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The Value of Liver Scannnig in Pediatric Age Group with Special Emphasis on Histopathological Correlation*

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Liver scanning by radiopharmacenticals has been accepted as one of the most useful diagnostic methods in the evaluation of liver disease.[1, 2]

In recent years radiopharmaceuticals have been extensively used to determine the morphological and functional state of liver by many investigators.[3, 4-5] ^{198}Au Colloid was the first radiopharmaceutical used to delineate the morphology of the liver in 1954.[6] In the following years ^{131}I labeled heat denatured human serum albumine, ^{131}I labeled Rose Bengal, ^{99m}Tc Sulfur colloid, ^{113m}In Colloid, and most recently ^{99m}Tc and ^{113m}In microspheres have been succesfully used for the same purpose.[7, 12] Among these ^{99m}Tc sulfur colloid and ^{113m}In colloid are the most frequently and widely used radiopharmaceuticals.

It is very well known that the consideration of radiation hazard to the child prevents the physician from requesting a test which will unavoidably result an internal radiation exposure to his patients. For this reason we felt that the discussion of the value, usefulness and the limitations of liver scanning in the pediatric age group merits a separate communication. In this investigation we wanted to evaluate the contribution of liver scanning in reaching the final clinical diagnosis by compar-

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ison of the findings of scintigraphy with tissue diagnosis. Scintigraphic findings have also been compared with the X-ray findings and preliminary clinical diagnosis.

Material and Method

Fifty patients with space-occupying lesions of liver or neighbouring organs and/or tissues and 50 patients with other than space-occupying lesions of the liver were selected for this study. In all of these 100 cases final diagnosis was established by needle biopsy, laparotomy, with or without incisional biopsy and post-mortem examination.

Range of ages of the patients were 0-17 years. Forty-two cases were females and 58 males. Table I. summarizes the distribution of age and sex of the patients.

TABLE I

SEX AND AGE DISTRIBUTION OF THE CASES

Sex	Age				Total
	0–5	6–10	11–15	16–17	
Female	17	15	9	1	42
Male	23	17	13	5	58
Total	40	32	22	6	100

In our studies ^{99m}Tc sulfur colloid and ^{112m}In colloid have been used as liver scanning agents. These radiopharmaceuticals were prepared by the methods described by Harper[9] and Goodwin[10] respectively. Two mCi of adult dose was adjusted for each case according to the weight of the patients.

The Picker "Magna Scanner V" with a five inch "Thallium Activated" NaI crystal and Nuclear Chicago "Pho-Gamma" Camera were used for the studies. Instruments were adjusted to the 141 keV and 395 keV photopeaks of ^{99m}Tc and ^{113m}In, respectively.

Scanning was started 15-20 minutes after the intravenous injection of the radiopharmaceuticals. Anterior, posterior and right lateral views of the organ were obtained routinely. No sedation was necessary during the entire course of the studies, except in few agitated and uncooperative patients.

Results

Patients were placed into six distinct categories according to their referral to the Department of Nuclear Medicine (Table II).

TABLE II

REASONS OF REFERRAL TO DEPARTMENT OF NUCLEAR MEDICINE

1. To differentiate the cause of hepatomegaly, splenomegaly or both,
2. For the diagnosis of suspected primary and secondary space-occupying lesions of liver,
3. To see the extension of the lesions in a neighbouring organ and/or tissue to the liver,
4. For the staging of lymphomas,
5. To differentiate a space occupying-lesion from a non-space-occupying-lesion,
6. For the evaluation of cancer chemotherapeutic agents and/or radiotherapy and operation.

Table III shows the correlation between the preliminary clinical diagnosis, X-ray and scintigraphic findings with the tissue diagnosis in cases of space-occupying lesions of liver and neighbouring organs.

19 Patients had had hydatid cysts (38 % of the 50 space-occupying lesions). Most of these patients were female. Ages varied between 5-15 years, with only one case under 5 years of age. In all of these cases scintigraphic findings were confirmed by the tissue diagnosis.

