

## C A S E R E P O R T

# SPECT/CT with $^{99m}\text{Tc}$ labelled heat-denatured erythrocyte to detect thoracic and abdominal splenic tissue

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**Summary.** Scintigraphy with  $^{99m}\text{Tc}$  labelled heat-denatured erythrocyte (DRBC) allows non invasive diagnosis of heterotopic splenic tissue implantation (splenosis) following splenic trauma or surgery. Single-photon emission computed tomography (SPECT) combined with computed tomography (CT) improves diagnostic accuracy of planar imaging through a more precise localization of functional findings. We report about two cases of splenosis occurring many years after splenectomy.  $^{99m}\text{Tc}$ -DCRBC scintigraphy was used for differential diagnosis of metastatic disease in one case and to assess an incidental finding at bone scan in the second one. SPECT/CT increased specificity of planar imaging, especially revealing combined (thoracic and abdominal) splenosis. ([www.actabiomedica.it](http://www.actabiomedica.it))

## Introduction

Splenosis is an heterotopic splenic tissue implantation following splenic trauma or surgery. It has been widely reported with an incidence of 16-67% (1). Generally, the splenic implants are numerous and located within the peritoneal cavity; however, extra-abdominal splenosis does occur, including pleural cavity, lung, pericardium, pelvis, and subcutaneous tissues. Splenosis may occur from months to years after accident or splenectomy. The correct identification of this condition is critical to avoid unnecessary procedures. The differential diagnosis of splenosis is challenging using conventional imaging (ultrasound, CT, and MRI) (2) and it include metastatic disease, hepatic or renal malignancies, lymphoma, pheochromocytoma, endometriosis, carcinomatosis, or adenopathy. Fine needle aspiration is considered the gold standard for a definitive diagnosis, but it is an invasive procedure not immune to complications especially bleeding. The use of  $^{99m}\text{Tc}$  labelled heat-denatured erythrocyte ( $^{99m}\text{Tc}$ -

DRBC) scintigraphy allows diagnosis confirmation demonstrating phagocytic ability in the ectopic splenic tissue. It should be considered as the technique of choice due to its great sensitivity and specificity, as previously described (3). We report two cases of patients with previous splenectomy referred to our Center to perform  $^{99m}\text{Tc}$ -DRBC scintigraphy for the differential diagnosis of thoracic and abdominal incidental findings at conventional imaging.

## Case #1

A 66-year-old man with previous post-traumatic splenectomy, forty-eight years earlier, was submitted to a CT scan for persistent cough. CT showed a solid nodule in the posterior basal segment of the left lung, left abdominal peri-renal masses and a right renal lesion inducing the suspicion of metastatic renal cancer. One month later the patient was submitted to right nephrectomy whit histological diagnosis of on-

cocytoma. Follow-up CT scan (2 months later) confirmed previously described lung and abdominal solid nodules stable in number and size. A  $^{99m}\text{Tc}$ -DRBC scintigraphy was then performed. The labeling procedure of heat-damaged RBC was previously described and validated (4). Planar images revealed multiple foci of uptake in the left hypocondrium (fig. 1). Hybrid SPECT/CT showed that one of the uptake foci corresponded to the nodule in the posterior basal segment of the left lung (fig. 2,3) suggesting the diagnosis of combined thoracic and abdominal splenosis.

## Case #2

A 72-year-old man was referred for a triphasic bone scintigraphy with  $^{99m}\text{Tc}$ -disphosphonate to evaluate painful prosthetic implant of the knee. In all the study phases, images showed abnormal uptake close to the tibial portion of the implant. Whole-body scan revealed intense radiopharmaceutical accumulation in the left hypocondrium (fig.4). To establish septic involvement of the prosthesis, scintigraphy with  $^{99m}\text{Tc}$  HMPAO-labeled leukocytes was subsequently performed and the whole body images confirmed accumulation of labelled cells in the left hypocondrium. The patient underwent splenectomy owing to Banti

