

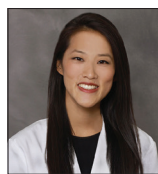
Thoracic Presentations of Small Round Blue Cell Tumors

Annalice Chang, Kyle Pfeifer, Peter Chen¹, Vivek Kalra, Myung Soo Shin

Departments of Radiology and ¹Pathology, Yale New Haven Hospital, New Haven, CT, USA

Address for correspondence:

Dr. Annalice Chang,
 Department of Radiology,
 Yale New Haven Hospital, 20 York St.,
 New Haven, 06510 CT, USA.
 E-mail: annalice.chang@yale.edu



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ABSTRACT

The term “small round blue cell” is frequently used as a cursory radiologic pathological correlation of aggressive tumors throughout the body. We present a pictorial essay of common and uncommon subtypes of small round blue cell tumors in the chest illustrating the characteristic radiologic findings of each lesion. In addition, we review the pathologic findings of each tumor subtype with characteristic hematoxylin- and eosin-stained photomicrographs and immunohistochemical and molecular studies. Represented tumors include small cell carcinoma, Ewing sarcoma, extranodal marginal zone B-cell lymphoma, embryonal rhabdomyosarcoma, desmoplastic small round cell tumor, and posttransplant lymphoproliferative disorder. Understanding and ability to recognize these lesions are essential to broaden the radiologist’s differential diagnosis and help guide patient care.

Key words: Radiologic-pathologic correlation, small round blue cell tumors, thoracic small round blue cell tumors

INTRODUCTION

The term small round blue cell tumors (SRBCTs) refers to similar appearing neoplasms composed of small, round, basophilic cells on hematoxylin and eosin (H and E) staining. Within the thorax, many SRBCTs appear as nonspecific pulmonary nodules or masses on imaging. Therefore, accurate diagnosis relies on a combination of clinical presentation, radiographic studies, and pathologic specimens. In this pictorial essay, we present a radiologic and pathologic review of SRBCTs in the thorax highlighting the characteristic radiologic images, histomorphology, immunohistochemistry, and molecular studies utilized to arrive at the diagnosis. Represented tumors include

small cell carcinoma, Ewing sarcoma, extranodal marginal zone B-cell lymphoma, embryonal rhabdomyosarcoma, desmoplastic small round cell tumor, and posttransplant lymphoproliferative disorder (PTLDs).

SMALL CELL LUNG CARCINOMA

Small cell lung carcinoma (SCLC) is a common, rapidly growing neoplasm that has a strong correlation with cigarette smoking.^[1] Patients present clinically with a cough, hemoptysis, or postobstructive pneumonia.^[1] Radiographically, SCLC presents as a centrally located bulky hilar/perihilar mass with associated adenopathy.

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Complications include displacement or narrowing of the tracheobronchial tree or vessels, pleural effusions, and/or metastases [Figure 1]. Histologically, SCLC is characterized by densely packed neuroendocrine cells with high mitotic activity. Positive immunostaining for chromogranin A or synaptophysin is confirmatory [Figure 2].

EWING SARCOMA

Ewing sarcoma commonly presents with nonspecific localized bony pain in children and adolescents. The most common locations include the pelvis, femur, spine, ribs, and skull.^[2] Radiographically, they present as an osseous lesion with aggressive periosteal reaction and soft tissue mass.^[2,3] Extra-osseous Ewing sarcoma can present in the thorax and arise from chest wall structures or soft tissues (Askin tumor), presenting as a pleural-based mass with an associated effusion.^[3] Histologically, they are characterized by sheets of small round cells (or rarely spindled cells) [Figure 3]. Positive immunostaining for CD99 [Figure 4] and t(11;22)(q24;q12) chromosomal translocation are distinguishing features.

