Role of Liver Scanning in the Preoperative Evaluation of Patients with Cancer

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[WITH SPECIAL PLATE]

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Summary: Liver scan characteristics and liver function tests of 72 patients with proved hepatic malignancy (54 metastatic, 18 primary) were evaluated. Well-defined focal defects were observed in 83% of patients with metastatic and 77% of patients with primary liver carcinoma. In 10% of the patients with metastatic liver disease the distribution of radioactivity was normal. Four or more biochemical liver function tests were normal in 33% of metastatic and 29% of primary liver cancer patients. Hepatic enlargement was present in the scan in 94% of the patients with liver metastases; however, data obtained from 104 necropsies of patients with hepatic metastases showed that only 46% had hepatomegaly. We recommend, therefore, that a liver scan should be performed before major tumour surgery in every patient with known malignancy regardless of normal liver size or normal liver function tests.

Introduction

Although liver scanning has been proposed as a sensitive test for the detection of hepatic metastases, its exact role in the management of a patient with malignancy has not been completely defined. In the present study patients with histological evidence of hepatic cancer were analysed in an attempt to determine the sensitivity of the liver scan for the detection of hepatic malignancy, especially metastasis, and the indications for a liver scan in patients known to have cancer in some other region of the body.

Materials and Methods

Seventy-two patients with proved hepatic malignancy (18 primary and 54 metastatic) who had had liver scans were studied. This group is referred to subsequently as the "scan group." In 68 cases the histological proof was obtained by needle biopsy and the interval between the two procedures was one week or less. In four cases histological confirmation was obtained at necropsy performed within one month of scanning. Only those biochemical tests done within two days of the radio-nuclide procedure were evaluated. Liver weight was calculated in each case from the scanning images (anterior and right lateral views) by the method of Rollo and DeLand (1968). The presence of abdominal symptoms, hepatomegaly, or abnormal liver-function tests were the usual indications for obtaining the liver scans.

The scans were performed 10-15 minutes after the intravenous administration of 2-6 mCi of ^{113m}In colloid or ^{99m}Tc

sulphur colloid. A 5-in. (13-cm.) crystal commercial rectilinear scanner having analogue circuitry was utilized with the count rate differential set at 100% (the minimum contrast enhancement possible without changing the circuitry). The scan images were interpreted independently by two observers without knowing the final diagnosis.

A control group of 120 necropsies of patients with hepatic malignancy (16 hepatoma and 104 metastatic) who had died during the period 1961-7 was selected from the records of the pathology department of Johns Hopkins Hospital. Weights of liver and spleen were recorded. Predicted normal liver weight for each patient was calculated from the nomogram of DeLand and Norn (1968). Livers weighing more than 2 standard deviations (S.D.) from the mean and spleens of over 200 g. were considered enlarged.

Results

Classification of Scan Patterns.—The liver scans were classified into three types: (1) homogeneous distribution of radioactivity; (2) patchy or nonhomogeneous distribution beyond statistical fluctuations without clear-cut focal lesions; and (3) well-defined focal defects. Examples of each are shown in Figs. 1, 2, and 3a and 3b (Special Plate). Each of these types was further divided, depending on the absence or presence of liver enlargement. The frequency of each type is summarized in Table I. The most striking findings were as follows: (1) Of the patients who had primary carcinoma of the liver (16 hepatoma, 2 cholangiocarcinoma) none were in type 1; 23% had patchy or nonhomogeneous distribution (type 2); and 77% had clear-cut focal defects (56% single and 21% multiple). None of these patients had more than two defects. (2) Of the patients who had metastatic tumours in the liver (54 cases) 10% had a homogeneous distribution of activity; 7% had a patchy nonhomogeneous pattern; and 83% had well-defined focal defects, single in 20% and multiple in 63%.

TABLE I.—Frequency of Each Type of Defect (%)

	Type 1		Type 2		Type 3	
	a	b	a	b	a	b
Primary (18) ..	0	0	6	17	0	77
Metastatic (54) ..	4	6	2	5	2	81

Type 1 = Uniform distribution of radioactivity.

Type 2 = Nonhomogeneous distribution of radioactivity.

Type 3 = Clear-cut focal defects.

a = Without hepatomegaly. b = With hepatomegaly.

Hepatomegaly.—In the "scan group" patients altogether 94% had significant hepatic enlargement (greater than 2 S.D. from the mean) (Table II). One patient with hepatoma and four with liver metastases had normal liver weights. This was in marked contrast to the incidence of hepatomegaly in the necropsy group. The possible significance of this finding is discussed elsewhere in the paper.

