplasic cholestatic jaundice associated with prostate cancer have been reported in the literature. We present a case of 57 years old patient who presented cholestatic jaundice revealing an underlying metastatic prostate cancer after detailed examinations including Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positon Emission Tomography (PET), and Endoscopic Retrograde Cholangiopancreatography (ERCP).

Cholestatic jaundice may be brought on by malignancies *via* identified pathways (e.g., bile duct obstruction or widespread hepatic infiltration). Through an unknown pathogenetic mechanism, paraneoplastic syndromes connected to malignancy, particularly renal cell carcinoma (Stauffer's syndrome) and malignant lymphoproliferative disorders, can cause a reversible form of cholestasis. There have been two cases documented in the medical literature of prostate cancer that originally manifested as cholestatic jaundice without any clear reason (i.e., blockage or invasion). We describe a patient who had pruritus and cholestatic jaundice when they first arrived. The diagnosis of prostate cancer was made throughout the diagnostic process. Conjugated bilirubin and alkaline phosphatase levels significantly rose, but transaminase and glutamyltranspeptidase levels only slightly increased. No signs of extrahepatic biliary blockage or hepatic metastases were found, according to the findings of the necessary studies carried out while the patient was hospitalised.

Keywords: Computed Tomography (CT) • Magnetic Resonance Imaging (MRI) • Positon Emission Tomography (PET)• Endoscopic Retrograde Cholangiopancreatography (ERCP)

Introduction

Cholestasis in patients suffering from malignancies can typically result from a bile duct obstruction either by the primary tumor itself, metastasis to the liver, or enlarged lymph nodes [1,2]. More rarely, in patients with advanced prostate cancer known as a silent cancer. However, prostate cancer presenting as cholestatic jaundice is extremely rare, and only very few cases of paraneoplastic cholestatic jaundice associated with prostate cancer have been reported in the literature [3-5]. Here, we describe a case of a patient with metastatic prostate cancer who presented with cholestatic jaundice and was treated with both surgical castration and chemotherapy.

Case Presentation

A 57 year old man was referred to our hospital because of jaundice, anorexia and weight loss which had persisted for 4 months with abdominal pain, dark urine, light-colored stools and pruritus. The liver and spleen were not palpable. Digital rectal examination revealed a stony hard prostate.

Initial liver function test results were as follows-ASAT of 560 U/L (Normal range: 7-52 U/L), ALAT of 780 U/L (Normal range: 13-39 U/L), alkaline phosphatase of 682 U/L (normal range: 34-104 U/L), gamma-glutamyltransferase of 1420 U/L (Normal range: 9-64 U/L), and total bilirubin of 16.2 mg/Dl (Normal range: 0.3-1 mg/dL), with direct bilirubin of 10.7 mg/dL (Normal range: ≤ 0.18). Prostate-Specific Antigen (PSA) was 500 ng/mL (Normal range: 0-4 ng/ml).

Magnetic resonance imaging revealed dilatation of intra and extra hepatic ducts, the common hepatic duct measuring 20 mm without evident tumor process in the bilio-digestive crossroads. Computed Tomography (CT) of the patient's chest, abdomen and pelvis showed enlarged lymph nodes in the middle mediastinum, and enlarged para-aortic lymph nodes with a large irregular heterogenous prostatic hypertrophy with numerous hypogastric lymph nodes. Prostate biopsy revealed adenocarcinoma (poorly differentiated, Gleason score-9:5+4). Endoscopic retrograde cholangiopancreatography was performed with placement of a stent.

