Perfusion Scintigraphy (Tc-99m MAA) During Surgery for Placement of Chemotherapy Catheter in Hepatic Artery: Concise Communication

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In 17 patients receiving regional hepatic chemotherapy, Tc-99m macroaggregated albumin imaging was used to aid arterial catheter placement and to assess perfusion patterns. Intraoperative imaging with a portable gamma camera allowed immediate monitoring of hepatic and extrahepatic perfusion patterns and assisted catheter manipulation when necessary to achieve optimal flow distribution. In all 12 patients with standard hepatic arterial anatomy, complete perfusion of both lobes of the liver was achieved, although three of them required intraoperative catheter manipulation and repeat imaging after initial placement. The remaining five patients had aberrant hepatic arterial anatomy, and complete perfusion was more difficult to achieve; they exemplified the need for dual catheters, ligation of accessory hepatic branches, and repeated imaging.

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A totally implanted drug-delivery system for hepatic chemotherapy has been developed at the University of Michigan Medical Center (*1*). A special small-bore silastic catheter is surgically placed in the hepatic artery and attached to a subcutaneously implanted Model 400 Infusaid pump. A critical aspect in the successful application of this chemotherapy system is the correct positioning of the arterial catheter during laparotomy to ensure maximal delivery of the chemotherapeutic agent to all involved portions of the liver, with minimal delivery to other sites where it could cause unwanted side reactions. Intraoperative use of perfusion imaging with technetium-99m macroaggregated serum albumin (Tc-99m MAA) has proven useful for assessing patterns of flow distribution as a guide to optimum catheter placement.

MATERIALS AND METHODS

The group studied consisted of 17 patients who underwent operative placement of chemotherapy catheters in the hepatic artery. A total of 42 hepatic artery Tc-99m MAA perfusion studies were obtained either intraoperatively (*17*) or during followup (*25*).

The patients ranged from 25 to 66 years old, mean 53. All had proven primary or metastatic hepatic neoplasms with the following distribution: colon carcinoma (*10*), hepatoma (*3*), carcinoid (*2*), cholangiocarcinoma (*1*), and islet-cell tumor of the pancreas (*1*).

Technique. *Presurgical imaging.* Before the operation, technetium-99m sulfur colloid liver scans and visceral angiograms are obtained in all patients. The liver scans serve as a baseline for assessing the extent of malignant disease in the liver, and later as guides for assessing the completeness of liver perfusion from the surgically implanted catheter (Fig. 1). The visceral angiograms serve as maps of regional vascular anatomy from which the number and initial locations of the chemotherapy catheters are determined (Fig. 2).

Operative imaging procedure. After initial surgical placement of the chemotherapy catheter in the common hepatic artery, 1–4 mci of Tc-99m MAA is injected slowly (0.5–1.0 ml/min) into the catheter to imitate the infusion rate and pattern of distribution of the chemotherapeutic agent as closely as possible. Imaging is accomplished with a mobile gamma camera with low-

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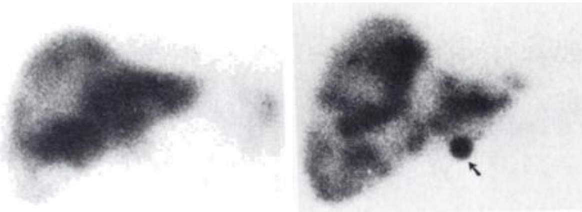

FIG. 1. Tc-99m sulfur colloid scan on a 54-year-old white male with adenocarcinoma of colon. Note multiple areas of photon deficiency due to metastases (left). Intraoperative Tc-99m MAA scan demonstrates perfusion of both lobes of liver (right). Arrow indicates focal area of activity at catheter tip.

energy, all-purpose, parallel-hole collimator; energy window is 30 keV, centered on 140 keV; output is fed to a nuclear medicine computer. The operative area is draped with a sterile sheet, and the camera head carefully positioned over the anterior abdomen. An anterior view is collected for a minimum of 60 sec. This image is displayed on the computer screen and compared with the preoperative anterior TcSC liver scan. If the images coincide, hepatic perfusion is considered satisfactory, and the study is complete. If the images demonstrate a

