RESIDUAL SPLENIC FUNCTION IN THE PRESENCE OF THOROTRAST-ASSOCIATED HEPATIC TUMOR: CASE REPORT

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A 50-year-old man had received intravenous colloidal thorium dioxide (thorotrast) 27 years previously. Scintiscans with both ^{99m}Tc-sulfur colloid and ^{131}I-rose bengal revealed an extensive intrahepatic defect. At operation, the lesion proved to be an infiltrating hemangiosarcoma. The spleen was small but the chronic internal radiation of the spleen had not completely destroyed the function of radiocolloid uptake. Review of the literature disclosed other cases in which the spleen was still capable of accumulating radiocolloid some years after thorotrast administration. In at least one other instance, radiocolloid uptake was not accompanied by splenic ability to clear Howell–Jolly bodies: a disassociation of splenic functions. The effects of the internal radiation dose to the spleen from thorotrast are discussed and compared with the effects of external radiation. The discrepancy between the effects of the two doses may be related to the high relative biologic effectiveness of the alpha rays from thorotrast compared with x-radiation, to nonuniformity of distribution, and to the effects of reticuloendothelial blockade.

The finding of intrahepatic tumors (particularly hemangiosarcomas) in a significant proportion of individuals who had received colloidal thorium dioxide (thorotrast) intravenously has been recognized for some years (*1*). We recently encountered such a patient in whom a scintiscan showed the presence of an intrahepatic mass. Since the spleen was functional in terms of ability to extract radiocolloid, we carried out calculations of the splenic radiation dose and compared this with the reported effects of external radiation on the organ.

CASE REPORT

A 50-year-old white man was admitted because of the recent onset of abdominal pain, vomiting, and diarrhea. The episode began about 5 days previously with pain along the right costal margin, made worse by motion. Initially there was nausea and vomiting, and oral intake nearly ceased. He had consumed alcoholic beverages until 2 years ago. Approximately 27 years prior to this, he had had a cerebral thrombosis and an arteriogram was performed. Physical examination showed him to be obese and dehydrated. He was afebrile, blood pressure was 120/70, pulse 100, and respiration 28. The abdomen was distended and bowel sounds were absent. There was abdominal tenderness, especially in the upper portion. Hemoglobin was 9.1 and white count 15,000 with 74% segmented forms. The platelet count was 50,000.

Nasogastric suction and intravenous fluids were begun and a blood transfusion was given. An abdominal x-ray showed a small opacified spleen and minimal densities in the liver. Areas consistent with lymph nodes were noted in the epigastrium; the appearance was characteristic of the effects of thorotrast. A recheck revealed that the arteriogram, performed at another hospital in 1948, was carried out with intravenous thorotrast.

A liver scan was performed after administration of ^{99m}Tc-sulfur colloid. The spleen was functional (Fig. 1) and clearly outlined on the scan. By measurement of the scan (and of a radiograph), the spleen was under 7 cm in length. A large superior hepatic defect, noted particularly on the right lateral view, was also seen on a scintiscan performed with

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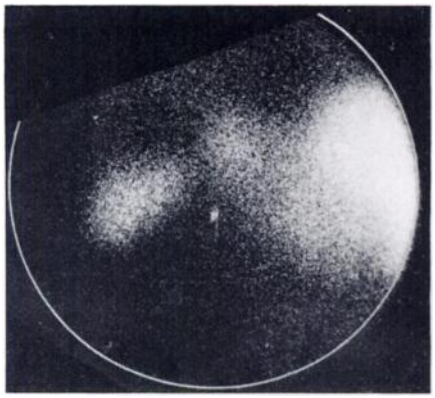

FIG. 1. Posterior ^{99m}Tc-sulfur colloid scintiscan showing uptake in spleen.

^{131}I-rose bengal (Fig. 2). Review of a smear of peripheral blood revealed occasional Howell–Jolly bodies.

The patient's symptoms were thought to be related to an intrahepatic tumor, perhaps impinging on the diaphragm or other structures. After a platelet infusion, a laparotomy was done. A large quantity of bloody fluid was aspirated from the peritoneal cavity. A 5-cm-diam tumor within and on the lateral aspect of the right lobe of the liver was found. This was covered by a clot. There was no extension to the hilus. Local nodes were all quite firm. The gallbladder and the right hepatic lobe were removed. Packed red blood cells, fluids, and frozen plasma were administered. The pathology report was of an hepatic hemangioendothelioma (hemangiosarcoma).

DISCUSSION

The most common malignant tumor associated with past thorotrast administration is the hepatic hemangiosarcoma, although other types of tumors, including those occurring within the liver, can be found (*2–4*). Relatively few observations, however, have been made on splenic function in these instances. Our patient's spleen was small, being more than two standard deviations below the adult average (*5,6*). Contraction of the spleen has been connected with thorotrast administration (*7*). In addition, internal irradiation of the spleen by means of beta-ray-emitting radionuclides, such as those delivered by microspheres, can also cause splenic contraction (*8*).

