CASE REPORTS

Discordant Hepatic Uptake between Tc-99m Sulfur Colloid and Tc-99m DISIDA in Hypervitaminosis A

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Scintigraphic findings in a patient with biopsy-proven hypervitaminosis A included markedly impaired hepatic uptake of Tc-99m sulfur colloid but essentially normal uptake of Tc-99m DISIDA. This case presents a potential cause for image discordance with these two agents.

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Discrepancy in the results of liver imaging with different radiopharmaceuticals—sulfur colloid preparation and iminodiacetic acid (IDA) derivatives—has been reported in a variety of clinical entities (*1*). We present a case of hypervitaminosis A in which discordant images were characterized by markedly impaired hepatic uptake of Tc-99m sulfur colloid in the face of a normal Tc-99m DISIDA image.

CASE REPORT

A 30-yr-old male presented with complaints of swelling and tingling in his hands and feet, increasing over a 6-wk period, and generalized weakness. Over a 6-yr period he had indulged in megavitamin therapy, which included an estimated daily intake of 2.5 g of vitamin B_6 (adult recommended daily allowance: 2.0 mg) and 60,000 IU vitamin A (adult recommended daily allowance: 5,000 IU). Pertinent physical findings included dry, cracked skin, cheilosis, hypopigmentation of the palms and forehead, and ingrown toenails. There was edema and absent deep tendon reflexes in the lower extremities, and a profound sensory neuropathy. There was no papilledema and the cranial nerves were intact.

Initial laboratory tests revealed the following: WBC 3900, hematocrit 32.3, platelets 92,000, SGOT 100 U/l (normal 7–29), SGPT 82 U/l (12–29), LDH 547 U/l (90–320), alkaline phosphatase 186 U/l (20–90), total bilirubin 2.2 mg/dl (0–1.2), and direct bilirubin 0.9 mg/dl (0–0.2). Vitamin A level was 99 mg/dl (20–80). The patient was advised to discontinue all fat-soluble vitamins and decrease water-soluble vitamin and mineral intake.

Over the next month, his liver function tests reverted to normal except for the alkaline phosphatase, which remained elevated at 189 U/l. A coagulopathy was noted, however, with PT 15.5 patient/10.7 control, PTT 71.4 patient/54.7 control, and bleeding time 17 min. Repeat serum vitamin-A level was normal (34 mg/dl). A sulfur colloid liver-spleen study demonstrated borderline liver enlargement with diminished hepatic uptake, splenomegaly with augmented uptake, and increased bone-marrow activity (Fig. 1). An ultrasound image of the portal vein revealed a diameter of 1.5 cm (normal <1.3 cm), and a lack of caliber variation of the splenic and superior mesenteric veins during respiration, both believed to be signs of portal hypertension (*2*).

One month later, after correction of his coagulopathy, he was readmitted for liver biopsy. A repeat liver-spleen study was essentially unchanged from the earlier study, aside from relatively increased pulmonary uptake of the colloid on the later examination. Hepatic imaging was also performed with Tc-99m DISIDA, which revealed normal extraction and excretion of the radiopharmaceutical (Fig. 2). Light and electron microscopy of the liver biopsy revealed excessive iron storage but no cirrhosis. There was perisinusoidal fibrosis and lipid droplets in prominent perisinusoidal cells (Ito cells), characteristic of liver disease secondary to hypervitaminosis A.

The patient was discharged with a diagnosis of hypervitaminosis A, presumed vitamin B_6 sensory neuropathy, and pancytopenia secondary to hypersplenism.