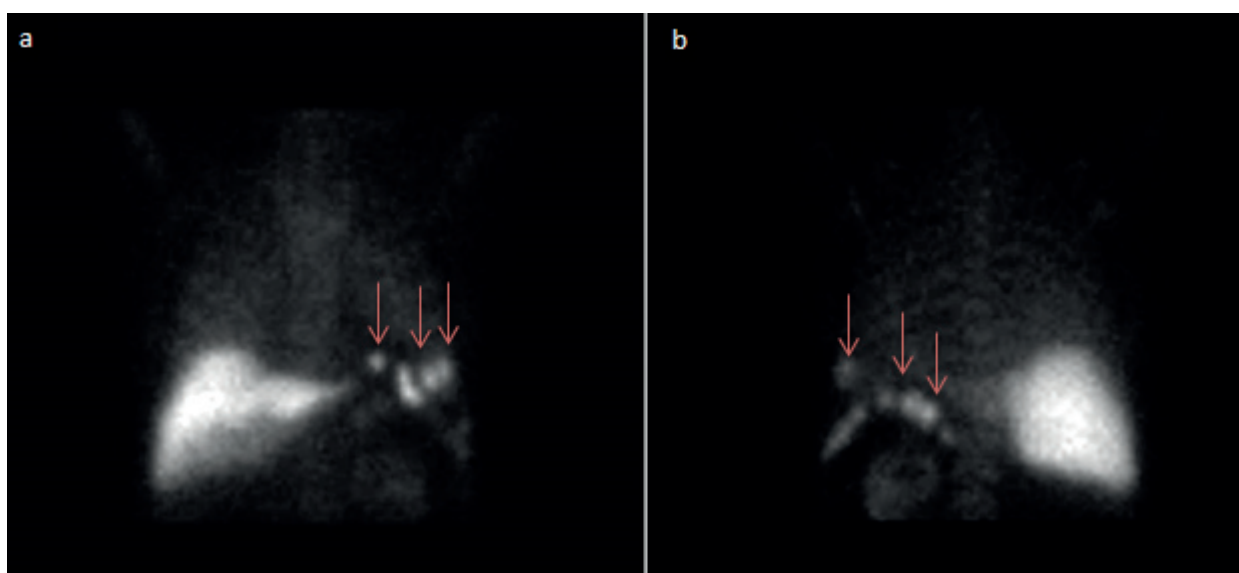
syndrome 60 years earlier. Therefore,  $^{99m}\text{Tc}$ -DRBC scintigraphy (planar images and SPECT/CT) was performed, confirming radiopharmaceutical accumulation in the left hypocondrium corresponding to solid tissue being consistent with splenosis (fig. 5,6).

## Discussion

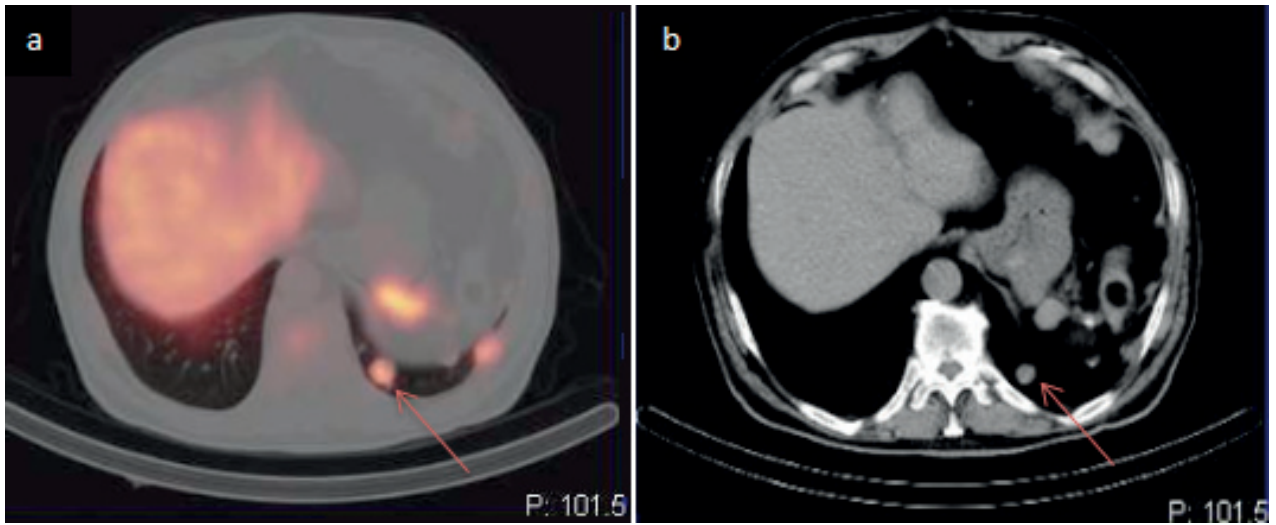
Splenosis is mostly asymptomatic and found incidentally on US, CT, and MRI examinations. However, heterotopic splenic tissue may be occasionally demonstrated during scintigraphy or PET scan performed with different tracers (5,6,7), as in case #2, in which splenic remnants after surgery were revealed by  $^{99m}\text{Tc}$ -HMPAO-labeled leukocytes and  $^{99m}\text{Tc}$ -disphosphonate scintigraphy.