Splenomegaly.—Of interest was the finding that 33% of the patients with primary carcinoma of the liver and 7% of the

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patients with metastatic tumours of the liver showed splenomegaly in the scan. The incidence of splenic enlargement as observed from the anterior scan views is also given in Table II.

TABLE II.—Incidence of Hepatosplenomegaly as Observed from the Scan Images (%)

	Hepatosplenomegaly	Splenomegaly*
Primary ...	94	33
Metastatic ...	94	7

* The splenic size could be assessed from the anterior view in only 42 cases (12 primary and 30 metastatic).

Biochemical Studies.—The results of the biochemical tests of liver function are summarized in Table III. It can be seen that the bromsulphalein (B.S.P.) retention was the most sensitive test in both types of malignancy. Except for the B.S.P. retention test, as many as four biochemical tests were within normal limits in 29% of the patients with primary carcinoma and 33% of the patients with metastatic carcinoma of the liver.

TABLE III.—Liver Function Tests

Test		Primary Carcinoma Liver: Patients in whom Tests were Done		Metastatic Carcinoma: Patients in whom Tests were Done	
		No.	%	No.	%
B.S.P. retention in 45 minutes	< 10% ..	0	0	2	10
	> 10% ..	6	100	18	90
Alk. phosphatase (K.A. units)	< 15 units ..	12	70	20	44
	> 15 units ..	5	30	26	56
S.G.O.T.	< 50 units ..	7	40	18	39
	> 50 units ..	10	60	26	61
S.G.P.T.	< 50 units ..	13	81	25	67
	> 50 units ..	3	19	12	33
A/G ratio	> 1.5 ..	4	25	11	38
	< 1.5 ..	12	75	27	62
S. Bilirubin mg./100 ml.	> 1.5 ..	6	37	28	70
	< 1.5 ..	10	63	12	30
Pr. time % or normal	> 80 ..	4	37	3	23
	40-80 ..	7	63	9	63
	< 40 ..	0	0	2	14

Necropsy Data.—In the necropsy group of patients with hepatic malignancies, liver weight greater than 2 S.D. from the mean was observed in 63% of the cases with hepatoma and 46% of those with metastatic liver carcinoma. Thirty-six per cent. of patients dying with hepatic metastases greater than 2 cm. in diameter had normal liver weight. The spleen weight was greater than 200 g. in 63% of the patients (10 cases) with hepatoma and 29% of those with liver metastases (29 cases) (Table IV). Splenic metastases were present in one case of hepatoma, while in the metastatic group 19 patients had splenic metastases. Five of the latter had splenomegaly. In two of these five cases the metastases were small and capsular and thus were not the causative factor for the splenomegaly. Twelve of the sixteen (75%) patients with hepatoma had evidence of coexistent cirrhosis (Laennec or postnecrotic type), while in those with metastases to the liver only two (2%) had coexistent cirrhosis.

TABLE IV.—Organ Size in Hepatic Malignancy (%) (Necropsy Series)

	Liver		Spleen	
	Normal	Enlarged*	Normal	Enlarged†
Primary (16) ...	37	63	37	63
Metastatic (104) ..	54	46	71	29

* Normal liver weight calculated from the nomogram of DeLand and North (1968). Liver weight above 2 S.D. was considered enlarged.

† Spleen weight above 200 g.

Discussion

The present study supports the concept that liver scanning is helpful in predicting which patients will subsequently be found by biopsy to have metastatic or primary carcinoma of the liver. Eighty-eight per cent. of the patients who had liver-punch biopsies that showed metastatic cancer (44 out of 50 cases) had well-defined focal defects in the liver scan. Thus the incidence

of false-negative liver scans in the presence of metastases which could be detected by biopsy was relatively low. Our data also suggested that liver scanning seemed to be carried out most often when the clinician detected enlargement of the liver. This was indicated by the difference in the incidence of hepatomegaly in the presence of liver metastases between the scan group and necropsy group of patients.

In this study we have also evaluated the role of biochemical tests as a screening procedure in the detection of hepatic malignancy. A high serum alkaline phosphatase has been considered to be more specific for hepatic metastasis than other liver-function tests in patients without bone disease or biliary obstruction (Smith and Williams, 1968; Yesner and Conn, 1963). But this test can be abnormal in a variety of other conditions, such as chronic infiltrative diseases of the liver due to sarcoidosis, Hodgkin's disease, tuberculosis, infectious hepatitis, or infectious mononucleosis (Ross *et al.*, 1956). Only 30% of the patients with primary carcinoma of the liver and 56% of those with metastatic liver cancer had high serum alkaline phosphatase. B.S.P. retention is a very sensitive test, but is also non-specific. No single biochemical test is both high-specific and sensitive for hepatic malignancy. Our results indicate that too much significance should not be given to the biochemical tests in predicting the presence or absence of hepatic malignancy.