Following hydatid cyst, cases of Wilm's tumors and abscess of liver took second place in prevalance, with 5 cases each. Scintigraphic findings also proved to be correct in all ten of these cases by tissue diagnosis.

In five cases of neuroblastoma, liver scintigraphy was performed to investigate metastasis. Scintigraphies have given false positive information in two out of these five cases in which the final diagnosis was established by incisional biopsy.

Only three cases of Hodgkin lymphomas were included in this study in whom biopsies of the liver were obtained by laparotomy. Scintigraphic findings were found to be correct in these three cases.

Three cases of hepatoblastoma have also been correctly described by scintigraphic studies. In addition to multiple cases of the same

TABLE III

SPACE-OCCUPYING LESIONS OF LIVER AND NEIGHBOURING ORGANS AND/OR TISSUES

Tissue Diagnosis		Hepatic Involvement		Clinical Diagnosis			X-Ray Diagnosis			Scintigraphic Diagnosis		
Type	Primary Site	+	–	Number of Cases	Correct	False	Correct	False Positive	False Negative	Correct	False Positive	False Negative
Hydatid Cyst	Liver	18	–	18	17	1	7	–	9	18	–	–
Hydatid Cyst	Spleen	–	1	1	1	–	–	–	1	1	–	–
Abscess	Liver	5	–	5	3	2	–	–	4	5	–	–
Wilm's Tumors	Kidney	5	–	5	5	–	5	–	–	5	–	–
Neuroblastoma	Abdominal	3	2	5	3	2	3	–	2	3	2	–
Hepatoblastoma	Liver	3	–	3	3	–	1	–	2	3	–	–
Hodgkin Lymphoma		3	–	3	3	–	–	1	2	3	–	–
Hemangioendothelioma	Liver	1	–	1	–	1	–	–	1	1	–	–
Burkitt's Lymphoma	Abdominal	2	–	2	1	1	–	–	2	2	–	–
Ileal Lymphosarcoma	Ileum	–	1	1	1	–	–	–	–	1	–	–
Embryoner Rabdomyosarcoma	Liver	1	–	1	–	1	–	–	1	1	–	–
Embryoner Adeno Carcinoma	Abdominal	1	–	1	–	1	–	–	1	1	–	–
Adeno Carcinoma of Colon	Colon	1	–	1	–	1	1	–	–	–	–	1
Metastatic Malignant Tumor (Type Unidentified)	Unidentified	1	–	1	1	–	–	–	1	1	–	–
Ewing's Sarcoma	Right Thorax	1	–	1	1	–	1	–	–	1	–	–
Adeno Carcinoma of Rectum	Rectum	1	–	1	–	1	1	–	–	–	–	–

TABLE VI

PATHOLOGIC PROCESSES OF LIVER OTHER THAN SPACE-OCCUPYING TYPE

Tissue Diagnosis		Number of Cases	Clinical Diagnosis		X-Ray Diagnosis			Scintigraphic Diagnosis		
			Correct	False	Correct	False Positive	False Negative	Correct	False Positive	False Negative
Postnecrotic Cirrhosis		10	10	–	–	–	10	9	1	–
Cirrhosis Non-Classified		7	6	1	2	–	5	6	1	–
Portal Cirrhosis		2	1	1	1	–	1	–	2	–
Chronic Hepatitis		3	2	–	–	–	2	2	–	–
Focal Hepatitis, Post Necrotic Scar		2	2	1	–	–	2	2	1	–
Cholangiolithic Hepatitis		2	2	–	1	–	1	2	–	–
Neonatal Hepatitis		1	1	–	1	–	–	–	1	–
Lupoid Hepatitis		1	–	1	–	–	1	1	–	–
Non-Specific Hepatitis		1	1	–	–	–	1	1	–	–
Vena Occlusive Diseases and Budd-Chiari Syndrome		3	2	1	–	–	3	2	1	–
Glycogen Storage Disease		3	2	1	–	–	3	2	1	–
Tuberculosis of Liver and Peritoneum		1	–	1	–	–	1	1	–	–
Hepatic Necrosis Submassive		1	1	–	1	–	–	1	–	–
Polycystic Disease of Liver		1	1	–	1	–	–	1	–	–
Hepatic Amebiasis		1	1	–	–	–	1	1	–	–
Kala-Azar		1	1	–	–	–	1	1	–	–
Dubin Johnson		1	1	–	–	–	1	1	–	–
Non-Specific Reactive Processes	a) Hydropic Degeneration	1	1	–	1	–	–	1	–	–
	b) Hepatic Central Lobular Hemoragic Necrosis, Circulatory Disturbance	1	–	1	1	–	–	1	–	–
	c) Triaditis	1	1	–	–	–	1	–	–	1
	d) Vacuolar Degeneration, Hepatic Fibrosis	2	1	1	2	–	–	2	–	–
	e) Non-Spesific Granulation Tissue	1	1	–	–	–	1	–	1	–
	f) Non-Specific Inflammatory Process	1	–	1	–	–	1	1	–	–
Normal*		2	1	1	–	–	–	–	2	–