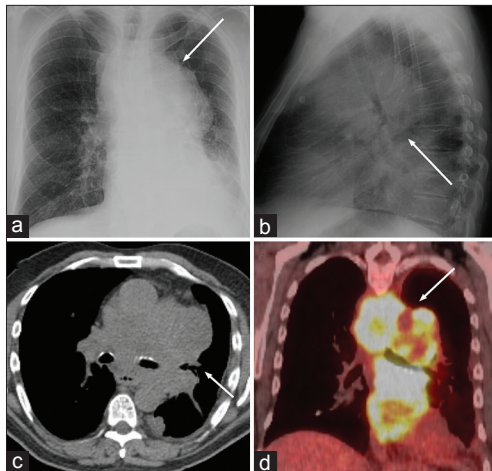


Figure 1: 59-year-old female smoker with shortness of breath diagnosed with small cell carcinoma. (a and b) Frontal and lateral chest radiographs show a large right mediastinal mass (arrow). (c) Axial computed tomography image on soft tissue windows demonstrates a multilobulated mass encasing the hilar structures (arrow). (d) Subsequent positron emission tomography scan shows an intensely fludeoxyglucose avid mass (arrow).

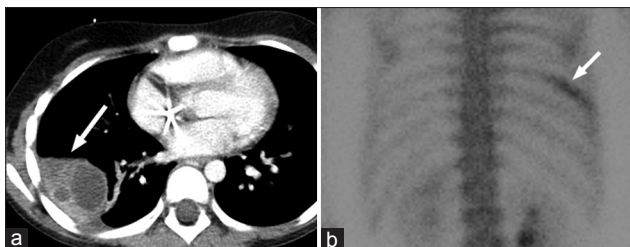


Figure 3: A 7-year-old female presenting with a cough with concern for pneumonia refractory to antibiotic treatment, diagnosed with Ewing sarcoma. (a) Axial computed tomography image on soft tissue windows shows a large necrotic soft tissue mass involving the right eighth rib (arrow). (b) There is increased radiotracer uptake in the same region on bone scan (arrow).

EMBRYONAL RHABDOMYOSARCOMA

Rhabdomyosarcoma is the most common childhood soft tissue tumor and often arises from the head, neck, and genitourinary system.^[4] Isolated thoracic rhabdomyosarcomas are unusual but can arise from the heart, lungs, pleura, airways, or mediastinum.^[4] Radiographically, they often present as a soft tissue mass, which erodes into the adjacent bone. Metastatic disease can present as pulmonary/pleural nodules [Figure 5]. The unifying histomorphologic feature is neoplastic cells that resemble embryonic skeletal myoblasts, which display positive immunostaining for myogenin and/or MyoD1 [Figure 6].

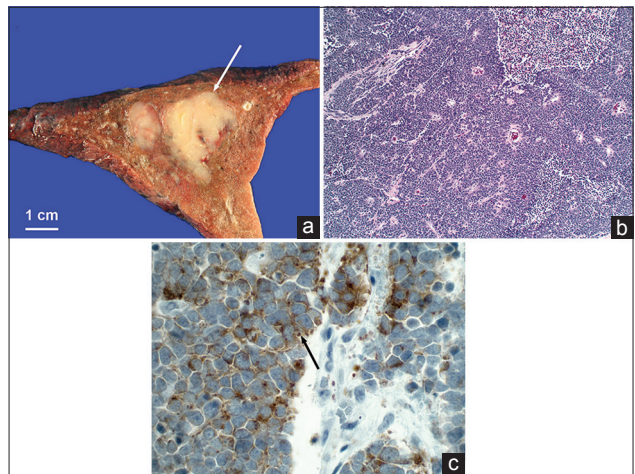


Figure 2: Pathology from patient in Figure 1. (a) Gross pathology shows white nodules compressing the bronchioles (arrow). (b) Densely packed, haphazardly arranged, monotonous sheets of small tumor cells interspersed with areas of necrosis (H and E, $\times 100$). (c) Positive cytoplasmic immunoreactivity for synaptophysin supports neuroendocrine differentiation (brown, arrow).