Choline PET-scan detected enlarged metastatic lymph nodes in the pelvis, abdomen and mediastinum, and hot lesions on several bones (Figures 1 and 2). Figure 1 showed-

- Hyper metabolic ranges in the prostate (SUV_{max} 6.80)
- Internal and external iliac hyper metabolic lymph nodes (SUV_{max} 9.23)
- Hypermetabolic range at the right ischium (SUV_{max} 8.44)

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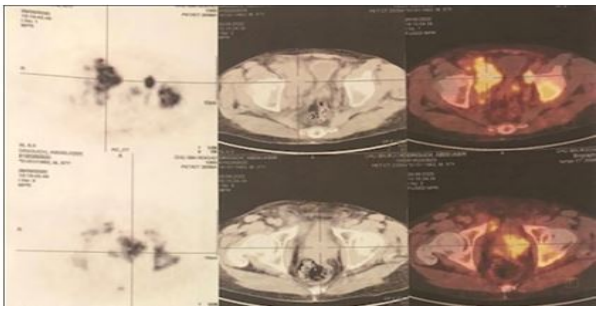

Figure 1: Choline PET-Scan.

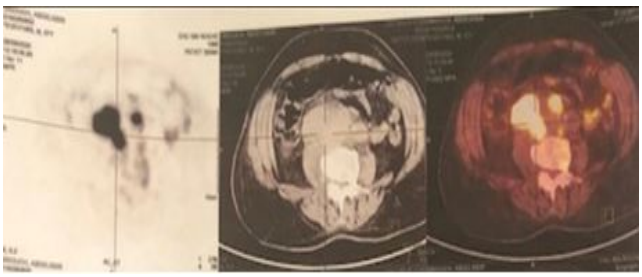

Figure 2: Choline PET-Scan Showed Hyper Metabolic Para-Aortic Lymph Nodes (SUV_{max} 10.02).

Six months after surgical castration, bilirubin levels returned to normal with jaundice regression. But PSA levels remained high and the CT showed stability according to Response Evaluation Criteria in Solid Tumors (RECIST). We added chemotherapy and the first cycle of docetaxel was initiated and well tolerated without any adverse event, including no elevation in liver enzymes.

Discussion

There are many case reports describing cholestasis as a paraneoplastic syndrome associated with several different malignancies [6,7]. Hong et al. reported some paraneoplasic syndromes associated with prostate cancer, they classified different types according to clinical symptoms [6].

Prostate cancer is the second urological malignancy associated with paraneoplastic syndrome after renal cell carcinoma [8].

Cholestasis syndromes may be present before a cancer diagnosis as in our case report. The pathogenesis is still unknown. Blay et al. reported that the cytokine, interleukin-6 (IL-6) is involved in the pathophysiology of cholestatsis in renal cell carcinoma (Stauffer's syndrome) [9].

Paraneoplastic cholestasis should be considered in the absence of metastatic infiltration of the liver, metastatic extrahepatic biliary duct obstruction, or an infectious etiology in prostate cancer.

Jaundice cholestasis due to prostate cancer can be improved with appropriate antiandrogen therapy and may be exacerbated by steroid use. Kang et al. suggest that administration of steroids may cause a sudden flare of paraneoplastic cholestasis, with elevation of bilirubin levels [10].

Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer (CHAARTED) trial demonstrated in patients with metastatic castration-naive metastatic prostate cancer that the administration of six cycles of docetaxel at the beginning of Androgen Deprivation Therapy (ADT) resulted in significantly longer survival of more than a year compared to ADT alone [11].

Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial also showed survival benefit in patients with metastatic prostate cancer treated with this combination [12].

In our case report, we safely treated the patient with surgical castration and we added chemotherapy: Docetaxel. Fortunately, this treatment approach resulted in excellent response.

Conclusion

Cholestatic jaundice present as the first manifestation of metatatic prostate cancer is uncommon. We have reported a case that was treated by combination of surgical castration and docetaxel, patient's symptoms and laboratory abnormalities were reversed few months. The patient's symptoms and the anomalies in the lab quickly improved after therapy with flutamide and leuprolide. We consider this patient's cholestatic jaundice to be a component of a paraneoplastic disease; the exact cause of cholestasis is still unknown. Malignancies, such as prostate cancer, should be looked into in patients with unexplained cholestasis.

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