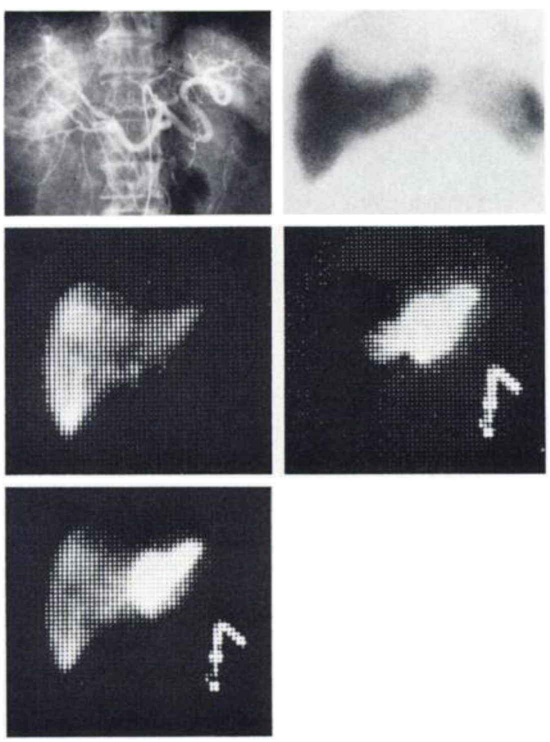

FIG. 2. Celiac angiogram on a 59-year-old white female with metastasis from colon shows left hepatic artery arising from left gastric (arrows) (upper left). Tc-99m sulfur colloid scan shows multiple hepatic metastases (upper right). Intraoperative Tc-99m MAA infusion into surgically placed catheter in common hepatic artery demonstrates perfusion in distributions of right and middle hepatic arteries (center left). Tc-99m MAA infusion into second catheter in left gastric artery (which has been ligated distal to left hepatic) demonstrates perfusion of left lobe of liver (center right). Activity due to first injection has been subtracted out. Image of superimposed infusions shows perfusion of entire liver (lower).

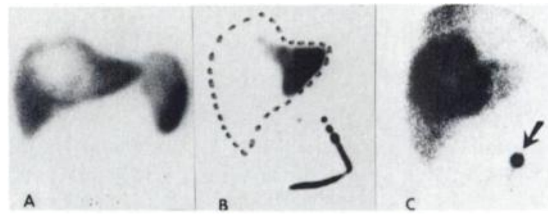

FIG. 3. Tc-99m sulfur colloid scan on a 66-year-old white female with metastases from colon (A). In a patient with standard hepatic anatomy, initial intraoperative Tc-99m MAA scan shows perfusion of left lobe only (B). After repositioning, perfusion of entire liver is demonstrated (C). There is hyperperfusion of tracer in large metastatic lesion in right lobe. Note lung uptake, indicating A-V shunting; also a small focal area of uptake at catheter tip (arrow) most likely due to Tc-99m MAA adherence to a small nonobstructing thrombus.

marked discrepancy, with either incomplete hepatic visualization or marked extrahepatic activity, the surgeon may elect to readjust the catheter and study the distribution again (Fig. 3).

In cases where the surgeon readjusts the catheter, the wound is redraped and a second 60-sec anterior liver view obtained. A second injection of Tc-99m MAA is then administered and, without moving the camera head, a third 60-sec anterior view is obtained. The perfusion pattern resulting from the second injection is determined by subtracting the second image from the third image. If perfusion is considered satisfactory, the study is complete. If not, the steps outlined above can be repeated.

In some cases, two catheters are required in order to perfuse the entire liver. For example, the right or left hepatic artery may arise as a branch of the left gastric or superior mesenteric. After the catheters are both in place, one of them is injected (preferably the one supplying the largest volume of liver) and an initial 60-sec image obtained. The second catheter is then injected and a second 60-sec image obtained. The combined perfusion pattern is compared with the baseline liver scan to assess completeness (Fig. 2). One or both catheters may require additional manipulation, guided by subsequent Tc-99m MAA injections using the subtraction technique described.