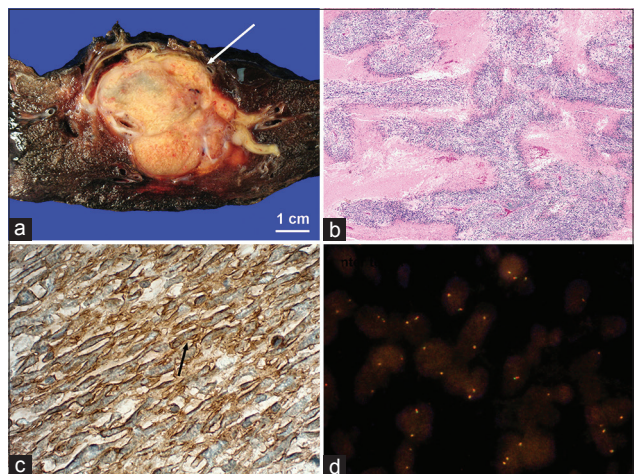


Figure 4: Pathology from patient in Figure 3. (a) Gross pathology shows a multilobular, yellow tumor arising from the chest wall (arrow). (b) Extensive geographic zones of necrosis with tumor cells around blood vessels imparting a striking "filigree pattern" (H and E, $\times 40$). (c) Strong immunoreactivity for CD99 confirms primitive neuroectodermal differentiation (brown, arrow). (d) Fluorescent *in situ* hybridization demonstrates negative SYT-SSX fusion gene which rules out the translocation found in synovial sarcomas and indirectly supports Ewing sarcoma.

DESMOPLASTIC SMALL ROUND CELL TUMOR

Desmoplastic small round cell tumors are rare neoplasms which typically arise in the abdomen and present with abdominal pain.^[5] Radiologic imaging demonstrates multiple abdominopelvic masses with a dominant

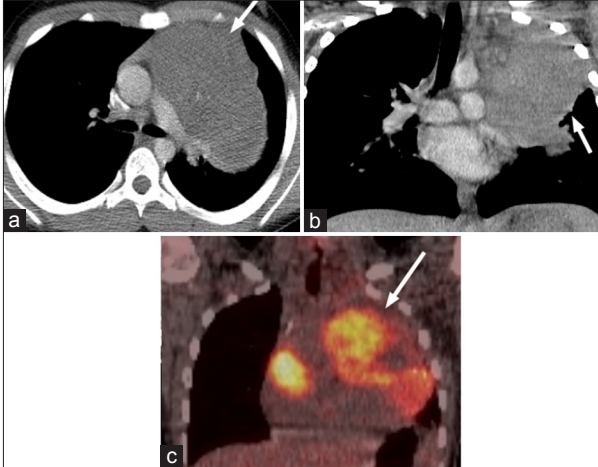


Figure 5: 13-year-old male presenting with a cough diagnosed with embryonal rhabdomyosarcoma. (a and b) Axial and coronal computed tomography images on soft tissue windows demonstrate a multilobulated left anterior mediastinal mass (arrows). (c) Subsequent PET scan demonstrates that this FDG avid lesion is contiguous with the pericardium (arrow).

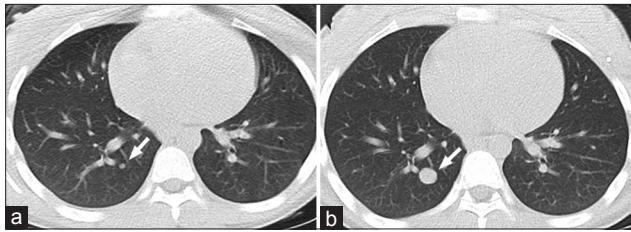


Figure 7: 12-year-old female with left shoulder pain diagnosed with desmoplastic small round tumor. (a) Axial computed tomography section on lung windows demonstrate a pulmonary nodule in the right lower lobe, which progressively enlarged over a year (b) (arrows).