* Clinical diagnoses of these two cases were FMF and Granulomatous Hepatitis.

pathologic processes, rare cases of other pathologies were present among space-occupying lesions. They are also listed in Table III.

Overall accuracy of liver scintigraphy in space-occupying lesions was 94 %, accuracy of preliminary clinical diagnosis was 78 %, and that of X-ray studies was 42 %. In this type of pathologic processes scintigraphic findings were false positive in 2 cases (4 %) and false negative in one case (2 %).

As seen in Table III, X-ray studies, especially intravenous pyelography (IVP) have given correct description of the lesions which are related with the kidneys.

Since the number of cases with hydatid cyst was considerably high the accuracy of liver scanning with the exclusion of these cases was reevaluated and was found to be 90 %.

Table IV summarizes the correlation of preliminary clinical diagnosis, X-ray and scintigraphic findings in cases with pathologies other than space-occupying lesions of the liver.

It this group 19 of the patients (38 %) have had different types of cirrhosis. Scintigraphic diagnosis was in keeping with tissue diagnosis in 15 patients (30 % of 50 cases). Preliminary clinical diagnosis was correct in 17 cases (34 %) and that of X-ray diagnosis was correct in 3 cases (6 %).

Eleven cases of different kinds of hepatitis were encountered in these series and tissue diagnosis was in agreement with scintigraphic diagnosis in 9 cases and scintigraphic findings were false-positive in two cases. Clinical diagnosis was correct in 10 and X-ray diagnosis in 2 cases.

In addition to multiple cases of cirrhosis and hepatitis, rare cases of other pathologies were present among non-space-occupying lesions. They are also listed in Table IV.

Overall accuracy of liver scintigraphy in cases other than space-occupying lesions of liver was 76 %. In this group scintigraphic findings have given false positive information in 11 cases (22 %) and false negative information in 1 case (2 %).

When the space-occupying and non-space-occupying lesions were evaluated together, the accuracy of scintigraphic findings was 85 %. Correct diagnosis was obtained in 85 cases, false positive in 13 cases, and false negative in 2 cases.

Discussion

Despite the modern instrumentation and improved laboratory diagnostic studies, early diagnosis and treatment of pathologies concerning liver is still one of the most important problem of pediatrics.

Scintigraphy of the liver by radiopharmaceuticals is one of the most most valuable diagnostic approaches to the problem.

