Biomedical Letters
2017 | Volume 3 | Issue 1|Pages 17-22

RESEARCH ARTICLE OPEN ACCESS

Splenic Metastases from Primary Lung Cancer on Magnetic Resonance Imaging (MRI): A Retrospective Study

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Abstract
The aim of this study is to evaluate and identify Magnetic resonance imaging (MRI) features of splenic focal lesions secondary to primary lung cancers. Thirteen patients with lesions to the spleen from primary lung cancer included transverse T1-weighted, spectral presaturation attenuated inversion recovery T2-weighted (SPAIR), post contrast arterial phase, post contrast venous phase images. Sixteen splenic lesions from lung cancer were identified as metastasis; all of the lesions showed a heterogeneous hypointense enhancement to splenic parenchyma on T1-weighted after intravenous contrast MRI and among them two of the patient's focal lesions were not detected by Computed tomography (CT) and Ultrasonography (USG) but detected by MRI. The primary malignancy included adenocarcinoma (n=6), squamous cell carcinoma (n=3), small cell carcinoma (n=2), squamous adenocarcinoma (n=1) and lung sarcoma (n=1). The majority of the lesions was solitary, with central necrosis, high intensity peripheral rim enhancement and well defined margins along with other abdominal visceral metastases. Splenic metastasis generally presents as a solitary, cystic or necrotic mass, lymphadenopathy and heterogeneous isointense enhancement after contrast on CT and MRI. Imaging findings correlated with clinical findings are sufficient to diagnose splenic metastases from lung cancers.

Keywords: MRI, splenic neoplasms secondary, CT, lung neoplasms/pathology.
Received January 2, 2017; **Revised** February 18, 2017; **Accepted** March 7, 2017
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***To cite this manuscript*:** Preeti H, Pradhan Kumar PA, Wang Y, Zhu H, Sun X. Splenic Metastases from Primary Lung Cancer on Magnetic Resonance Imaging (MRI): A retrospective study. Biomed Lett 2017; 1(1):17-22.

1. Introduction

Spleen is the largest lymphatic organ in the body which is mesodermal in origin [1-3]. It is located in the left hypogastric quadrant of the abdomen and is fixed in the intraperitoneal position under the 9th to 11th intercostal spaces by splenorenal, splenocolic, splenogastric and phrenicosplenic ligaments [4]. The splenic trabecular arise from internal capsule, subdividing organ into two compartments, namely the red and white pulps separated by marginal zone. The white pulp plays a role in the immune system as it produces lymphocytes, plasma cells and antibodies and the red pulp filters the blood removing antigens, microorganisms and defective red blood cells [2,5,6].

Although the spleen is the most vascular organ in the body, it is an infrequent site for metastatic disease [7]. Splenic resistance for metastatic seeding is probably due to its high density of immune –system cells and high concentration of angiogenesis inhibition factor [8].

Splenic metastases from solid tumors are rare[7] and most often they are part of metastatic disease and usually reported at autopsy, with an average incidence of 7%[9] .The most common tumors that metastasize to the spleen are lung tumors, breast tumors, and melanoma, with the latter having the highest predilection[10, 11].

Lung cancer is one of the most common cancers that metastasize to the spleen [12]. By contrast, however, reports of splenic metastasis from lung cancer either at the time of initial diagnosis or during the clinical course is extremely rare [7]. In an earlier series of lung cancer patients, only 12 of 997 consecutive cases had splenic involvement [13]. The incidence of metastasis to the spleen in patients with lung cancer is variable [14, 15].

