Nuclear Medicine Procedures for Evaluating Organ Rejection

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Changes that occur in the morphologic and functional status of a transplanted organ are of great concern to the transplant surgeon. Of particular interest is the period during which the host is conducting a severe rejection campaign against the newly acquired organ. Surgeons have come to rely extensively on nuclear medicine procedures for information which enables them to provide the best patient management possible. At the University of Colorado Medical Center, diagnostic nuclear medicine procedures have now been used on more than 300 human renal and 60 human hepatic homograft recipients with ages ranging from several months to well into the fifth decade.

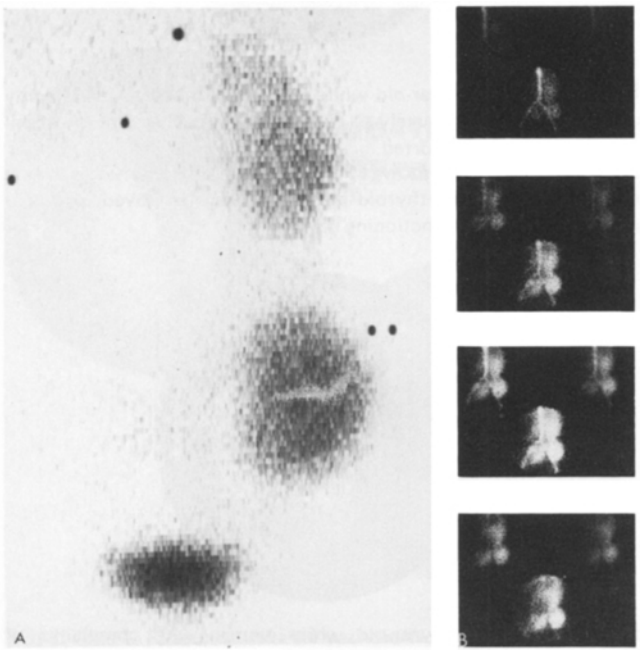

FIG. 1: (A) Rectilinear scan of anterior abdomen using ^{197}Hg-chlormerodrin. From top to bottom, native kidney, transplanted kidney, bladder. (B) Renal blood flow study with ^{99m}Tc-pertechnetate. Serial 3-sec images illustrate blood transit through aorta and iliac vessels into both kidneys.

Renal Transplantation

The most consistent and reproducible data have been obtained in studies following renal transplantation. Three radiopharmaceutical preparations are used routinely. Approximately 1 1/2 hr after the intravenous injection of ^{197}Hg-chlormerodrin (4 μCi/kg of body weight) the initial phase of the series begins. The patient is placed in the supine position and the collimator of a 5-in. rectilinear scanner is focused midway through the organ of interest. The homograft is easily palpated in its site of residence, just beneath the skin in the iliac fossa. Subsequently, the entire lower abdomen is scanned to achieve bilateral comparison. In cases of renal autotransplantation (patient's own kidney removed and following vascular reconstruction placed in the iliac fossa) the entire anterior abdomen is scanned to demonstrate tubular activity (Fig. 1) in both the native and transplanted organ (*1*).

Next, the patient is positioned before a dual-probe scintillation detector system. Using the ^{197}Hg-chlormerodrin administered previously, the kidney is located. Following localization, 0.9 μCi of ^{131}I-sodium iodohippurate (per kilogram of body weight) are injected intravenously as a bolus. The electronics of the dual-probe system are set with a time constant of 1 sec and a speed of 12 in./1 hr. Probe position is of critical concern because of the near proximity of the renal homograft to the bladder. By using both probes, one may either record activity in the bladder or, in the case of the autotransplant, the native kidney for comparison. Now the third procedure involves evaluation of blood flow to the homograft (perfusion). In most cases, the kidney is anastomosed to one of the internal iliac vessels. Following the intravenous administration of 10 mCi of ^{99m}Tc-pertechnetate as a bolus (*1*), the progression of its transit is recorded by a scintillation camera data-store sys-

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tem with subsequent playback and hard-copy recordings obtained at 3-sec intervals. (Fig. 1B). A divergent collimator is used in most instances as a means of comparing contra-lateral vessels as well as blood flow through the abdominal aorta. The flux from this dose of ^{99m}Tc-pertechnetate is much higher than that of ^{197}Hg-chlormerodrin (10 mCi instead of 250 μCi) and the energy range (140 keV compared with 77 keV) is different enough that the ^{197}Hg-chlormerodrin does not produce a significant image under these conditions (Fig. 2). A complete renal evaluation series may be satisfactorily completed in about 1 hr.

Liver Transplantation

Valuable information was obtained from radionuclide studies conducted on initial hepatic homograft recipients in the late 1960s. It became evident that data concerning the functional integrity of the liver (polygonal cells) and morphologic changes (reticuloendothelial cell uptake uniformity) could be monitored by using noninvasive nuclear medicine techniques. Polygonal cell function is studied following the intravenous injection of 100 μCi of ^{131}I-rose bengal. A 20-min retention examination as described elsewhere (*2-4*) is carried out, followed by rectilinear scanning of the entire anterior abdomen. Twenty-four hours later, a second rectilinear scan of the anterior abdomen is obtained demonstrating the presence or absence of the rose bengal preparation in the gut. The abdominal scans require about 45 min to complete.