Detection of splenic tissue by leukocyte scintigraphy is always incidental and due to uptake of  $^{99m}\text{Tc}$ -HMPAO-labeled leukocytes by phagocytic Kupffer cells of the reticuloendothelial system (8).

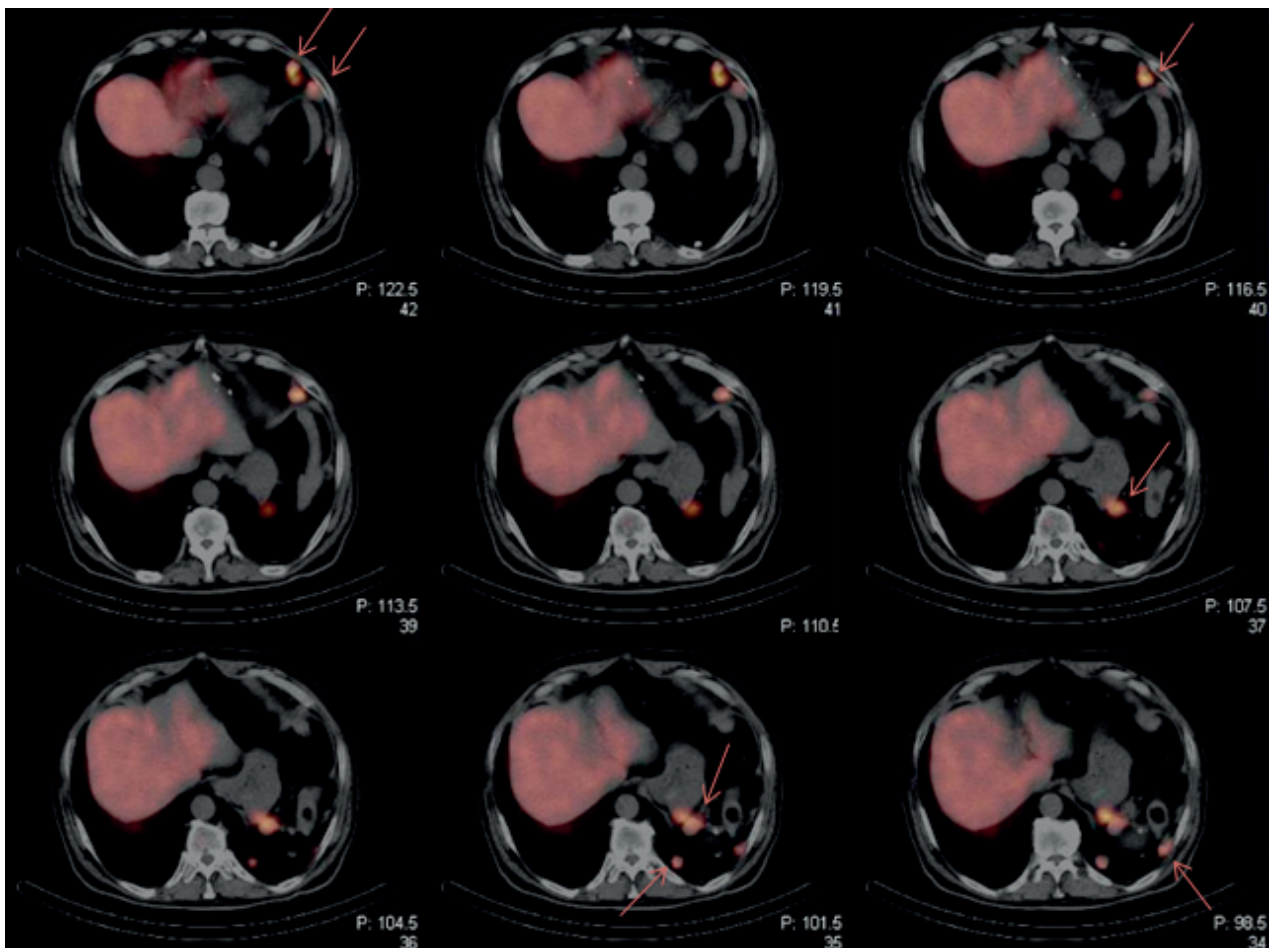
For many years, the most commonly used radiopharmaceutical for imaging the spleen was Tc-99m sulfur colloid (SC). However, heat-denatured RBC scintigraphy has demonstrated superior sensitivity in the identification of residual or heterotopic splenic tissue in adults (9,10) and children (11).



