The aim of the study is the assessment of the value of SPECT (single photon emission computerized tomography) using 99mTc-labeled red blood cells in the detection of liver hemangioma, in comparison to planar imaging. With planar red blood cell scintigraphy, sensitivity of the method was 76%, specificity 98%, positive predictive value 98% and negative predictive value 79%. With SPECT, sensitivity of the method was 95%, specificity 98%, positive predictive value 98% and negative predictive value 94%. The smallest lesion detected by planar red blood cell scintigraphy was 1.2 cm, and with SPECT red blood cell scintigraphy 0.8 cm. The use of 99mTc-labeled red blood cells SPECT improved the sensitivity much more in smaller lesions (0.8 to 2 cm), than in bigger ones (2-5 cm). SPECT with radiolabeled red blood cells significantly improves the results of scintigraphic findings, especially in the small lesions.

Key words: hemangioma, SPECT, 99mTc-red blood cells

INTRODUCTION

Hepatic hemangiomas are present in 0.4 -7% of the population and are the most frequent benign tumors of the liver. They are usually small, but rarely can be very large. The vast majority of hemangiomas of the liver never cause symptoms or health problems. They are more common and usually larger in women than in men. Pregnancy and estrogen-based medications can cause their growth. In most of the patients hemangiomas are asymptomatic and discovered incidentally during diagnostics procedures (US, CT, MRI), as well as at laparotomy or autopsy. Only 10% of hepatic hemangiomas reach dimensions that need surgical treatment especially if they are causing symptoms. Although benign, they may influence the organ function, depending on their size and position, causing pain, nausea or enlargement of the liver. Rarely, larger hemangiomas can rupture, with severe pain and bleeding into the abdomen that may be even life threatening. Rarely, if thrombocytopenia is present due to large hemangiomas, laboratory blood tests are required. When a hemangioma is suspected it must be confirmed, in order to exclude the presence of another type of tumor, particularly a malignant one. A biopsy of suspected hemangiomas is avoided because of their benign nature and the potential risk of bleeding. The most of liver hemangiomas require no treatment. In the diagnosis, ultrasound, 99mTc red blood cell scintigraphy with single-photon emission computed tomography (SPECT), CT with contrast, MRI, as well as angiography is performed. Recently, fusion SPECT/CT and SPECT/MRI imaging as well as imaging with hybrid SPECT/CT cameras are employed.

The aim of the study is the assessment of the value of SPECT (single photon emission computerized tomography) in the detection of liver hemangioma, in comparison to planar imaging.

PATIENTS AND METHODS

The study was performed with ECAM Siemens camera. In all the patients, planar scintigraphy was performed 180 min after red blood cell labeling by i.v. application of Sn-pyrophosphate and, 20 min after of 740 MBq 99mTc pertechnetate. Planar imaging was performed in anterior, posterior and right lateral position, using matrix 128x128, 500 000 imp/view. SPECT (single photon emission computerized tomography) was performed with the same camera, with non-circular orbit, 360 degrees, 6 degrees and 30 s per view, step and shoot mode. Reconstruction was performed using Butterworth filter, order 6, cut off frequency 0.25. Analysis was performed using slice reconstruction (coronal, transversal, sagittal), as well as a dynamic three-view display of SPECT slices.

We investigated 84 patients, 59 women and 25 men between 20 and 63 years old (mean age, 42 years). There is a total of 104 liver lesions, 88 in the right (68 single, 20...
multiple) and 16 in the left (12 single, 4 multiple) lobe, range from 0.5 to 6 cm. The diagnosis was confirmed according to clinical finding (after 1 year of follow up), surgery and biopsy. In the investigation, laboratory liver function tests and tumor markers assessment was included, as well as ultrasound (with Doppler) (Figure 1), planar liver radiocolloid scintigraphy (Figure 2a), CT, MRI and angiography.

RESULTS

With planar blood pool scintigraphy, there were 42 true positives (TP), 13 false negative (FN), 1 false positive (FP) and 48 true negative (TN) lesions. Thus, sensitivity of the method was 76%, specificity 98%, positive predictive value 98% and negative predictive value 79%. With SPECT, there were 52 TP, 3 FN, 1 FP and 48 TN lesions. Thus, sensitivity of the method was 95%, specificity 98%, positive predictive value 98% and negative predictive value 94%. The smallest lesion detected by planar RBC scintigraphy was 1.2 cm, and with SPECT RBC 0.8 cm. The use of SPECT improved the sensitivity 13% for lesions from 0.8 to 2 cm, and 5% in those from 2-5 cm.

