From suspicion of liver metastases to the diagnosis of Wilson disease in a patient with seminoma

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Wilson disease is an autosomal recessive disorder characterized by copper accumulation in the liver, brain, kidneys, and cornea due to inadequate biliary copper excretion. It should be considered especially in young patients who have findings of liver disease with unexplained etiology. Clinical presentation of the disease can be variable, and different types of parenchymal changes of the liver can be seen on imaging modalities. Multiple nodular lesions mimicking metastases can be detected. This condition can obligate physicians to screen for a malignant disease. Moreover, it may cause misdiagnosis as advanced stage of disease when coexistent with a malignancy. The coexistence of Wilson disease with some malignant diseases has been reported; however, coexistence with seminoma was not reported before. Approximately 40% of testicular cancers are pure seminoma. Liver metastases are rare in seminoma.

In this article, a case of Wilson cirrhosis is reported. The patient was first followed with diagnosis of seminoma with suspicion of liver metastases.

Key words: Wilson disease, nodular lesions, liver metastases, seminoma

INTRODUCTION

Wilson disease is an autosomal recessive disorder characterized by copper accumulation in the liver, brain, kidneys, and cornea due to inadequate biliary copper excretion. Initial findings may be chronic or fulminant liver disease, progressive neurologic disorder without clinical liver dysfunction, isolated acute hemolysis, and psychiatric disorders (1). Clinical presentation of the disease can be variable, and different types of parenchymal changes of the liver can be seen on imaging modalities. Multiple nodular lesions mimicking metastases can be detected (2,3).

Approximately 40% of testicular cancers are pure seminoma (4). The frequency of liver metastases at presentation of all germ cell cancers is 24%. Liver metastases are less frequent in seminoma (5).
In this article, a case of Wilson cirrhosis without any symptoms of liver or neurologic disease is reported. The patient was initially diagnosed and treated as liver metastases of a seminoma.

CASE REPORT

A 27-year-old man was admitted to our clinic with findings of chronic liver disease. He had no symptoms. His history revealed that he had undergone a right orchiectomy at a different center because of a mass lesion in the right testis. The histopathologic examination of the lesion was reported as “pure seminoma”. Initial laboratory investigations showed the following results: hemoglobin: 15.4 g/dl, leukocyte: 4,100/mm³, thrombocyte: 117,000/mm³, alanine aminotransferase (ALT): 102 U/L (0-34 U/L), aspartate aminotransferase (AST): 46 U/L (0-31 U/L), gamma-glutamyl transpeptidase (GGT): 72 U/L (0-38 U/L), alkaline phosphatase (ALP): 307 U/L (30-120 U/L), total bilirubin: 0.6 mg/dl, lactate dehydrogenase (LDH): 206 U/L (0-248 U/L), alpha fetoprotein (AFP): 8.01 IU/ml (0.5-5.5 IU/ml), and beta-human chorionic gonadotropin (βhCG): 25.1 mIU/ml (0.01-5 mIU/ml). Abdominal ultrasonography (USG) showed splenomegaly, heterogeneity of the liver parenchyma and hypoechoic nodular lesions in the liver, which were considered as metastases. Computed tomography (CT) of the liver confirmed the presence of the multiple hypodense lesions, which were reported as metastases (Figure 1A) and dilatation of portal vein and splenomegaly (Figure 1B). Histological examination of the fine needle aspiration biopsy of the lesions revealed the enlargement of the portal areas, bridging necrosis and regenerative changes, but no tumor cells. Despite the findings on the biopsy specimen, three courses of bleomycin, etoposide and cisplatin (BEP) regimen had been given at an oncology clinic because of the seminoma history, suspicion of liver metastases by imaging findings and a minimal increase in the AFP level. No significant alterations were observed on the follow-up USG and CT following the chemotherapy. Abdominal CT showed multiple hypodense lesions in liver (Figure 2A) and dilatation of portal vein and splenomegaly (Figure 2B). The patient was referred to our clinic because of the parenchymal findings suggestive of chronic liver disease on the histologic examination of the nodular lesions. Laboratory investigations at the admission showed the following results: hemoglobin: 14.5 g/dl, leukocyte: 3,100/mm³, thrombocyte: 74,000/mm³, prothrombin time: 12 seconds, ALT: 43 U/L, AST: 25 U/L, GGT: 115 U/L, ALP: 307 U/L, LDH: 295 U/L, total bilirubin: 0.4 mg/dl, albumin: 4.6 g/dl, AFP: 11.5 ng/ml, βhCG: 0.1 mIU/ml, HBsAg, anti-hepatitis C virus (HCV), antinuclear antibodies (ANA), anti-smooth muscle actin (ASMA), anti-liver-kidney-microsome (LKM), and antimitochondrial antibodies (AMA) were negative. Ferritin level, transferrin saturation, and alpha 1 antitrypsin level were normal. Ceruloplasmin level was 15 mg/dl (25-63 mg/dl) and 24-hour urinary copper level was 117 μg (2-80 μg/L). Kayser-Fleischer corneal ring was not detected on the eye examination. Upper gastrointestinal endoscopy showed first-degree esophageal varices. Cranial magnetic resonance imaging was normal. D-penicillamine challenge test was performed, and 24-hour urinary copper level