The most specific method of establishing the diagnosis is by tissue examination—by either open or closed biopsy. Blind needle biopsy, however, occasionally fails to detect the lesion. In one large series of needle biopsies of the liver performed on cadavers immediately before the necropsy, metastases were detected in less than 50% of cases with hepatic metastases (Conn and Yesner, 1963). Even large hepatomas may be missed by blind biopsy (*New England Journal of Medicine*, 1968). Liver scanning helps in the selection of the proper biopsy site. In the present series random needle biopsies were initially negative in five cases, while subsequent biopsies after proper selection of the biopsy site from the scan images yielded positive results.

Although the incidence of false-positive liver scans has been reported to be as high as 29% in selected patients with cirrhosis (Johnson and Sweeney, 1967), which occasionally poses problems in the diagnosis of hepatoma, we believe that with proper technique and interpretation the number of false-positive scans can be reduced. The incidence of false-negative or non-specific scan pattern (without clear-cut focal defects) in our series of primary carcinoma of the liver was 23%; if we consider cases of hepatoma alone this incidence becomes 25%. A non-homogeneous distribution pattern (Type 2) is not unexpected in hepatoma because of the frequent association of cirrhosis and hepatoma. Fifty per cent. of hepatoma patients in the scan group and 75% in the necropsy group had coexistent cirrhosis. Hepatoma occurs as a complication in up to 33% of cases with alcoholic cirrhosis (Stone *et al.*, 1968). A well-defined focal defect in the scan of a cirrhotic patient always increases the probability of hepatoma. Absence of clear-cut defects, however, does not exclude the presence of hepatoma. Single clear-cut focal defects were seen in 56% of cases with primary liver carcinoma. Since hepatomas can originate as a multicentric tumour (Passaro, 1966), multiple focal defects do occur, as seen in 21% of our cases. None of the patients with primary liver carcinoma had a normal scan pattern.

Despite the fact that focal defects can occur in patients with liver abscesses, cysts, angiomas, etc. (McAfee *et al.*, 1965), multiple focal defects in a patient with known cancer in some region of the body are most likely due to metastasis. Well-defined focal defects were seen in 83% of our patients with metastatic liver cancer; 29 cases (54%) had three or more focal defects. Ninety per cent. of the patients with metastatic liver cancer who had hepatic enlargement in the scan showed well-defined focal defects. We believe that if no clear-cut focal defects are seen in patients with an enlarged liver suspected as being due to metastases the probability of metastases is very low.

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FIG. 1.—Liver scan showing enlarged liver with uniform distribution of radioactivity (Type 1b).

FIG. 2.—Scan showing nonhomogeneous distribution of activity (Type 2b). Splenic enlargement is also seen here.

FIG. 3a.—Scan with well-defined focal defects. Note the normal size of the liver (Type 3a).

FIG. 3b.—Clear-cut focal defects with massive enlargement of the liver (Type 3b).

Seven per cent. of the patients with liver metastases had a nonhomogeneous scan pattern similar to that seen in cirrhosis. Hence in noncirrhotic patients suspected of hepatic metastases the presence of even a nonhomogeneous pattern should arouse suspicion of malignancy. Similarly, since metastases to a cirrhotic liver are very rare (only 2% in our necropsy series), the diagnosis of metastasis in patients with known cirrhosis should be made cautiously even when there are focal defects. In rare instances the radioactivity distribution pattern may be entirely normal (10%). Because of the incidence of false-negative and false-positive liver scans, we believe that biopsy should be performed as the next step to the scanning procedure for confirmation of the diagnosis after proper selection of the biopsy site from the scanning image.

In the necropsy group hepatomegaly was present in only 46% of patients with metastatic liver disease, which strongly suggests the possible value of a liver scan in every patient with a known primary cancer, even in the absence of liver enlargement. In 36% of the patients with metastatic lesions larger than 2 cm. in diameter the liver was normal in size. In 45% of the entire 104 patients with liver metastases in the necropsy group metastasis to the liver was not suspected during life. This is consistent with the hypothesis that many cases of metastatic liver disease are missed because suspicion is not aroused in the absence of hepatic enlargement. Fruitless surgery can at times be avoided and the prognosis more accurately assessed if the presence or absence of metastases is established.