Morphology of the homograft is determined both pre- and postoperatively using ^{99m}Tc-sulfur colloidal preparations (*3, 5-8*). Three and 5-in. rectilinear scanners, a ten-crystal rectilinear scanner, and a scintillation camera system have all been used for these morphologic procedures, but since size relationships are extremely important in the liver homograft series, the 5-in. rectilinear scanner has gained the greatest utility. Scanning time necessary for completing the four-view liver series is approximately 50 min. For the most part, the examinations described are easily accomplished as shown by the fact that they are performed twice a week during the immediate postoperative period.

Discussion

Experimental studies derived from canine recipients as conducted by the author (*4,9*) and others (*7, 8, 10*) provide a basis for the use of nuclear medicine studies as they apply to human organ transplantation. These procedures and clinical experience have provided information concerning the changes which can be detected by nuclear medicine procedures. Many entities in addition to rejection may yield an abnormal renal transplant

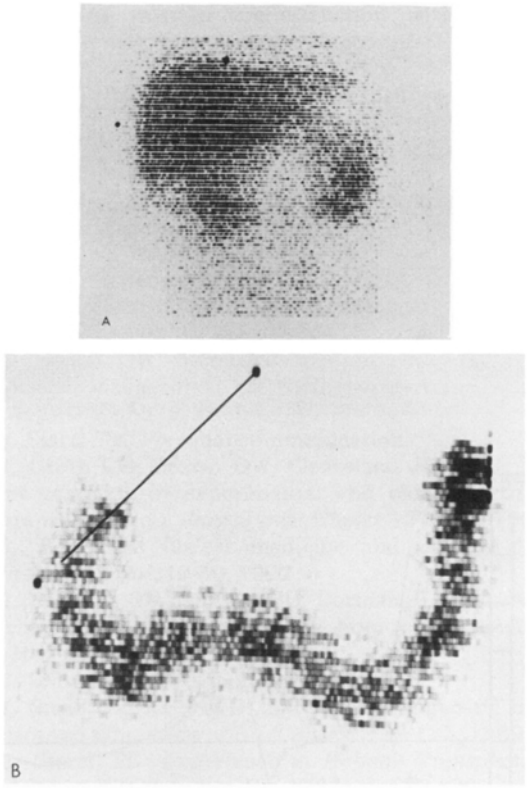
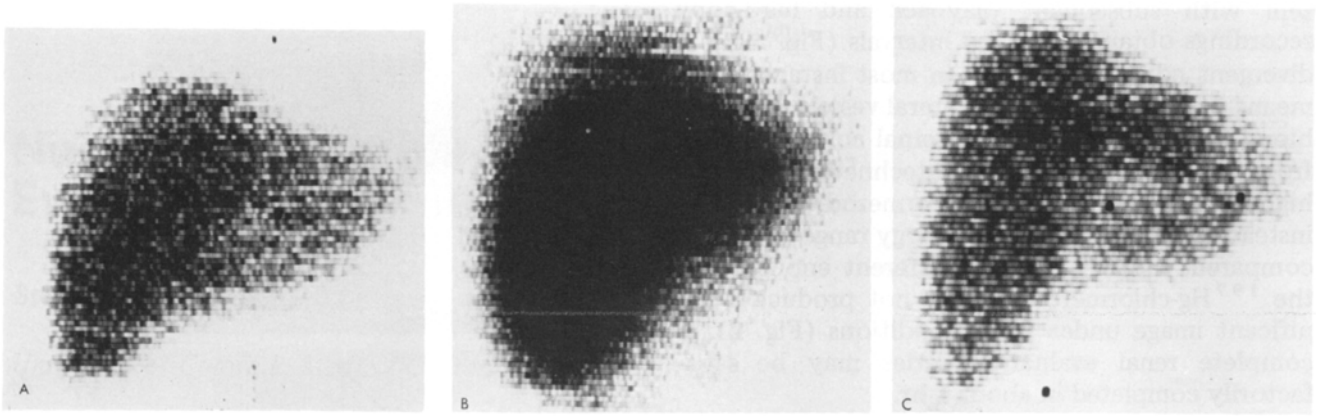


FIG. 2: (A) Anterior rectilinear scan of abdomen demonstrating abnormal accumulation of ^{131}I-rose bengal in polygonal cells of liver and bilateral kidneys at 24 hr. (B) Normal distribution pattern of rose bengal at 24 hr gives no evidence of radiopharmaceutical in liver parenchyma.

evaluation series. These more commonly include acute tubular necrosis (ATN), renal artery obstruction, and ureteral obstruction. In some cases, an episode of the latter may mimic a mild rejection. In both, the renogram shows a good early phase but a continued rise rather than drop in the later phase. Renal scans obtained using ^{197}Hg-chlormerodrin usually reveal a sharply delineated transplanted organ, provided technical considerations are correct. Acute rejection and arterial stenosis or occlusion may yield identical findings on a rectilinear scan. Both show progressively decreased renal uptake and increased hepatic concentration of the radiopharmaceutical (*5, 7, 10, 11*). During rejection, serial images, if obtained at proper intervals, will show an increase in the size of the organ followed by a gradual return to normal after steroid treatment. Dynamic studies using ^{99m}Tc-pertechnetate will provide useful information about the patency and viability of the anastomosed renal artery as well as an idea of renal homograft size (*1*). Probe or detector placement are of the utmost importance in all studies of the transplanted kidney.