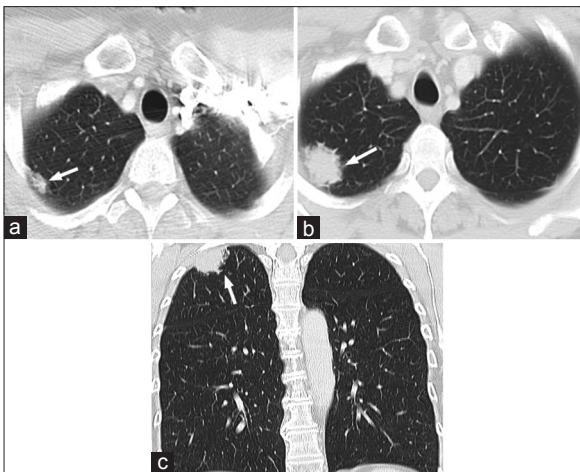


Figure 9: A 56-year-old female with abdominal pain diagnosed with gastric extranodal marginal B-cell lymphoma. (a) Four years after diagnosis, computed tomography images on lung windows demonstrate a spiculated lesion at the right lung apex (arrow) with subsequent growth over a year (b and c) (arrows).

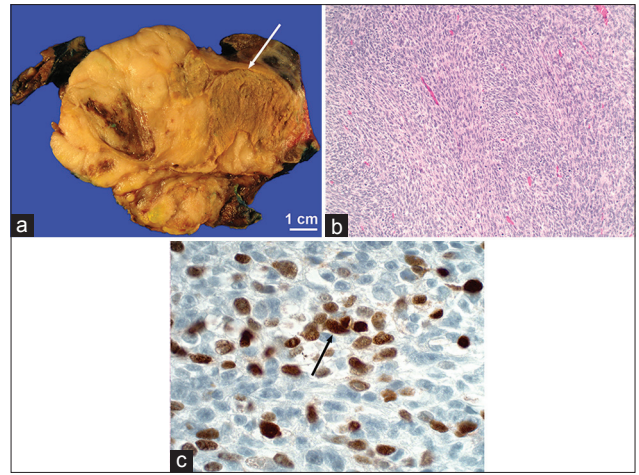


Figure 6: Pathology from patient in Figure 5. (a) Gross pathology shows a tan, poorly circumscribed tumor (arrow). (b) Fascicles of fusiform cells (H and E, $\times 100$). (c) Positive immunoreactivity for myogenin confirms primitive skeletal muscle differentiation (brown, arrow).

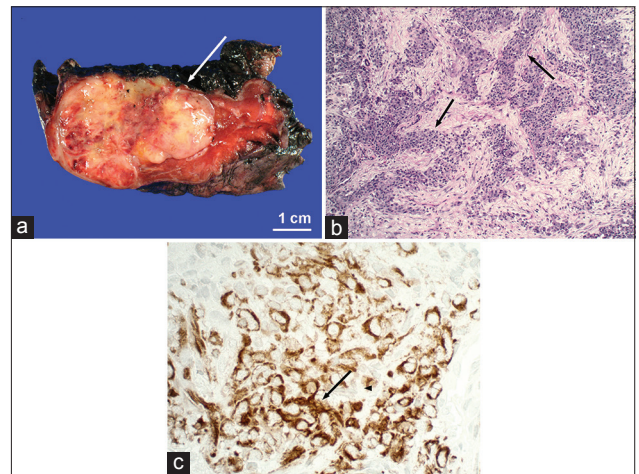


Figure 8: Pathology from patient in Figure 7. (a) Gross pathology shows grey-white pulmonary nodules with foci of necrosis and hemorrhage (arrow). (b) Multiple sharply demarcated nests surrounded by prominent desmoplastic stroma (arrows) (H and E, $\times 100$). (c) Positive immunoreactivity for vimentin confirms mesenchymal differentiation (brown, arrow).

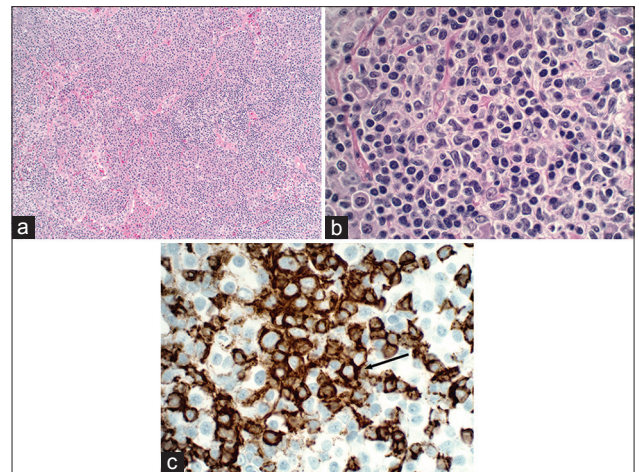


Figure 10: Pathology from patient in Figure 9. (a) Architectural effacement by the proliferation of atypical lymphoid cells, which show centrocyte, monocytoid, and plasmacytoid features on $\times 400$ (H and E, $\times 100$) (b). (c) Strong membranous immunoreactivity for CD20 confirms B-cell lineage (brown, arrow).