The pathology of thorotrast within the spleen has been described (*9*). Initially, thorotrast is diffusely distributed throughout splenic tissue, in the reticuloendothelial cells. On the average, 72% of the injected dose of thorotrast is deposited in the liver and 12% in the spleen (*10*). From this estimate we have the following average concentrations:

Liver: 72%/1,500 gm = 0.048%/gm;
Spleen: 12%/150 gm = 0.080%/gm.

The splenic concentration of thorotrast is thus about 1.7 times that of the liver. In individual cases, however, this varies over a wide range (*10*). An eventual redistribution occurs; some thorotrast is apparently translocated to local lymph nodes. Later, thorotrast distribution in the spleen develops foci near small arteries and this lack of homogeneity causes difficulties in calculating radiation dose. Assuming a more uniform distribution, Looney (*10*) estimated that, following intravenous administration of a 25-ml conventional dose of thorotrast, the spleen would receive a radiation dose of 0.8 rads per week for life. In the present case, this would amount to (0.8 rads/week) × (52 weeks/year) × (27 years), or 1,123 rads. Recall, however, that the distribution is nonuniform after a number of years (with "hot spots" appearing); that the spleen becomes progressively smaller, making the radiation effects per unit volume more intense; and that the alpha emissions of thorium have a relative biologic effectiveness considerably greater than 1—probably closer to a value of 10. We can compare the estimated radiation dose to the spleen due to thorotrast with that reported for external irradiation (*11*). Short-term delivery of 2,000 rads of x-rays to the abdomen did not result in any gross impairment of the spleen's ability to accumulate ^{99m}Tc-sulfur colloid (the actual dose to the spleen may have been less). The histopathology of the x-irradiated spleen (*17*) is quite different from that of the spleen chronically irradiated by thorotrast (*9*).

The somewhat scanty data on the functional effects of thorotrast on the spleen are summarized in Table 1. In most cases the spleen, although containing thorotrast, retains the ability to concentrate circulating radiocolloid. At some point, however, a functional asplenia is produced, perhaps due to the

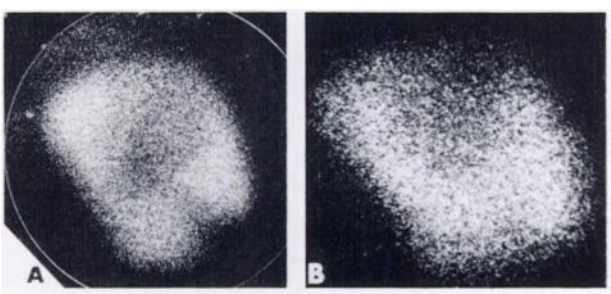

FIG. 2. Right lateral scintiscans, with slight differences in magnification and angulation, showing large hepatic defect. Scanning agents were ^{99m}Tc-sulfur colloid (A) and ^{131}I-rose bengal (B).

TABLE 1. FUNCTIONAL EFFECTS OF THOROTRAST

Authors	No. of cases	Splenic ability to accumulate radiocolloid?	Howell–Jolly bodies or RBC abnormalities?
Johnson et al (12)	1	Yes*	?
Spencer et al (13)	1	No†	Yes
Johnson and Babb (3)	1	Yes‡	Yes
Langlands and Williamson (14)	35	?	Yes (34/35)
Janower et al (15)	30	?	No
Present case	1	Yes†	Yes

* ^{51}Cr-denatured erythrocytes.
† ^{99m}Tc-sulfur colloid.
‡ Agent not stated.

chronic irradiation or to the loading effect of thorotrast on the reticuloendothelial cells as the spleen decreases in size.

On the other hand, what about other functions, such as the removal of Howell–Jolly bodies from circulating erythrocytes? In the case reported by Johnson and Babb (*3*) and in our case, the spleen was capable of taking up radiocolloid but could not completely clear Howell–Jolly bodies. A similar dissociation of splenic functions has been described in patients under acute hematologic stress, in whom an "overload" of Howell–Jolly bodies was present (*16*). Our patient was probably under such stress, as manifested by the leakage of blood from the tumor and the low hemoglobin and platelet counts. A bone-marrow aspiration showed normoblastic erythroid hyperplasia consistent with continued hemorrhage. Interestingly, in the report of Langlands and Williamson (*14*), 34 of 35 patients with intrasplenic thorotrast had circulating Howell–Jolly bodies. In the case described by Johnson et al (*12*) the thorotrast-laden spleen still possessed the ability to accumulate ^{51}Cr-tagged heat-denatured erythrocytes.

The dissociation of splenic functions brings us back to the striking difference between the effects of acute external irradiation and chronic internal radiation on the spleen. Nonuniformity of distribution, a high relative biologic effectiveness of the alpha emissions, and chronic blockade of reticuloendothelial cells may all play a role in the thorotrast effect. Thorotrast use in animals might provide a model for studying these effects and in elucidating the time course of the dissociation of splenic activities.

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