Improved Evaluation of Technetium-99m-Red Blood Cell SPECT in Hemangioma of the Liver

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This paper reports the results of a prospective study carried out to evaluate a new reading method of tomographic ^{99m}Tc red blood cell (RBC) imaging in liver hemangiomas. For this purpose, assessment of planar imaging and conventional, static ^{99m}Tc-RBC SPECT presentation (x-ray type film) (Method 1) was compared to a dynamic three-view display of SPECT slices (Method 2) in 21 patients with 56 hemangiomas and 18 patients with malignant liver lesions. Of the 56 hemangiomas, 47 were diagnosed by US, 6 by CT and 56 by MRI. Twenty-nine (52%) hemangiomas were detected by planar scintigraphy and 38 (68%) by SPECT Method 1, whereas 53 (95%) were visualized by SPECT Method 2. Comparing Methods 1 and 2 in hemangiomas ≤ 1.0 cm, 1.1–2.0 cm and 2.1–3.0 cm in diameter, Method 2 improved sensitivity from 18% to 82%, 50% to 93% and 82% to 100%, respectively. The smallest hemangioma detected with Method 2 was 0.5 cm in diameter; with Method 1, 0.9 cm; and with planar imaging, 1.0 cm. As assessed by evaluation of the metastases and carcinomas, the specificity for hemangioma was 100%, independent of the method applied, resulting in a positive predictive value of 100%. This study suggests that evaluation of dynamically displayed ^{99m}Tc-RBC SPECT studies is superior to conventional reading of static display and comparable to MRI in liver hemangioma ≥ 1 cm. Therefore, this approach is suggested as an alternative to MRI for confirming the diagnosis of liver hemangioma ≥ 1 cm if planar imaging is negative. This option is available with most modern computer software systems and saves additional disbursement.

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The continuing development of high resolution real-time sonographic equipment in addition to the continuously rising spread of sonographic scanners leads to an increase in the detection of focal intrahepatic lesions. Cavernous hemangioma is the most common benign tumor of the liver (*1*). Thus, there is an increasing need to distinguish hemangioma from malignant tumors or metastases. Computed tomography (CT) has been reported in several articles to be a relatively poor imaging technique for diagnosing cavernous hemangioma of the liver (*2–4*). Angiography and biopsy can usually establish the diagnosis with certainty but are not without risk. Technetium-99m red blood cell (RBC) imaging is a highly specific test for hemangioma (*2,5,6,7*); however, its sensitivity for hemangioma less than 2–3 cm in diameter is rather limited compared to magnetic resonance imaging (MRI) (*2,5,8,9*). Therefore, this study evaluates an alternative reading of ^{99m}Tc-RBC single-photon emission computed tomography (SPECT). For this purpose, assessment of planar imaging and conventional, static ^{99m}Tc-RBC SPECT presentation were compared to dynamic display of SPECT slices.

MATERIAL AND METHODS

From 1985 to 1990 ^{99m}Tc-RBC scanning was performed in 39 patients with focal lesions of the liver. There were 24 females and 15 males aged 31–74 (average 55.3 yr). Of these patients, 21 had hemangiomas (Fig. 1). All patients had initial US. Confirmation of diagnosis was made by CT and MRI in addition to clinical and imaging follow-up over 1.5–6 yr. Supplementary cytology and histology were available in five patients with a known primary diagnosis of malignancy and in one patient with myxoma. Of the control group (18/39 patients), 3 patients had hepatocellular carcinoma and 15 had metastases (26 lesions) (Table 1). Metastases were confirmed by biopsy in all patients.

Scintigraphic Imaging

All patients had a ^{99m}Tc-RBC study utilizing in vivo/in vitro labeling technique of red blood cells (*10*). Scintigrams were acquired 2 hr after intravenous injection of 700–800 MBq ^{99m}Tc-labeled RBC. No initial flow studies were obtained. Planar imaging was performed for a total of 750,000 counts in anterior, posterior and right lateral projection using a large field of view gamma camera with a low-energy, all-purpose collimator. SPECT was obtained using a dual-head, large field of view gamma camera (Dyna Digital Camera, Picker International, Northford, CT) with low-energy, all-purpose collimators (180°