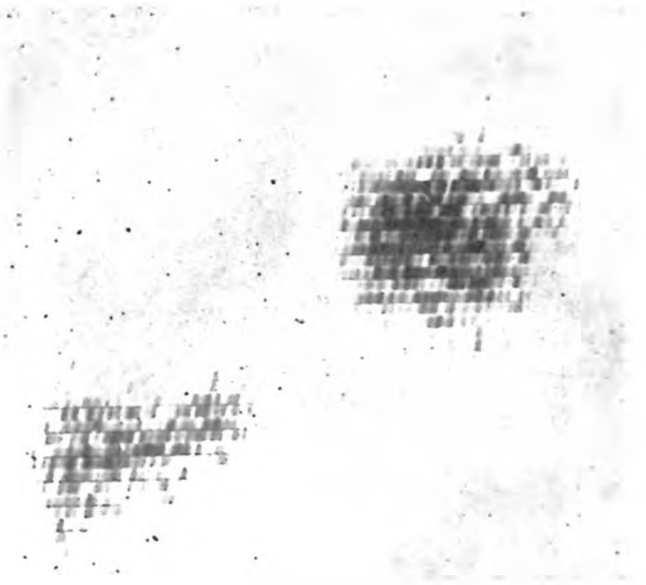
In space-occupying lesions of liver and neighbouring organs and/or tissues, liver scanning gives information about the size of the lesions and in many of the cases about the type of the lesions as in cystic formations. Figure 1 shows the liver scanning of a patient with a single hydatid cyst of the liver. Figure 2 shows the liver scanning of a patient with multiple hydatid cysts of the liver. As can be seen from Figure 1 and 2, total area of the liver is not very much enlarged despite of a large liver indicated on palpation. Radiactivity is not present or very slight in the cystic areas and the borders of the lesions show smooth, concave lines. With these characteristics of the lesions one can inform the physician about a cystic lesion which is vital to know before the operation.

Abscesses of the liver were important to differentiate from cystic lesions since scintigraphic findings resembled that of cysts in regard to their multiplicity in number and quite circumscribed outlines. Nevertheless, there was almost always some radioactivity in the lesions and the borders were infiltrative in appearance and not as smooth as in cystic lesion. With this scintigraphic information in addition to that of clinical findings, final diagnosis of abscess of liver was considerably easy to reach, Figure 3.

In primary and secondary malignant space-occupying lesions of the liver the organ was strikingly enlarged. Site of the lesion were hypoactive and it showed non-homogeneous concentration of the radioactive complex. The borders of the lesions were not clearly defined as seen in Figure 4, which demonstrates a case of hepatoblastoma of the liver.

Extension of the space-occupying lesions of a neighbouring organ and tissue to the right hypochondrium has given a special appearance to the scanning image of liver as in Wilm's tumors of the right kidney region. Lesions were not in the liver but the borders of liver near the affected organ were distorted and normal morphology of the liver was changed.[1] Figure 5 demonstrates such a case of Wilm's tumor extending to the lower part of the liver.

In Hodgkin lymphomas of our series, liver and spleen were both involved. Both organs were significantly enlarged in size. Radioactivity



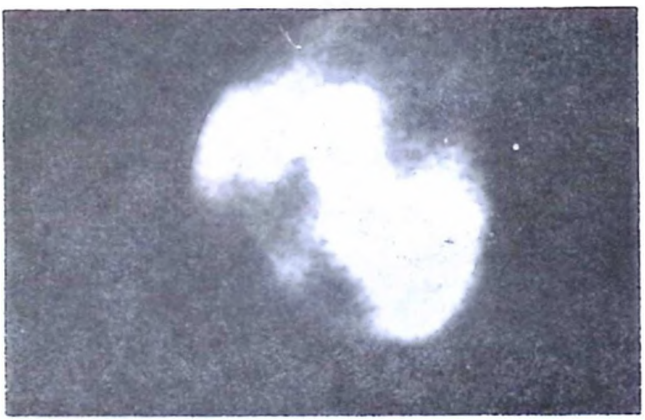
Anterior view.

Right lateral view.

Figure 1

The liver scanning of a patient with a single hydatid cyst, in the upper part of right lobe.

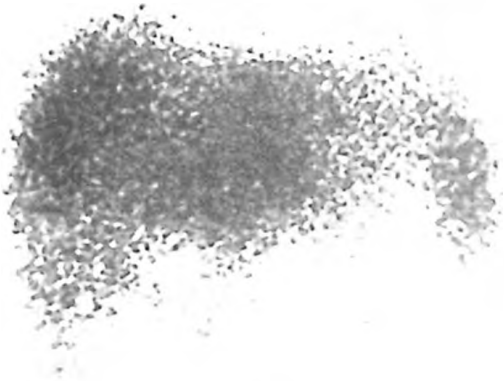
Anterior view.