Nonoperative follow-up studies. Following complete implantation of the catheter and chemotherapy pump, the catheter can be accessed via a sideport for followup studies of the catheter patency and perfusion pattern (*1*). One to four mCi of Tc-99m MAA is injected slowly (0.5–1.0 cc/min) via the sideport. Images (500,000 counts) are obtained in the anterior, posterior, and both lateral views. The images include the lower portions of the lung fields and the entire abdomen.

RESULTS

Initial visceral arteriograms demonstrated standard hepatic arterial anatomy in 12 of the 17 patients. Each of the 12 received one catheter. The other five had variations consisting of a replaced right hepatic artery to the superior mesenteric artery (*2*), a replaced left hepatic artery to the left gastric artery (*2*) and a single case where the left hepatic artery was not visualized, possibly due to compression by tumor. Three of these patients received two catheters. The patient in whom the left hepatic artery was not seen received a catheter in the proper hepatic artery via the gastroduodenal, and the remaining patient received a similar placement with ligation of a small accessory right hepatic artery arising from the superior mesenteric artery. In 11 of the 17 cases, only one intraoperative Tc-99 MAA injection was required. However, three patients required two injections, and the remaining three required three, four, and, five injections respectively.

Of the 12 patients with standard hepatic arterial anatomy, nine showed perfusion of both lobes after the initial injection (Fig. 1). In the remaining three, catheter manipulation with repeated Tc-99m MAA study resulted in perfusion of both lobes of the liver.

Of the five patients with variant anatomy by hepatic arteriogram, only one had perfusion of both lobes after the first injection. Note that two of these five patients had no chance of complete perfusion from the outset (one with a nonvisualized left hepatic on angiography and one with a surgically ligated accessory right hepatic). Subsequent catheter manipulation and scanning resulted in unequivocally complete perfusion of both lobes of the liver in one of the two remaining patients. In the last patient, who required two catheters because of a right hepatic artery transferred to the superior mesenteric artery, a small portion of the left lobe was not perfused. Of the 14 patients who had complete perfusion of both lobes, confirmed by Tc-99m MAA study after intraoperative placement of the catheter, only one had a subsequent study showing less than complete perfusion of the liver. The followup study was done approximately one week after surgery and the change was due to a blood clot in the common hepatic artery, documented by angiography, which led to redirection of blood flow.

Lung uptake, above background, was seen in nine studies on eight patients (Fig. 3C). It occurred only once on an initial study and appeared in the other patients an average of three months after pump placement.

Extrahepatic abdominal uptake occurred in nine studies on seven patients (Fig. 4). This was seen only once on an initial study and after an average of two months in the patients with gastrointestinal activity on follow-up studies. Five of the patients had clinical symptoms of chemotherapy toxicity, including mild gastritis and diarrhea in four and more severe gastritis and UGI bleeding in one. Extrahepatic uptake may be due to placement of the catheter tip proximal to branches leading to other abdominal structures; to clotting or tumor encasement of the hepatic artery, with backflow into the mesenteric and splenic arteries; or to flow into extrahepatic collaterals that may be formed subsequent to surgical ligation of the gastroduodenal or splenic arteries.

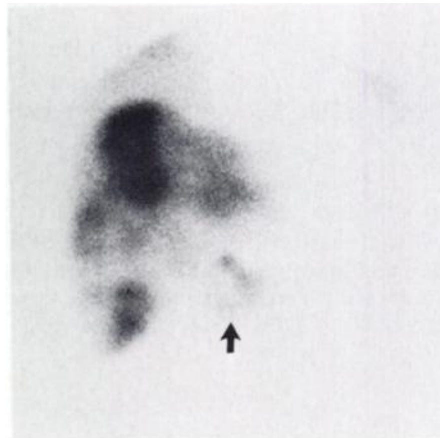

FIG. 4. Small area of extrahepatic activity is demonstrated subjacent to porta (arrow).

An important additional finding was the presence of focal areas of increased tracer at the end of the catheter or in the course of the proper hepatic artery (Figs. 2,3). This was felt to represent blood clot with adherence of Tc-99m MAA. The finding was seen to some degree in 19 studies on nine patients and was confirmed by angiography in one. The presence of this focal uptake did not correspond with a change in flow pattern or apparent obstruction to flow in any of the remaining eight patients.