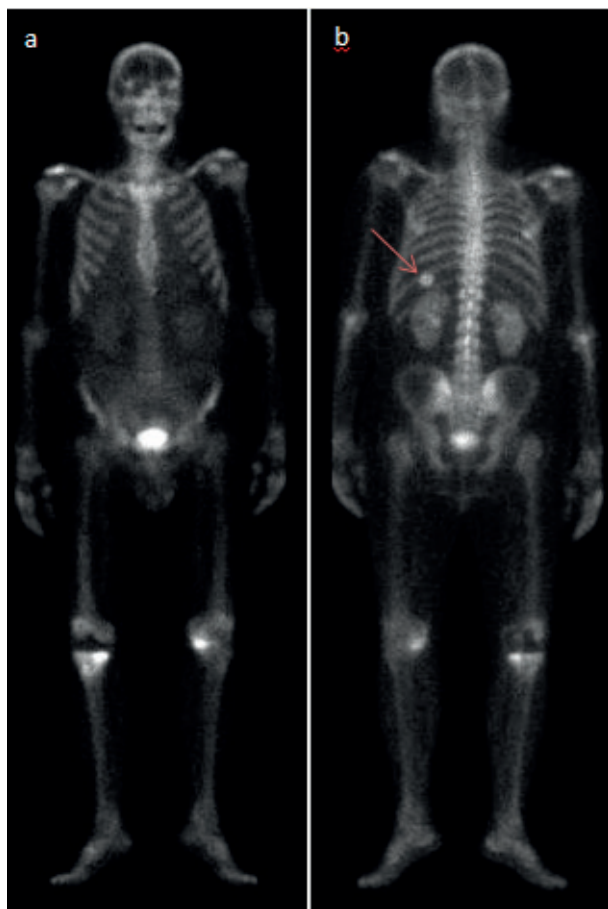
**Figure 1.**  $^{99m}\text{Tc}$ -DRBC scintigraphy (planar imaging): anterior (a) and posterior (b) view demonstrating multiple foci of labeled red blood cells accumulation (red arrows).



**Figure 2.**  $^{99m}\text{Tc}$ -DRBC SPECT/CT: labeled RBC accumulation in the left lung (a) corresponding to the solid nodule (red arrow) in the posterior basal segment at the CT scan (b).



**Figure 3.**  $^{99m}\text{Tc}$ -DRBC SPECT/CT: fused images of spleen remnants in the abdomen and left lung (red arrows)



**Figure 4.** Bone scan with  $^{99m}\text{Tc}$ -HDP: whole body anterior (*a*) and posterior (*b*) view demonstrating focal tracer accumulation near the upper pole of the left kidney (red arrow).

Occasionally, splenosis can mimic metastatic malignancy on imaging and pose a diagnostic challenge, as in case #1, submitted to surgery for a renal lesion. Locations of splenosis especially in the hepatic, or lung parenchyma, may be confused with neoplastic lesions and may lead to unnecessary surgery.

In this context, PET/CT largely used to assess cancer may pose this diagnostic challenge with growing frequency, as in the case of intrapancreatic mass suspected for neuroendocrine tumors (NETs) (6). Indeed, PET imaging of NETs with labelled-peptides ( $^{68}\text{Ga}$ -DOTATOC,  $^{68}\text{Ga}$ -DOTATATE,  $^{68}\text{Ga}$ -DOTANOC) may determine false positive results (6) due to the presence of SSTRs on the surface of splenic lymphocytes.