Since most of the patients are asymptomatic, splenic metastasis are usually found incidental during abdominal imaging examination. Radiologically, metastases disseminate in such a manner that it is hard to differentiate from primary splenic lesions, which causes a diagnostic dilemma with primary lesions of spleen particularly for solitary lesions in patients with a history of malignant diseases. Computed tomography and ultrasonography are commonly used for initial evaluation with magnetic resonance imaging reserved as a useful problem-solving tool for characterizing atypical and uncommon lesions. The value of magnetic resonance

imaging lies in classifying these lesions as either benign or malignant by virtue of their signal-intensity characteristics on T1- and T2-weighted imaging and optimal depiction of internal hemorrhage [16]. The challenge for the clinician is to discern the relatively rare finding of splenic metastasis from the more common splenic pathology such as lymphoma, abscess hemangioma and infarct. In this study, a retrospective analysis was done to determine the incidence, location of primary tumor, MRI feature of splenic lesion enhancement pattern after contrast administration with an emphasis on metastasis. Because of the rarity of the splenic metastasis radiologist need to be more familiar to categorize incidentally detected splenic lesions as for radiological diagnosis.

2. Materials and Methods

2.1 Patients

In this retrospective study, all patients with a proven splenic lesion on radiological imaging from January 2010 to December 2015 were included. Patient's data were retrieved from the hospital's centralized data system, including clinical, pathological and radiological files. Thirteen lung cancer patients with focal splenic lesions were included in this retrospective study. Criteria for the inclusion were the presence of focal splenic lesion confirmed by imaging ,MRI scan of the splenic lesion, known primary lung cancer and correlative supportive imaging as CT and USG) ,available clinical data included patient demographics (gender, age), primary tumor site and other metastatic sites. The study was approved by the ethics committee of Tongji University affiliated Shanghai Pulmonary Hospital, Shanghai, China.

2.2 MRI equipment and scan parameter

A Philips Acheiva 1.5 tesla MRI scanner with Sense –Body receiver coil and B transmit coil were used. All patients had unenhanced and contrast enhanced abdominal MRI in head first-supine position. Parameters included for T1 weighted were scanning sequence – GR (gradient recalled), TR -10 ms, TE-4.6 ms, slice thickness 9 mm, spacing between slice 9.89 mm coding scheme designator DCM (DICOM File Format) flip angle of 15°, window center of 237 and window width of 468[D]. Parameters for spectral pre-saturation attenuated inversion recovery T2 weighted (T2 SPAIR) were spin-echo sequence, TR 425.5 ms, TE 80ms, slice thickness 9mm and spacing between slice 9.89mm, flip angle of 90°, window center 201 and window width 350[D]. Contrast enhanced MRI T1-weighted sequence was performed after intravenous injection of Gadodiamide 287 mg (GE Healthcare Ireland) at the dose of 0.2mmol/kg body weight.

2.3 Image analysis

MRI images were retrospectively evaluated by experienced radiologists at Shanghai Pulmonary Hospital, who were blinded to the clinical information and histological diagnosis. The patients were evaluated for age, gender, the number of lesions and quantitative analysis of all the lesions in the study .Imaging data were reviewed for splenic metastasis. The features assessed were a multiplicity, size, margin, enhancement pattern, homogeneity and extra splenic metastases. Lesions were assessed for the increment or decrement of signal intensities to the surrounding spleen parenchyma in T1 and T2 weighted images and spleen was compared with liver for the difference in signal intensities. MRI images were also compared with available CT and USG for further evaluation of the lesions.

3. Results

3.1 Clinical and histological features

A total of 13 male patients aged 43 to 79 years (mean age 53.14 years) with 16 splenic metastases from lung cancer were identified. Identified primary tumors in the lung were adenocarcinoma (n=6), squamous cell carcinoma (n=3), small cell lung carcinoma (n=2), squamous adenocarcinoma (n=1) and lung sarcoma (n=1).

3.2 Image characteristics

All of the sixteen splenic lesions were detected by MRI, whereas four lesions from squamous adenocarcinoma and lung sarcoma were not detected by CT and USG. During precontrast MRI, thirteen splenic lesions appeared as hypo intense nodules, two as hyper intense nodules and one as isointense nodules in T1-weighted image and as hyper intense (16) in T2-weighted images. The lesions were solitary in 10 patients and multiple in 3 patients. The sizes of the lesions were found to be as small as 0.94*0.54cm from lung sarcoma (**Figure 1**) to a maximum of 10.38*7.18cm from squamous cell carcinoma (**Figure 2**). The splenic nodules arising from adenocarcinoma (**Figure 3**) had irregular margins while those from small cell carcinoma, squamous cell carcinoma, squamous adenocarcinoma (**Figure 4**) and lung sarcoma had well defined margins. Sixteen splenic lesions from lung cancer were identified, all of the lesions showed a