DISCUSSION

Discrepancy between liver images obtained with sulfur colloid preparations and iminodiacetic acid derivatives presumably results from functional differences in uptake of the agents: the former are trapped in the perisinusoidal space of Disse, whereas the latter are actively extracted and excreted by hepatocytes. Often, focal pathologic processes may disrupt both mechanisms equally, resulting in a high degree of concordance between the images obtained with these two different hepatic tracers (*3*). Nevertheless, focal discordant uptake (defect on colloid image, activity with hepatobiliary agents) has been reported in a variety of entities

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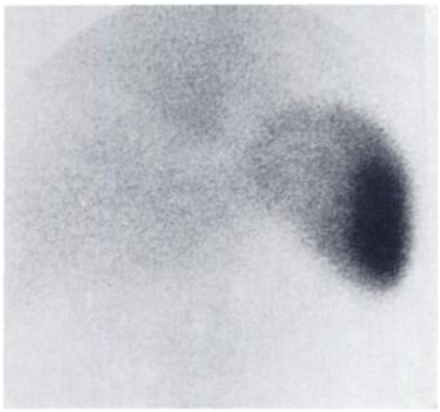

FIG. 1. Anterior image from initial Tc-99m sulfur colloid image, showing diminished hepatic uptake but augmented uptake in enlarged spleen. Bone-marrow uptake is also present.

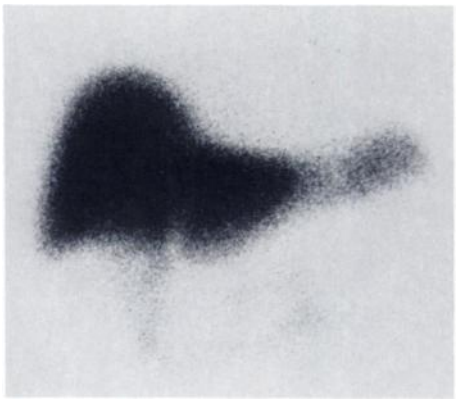

FIG. 2. Anterior image from Tc-99m DISIDA study, at 5 min after injection. There is extraction of tracer, and early gut activity. Gallbladder was well seen at 20 min after injection.

including hepatocellular adenoma (*1*), focal nodular hyperplasia (*4*), and hepatocellular carcinoma (*5*). Nonfocal discordance has been described in acute hepatitis (essentially normal colloid images with abnormal hepatobiliary image) (*6*) and chronic alcoholic liver disease (diminished colloid uptake with normal clearance of hepatobiliary agent) (*7*).

Liver disease secondary to hypervitaminosis A is characterized by perisinusoidal fibrosis, central-vein sclerosis, and lipid droplets in prominent fat-storing cells—referred to as perisinusoidal cells or Ito cells. These fat-storing cells are located underneath the endothelial lining within the space of Disse, usually in recesses between hepatocytes. Russell reported abnormal sulfur colloid liver images—characterized by diminished hepatic uptake, hepatosplenomegaly, and augmented splenic and bone-marrow uptake—in two patients with hypervitaminosis (*8*). Despite lack of morphological evidence of cirrhosis, both of these patients presented with ascites and portal hypertension, and it was suggested that their physical findings could result from obstruction of sinusoids and obliteration of the space of Disse. Rat experiments have subsequently demonstrated elevation of portal venous pressure after vitamin A administration—attributed to enlarged Ito cells bulging the endothelial lining into the sinusoidal lumen and compromising the microcirculation—which was well correlated with diminished volume of the sinusoidal lumen (*9*).

Adequate perfusion of the sinusoids with portal-venous, rather than arterial, blood is considered to be a prerequisite for efficient phagocytic function. Horisawa et al. have suggested that the characteristic hepatic colloid image pattern of chronic liver disease results from poor extraction of colloid due to intrahepatic shunts bypassing the hepatic reticuloendothelial system (*10*). We postulate that this same mechanism accounts for the sulfur colloid image abnormalities seen in cases of hypervitaminosis A. That is, volume decrease of the sinusoids secondary to increased volume of fat-storing cells results in elevation of portal-venous pressure and intrahepatic shunting. With diminished blood flow in the hepatic sinusoids, the colloidal particles are not as effectively trapped in the space of Disse.

The resultant pattern in the current case, characterized by decreased liver uptake of the colloid with redistribution into the spleen and bone marrow, correlates well with the ultrasound evidence of portal hypertension as well as the histologic findings. This mechanism does not necessarily affect hepatocyte function, thus accounting for the discordance between Tc-99m sulfur colloid and Tc-99m DISIDA images of the liver.

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