On the other hand, PET/CT with different tracers as  $^{18}\text{F}$ -FDG or  $^{68}\text{Ga}$ -DOTATOC may be used to exclude (12) or confirm (fig. 7) malignancy in the

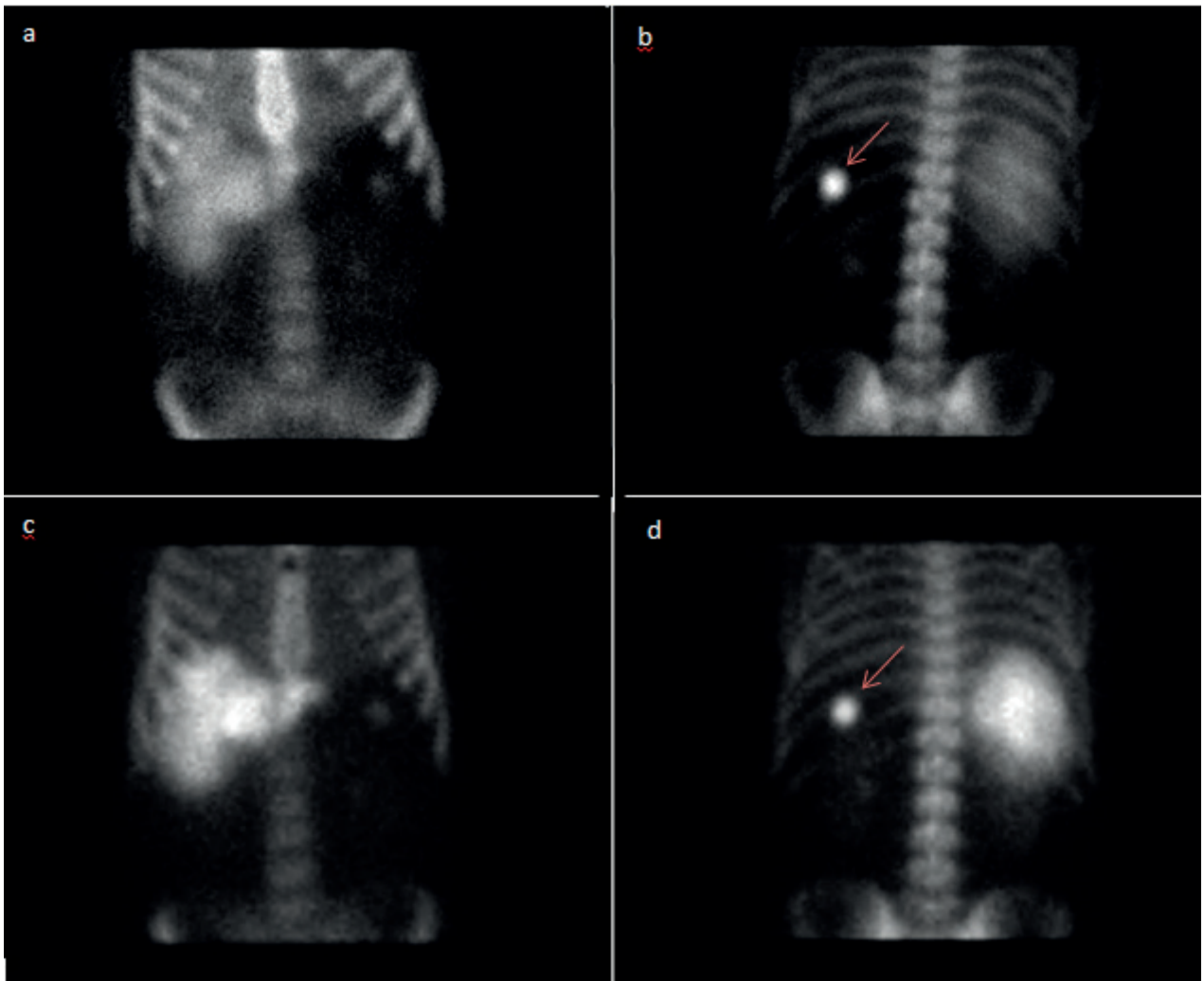
case of abdominal implant associated to inconclusive conventional imaging in oncologic patients.

Nonetheless, PET/CT does not definitively assess the presence of splenosis, always requiring the use of specific tracers targeting the hemocatheretic function of the spleen as  $^{99m}\text{Tc}$ -DRBC.