From a clinical standpoint, 14 of the 17 showed a response to chemotherapy. A partial response was defined as at least a 30% decrease in the sum of the palpable liver size below the costal margin in the right midclavicular line and below the xiphoid process. All respondees showed at least a 50% reduction in the product of the longest perpendicular diameters of measurable nodules by liver scan.

DISCUSSION

Tc-99m MAA imaging has been used by several investigators to assess catheter-controlled perfusion patterns in chemotherapy (*2–6*). However, none of the previous studies have used the technique prospectively for actual guidance of catheter placement at surgery, nor have they taken advantage of computer subtraction techniques to permit the effects of catheter manipulation to be assessed by serial Tc-99m MAA injections.

Assessment of catheter placement before the infusion of chemotherapeutic agents has been difficult without the use of radiotracers. There are significant drawbacks to both angiography (high flow rate, catheter recoil, flow reversal) and fluorescent dyes (marking surface flow only).

The Tc-99m MAA technique with the surgically implanted chemotherapy pump allows slower infusion rates to be used, more closely simulating the chemotherapeutic infusion rate. Catheter recoil and flow reversal are not problems. Perhaps, more importantly, Tc-99m MAA provides a map of perfusion at the capillary level, which is not provided by contrast angiography or fluorescent dyes.

The question of normal versus variant vascular anatomy has not been previously addressed, and this has made a large difference in the probability of successful catheter placement in this study. In the patients with normal anatomy, all had optimal catheter placement. On the other hand, among the five patients with variant arterial anatomy, only one initial catheter placement resulted in complete perfusion of both lobes of the liver, and in only two of the five cases was complete perfusion achieved.

The finding of lung uptake in half of the patients is significant. The lung activity is indicative of arteriovenous shunting, which is well recognized to be increased in tumor neovascularity. This finding taken alone is not new. It is of great interest, however, that we observed lung uptake only once on an initial study. The eight other instances of lung uptake were on followup scans during chemotherapy in seven patients, and it seems likely that shunting must have increased with time. Possibly a positive response to chemotherapy, with a decrease in cellularity of tumors, could result in increased AV shunting. Alternatively, there may be increased shunting due to development of cirrhosis as a result of the chronic chemical toxicity.

Extrahepatic uptake in the gastrointestinal tract and other abdominal viscera has not been fully investigated. Again the increased incidence of this finding with time has not been reported previously, and the causes await elucidation. However, analysis of extrahepatic areas is an important adjunct to the hepatic perfusion analysis because it warns the clinician to be alert for toxic side effects. The finding of marked lung or gastrointestinal uptake is clinically important because it may require alteration of the chemotherapeutic regimen.

Optimal catheter placement is a key element in successful regional chemotherapy. The current approach using a completely implantable system offers the potential for long-term therapy, but it imposes a strict burden on the surgeon to optimize catheter placement at the time of laparotomy. Intraoperative scintigraphy of hepatic artery perfusion with Tc-99m MAA is a sensitive technique that is feasible in the operating room through the utilization of mobile gamma cameras and computer systems.

ACKNOWLEDGMENT

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George Simon Memorial Fellowship Award

The Fourth Annual George Simon Memorial Fellowship Award, given by the Fleischner Society for the best submitted work relating to the imaging of the respiratory system, has been given to H. Dirk Sostman of Yale University for his paper "Experimental Studies with ^{111}Indium Labeled Platelets in Pulmonary Embolism."

Entries for the Fifth George Simon Award are now being accepted. The paper can represent the work of more than one investigator, but the senior author should be the applicant and responsible for the majority of the work. Applicants should be no older than 40 years. Papers which have been published or submitted elsewhere are not eligible. The award consists of an all-expense-paid trip to the 1983 Fleischner Society Meeting, New York City in May, plus a cash prize. All submissions must be in the form of a complete scientific paper, not longer than 25 pages (double spaced) and should be sent in triplicate to:

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Papers must be sent on or before January 1, 1983