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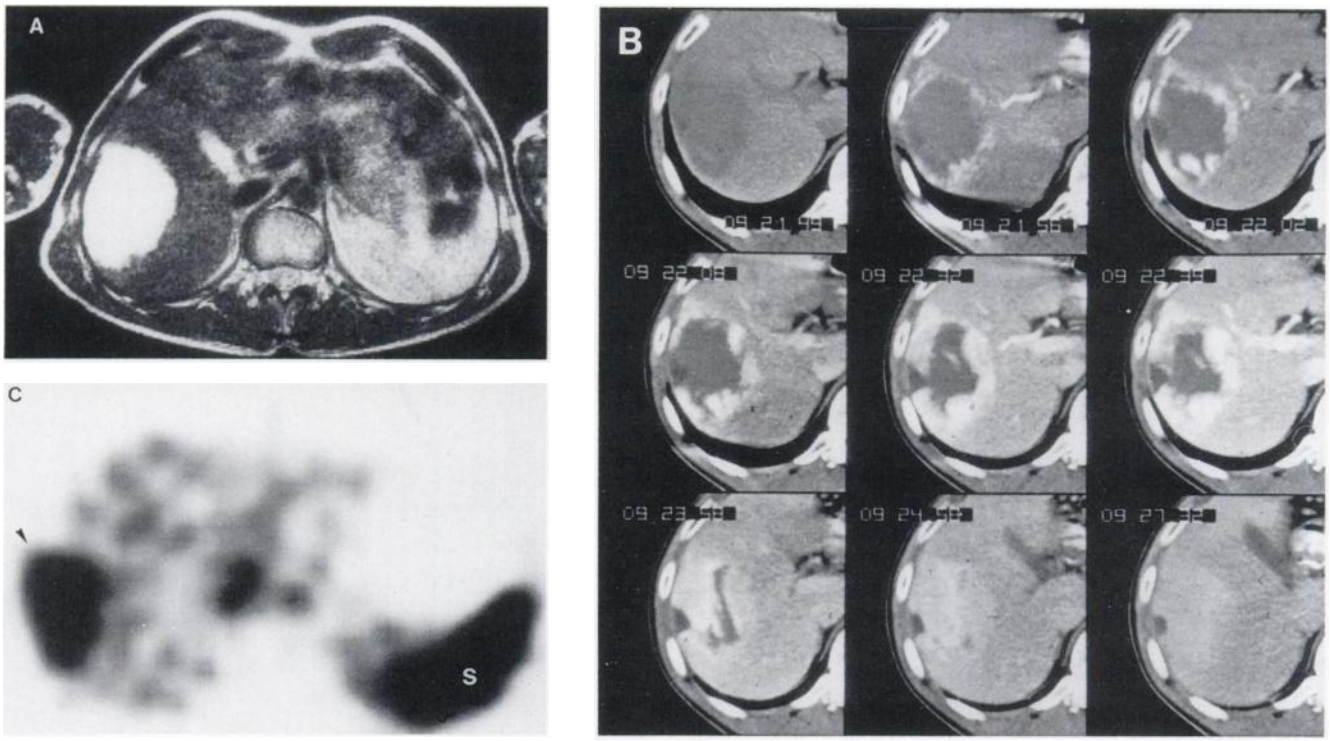

FIGURE 1. Typical appearance of hemangioma in MRI, CT and ^{99m}Tc-RBC SPECT. (A) Transverse T2-weighted image shows a large lesion with increased signal intensity in the right lobe of the liver. (B) Sequential CT images at the same level demonstrate characteristic appearance with early peripheral enhancement followed by filling in of the central part. (C) Transverse slice of RBC SPECT shows a large area with increased activity uptake (arrowhead). The spleen (S) is depicted.

rotation, 32 angle steps, 64 projections, 40 sec per angle step, 64 × 64 pixel matrix). A series of transverse slices 6 mm thick were reconstructed using filtered backprojection. No attenuation correction was applied. Coronal and sagittal views were reconstructed from transverse slices without any additional filtering.