![Figure 1](image1). Abdominal CT shows multiple hypodense nodular lesions in liver (A), dilatation of portal vein and splenomegaly (B).
was detected as 570 μg. Due to these findings, a liver biopsy was performed again to confirm the diagnosis of Wilson disease. Level of copper per gram of dried liver tissue was detected as 657 μg (normal: <250μg), and histologic examination of the liver was reported as cirrhosis. The diagnosis of Wilson cirrhosis was made with these findings, and D-penicillamine 1200 mg/day and zinc sulfate 3x50 mg/day therapies were started. The patient is now in the third year of follow-up and has had no symptoms that can be related to seminoma or liver disease. The hypodense nodular lesions, which were detected on prior images, were not observed on a follow-up abdominal CT. It shows only minimal heterogeneity of liver parenchim (Figure 3A) and dilatation of portal vein and splenomegaly (Figure 3B).

**DISCUSSION**

Wilson disease should be considered especially in young patients who have findings of liver disease with unexplained etiology. Although the exact pathogenetic association and predisposition have not been found, the coexistence of Wilson disease and intraabdominal malignancies such as adenocancer, hepatoma and cholangiocellular cancer has been reported (6). However, to our knowledge, a coexistence of seminoma and Wilson disease has not been reported to date. Although parenchymal heterogeneity is frequently observed on imaging modalities in Wilson disease, multiple nodular lesions mimicking metastases are detected less frequently. These nodular lesions are best identified by USG (2,3). Parenchymal necrosis, regeneration

**Figure 2.** Abdominal CT, after three courses of BEP regimen, shows multiple hypodense lesions in liver (A) and dilatation of portal vein and splenomegaly (B). There were no significant differences between before and after chemotherapy images.

**Figure 3.** Abdominal CT, in the third year of D-penicillamine and zinc sulfate therapy, shows minimal heterogeneity of liver parenchyma (A), dilatation of portal vein and splenomegaly (B), but no nodular lesions.
and scarring can be causes of morphologic changes (3). It is known that increased echogenicity and heterogeneity of the liver can be observed in the extended period of disease because of steatosis and parenchymal fibrosis (3,7,8). Akpınar et al. (3) classified the parenchymal changes in Wilson disease under three main headlines: 1- Simple parenchymal heterogeneity, 2- Parenchymal heterogeneity with multiple hypoechoic nodules, and 3- Parenchymal heterogeneity with multiple alternating hyper-hypoechoic nodules. Akhan et al. (9) reported that multiple hypoechoic nodules were detected on USG in 14% of patients with Wilson disease, and these lesions were observed as hypodense nodules on CT.

In the initial evaluation of our case, parenchymal heterogeneity and multiple hypoechoic nodules in the liver were detected on USG; however, these lesions were considered as metastases because of the concurrent diagnosis of seminoma. The frequency of liver metastases at presentation is 24% of all germ cell cancers, and this condition is less frequent in seminoma (5). Pure seminomas, by definition, are not thought to produce AFP. However, several case reports have described pure seminoma with borderline elevations in serum AFP (10.4 to 16 ng/ml) (10). Elevated levels of tumor markers indicate poor prognosis in addition to liver metastases (4,11). The most effective chemotherapy regimen for metastatic disease is BEP (12). Despite no significant increase in AFP level and the histopathologic findings of nodular liver lesions, three courses of BEP regimen were administered to our patient because of the USG and CT features of the nodular lesions, which were considered as metastases. However, no significant alterations were observed on the follow-up USG and CT after the chemotherapy.

The presence of hypoechoic nodular lesions in Wilson disease was reported as a predictive factor for good prognosis and good response to treatment (2,13). Additionally, five years after D-penicillamine therapy, disappearance of these nodular lesions and parenchymal heterogeneity was reported in the literature (14). Our patient is in the third year of D-penicillamine and zinc sulfate therapies, and no symptoms have been seen that can be related to seminoma or liver disease. The nodular lesions disappeared on follow-up abdominal CT.

In conclusion, multiple nodular lesions mimicking metastases may be detected on imaging modalities of the liver in Wilson disease, and these lesions can disappear after the treatment. Moreover, consideration of this condition is important, especially in patients with a concurrent diagnosis of a malignant disease, to ensure accurate evaluation about the disease stage and avoid unnecessary chemotherapies.

REFERENCES