heterogeneous isointense enhancement to splenic parenchyma on T1-weighted arterial phase after intravenous contrast MRI. The majority of the lesions were solitary (**Table 1**) with rim enhancement of high signal in post contrast phase. In CT thirteen lesions showed hypodense and one showed isodense attenuation while in two cases; it did not detect any lesions. Regarding USG only solitary lesions were detected; they were seven hypo-echoic two hyper-echoic one iso-echoic whilst multiple lesions were either not detected or well differentiated. All 13 cases had accompanying metastasis to other abdominal organs found mostly in the liver (n=9), the kidneys (n=5), adrenal glands (n=3) and pancreas (n=1) (**Supplementary Data 1**). The splenic lesion from small cell lung carcinoma displayed a peripheral rim of high signal intensity, central enhancement with target sign appearance in contrast MRI, which can be a helpful characteristic finding. (**Figure 5**).

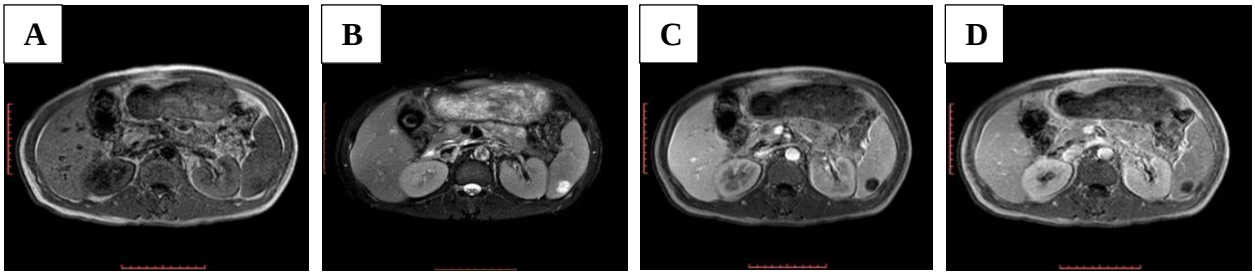

Figure 1 (A-D): 46 year old man with splenic metastasis from primary lung sarcoma. On precontrast transverse T1 weighted MRI (A) the lesion appears as hypointense and on T2 weighted SPAIR image (B) lesion appears as hyperintense. On post contrast arterial phase(C) the lesion appears round with slightly enhanced center with peripheral rim of high signal intensity appearing as target sign, where as it appears as a homogenous enhancement in the venous phase (D).

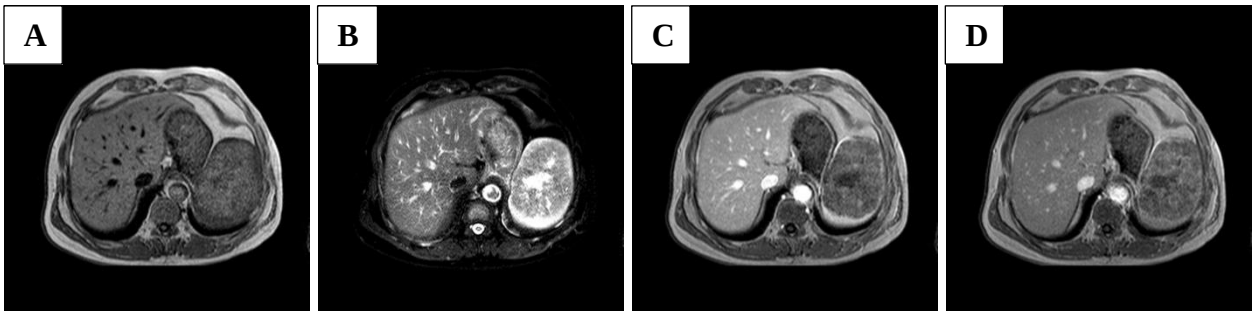

Figure 2 (A-D): 57 year old man with splenic metastasis from primary squamous cell lung carcinoma. On precontrast transverse T1 weighted (A) and on T2 weighted SPAIR image (B) lesion appears as hyperintense. On post contrast arterial phase (C) the solitary lesion shows heterogeneous isointense enhancement, whereas it appears as homogeneous enhanced on venous phase (D) with enlarged spleen.

