Use of the ^{198}Au liver scan in assessing the therapeutic effect of penicillamine in Wilson's disease

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Summary

In a 14-year-old girl Wilson's disease was found to be the etiologic basis of an active liver cirrhosis diagnosed months previously. Specific therapy with D-penicillamine caused remarkable clinical and biochemical improvement. Repeated liver scans using ^{198}Au revealed increased liver uptake of the ^{198}Au while the size of the spleen decreased. It is proposed that repeated liver scintiscanning may provide another easily performed and safe test for evaluation of the effect of therapy in these patients.

Introduction

The hepatic form of Wilson's disease in which neurological dysfunction may be slight or absent has been recognized as a clinical variant for many years (Kehrer, 1930). Patients with this form of disease show considerable improvement following penicillamine therapy (Sternlieb and Scheinberg, 1964; Lange, 1968).

The present report concerns a 14-year-old girl with advanced cirrhosis of the liver due to Wilson's disease, in whom clinical and biochemical improvement during 1 year of penicillamine treatment was associated with a considerable improvement of the ^{198}Au liver scan. This appears to be the first case report in which serial liver scans have been used to document the favourable response of the liver to penicillamine therapy in Wilson's disease.

Case report

B.A. was born in Israel to parents of Moroccan origins and had a normal childhood and pubertal

development until the summer of 1971, when, at the age of 14, amenorrhea, abdominal distention, fatigue and weakness developed over a period of 6 months. She was found to have ascites, splenomegaly, hypochromic anemia, esophageal varices, and laboratory tests indicative of liver disease, Table 1.

On laparotomy the liver was found to be moderately enlarged with a nodular surface, and the surgical liver biopsy revealed a macronodular cirrhosis with infiltrates of chronic inflammatory cells. Treatment with a low salt diet, 25 mg of prednisone per day and diuretics reduced the ascites, yet the patient continued to be anaemic, amenorrhoeic and fatigued. The neurological examination was normal. In December 1971 the patient was referred to our ward.

The diagnosis of Wilson's disease was confirmed by the finding of bilateral Kayser-Fleischer ring on slit lamp examination. Repeated examinations revealed a serum ceruloplasmin concentration of 16-18 mg/100 ml; 24-hr urinary copper excretion was 330 μg . ^{198}Au liver scan showed very low uptake by the liver, and a high concentration of ^{198}Au in the enlarged spleen (Fig. 1).

Treatment with D-penicillamine, 2 g daily, was initiated. The menses reappeared and became regular 8 months later, the ascites disappeared completely, the splenomegaly decreased in size. Liver function tests improved (Table 1), and oesophageal varices diminished in size. Repeated ^{198}Au liver scans revealed marked improvement in the uptake of ^{198}Au by the liver (Figs. 2 and 3).

TABLE 1 Laboratory data in a case of Wilson's disease

	3 December 1971	12 December 1972	Normal values
Haemoglobin g/100 ml	9.6	14	14 $\pm$ 2
Leucocytes/mm ³	2660	4500	5000-10,000
Thrombocytes/mm ³	140,000	48,000	150,000-300,000
Albumin g/100 ml	2.5	3.9	3.5-5.5
Globulin g/100 ml	4.2	3.0	1.5-3.0
Bilirubin mg/100 ml	2.3	1.3	0.2-1.0
SGOT mlu/ml	260	110	10-50
Alkaline phosphatase mlu/ml	140	145	30-80
Vit B ₁₂ pg/ml	1900	1100	220-800
Prothrombin %	40	65	60-100

FIG. 1. Hepatic scintiscan performed in December 1971 (using ^{198}Au).

FIG. 2. Hepatic scintiscan performed in March 1972, 3 months after initiation of penicillamine therapy.

FIG. 3. Hepatic scintiscan performed in December 1972, 12 months after initiation of penicillamine therapy.

Family history

The parents were first cousins, both born in Morocco. There was no positive history of neurological or liver disease, or of early deaths in the family. The patient has two brothers and one sister.

The sister and one brother had normal levels of serum ceruloplasmin and of 24-hr copper excretion. In both, liver function tests were normal, and no Kayser–Fleischer ring was detected. However, the 4-year-old brother was found to have a ceruloplasmin concentration of 10 mg/100 ml and a 24-hr urinary copper excretion of 117 μg . A liver biopsy sample showed copper content of 1060 $\mu\text{g/g}$ of dry liver. No Kayser–Fleischer rings were detected, the liver function tests were normal, and an ^{198}Au liver scan was normal.

Discussion

The clinical picture of Wilson's disease varies considerably from case to case. Prior to admission our patient had been diagnosed as suffering from acute juvenile cirrhosis of the liver, with jaundice, hypergammaglobulinaemia, portal hypertension and amenorrhea.

The availability of an effective treatment which is easily administered makes it imperative that all young patients with liver cirrhosis or chronic active hepatitis (Sherlock, 1961; Sternlieb and Scheinberg, 1972), be examined specifically for Wilson's disease. On prolonged treatment with D-penicillamine the liver function is often improved, jaundice and ascites disappear, and the histological changes may be reversed even in advanced cases (Falkmer, Samuelson and Sjölin, 1970; Levi *et al.*, 1967). In our case marked clinical and biochemical improvement commenced within the first months of treatment. Hepatocellular function improved (Table 1), the portal hypertension diminished and concomitantly ^{198}Au uptake by the liver increased.

Injected ^{198}Au colloid is ingested by virtually all cells of sinusoidal origin (Bissell, Hammaker and Schmid, 1972).

Scintiscans of the liver performed in cirrhotic patients show a decrease in the hepatic uptake of ^{198}Au with an increase of activity in the extrahepatic reticuloendothelial system (RES) such as the spleen and bone marrow. This uptake of ^{198}Au in the extrahepatic RES in the presence of cirrhosis is thought to result from both a change in hepatic blood flow due to portal hypertension, and to proliferation of the reticuloendothelial cells (Cohen, 1969). It is therefore probable that in this patient the considerable increase in hepatic ^{198}Au uptake reflects objective improvement of liver circulation and a reduction in the portal hypertension (also confirmed clinically by disappearance of the ascites and reduction in the size of the oesophageal varices and splenomegaly).

Since patients with Wilson's disease are the only patients with chronic 'hepatitis' for whom specific and effective therapy is available, repeated liver scans in such patients may provide another easily

performed and safe test for objectively evaluating the effect of penicillamine therapy, particularly in patients in whom there may be a contraindication to repeated liver biopsy.

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