Right lateral view.

Posterior view.

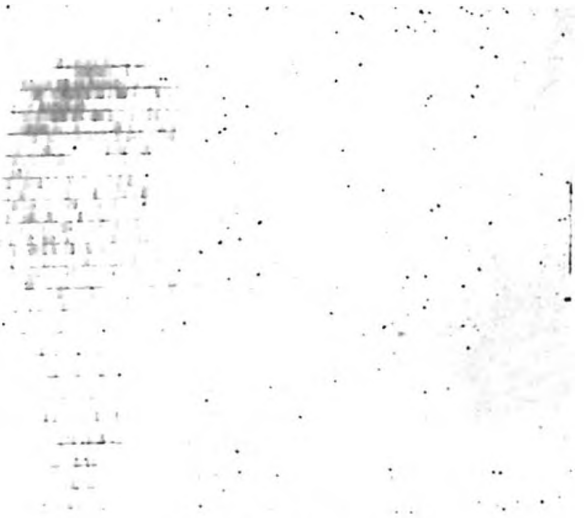
Figure 2
The liver scanning of a patient with multiple hydatid cysts of the liver.



Anterior view.

Right lateral view.

Figure 3
The liver scintigraphy of a patient with multiple abscesses in the lower part of the right lobe of liver.



Anterior view.

Lateral view.

Figure 4
A case of hepatoblastoma.

Anterior view.

Right lateral.

Figure 5

A liver scanning of a case with a Wilm's tumor of right kidney which is extended to the lower part of the liver.

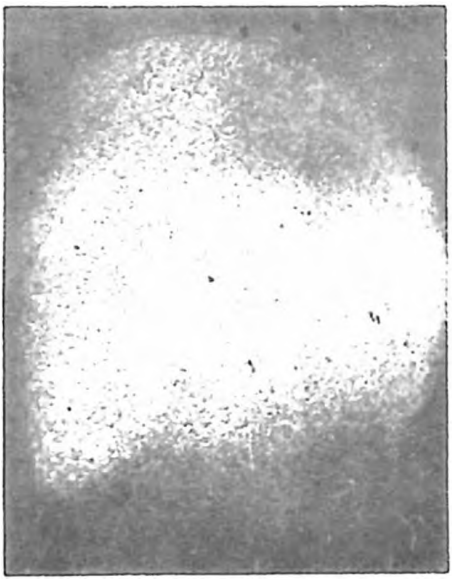
was unevenly distributed. In addition to this finding in two out of three cases findings suggestive of small space-occupying lesions were also present. Only these three cases in which open biopsies were available were included in this study.

As seen in Table IV, the percentage of different types of cirrhosis among the non-space-occupying lesions of liver was 38 % in our 50-case series. In this study scintigraphic findings of cirrhosis were found to be specific for this type of disorder. The liver was enlarged in the pediatric age group in contrast to that of adults, no distortion of liver shape and decreased liver size were observed. Spleen was significantly enlarged and contained more radioactivity than the liver. Distribution of radioactivity in liver was non-homogeneous and showed a patchy appearance. In most of the cases vertebral colon was slightly while in some cases clearly observable. These findings all together were strongly suggestive of liver cirrhosis. Figure 6 demonstrates study of a case with cirrhosis.

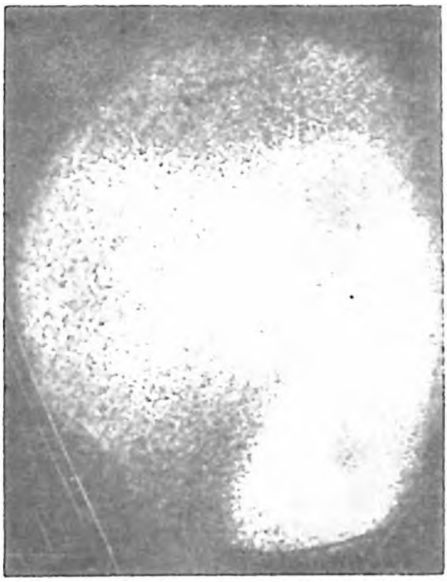
In pathologic processes with functional impairment of the liver the organ was enlarged, in most cases, enlargement of the left lobe of the liver was more pronounced than that of the right lobe. Radioactivity also showed uneven distribution in this type of cases. These scintigraphic findings were suggestive of functional impairment of the liver. However it was not possible to indicate the exact nature of this type of pathologic processes as in the cases of cirrhosis.