Discussion

World population incidence of focal splenic lesions ranges from 0.103 to 0.20 % of which metastases accounts for 4.85 %[6]. The lung was the primary tumor site in 21% patients in a retrospective analysis of 92 patients with splenic tumors recorded over a 25-year period [11]. The incidence of spleen metastasis is considered to differ among histologic types of lung cancer [13-15]. Splenic metastases originated from bronchoalveolar carcinoma, adenocarcinoma, SCLC, and pulmonary carcinoid primary tumors [17]. In previous studies small cell lung cancer and adenocarcinoma have been recognized to be the most common cell types likely to metastasize to the spleen and squamous cell lung carcinoma the least likely [14, 15]. However, in this retrospective study of lung cancer lesions we identified 13 patients with 16 splenic metastases, 6 were from adenocarcinoma, 3 from squamous cell carcinoma, 2 from small cell carcinoma, 1from squamous adenocarcinoma and 1 from lung sarcoma. To the best of our knowledge, this is the first report showing squamous adenocarcinoma and lung sarcoma metastasizes to spleen. These results suggest that the spleen is a possible site for metastatic seeding in patients with advanced or recurrent lung cancer

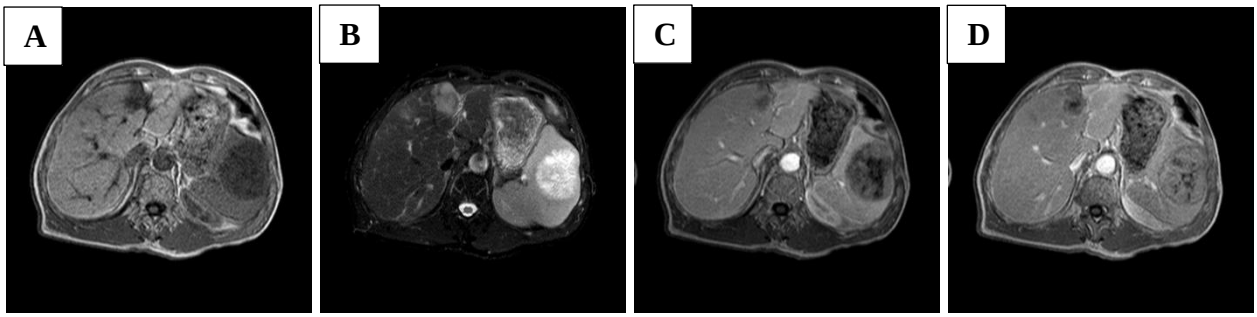

Figure 3(A-D): 60 year old man with splenic metastasis from primary lung adenocarcinoma. On precontrast transverse T1 weighted MRI (A) the lesion appears as hypointense and on T2 weighted SPAIR image (B) lesion appears as hyperintense. On post contrast arterial phase (C) the lesion appears as heterogeneous enhancement with central necrosis and the lesion fades rapidly and shows a homogeneous enhancement with poorly defined margins in the venous phase (D) with multiple liver metastases.