Suspected postoperative complications or changing liver function tests (LFTs) lead one to expect



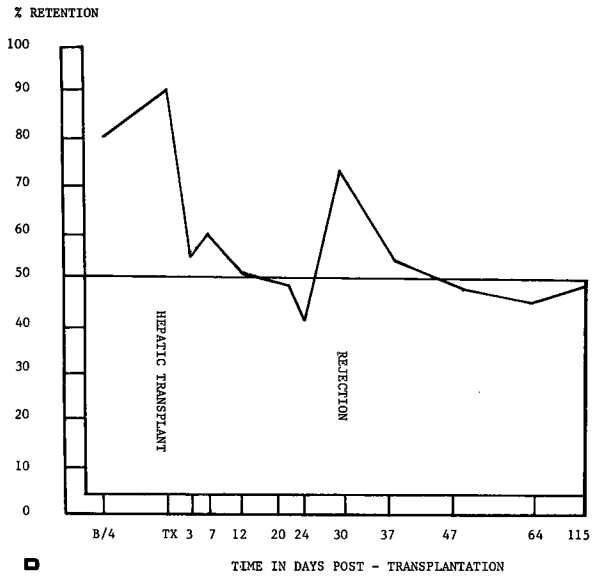


FIG. 3. Serial anterior rectilinear scans of liver using ^{99m}Tc-sulfur colloid. (A) Before rejection. (B) During rejection. (C) Following rejection. Note changes in hepatic size. (D) Typical findings of rose bengal retention values during pre- and postoperative course.

to obtain an abnormal liver series. It has also been our experience that abnormalities of the liver parenchyma are occasionally found with radionuclide scanning in the presence of normal LFTs and in the face of a complete lack of clinical signs of rejection. A 20-min retention study and a 24-hr rectilinear scan of the anterior abdomen may confirm the presence of a complete intrahepatic or extrahepatic biliary obstruction (Fig. 2). The normal half-time for the iodinated preparation in the liver is 90 min. From this, one may deduce that the liver should be essentially free of rose bengal by the 24-hr scan. An important and sometimes confusing technical consideration is the fact that the kidneys are often visualized. Occasionally it is difficult to distinguish the renal systems from the bowel.

Rejection of the liver homograft may be followed using serial tests with ^{99m}Tc-sulfur colloid and the rectilinear scanner. Marked size increase is noted during the rejection period. Increase is also noted in the 20-min rose bengal retention value (Fig. 3). After the administration of the appropriate medication, the liver will decrease in size. This phenomenon requires several days to weeks to be reversed, but at its completion the homograft will have returned essentially to its previous size (*3, 5, 6, 12*). The distribution of radiocolloid in the reticuloendothelial system plays an important part in the evaluation of graft rejection. In many cases, vast concentration of the colloidal radiopharmaceutical may be visualized in the extrahepatic sites—the bone marrow (*5, 12, 13*). The findings are consistent with those seen in severe cirrhosis except that on occasion we have also seen lung uptake of the colloidal material (Fig. 4), a phenomenon described elsewhere (*3, 8, 13, 14*). In scans performed several weeks after transplantation and after rejection reversal, the RE extrahepatic sites are relatively free of the radiopharmaceutical preparation. This is felt to be indicative of hepatic reticuloendothelial function. By this point in time, the 20-min rose bengal retention values have also dropped to within normal or a high-normal range.

Summary

Nuclear medicine procedures, as performed at our institutions, and as described by Loken, et al (*15*) and others (*1, 5, 11*), have proven to be of valuable assistance in the management of the postoperative renal and hepatic transplant recipients. Although we cannot always determine with certainty the nature of the lesion in these patients, correlation of nuclear medicine studies with the rest of the clinical information significantly improves the results of these new surgical procedures. The technical quality of the tests described is of great importance if they are to achieve their maximum potential usefulness. Postoperative studies have been obtained on renal homograft recipients for as long as ten years. Serial studies have been

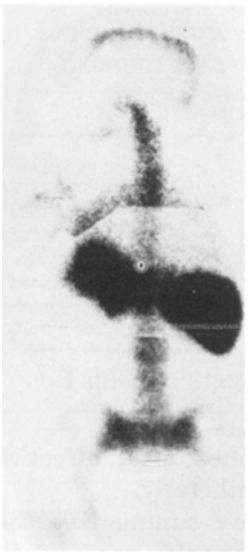


FIG. 4. Anterior example of scintillation camera study showing marked reticuloendothelial cell uptake of ^{99m}Tc-sulfur colloid preparation.

performed on hepatic homograft recipients for more than 42 months at the present time.

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