Scintigraphic studies were decidedly useful in cases whom hepatomegaly was present but other diagnostic studies were unsubstantial about a space-occupying lesion.

In the entire course of the illness, to reach the diagnosis, patients receive a number of roentgenologic studies like flat plate of the abdomen, intravenous pyelograply (IVP), X-ray of the oesophagus and stomach, small bowel series; considering the radiation dose received by these studies, a liver scanning exposes the patient to a far negligible amount of radiation hazard. Table V summarizes the radiation dose received by some of X-ray studies and by liver scanning.[16, 17] Although the importance and the value of liver scanning in pediatric age group as a diagnostic tool have been emphasized by many investigators, a correlation of the scintigraphic findings to histopathological diagnosis have not been studied in those series found in literature. For this reason we are not able to compare our results with others.[13, 14, 15] However, our correlative values are closely related to the values which are obtained from the critical evaluations of liver scanning and other laboratory diagnostic studies performed on adult cases by other investigators.[18, 19]



Anterior view of liver.



Anterior view of spleen.

Posterior view of spleen.

Figure 6

The scintigraphic appearance of the liver cirrhosis. (Cold area in the spleen belongs to a lead marker which indicates the lower pole of the spleen.)

TABLE V

WHOLE BODY AND LIVER DOSES OF COMMONLY USED LIVER SCANNING AGENTS AND SOME DIAGNOSTIC X-RAY STUDIES IN ADULTS

Radiopharmaceutical	Administered Dosage	Whole Body Dose in Rads	Liver Dose in Rads
^{99m}Tc-S Colloid	2 mCi	0.03–0.1	0.66–2.1
^{198}Au Colloid	150 mCi	0.35	5.7
^{131}I Aggregated Albumin	500 uCi	0.05	0.30
^{131}I Rose Bengal	150 uCi	0.05–0.15	0.25–0.50
^{113m}In Colloid	2 mCi	–	0.7–3.5
Gastrointestinal Series and Barium Enema	–	1400.0	–
Intravenous Pyelography	–	970.0	–

Conclusion

Liver scintigraphy in the pediatric age group has been found to be one of the most valuable diagnostic studies by our evaluation. It is convenient to perform and it can also be applied without any hazardous effects to the patient. In many cases it furnishes the clinician with the diagnostic information without subjecting the patient to the more elaborate tests.

Liver scintigraphy is especially useful in differentiation of the space-occupying lesion from the non-space-occupying type. This study gives considerable advantage to the physician indicating the number, localization and the type of the lesions as in cystic lesions and abscesses, since it is very important to know before the operation.

It is an easy means of control of the results of surgery and chemo therapy as again in the cases of cysts, abscess, neuroblastoma and Wilm's tumors.

To plan the consequent course of the treatment, early detection of metastasis to the liver in neoplastic processes is very important. It is more so in surgical cases before and after operation. This objective is established with the utmost economy of time and material by performing a liver scintigraphy. Since the accuracy of this particular approach is very high in space-occupying lesions (90 %) and fairly good in non-space-occupying lesions (76 %) of the liver, in our opinion this study should be obtained prior to any other diagnostic study in all the cases in whom a pathology concerning the liver is being entertained.

Summary

Liver scintigraphy is one of the most practical and appropriate diagnostic tests in shedding light to the liver disorders.

A liver scintigraphy is imperative to differentiate space-occupying lesions, from non-space-occupying lesions of the liver and neighbouring organs.

It is very useful for follow-up studies of the cases who had had operations and chemotherapy.

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