Image Interpretation

Scintigraphic studies were evaluated prospectively. Technetium-99m RBC planar and SPECT studies were each reviewed blinded in random order without knowledge of the diagnosis and lesion location. SPECT interpretation was made in two different ways:

1. Conventional static method, images were displayed in black and white on x-ray type films. Transverse, sagittal and coronal slices were evaluated simultaneously.
2. Dynamic display method, transverse, coronal and sagittal views were displayed side by side, without any smoothing, one cross-section per view, on a monitor screen with the option of sequential step-by-step viewing and cine display of the set of slices. Each slice could be identified by

TABLE 1
Final Diagnosis and Scintigraphic Results for 39 Patients

Diagnosis	No. of lesions	Focal uptake		
		SPECT Method 1	SPECT Method 2	Planar
Primary heptic tumors				
Hemangioma	56	38	53	29
Hepatocellular carcinoma	4	0	0	0
Metastasis				
Carcinoid	5	0	0	0
Colon cancer	8	0	0	0
Breast cancer	2	0	0	0
Thyroid cancer	2	0	0	0
Leiomyosarcoma	3	0	0	0
Rhabdomyosarcoma	1	0	0	0
Non-Hodgkin's lymphoma	1	0	0	0

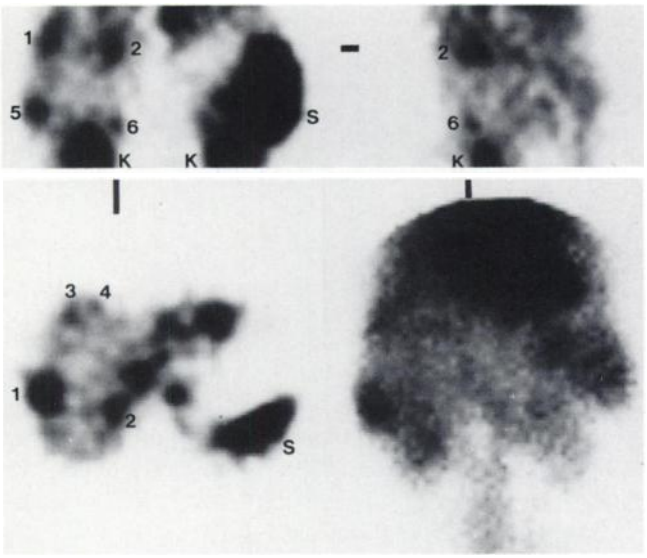

FIGURE 2. Monitor display as evaluated with Method 2. Coronal (upper left), sagittal (upper right), transverse view (lower left), and ventral topogram are displayed simultaneously with the option of step-by-step movie presentation of the whole set of slices of the three views. With "dynamic" display, a review of the whole three sets of slices enables differentiation of blood vessels and small hemangiomas. Each slice can be identified by the small horizontal and vertical tic marks at the corresponding slices. The three views show different aspects of multiple (1–6) hemangiomas. The spleen (S) and the kidneys (K) are depicted.

horizontal and vertical tic marks at the orthogonal slices (Fig. 2).

In planar imaging, a focal lesion of the liver was considered to be a hemangioma if there was definite increased blood pool activity compared to the activity of adjacent normal liver tissue. In evaluation of the static SPECT images (Method 1), the focal activity had to be equal to or greater than the activity of the aorta or vena cava in at least two views. Additionally, in dynamic display (Method 2), a lesion was interpreted as hemangioma-positive if there was increased radiotracer uptake compared to the adjacent liver tissue and equal or greater activity accumulation compared to the closest intrahepatic vessel that could be identified by watching the course of increased activity in the three-view movies.

US, CT and MRI

All 39 patients had sonographic examination using a high-resolution, real-time scanner (Picker International, LCS 7000) with a 3.5 MHz transducer. A presumptive diagnosis of hemangioma was made when a hyperechoic, sharply marginated lesion was detected.

Precontrast and contrast-enhanced CT studies were performed using a Somatom DRH (Siemens). The scanning time was 3 or 5 sec at 125 kV and 230 mAs; section thickness was 8 mm. Dynamic contrast-enhanced CT of a given section was performed with a frequency of 10 images/min. A diagnosis of hemangioma was only made when the typical criteria described by Freeny et al. (*3*) were present.