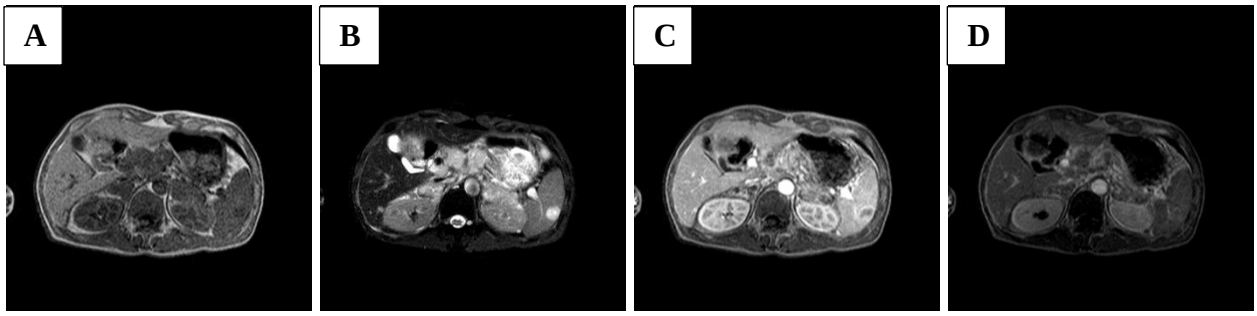

Figure 4 (A-D): 54 year old man with splenic metastasis from primary squamous adenocarcinoma of the lung. On precontrast transverse T1 weighted MRI (A) the lesion appears as hypointense and on T2 weighted SPAIR image (B) lesion appears as hyperintense. On post contrast arterial phase (C) the solitary lesion shows heterogeneous enhancement with well-defined margin and peripheral rim of high signal intensity, whereas it appears as homogeneous enhancement in the venous phase (D).

Table1: Demographic and histological data of 13 patients with splenic metastases

Age/gender	Primary cancer site	Tumor subtypes	No. of lesions in spleen
60/M	*Right lung*	Adenocarcinoma	Solitary
79/M	Left lung	Adenocarcinoma	Solitary
67/M	Right lung	Adenocarcinoma	Solitary
48/M	Right lung	Adenocarcinoma	Multiple
55/M	Left lung	Adenocarcinoma	Solitary
43/M	Left lung	Adenocarcinoma	Solitary
68/M	*Left lung*	Small cell carcinoma	Solitary
51/M	Left lung	Small cell carcinoma	Solitary
57/M	Left lung	Squamous cell carcinoma	Solitary
59/M	Right lung	Squamous cell carcinoma	Solitary
57/M	Right lung	Squamous cell carcinoma	Solitary
54/M	Right lung	Squamous adenocarcinoma	Multiple
46/M	Left lung	Lung sarcoma	Multiple

irrespective of histological type. There may be four types of radiological classification of splenic metastasis dependent on pathological examination, which is as solitary, multiple, microsco pic and diffuse. In our study the most common nodules were solitary which was in agreement with recently published studies that report solitary nodule type to be the most common [13, 18, 19].

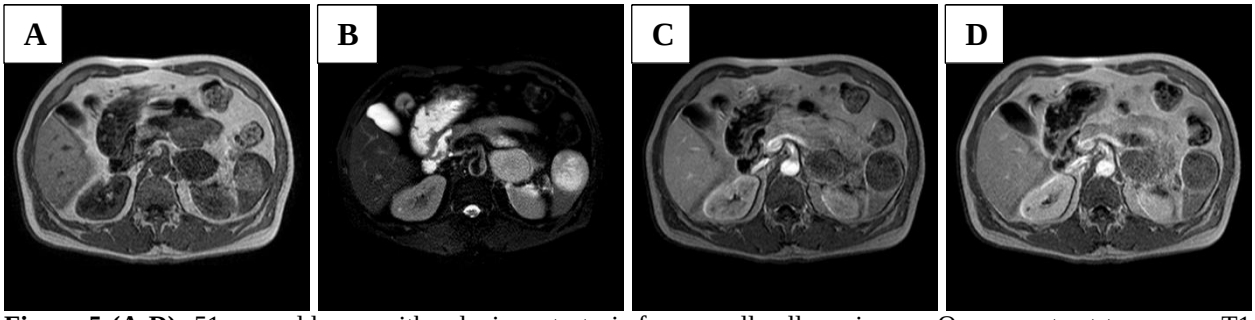

Figure 5 (A-D): 51 year old man with splenic metastasis from small cell carcinoma. On precontrast transverse T1 weighted (A) and on T2 weighted SPAIR image (B) lesion appears as hyper intense. The lesion appear round with well –defined margins on post contrast arterial phase (A) and appears as homogeneous enhancement with peripheral of high signal intensity as a target sign appearance in venous phase (D).