The presence of splenomegaly has been reported as a rare occurrence in metastatic liver disease (*New England Journal of Medicine*, 1968). In our necropsy series 29% of patients had an enlarged spleen. The discrepancy, however, regarding the incidence of splenomegaly in patients with liver metastasis in the scan group (7%) and the necropsy group (29%) had two possible explanations. Firstly, it is recognized that even with

an enlarged spleen the anterior view may fail to detect the enlargement, and in these cases the posterior and left lateral views are necessary. Secondly, splenic enlargement may be a late manifestation of metastatic disease of the liver. Fenster and Klatskin (1961) reported a 33% incidence of splenomegaly in patients with hepatic metastases. The mechanism of splenic enlargement is thought to be secondary to portal hypertension or metastasis to the spleen. Splenomegaly without parenchymal metastasis occurred in 26% of our necropsy series. Pancreatic carcinoma most commonly produces splenomegaly by pressure or occlusion of the portal or splenic vein from direct extension of the tumour. In our necropsy series there was enlargement of the spleen in five of nine cases with carcinoma of the pancreas. All were due to splenic congestion. Although metastases to the spleen were found in 19 cases from the necropsy series, in only three could the splenomegaly be attributed to splenic metastases.

REFERENCES

- Conn, H. O., and Yesner, R. (1963). *Annals of Internal Medicine*, **59**, 53.
DeLand, F. H., and North, W. A. (1968). *Radiology*, **91**, 1195.
Fenster, L. F., and Klatskin, G. (1961). *American Journal of Medicine*, **31**, 238.
Johnson, P. M., and Sweeney, W. A. (1967). *Journal of Nuclear Medicine*, **8**, 451.
McAfee, J. G., Aulsebrook, R. G., and Wagner, H. N., jun. (1965). *Archives of Internal Medicine*, **116**, 95.
New England Journal of Medicine, 1968, **279**, 1046.
Passaro, E. (1966). *Journal of Woodsworth General Hospital*, **10**, 61.
Rollo, F. D., and DeLand, F. H. (1968). *Radiology*, **91**, 1191.
Ross, R. S., Iber, F. L., and Harvey, A. M. (1956). *American Journal of Medicine*, **21**, 850.
Smith, L. B., and Williams, R. D. (1968). *Archives of Surgery*, **96**, 693.
Stone, W. D., Islam, N. R. K., and Paton, A. (1968). *Quarterly Journal of Medicine*, **37**, 119.
Yesner, R., and Conn, H. O. (1963). *Annals of Internal Medicine*, **59**, 63.

Kidney Function after Renal Arterial Embolism

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Summary: Seven patients with atrial fibrillation had acute unilateral renal pain associated with suppression of function in the affected kidney. This was ascribed to renal embolism. Arteriography performed in four patients showed abnormalities in the renal arterial tree in three, though thrombus in a main artery was present in only one.

Considerable function returned spontaneously to the affected kidney in six patients as judged by intravenous pyelography or renography. In two patients the sole functioning kidney was affected, leading to acute oliguric renal failure, but renal function recovered in each case. The routine use of anticoagulants in persistent atrial fibrillation is justified by such cases.

Introduction

Successful renal arterial embolectomy has been reported in patients operated on soon after the embolus had occurred

(Duncan and Dexter, 1962; Brest *et al.*, 1964; Smithwick *et al.*, 1964; Erskine and Blaisdell, 1965; Loomis *et al.*, 1966; Halpern, 1967; Goldsmith *et al.*, 1968). Improvement in renal function after embolectomy delayed for several weeks has also been reported (Perkins *et al.*, 1967; Peterson and McDonald, 1968), but it is generally believed that renal function is unlikely to return after major embolism without early surgical intervention. Thus kidney function returned in only 2 out of 18 cases of renal embolism reported by Goldsmith *et al.* (1968) and in 4 out of 20 cases described by Regan and Crabtree (1948). As renal emboli usually occur in patients with heart disease, in whom surgery is likely to be hazardous, it is particularly desirable that a decision to undertake renal arterial embolectomy should be based on a knowledge of the likely consequences of non-intervention. Yet observations on the course of renal embolism studied after early diagnosis are comparatively few, presumably because correct antemortem diagnosis of renal infarction appears to be rare. Thus the diagnosis had been made in life in only 1 of the 143 cases studied at necropsy by Barney and Mintz (1933) and in only 2 of the 205 cases reported by Hoxie and Coggin (1940).

The present report describes the course of seven cases in which renal embolism was associated with suppression of kidney

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