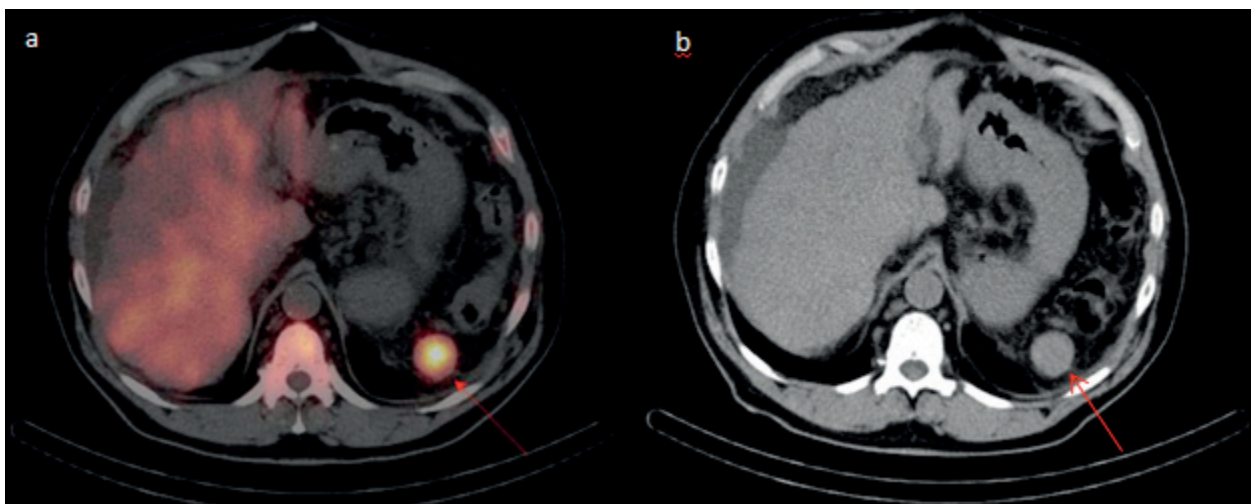
Scintigraphy with  $^{99m}\text{Tc}$ -DRBC provides selective splenic imaging allowing the noninvasive diagnosis of this entity avoiding more aggressive diagnostic techniques such as fine needle aspiration or laparotomy.

The additional use of hybrid imaging (combining SPECT and CT) improves specificity through a more precise localization of ectopic splenic tissue. Indeed, in case #2, planar imaging alone didn't allow accurate localization of labeled RBC accumulation in the left lung, being the uptake site confused with left hypocondrium, as for the other abdominal nodules. Combined intrathoracic and intraperitoneal splenosis have been previously described (13) but the added value of SPECT/CT is only occasionally reported as in one woman with previous splenectomy following a road accident (14), to assess lung nodules incidentally discovered in a chest radiograph forty-seven years after a car accident (3) and to characterize an incidental liver lesion discovered on abdominal ultrasound diagnosed as intrahepatic splenosis (15). SPECT/CT has been used with radiolabelled colloids to detect accessory spleen mimicking pancreatic tumour (16). Before hybrid technology was available in the clinical routine, SPECT alone was used to increase detection accuracy of planar imaging in localizing  $^{99m}\text{Tc}$ -DRBC or radiolabelled colloids accumulation (17, 18). However, Ekmekçi S. et al. demonstrated that there was no contribution of SPECT alone to planar imaging with  $^{99m}\text{Tc}$ -DRBC in detecting splenosis or accessory spleen in splenectomized and nonsplenectomized patients (112 scintigraphic scans of 96 patients).  $^{99m}\text{Tc}$ -DRBC scan showed high specificity in the detection of accessory spleens/splenosis with no false positive results in patients who underwent surgery (19). Fusion of transmission (SPECT) and emission (CT) tomography (called TET) for correct localization of ectopic splenic tissue was assessed for the first time by Horger M et al. in 7 patients with haematological disorders (20). Diagnostic impact of fused images was highest for intrahepatic, pulmonary or pleural splenic implants. Utilization of SPECT/CT increased accuracy in