Perhaps due to higher blood flow compared to the left lung with the right lung, splenic metastases are most often associated with carcinoma of the left lung as per most reports, which is also in agreement with Kinoshita et al on autopsies [8].Our study comprised of 7 cases metastasizing from left lungs and 6 from right lung which shows both are likely to metastasize.

Since the majority of patients are asymptomatic in the early stages of such metastases, it is really hard to detect splenic metastases early enough. However, some patients harboring splenic metastases do complain of fatigue, weight loss, fever, abdominal pain, splenomegaly, anemia, or thrombocytopenia [20]. In this study we also found all the patients to be asymptomatic and the lesions most often found incidentally on imaging performed in patients with known malignancy during MRI abdominal examination for further evaluation of possible metastatic seeding. None the less the ongoing advances in imaging modalities may aid in diagnosing splenic metastasis beforehand, and thus facilitating better disease management.

On MRI, metastases typically appear as hyper intense masses on T2-weighted images and hypo- to isointense masses onT1-weighted images with inhomogeneous contrast enhancement, usually with peripheral ring-like pattern [21-23]. Central tumor necrosis is seen as regions of hyper intensity on T2-weighted images [24].Consistent with our findings, on unenhanced T1-weighted image splenic metastases appeared to be hypo intense compared to splenic parenchyma except for one case each small cell carcinoma and from squamous cell carcinoma, they showed hyper intense enhancement. On T2-weighted image all splenic lesions showed hyper intensity. After intravenous administration of contrast, splenic lesions were heterogeneously isointense enhanced during the arterial and venous phase of T1-weighted contrast image. In terms of enhancement pattern the lesions that were large usually demonstrated high intensity peripheral rim enhancement with an isointense area of cystic or necrotic appearing like a target sign. In our study MRI detected smaller focal lesions which were not detected by USG nor CT, which suggest that MRI is more sensitive towards detecting smaller lesions.

In a review of 13 cases of splenic metastasis from lung carcinoma, Ando et al. report 6 patients who did not undergo splenectomy, 4 (67%) went on to have a splenic rupture with associated poor outcomes[25]. When an isolated metastasis is confirmed, most investigators agree that a splenectomy should be performed to prevent further metastatic seeding to the distal areas from the spleen and to avoid possible splenic rupture and provides the potential cure for extended survival [26].

The clinical findings, patient's history, lymphadenopathy or metastasis to other organs may aid in the diagnosis of metastatic disease. In our study patients had accompanying metastasis to other abdominal organs, including liver, adrenal gland, kidney and pancreas which also suggest advanced disease with poor prognosis. It is noteworthy that majority of the patients exhibited more than one metastatic site in the abdomen which can suggest that splenic mass accompanying metastasis to other abdominal organs in patients with a known lung cancer should be regarded as a metastasis [13]. The search for additional clinical findings such as lymphadenopathy or diseases in other organs may aid in the diagnosis of metastatic diseases.

MRI is not considered as a first line routine technique because most of the splenic lesions are easily detected during CT scan; but can be considered for the detection of smaller splenic lesions and lesions which are either necrotic or hemorrhagic which suggests MRI can be a better diagnosing module for

the staging of tumors which can help in predicting better survival.

As patients with splenic metastases usually present with advanced metastatic disease, the clinical context and imaging findings are usually sufficient for diagnosis [27].

Limitations

The limitations of this study relate to its retrospective nature and relatively limited number of cases due to the rarity of spleen metastasis.

Conclusion

Splenic metastasis is a rare occurring and usually presents as a solitary, cystic or necrotic mass, lymphadenopathy and heterogeneous isointense enhancement after contrast on MRI and CT. Findings of splenic lesions in addition with known malignancy and clinical history are suggestive of metastasis, although splenectomy may be required for histological subtyping and definitive diagnosis.

Acknowledgements

Authors are thankful to Ashish Kumar Pradhan for his help in manuscript writing up and editing.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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