mass arising from the retrovesical/retrouterine space.^[5] Thoracic dissemination may manifest as pulmonary nodules or pleural involvement [Figure 7].^[5] The defining histologic feature is that of desmoplastic stroma enveloping irregular nests of cells [Figure 8]. Positive immunostaining for vimentin [Figure 8] and t(11;22)(p13;q12) chromosomal translocation are distinguishing features.^[6]

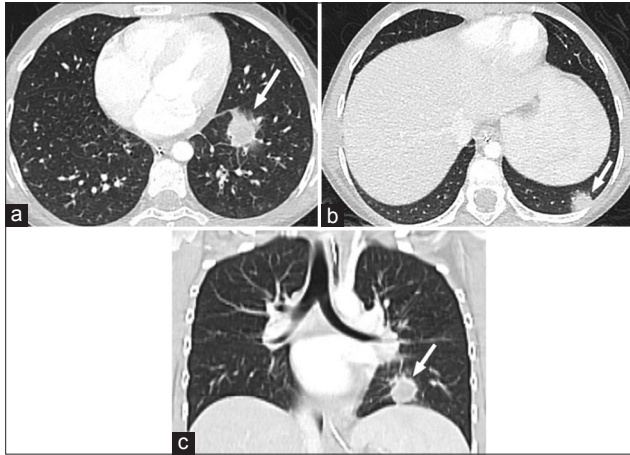


Figure 11: A 10-year-old female status postliver transplant for Wilson disease diagnosed with the posttransplant lymphoproliferative disease. (a-c) Axial and coronal computed tomography sections on lung windows show two pulmonary nodules in the left lower lobe ten months after transplant (arrows).

EXTRANODAL MARGINAL B-CELL LYMPHOMA

Extranodal marginal B-cell lymphoma or mucosa-associated lymphoid tissue, often arises from the gastrointestinal tract.^[7] Within the lungs, they can present as metastatic disease or primary bronchial-associated lymphoid tissue lymphoma. Radiographically, they appear as lung

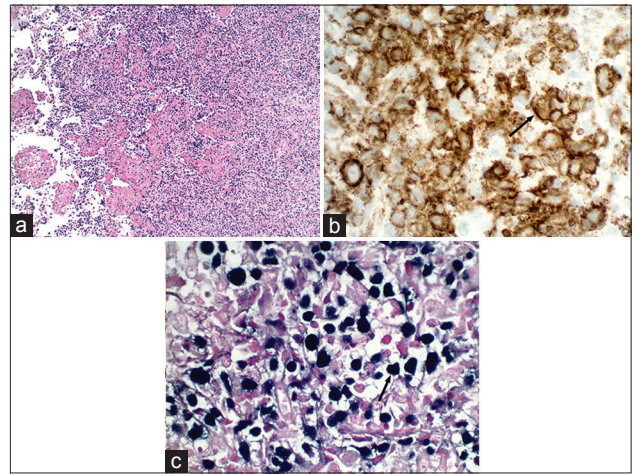


Figure 12: Pathology from patient in Figure 11. (a) Effacement of normal architecture by the proliferation of large atypical lymphoid cells (H and E, ×100). (c) Strong reactivity for CD20 confirms B-cell lineage (brown, arrow). (d) Positive Epstein-Barr encoding region *in situ* hybridization detects Epstein-Barr virus in neoplastic B-cells (dark blue, arrow).