All patients had an MRI scan on a 0.23 T superconducting magnet (Brucker, BMT 1100). Imaging was done using multi-

TABLE 2
Imaging Data of 21 Hemangioma-Positive Patients

Patient no.	No. of lesions	Size (cm)	US*	MRI†	CT†	Planar†	SPECT Method 1†	SPECT Method 2†
1	1	4.0	+	+		+	+	+
2	5	4	+	+	+	+	+	+
		2.1	+	+		−	+	+
		1.5	+	+		−	−	+
		1.3	+	+		−	−	+
		0.5	+	+		−	−	+
3	3	1.8	+	+	+	−	−	+
		1.2	+	+		+	+	+
		1	+	+		−	−	+
4	5	3.5	+	+		+	+	+
		2.5	+	+		−	+	+
		1.2		+		−	+	+
		1		+		−	−	+
		0.9		+		−	+	+
5	3	3.5	+	+	+	−	+	+
		1	+	+		+	+	+
		0.8	+	+		−	−	+
6	1	4	+	+		+	+	+
7	1	5	+	+		+	+	+
8	1	8	+	+	+	+	+	+
9	6	7	+	+		+	+	+
		3	+	+		+	+	+
		3	+	+		−	+	+
		2.8		+		+	−	+
		2.5		+		−	+	+
		2		+		−	−	+
10	3	4.5	+	+	+	+	+	+
		1	+	+		−	−	−
		1		+		−	−	−
11	3	6	+	+		+	+	+
		1	+	+		−	−	+
		1		+		−	−	+
12	2	4.5	+	+		+	+	+
		2		+		−	+	+
13	4	5	+	+		+	+	+
		5	+	+		+	+	+
		2	+	+		+	+	+
		2	+	+		−	−	+
14	2	7	+	+		+	+	=
		1	+	+		−	−	+
15	2	5.3	+	+	+	+	+	+
		2.7	+	+		+	+	+
16	4	2.9	+	+		+	+	+
		2.6	+	+		+	+	+
		2.2	+	+		−	−	+
		1.7	+	+		−	−	+
17	3	4.4	+	+		+	+	+
		3.8	+	+		+	+	+
		1.7	+	+		−	+	+
18	4	2.8	+	+		+	+	+
		1.9	+	+		−	+	+
		1.8	+	+		+	+	+
		1.3	+	+		−	−	−
19	1	5.5	+	+		+	+	+
20	1	5	+	+		+	+	+
21	1	5	+	+		+	+	+

*Suspicion of hemangioma.
†Confirmation of hemangioma.

TABLE 3
Hemangioma Size and Its Detection with Planar Scintigraphy and SPECT Methods 1 and 2

Applied technique	No. of hemangiomas (% of total) by size (cm)					
	≤1	1.1–2.0	2.1–3.0	3.1–4.0	>4.0	Total
Planar	1 (9)	3 (21)	6 (55)	5 (83)	14 (100)	29 (52)
SPECT Method 1	2 (18)	7 (50)	9 (82)	6 (100)	14 (100)	38 (68)
SPECT Method 2	9 (82)	13 (93)	11 (100)	6 (100)	14 (100)	53 (95)
Total lesions	11	14	11	6	14	56

slice multiecho technique. T1-weighted axial sequences were acquired with TE 33 msec and TR 400 msec. T2-weighted sequences were obtained with TR 1800 msec and TE 33, 66, 99 and 132 msec. T2 relaxation time was calculated as described elsewhere (*11*). A diagnosis of hemangioma was made on the basis of the long T2 (*8*).

The section thickness was 8 mm at 4 mm gaps using a 256 × 256 matrix and two averages. Size of hemangioma was measured by MRI or CT. When appropriate lesions were detected with the above imaging modalities, the patients were referred for scintigraphy.

RESULTS

A total of 56 lesions were detected on US, CT and MRI. US found 47 lesions in the 21 patients with hemangioma. All 56 liver hemangiomas were diagnosed with MRI. CT disclosed 6 hemangioma-positive lesions. The size of the hemangiomas ranged from 0.5–8.0 cm (Table 2). Twenty-five hemangiomas measured less than 2.1 cm and 11 were less than 1.1 cm.