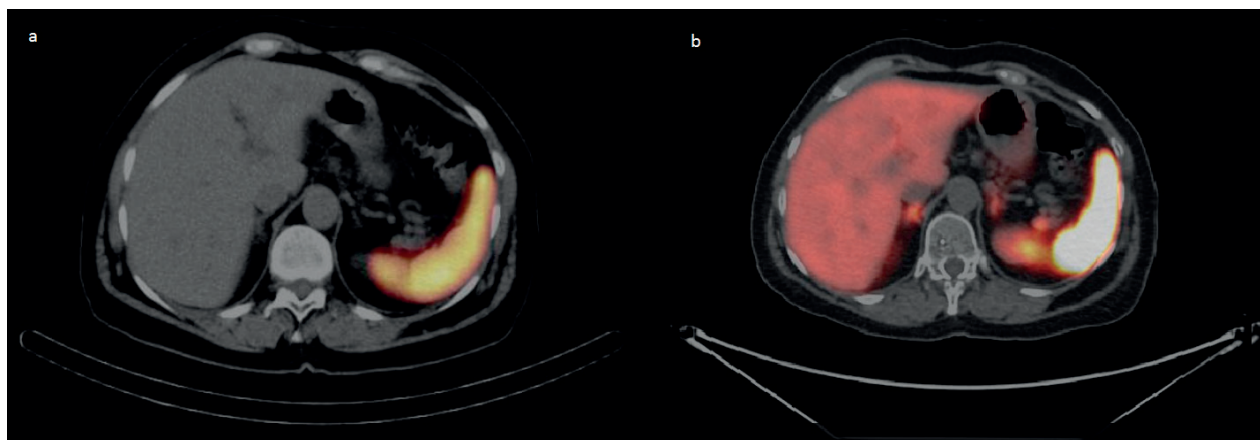




**Figure 5.** Scintigraphy (planar images) with  $^{99m}\text{Tc}$ -HMPAO-labeled leukocytes (*a, b*) and  $^{99m}\text{Tc}$ -DRBC (*c, d*): anterior (*a, c*) and posterior (*b, d*) views demonstrating accumulation of labeled blood cells in the left hypochondrium (red arrows).



**Figure 6.**  $^{99m}\text{Tc}$ -DRBC SPECT/CT: accumulation of labeled red blood cells (red arrow) in the solid tissue (fused image *a*) localized in the left hypochondrium at the CT scan (*b*)



**Figure 7.** 68-year-old woman with a lesion of the pancreatic tail (12x11 mm). MR signal similar to the spleen suggested the presence of splenic tissue or neuroendocrine tumor. The CT scan was also inconclusive. Combination of  $^{99m}\text{Tc}$ -DRBC scintigraphy (planar images and SPECT/CT) (a) and  $^{68}\text{Ga}$ -DOTATOC PET/CT (b) provided the final diagnosis of NET excluding splenic tissue.

identifying spleen remnants in a patient with recurrent idiopathic thrombocytopenic purpura and thrombocytopenia after splenectomy, undergoing surgery with intraoperative gamma probe (21). Moreover, SPECT/CT demonstrated better performance compared to planar imaging in localizing splenic morsels using labeled colloidal stannous chloride in 19 patients with spleen autoimplantation as a protective measure after splenectomy in hepatosplenic schistosomiasis (22).

## Conclusion

Radiolabelled heat-damaged red blood cell scintigraphy is a reliable, sensitive and non invasive imaging method to confirm the presence of functioning splenic tissue avoiding diagnostic pitfalls and misinterpretations. Adding SPECT/CT to planar imaging may be helpful in equivocal cases to accurately localize uptake foci especially in combined thoracic and abdominal splenosis.

Finally, SPECT/CT with  $^{99m}\text{Tc}$ -DRBC may complete the diagnostic algorithm of oncological patients previously submitted to PET/CT.

## Disclosure

The authors have stated that they have no conflicts of interest.

## References

1. Yildiz, A. E., Ariyurek, M. O., & Karcaaltincaba, M. (2013). Splenic anomalies of shape, size, and location: pictorial essay. *The Scientific World Journal*, 2013.
2. He, Z., Xu, X., Wei, Q., Ke, Q., & Zheng, S. (2015). Successful diagnosis of intrahepatic splenosis mimicking hepatic tumor: P96. *Surgical Practice*, 19.
3. Yuste, Jose R., et al. "Posttraumatic intrathoracic splenosis: from clinical suspicion to noninvasive diagnosis." *The American journal of medicine* 127.11 (2014): e3-e4.
4. Sammartano, A., Scarlattei, M., Migliari, S., Baldari, G. and Ruffini, L. 2019. Validation of in vitro labeling method for human use of heat-damage red blood cells to detect splenic tissue and hemocateretic function. *Acta Bio Medica Atenei Parmensis*. 90, 3 (Sep. 2019), 275-280. DOI:<https://doi.org/10.23750/abm.v90i3.7767>.
5. Baldari G, Sindoni A, Belletti A, et al.  $(^{99m}\text{Tc})$  disphosphonate uptake due to splenosis: incidental finding 60 years after splenectomy. *Clin Nucl Med* 2015;40:533-5.
6. Zurek Munk-Madsen, Maria, et al. "Intrapancreatic accessory spleen mimicking malignant tumor: three case reports." *Acta radiologica open* 8.6 (2019): 2058460119859347.
7. Barber, Thomas W., et al. "Ga-68 octreotate PET/CT and Tc-99 m heat-denatured red blood cell SPECT/CT imaging of an intrapancreatic accessory spleen." *Journal of medical imaging and radiation oncology* 60.2 (2016): 227-229.
8. Cuneyt Turkmen and Ebru Yormaz. Incidental Detection of Multiple Abdominopelvic Splenosis Sites During Tc-99m HMPAO-Labeled Leukocyte Scintigraphy. *Clin Nucl Med* 2006;31: 572-574.
9. Hagan I, Hopkins R, Lyburn I. Superior demonstration of splenosis by heat-denatured Tc-99m red blood cell scintigraphy compared with Tc-99m sulfur colloid scintigraphy. *Clin Nucl Med*. 2006 Aug;31(8):463-6

