

Acute Mixed Hepatitis Induced by Propylthiouracyl. Case Report

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Abstract

29-year-old woman with Graves' disease oral propylthiouracil, 200 mg per day. After 18 days she presented mixed type hepatitis. In this case, propylthiouracil induced a mixed pattern of cytotoxic and cholestatic hepatitis. Up to now, in english literature only one case report (Propylthiouracil-induced only cholestatic jaundice). But this case is cholestatic hepatitis. According to our knowledge, there was no published mixed type hepatitis of PTU. To our knowledge, this is the first case in the literature.

Early recognition of PTU-induced hepatic failure and prompt withdrawal of the drug may prevent progression from mild to severe disease, it may be prudent to discuss signs and symptoms of liver disease and other side effects with patients. Jaundice, pruritus, dark urine, abdominal pain, anorexia, or malaise should signal a patient to seek medical attention.

Introduction

Hepatotoxicity was first reported as a side-effect of propylthiouracil (PTU) therapy 50 years ago [1]. PTU-associated hepatotoxicity is a rare and life-threatening complication of antithyroid drug treatment of hyperthyroidism. The estimated incidence of antithyroid drug-associated hepatotoxicity is less than 0.5% [2], although the true incidence is unknown [3,4]. PTU hepatotoxicity occurs at all ages and, like thyroid disease [5], shows a female predominance. The presentation of PTU hepatotoxicity is clinically nonspecific.

Abnormalities or worsening of liver function tests suggest the diagnosis. The mechanism of antithyroid drug hepatotoxicity is not known, although positive lymphocyte sensitization studies in some patients who developed PTU hepatotoxicity suggest an immune reaction to PTU. Nonspecific hepatocellular necrosis is typically found on liver biopsy [3]. Based on the severity of the disease process, the pathological findings may range from early signs of hepatocellular inflammation and swelling to submassive hepatic necrosis. This case was presented with both cellular and cholestatic hepatitis.

Case Report

The patient, a 29-year-old woman, was diagnosed with Graves' disease two weeks before her presentation, and a regimen of oral propylthiouracil, 200 mg per day, was started. baseline laboratory values were normal. Then she presented to the Department of Endocrinology with nausea, 'yellowish' appearance.

Propylthiouracil (PTU) was discontinued at that time. On questioning, she reported no recent travel history and no acetaminophen, alcohol, or injection drug use. She had no history of hepatitis exposure, blood transfusion, or other ingestions. On physical examination, her skin was jaundiced, and her sclerae were icteric; exophthalmos and lid lag were apparent. The other systems were showed nothing abnormal. Her laboratory profile at admission was notable for Acute cholestatic hepatitis with aspartate aminotransferase 634IU/ml (normal <40 IU/ml), alanine aminotransferase 979 IU/ml (normal <40 IU/ml), alkaline phosphatase 955 IU/ml (normal <240 IU/ml), and gamma-glutamyl transpeptidase 456IU/ml (normal <38 IU/ml), total bilirubin 8,3mg/dl (normal,0,1 to 1,1 mg/dl), direct bilirubin 5,7 mg/dl (normal, 0,1 to 0,4 mg/dl), International Normalized Ratio (INR) 1,8 (normal 0,8 to 1,4). Tests for hepatitis A antibody immunoglobulin(Ig) M, hepatitis B surface antigen, and hepatitis B core immunoglobulin-M,

cytomegalovirus, epstein-barr virus, herpes simplex viruses hepatitis C and human immunodeficiency virus antibodies were all negative. A right upper quadrant abdominal ultrasonogram showed no sign of biliary dilation, and the liver, pancreas, and kidneys all appeared normal. Autoimmune hepatitis markers including antinuclear antibody and smooth muscle antibody were negative with normal levels of serum immunoglobulin.

After giving up propylthiouracil, liver enzymes normalized rapidly and were within normal limits 12 days after the first admission. Liver biopsy was not performed because the results of liver function tests were normal.

Discussion

Hepatotoxicity is a rare and life-threatening complication of thionamide therapy. Serum aminotransferase concentrations increase transiently in up to one-third of patients taking PTU; this abnormality may be associated with focal hepatic necrosis on liver biopsy [6]. The estimated incidence of antithyroid drug-associated hepatotoxicity is less than 0.5% [2]. A literature survey published in 1997 reported 49 cases of hepatotoxicity, 28 associated with PTU (including 7 deaths) and 21 associated with methimazole (including 3 deaths) [3]. There was no relationship between a fatal outcome and either the dose or duration of thionamide treatment.

Over the past 20 years, 22 cases of severe hepatotoxicity in adults in the US resulted in nine deaths and five liver transplants. Over the same period, 12 children developed liver failure resulting in three deaths and six liver transplants. It was estimated that this complication occurs

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in 1:10,000 adults taking PTU, with an even greater risk in children (1:2,000) [7,8].

In this case, propylthiouracil induced a mixed pattern of cytotoxic and cholestatic hepatitis. Up to now, in english literature only one case report (Propylthiouracil-induced only cholestatic jaundice [9]). But this case is cholestatic hepatitis. According to our knowledge, there was no published mixed type hepatitis of PTU. This is the first case.

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