Hemangiomas were always presented as hypervascular lesions (n=52) (Figure 2 b,c,d), although in 3 of them, hypovascular zone was found in the center. From 48 tumors that were not proved to be hemangiomas, 3 were adenomas (one isovascular and two hypovascular), 2 were focal nodular hyperplasias (one hypovascular and one isovascular), 15 were hepatocellular carcinomas (11 isovascular or descreetly bipervascular and 4 isovascular with necrotic lesions). From 28 tumors which proved to be metastases of carcinomas (colorectal, lung, bronchal, lymphoma), all the lesions were hypovascular. FP finding obtained by both methods was caused by the superposition of the activity from the vascular structure.

DISCUSSION

The majority of the results obtained by both methods were TP or TN. FP finding obtained by both methods was caused by the superposition of the activity from the vascular structure, i.e. small aneurysm. FN findings were obtained mostly because of the small size of the lesions, 13 with planar scintigraphy and 3 with SPECT (lesions from 0.5-0.8 mm). According to our investigation, hemangiomas are nearly always presented as hypervascular lesions, while other liver tumors may be presented as hypovascular and isovascular zones. With SPECT, sensitivity and negative predictive value are improved. Also, SPECT allows detection of smaller lesions. These parameters are especially improved for lesions from 0.8 to 2 cm. SPECT is a time consuming procedure, including acquisition and processing, so first, the planar imaging with radiolabeled red blood cells should be performed. However it is necessary all the cases when planar imaging is negative, particularly in smaller lesions.

Literature data are similar to ours. Thus, according to Tsai et al. there was no specific US pattern that would differentiate giant hepatic hemangioma from other giant liver masses, but 99mTc red blood cell SPECT appeared to separate them clearly. Intenza et al. proved the value of SPECT in additional diagnosis of cavernous hemangioma with 99mTc red blood cell imaging, because although fourteen of hemangiomas were detected by planar imaging, two were detected by SPECT only. However, he also proved that two patients with large hemangiomas had false-negative scans. El Desouki et al. proved that 99mTc red blood cell scintigraphy is the noninvasive technique most helpful in the diagnosis of hepatic hemangioma, especially in those at risk for lesion rupture or bleeding. According to him, SPECT should be performed whenever planar imaging fails to show the lesion by 2 hours. Also, US should precede scintigraphy for determination of the size and the location of the lesion. Location is important.
for optimal gamma camera acquisition, while lesions less than 1 cm can hardly be detected, because of the spatial resolution of gamma cameras. According to Bonanno et al., 599mTc red blood cell scanning is considered a highly specific technique for the study of hepatic hemangiomas, although planar imaging displays poor sensitivity for the identification of small lesions. His results confirm a high specificity of 99mTc red blood cell scanning with SPECT (100%). SPECT significantly improves the detection of hemangiomas (71%) compared to the delayed static study (52%), with the largest gain for lesions between 2-3.5 cm (83% versus 51%). However, also SPECT has difficulty in detecting lesions of less than 2 cm. Madacsy et al. obtained the sensitivity of planar 99mTc red blood cell scintigraphy 75% and the specificity 100%. He concluded that, although planar imaging is probably sufficient for all large or superficial hemangiomas, delayed SPECT should be used with small (2-3 cm) or deeply seated lesions. Similar to our findings, Krause et al. concluded that the specificity and positive predictive values for hemangioma was 100%. This study suggests that evaluation of dynamically displayed 99mTc red blood cell SPECT studies is comparable to MRI in liver hemangioma bigger than 1cm. Kagei et al. obtained in 40 hemangiomas, sensitivity for planar 99mTc red blood cell imaging 35%, SPECT 50%, US 53%, dynamic CT 82% and angiography 81%, respectively. When the tumor size was greater than 2.2 cm by 99mTc red blood cell SPECT and 2.8 cm by planar imaging, their sensitivity for both methods was 100%. Specificity for planar 99mTc red blood cell imaging was 100%, SPECT 95%, US 81%, dynamic CT 100% and angiography 83%, respectively. However one patient with hepatocellular carcinoma diagnosed by angiography showed increased uptake on SPECT. Because of the highest accuracy for SPECT in hemangioma greater than 2.0 cm, SPECT should be considered to be the method of choice for noninvasive diagnosis of hemangioma.