10. Hagman TF, Winer-Muram HT, Meyer CA, et al. Intrathoracic splenosis: superiority of technetium Tc 99m heat-damaged RBC imaging—selected reports—red blood cell. *Chest*. 2001;120:2097.
11. Ehrlich CP, Papanicolaou N, Treves S, Hurwitz RA, Richards P. Splenic scintigraphy using Tc-99m-labeled heat-denatured red blood cells in pediatric patients: concise communication. *J Nucl Med*. 1982 Mar;23(3):209-13
12. Koç ZP, Özcan Kara P, Tombak A. Splenosis Mimicking Lymphoma Relapse Confirmed by (18)F-FDG PET/CT and Tc-99m Nano-colloid Scintigraphy Thirty Years After Splenectomy for Trauma. *Mol Imaging Radionucl Ther*. 2019 Mar 19;28(1):38-40
13. Sánchez Aguilar M, Fernández López R, Tirado Hospital JL, García Gómez FJ. Thoracoabdominal splenosis. *Med Clin (Barc)*. 2017 Mar 3;148(5):242. doi: 10.1016/j.medcli.2016.05.012. Epub 2016 Jun 23. English, Spanish. PubMed PMID:27345847.
14. Williams, Kirryn, and Graham Simpson. "Thoracic splenosis: diagnosis without invasive investigations." *Respirology case reports* 5.6 (2017): e00274.
15. Tamm, Alexander, et al. "Heat-damaged RBC scan: a case of intrahepatic splenosis." *Clinical nuclear medicine* 40.5 (2015): 453-454.
16. Pachowicz, M., et al. "Accessory spleen mimicking pancreatic tumour: evaluation by 99mTc-labelled colloid SPECT/CT study. Report of two cases and a review of nuclear medicine methods utility." *Folia morphologica* 74.4 (2015): 532-539.
17. Williams, Gethin, et al. "Splenic implants detected by SPECT images of Tc-99m labeled damaged red blood cells." *Clinical nuclear medicine* 31.8 (2006): 467-469.
18. Marrero, Tirsia M. Ferrer, Valentin Prieto-Centurion, and Howard A. Jaffe. "Thoracic splenosis: History is the key." *Respiratory medicine case reports* 22 (2017): 251-253.
19. Ekmekçi , Diz-Küçükaya R, Türkmen C, Adalet I. Selective Spleen Scintigraphy in the Evaluation of Accessory Spleen/Splenosis in Splenectomized/Nonsplenectomized Patients and the Contribution of SPECT Imaging. *Mol Imaging Radionucl Ther*. 2015 Feb 5;24(1):1-7. doi: 10.4274/mirt.40085. PubMed PMID: 25800591; PubMed Central PMCID: PMC4372766.
20. Horger M, Eschmann SM, Lengerke C, Claussen CD, Pfannenbergl C, Bares R. Improved detection of splenosis in patients with haematological disorders: the role of combined transmission-emission tomography. *Eur J Nucl Med Mol Imaging*. 2003 Feb;30(2):316-9.
21. Alvarez R, Diehl KM, Avram A, Brown R, Piert M. Localization of splenosis using 99mTc-damaged red blood cell SPECT/CT and intraoperative gamma probe measurements. *Eur J Nucl Med Mol Imaging*. 2007 Jun;34(6):969. Epub 2007 Apr 25. PubMed PMID: 17457584.
22. Brandão SC, Gondra Lde A, Viana RA, Andrade LR, Brandt CT. Late splenosis evaluation after autoimplantation of spleen morsels in major omentum in hepatosplenic schistosomiasis patients using SPECT/CT imaging. *Clin Nucl Med*. 2012 Apr;37(4):372-3. doi: 10.1097/RLU.0b013e31823ea497. PubMed PMID: 22391708

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