Of the 56 hemangiomas, 29 were shown by planar imaging, 38 by Method 1 and 53 by Method 2 SPECT evaluation. The results of ^{99m}Tc-RBC imaging of hemangiomas are summarized in Table 3 by categorizing the hemangiomas into five groups according to size. Planar imaging sufficiently detected hemangiomas > 3.0 cm, SPECT Method 1 (static display) > 2.0 cm and SPECT Method 2 (three-view dynamic display) > 0.5–1.0 cm. Hemangiomas ≤ 1.5 cm in diameter were only detected incidentally in either planar image or SPECT Method 1 evaluation. The sensitivity of planar scintigraphy was 52%; of SPECT Method 1, 68%; and of SPECT Method 2, 95%. In a comparison of Methods 1 and 2, for hemangiomas ≤ 1.0 cm, 1.1–2.0 cm and 2.1–3.0 cm in diameter, sensitivity was considerably improved by Method 2 from 18% to 82%, 50% to 93% and 82% to 100%. The relation between the size of hemangioma and scintigraphic results is shown in Figure 3. In comparison to MRI, Method 2 did not identify one of four hemangiomas in one patient and two of three in another. Of the three hemangiomas not identified by Method 2, two were located adjacent to the heart and one was located adjacent to a fork of a large intrahepatic vessel. The smallest hemangioma detected with Method 2 was 0.5 cm in diameter; with Method 1, 0.9 cm; and with planar imaging, 1.0 cm. All metastases and hepatocellular carcinomas correctly showed normal or reduced activity accumulation in ^{99m}Tc-RBC scintigraphy (Table 1). As assessed by evaluation of the metastases and the carcinomas, the specificity for hemangioma was 100%, independent of the method applied, resulting in a positive predictive value of 100%.

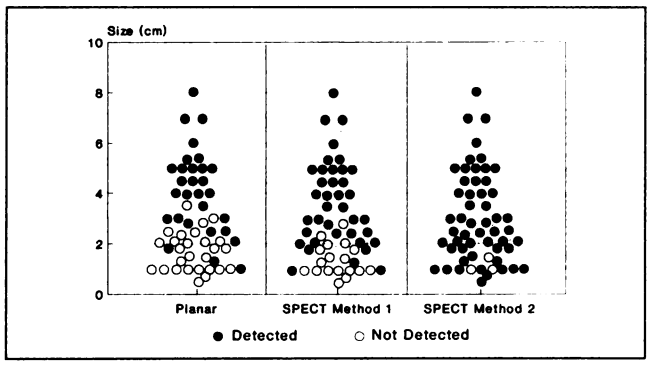

FIGURE 3. Relationship between hemangioma size and scintigraphic results with planar imaging, SPECT Method 1 and SPECT Method 2 evaluation. Independent of SPECT method applied, the tomographic technique was superior to planar imaging. Method 2 identified most hemangiomas <2.1 cm, which were not detected by Method 1 or planar scintigraphy.

DISCUSSION

Suspected cavernous hemangioma is the most common benign tumor of the liver. The incidence of this focal lesion ranges from 0.4%–7.3% (*1*). Thus, it is a major differential diagnosis if a focal liver lesion is discovered by US. Because the course of hemangioma is usually uncomplicated, differentiation from other lesions, such as metastases, is essential to avoid unnecessary or risky examination and treatment. US is sensitive but not specific for evaluating hepatic hemangioma (*12,13*). Using CT, there is some evidence that metastatic lesions and hepatoma may have an appearance similar to that of hemangioma (*2,14*). If strict criteria are used, diagnosis of hemangioma can only be ascertained in 55%–86% (*3,4*). Recent studies have claimed that MRI is the most sensitive modality (*8,9,15,16*) for detecting hepatic hemangiomas and is known to accurately distinguish them from most malignant liver lesions. On the other hand, ^{99m}Tc-RBC SPECT is the most specific technique; only a few

false positive studies have been reported (*17–20*). However, sensitivity of conventional ^{99m}Tc-RBC imaging is not fully satisfactory (*2,5,6,7,21*). The majority of hemangiomas are less than 5 cm (*1*) and many are less than 2 cm in diameter (present study 45%). With planar imaging technique, hemangiomas ≥ 3 cm in diameter and, with conventional SPECT evaluation, hemangiomas ≥ 2 cm can be identified with high sensitivity (*5,22,23*).