In order to improve sensitivity and specificity, different authors proposed improvements. Thus, Zincirkeser et al. recommends for the detection of hemangiomas located in the unusual position, the mismatch of the SPECT delayed images between the 99mTc-red blood cells and the 99mTc-sulfur colloid scans. Schillaci et al. in order to delineate the activity from vascular system, used red blood cell SPECT/CT hybrid imaging for accessing at the same time morphology and function, and proved it to be the feasible and useful in the identification or exclusion of suspected hepatic hemangiomas located near regions with high vascular activity. Dwamena et al. suggested that increased perfusion on radionuclide blood-volume imaging of hepatic hemangiomas may be a scintigraphic marker of arterioportal venous shunting, which may identify patients with increased risk for spontaneous rupture or identify them for the development of portal hypertension. Although the method is very specific, some limitations causing FP findings with 99mTc red blood cell imaging, both planar and SPECT are presented by some authors. Thus, Ji et al. proved FP finding with 99mTc red blood cell SPECT in hepatocellular carcinoma, caused likely by peliosis. Lim et al. with 99mTc red blood cell

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**FIGURE 2 B**

BLOOD POOL SCINTIGRAPHY WITH 99mTC - RADIOLABELLED ERITHROCYTES SHOWS HIPERVASCULARISATION IN THE SAME REGION, WHICH CONFIRMS

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**FIGURE 2 C**

C) AND D) SPECT WITH 99mTC - RADIOLABELLED ERITHROCYTES SHOWED APART OF LARGE HEMANGIOMA IN THE LEFT LOBE, MULTIPLE SMALL HEMANGIOMAS IN THE RIGHT LOBE.
SPECT, showed that the appearance of hepatic adenomas can vary on $^{99m}$Tc red blood cell SPECT, depending on whether dilated sinusoid and hepatic adenomas show blood pooling, sometimes mimicking hemangioma. The same author described the case of hepatocellular carcinoma mimicking cavernous hemangioma on $^{99m}$Tc red blood cell liver SPECT. Also, Shih et al. showed false-positive results for hepatic hemangioma on $^{99m}$Tc red blood cell SPECT caused by a liver metastasis from small-cell lung carcinoma. Also, according to Park et al., an early “blush” on $^{99m}$Tc red blood cell hepatic scintigraphy can be a diagnostic feature of infantile hemangioendothelioma.

CONCLUSION

The main problem for the detection of hepatic hemangioma with $^{99m}$Tc red blood cell scintigraphy is the size of the lesion. This may be partly overcome by SPECT. With SPECT, sensitivity and negative predictive value is improved. These parameters are especially improved for lesions from 0.8 to 2 cm. Thus, SPECT is recommended in all the cases when planar imaging is negative, particularly in smaller lesions. The best solution for the detection of liver hemangioma is hybrid SPECT/CT imaging which combines anatomic and functional imaging at the same time.

SUMMARY

$^{99m}$Tc LEUKOCITA SPECT I PLANARNA SCINTIGRAFIJA U DIJAGNOZI HEMANGIOMA JETRE

Cilj rada je procena vrednosti scintigrafije pomoću SPECT-a (single photon emission computerized tomography) $^{99m}$Tc obeleženim eritrocitima u otkrivanju hemangiama u poredjenju sa planarnim snimanjem. Planarnom scintigrafijom, senzitivnost metode je 76%, specifičnost 98%, pozitivna prediktivna vrednost 98% i negativna prediktivna vrednost 79%. Primenom SPECT-a senzitivnost metode iznosi 95%, specifičnost 98%, pozitivna prediktivna vrednost 98% i negativna prediktivna vrednost 94%. Najmanja lezija otkrivena pomoću planarne scintigrafije obeleženim eritrocitima iznosi 1.2 cm, a primenom SPECT-a 0.8 cm. Primena SPECT-a povećava senzitivnost više kada su u pitanju manje lezije (0.8 to 2 cm), nego veće (2-5 cm). SPECT pomoću obeleženih eritrocita značajno povećava preciznost scintigrafskog ispitivanja, posebno kod manjih lezija.

Ključne reči: hemangiom, SPECT, $^{99m}$TC crvena krvena zrna

REFERENCES