The detection of focal activity accumulation is mainly a function of image contrast which is increased by SPECT. In agreement with the literature, the present study demonstrates the improvement in sensitivity of SPECT technique in comparison with planar imaging technique (*5,7,24*). SPECT enables discrimination of activity of a lesion from that of overlaying liver tissue. Consequently, SPECT has the potential of identifying focal uptake even in small and central lesions. However, due to great blood vessels, distribution of activity is not completely homogeneous even in normal liver tissue. Hence, the conventional static evaluation of small lesions is limited. The results achieved with Method 1 are comparable to those reported by Kudo et al. and Birnbaum et al. (*5,9*). Assessment of dynamically displayed SPECT studies (Method 2) allows tracing of areas of increased activity simultaneously in three views and therefore enables differentiation of blood vessels from focal activity even in small hemangiomas. Due to this advantage, hemangiomas as small as 1 cm were reliably detected using Method 2. The sensitivity could be increased while specificity remained 100%. Further improvement in detection of smaller lesions (<1 cm) can be expected when dynamic display evaluation (Method 2) is applied to high resolution triple-headed SPECT systems. Even with static evaluation, using a triple-headed camera helped Ziessman et al. achieve better results than in previous studies (*25*).

Technetium-99m-RBC flow phase imaging recommended for further differential diagnosis was considered as noncontributory since specificity in the present study was 100% without assessment of flow. Moreover, only five false-positive cases have been reported in the literature, yielding increased uptake on delayed imaging (*17–20*). Nevertheless, flow imaging is still discussed controversially since variably decreased or increased perfusion in both hemangiomas and other tumors has been reported (*5–7,20,21,26,27*). Thus, combined evaluation of flow and delayed studies will lead to a loss in sensitivity rather than a gain in specificity. Moreover, as mentioned before, resolution of planar imaging is rather limited and dynamic flow studies in SPECT technique will not be available until faster SPECT cameras are commonly used.

We propose the approach outlined in Figure 4 for the diagnosis of liver hemangioma. In this algorithm, SPECT and MRI are equivalent. If typical findings of liver hemangioma are present on either study, the diagnostic workup should be terminated.

In conclusion, the results show that evaluation of dynamically displayed ^{99m}Tc-RBC SPECT studies is superior to conventional reading of static display and comparable to MRI. Therefore, this approach is suggested for confirming the diagnosis of liver hemangioma ≥ 1 cm if planar imaging and conventional reading of the tomograms are negative. The dynamic SPECT display software is included in most currently available computer software systems and needs no additional disbursement.

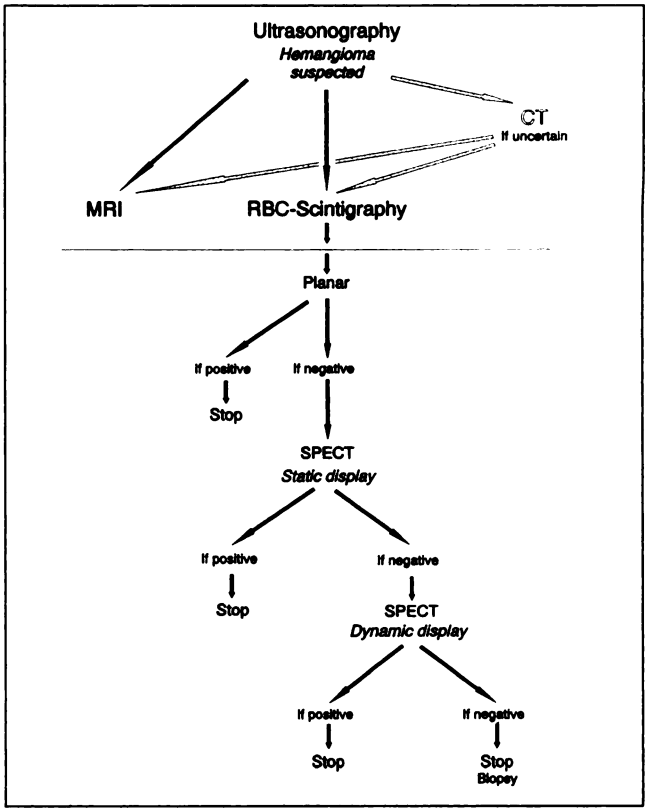

FIGURE 4. Proposed algorithm for diagnostic workup of liver hemangioma. Since accuracy of RBC SPECT and MRI is comparable in hemangioma ≥ 1 cm, both imaging procedures play similar roles. Whenever imaging is positive for hemangioma, no further test is indicated. If planar RBC scintigraphy is negative, SPECT has to be performed. When evaluation of statically displayed SPECT studies is negative, analysis of dynamic display is proposed. In definitively negative RBC studies, biopsy or prolonged follow-up are the remaining procedures.

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