Table 1: Summary of characteristics of thoracic small round blue cell tumor

	Demographics, age group	Intrathoracic location	Imaging characteristics	Pathologic basis of differential diagnosis
Small cell carcinoma	Cigarette smokers, usually over 60 years of age	Lungs (metastases)	Centrally located bulky hilar/perihilar mass, with possible associated narrowing of tracheobronchial tree/major vessels	Densely packed cells with haphazardly arranged geographic areas of necrosis interspersed between clusters of viable tumor; positive cytoplasmic staining for CD56 and CD57
Ewing sarcoma	Children, adolescence, slight male predominance	Lungs (metastases); soft tissues or osseous structures of chest wall (Askin tumor)	Noncalcified pulmonary/pleural nodules of varying sizes; Askin tumor - pleural-based mass with pleural effusion	Small cells with extensive geographic zones of necrosis around blood vessels; positive staining for CD99; nonrandom reciprocal translocation between chromosomes 11 and 22 (t[11; 22] [q24; q12])
Embryonal rhabdomyosarcoma	Young children with small peak in adolescence	Lung, pleura, heart, pericardium, airways, mediastinum (primary)	Soft tissue mass with enhancement that often erodes the adjacent bone	Neoplastic cells with varying degrees of resemblance to embryonic skeletal myoblasts at different stages of differentiation; positive nuclear staining for myogenin/MyoD
Desmoplastic small round cell tumor	Adolescence, slight male predominance	Pleura (metastases)	Multiple abdominopelvic soft tissues masses, dominant mass from the retrovesical or retrouterine space	Desmoplastic stroma that envelops the sharply demarcated nests of cells; positive staining for vimentin, epithelial membrane antigen, desmin; fusion translocation between Wilms tumors and Ewing sarcoma genes
Extranodal marginal B-cell lymphoma	Average age over 60, female predominance	Lungs (metastases or primary [bronchial-associated lymphoid tissue])	Lung nodules/masses or airspace consolidations	Atypical lymphoid cells with centrocyte, monocytoid and plasmacytoid features causing architectural effacement; positive staining for CD 20
Posttransplant lymphoproliferative disorder	Posttransplant, most commonly after multivisceral transplants	Lungs, pleura	Lung nodules/masses randomly distributed throughout lung, homogenous but may demonstrate hazy halo with central necrosis	Majority are B-cell neoplastic proliferations with positive B-cell markers (i.e., CD 20); positive Epstein-Barr encoding region <i>in situ</i> hybridization

nodules/masses or airspace consolidations [Figure 9].^[8] Immunohistochemically, these neoplastic cells typically express IgM and stain strongly for CD20 [Figure 10].

POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDER

PTLDs are lymphoid or plasmacytic proliferations that develop as a consequence of immunosuppression following organ transplantation. The abdomen is most frequently involved. Thoracic manifestations are less common, presenting as randomly distributed pulmonary nodules [Figure 11].^[9] A characteristic feature of PTLD is its association with Epstein–Barr virus infection, which can be detected by Epstein–Barr encoding region *in situ* hybridization [Figure 12].

DISCUSSION/CONCLUSION

SRBCTs are a heterogeneous group of aggressive neoplasms [Table 1]. Within the thorax, many of these lesions appear as nonspecific pulmonary nodules/masses radiographically and can be difficult to diagnose definitively without soft tissue sampling. On H and E staining, SRBCTs often appear similar, and immunohistochemistry and cytogenetics help distinguish between the entities. Understanding these lesions can broaden the radiologist's differential diagnosis and help guide patient care.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Carter BW, Glisson BS, Truong MT, Erasmus JJ. Small cell lung carcinoma: Staging, imaging, and treatment considerations. *Radiographics* 2014;34:1707-21.
2. Ludwig JA. Ewing sarcoma: Historical perspectives, current state-of-the-art, and opportunities for targeted therapy in the future. *Curr Opin Oncol* 2008;20:412-8.
3. Murphey MD, Senchak LT, Mambalam PK, Logie CI, Klassen-Fischer MK, Kransdorf MJ. From the radiologic pathology archives: Ewing sarcoma family of tumors: Radiologic-pathologic correlation. *Radiographics* 2013;33:803-31.
4. McCarville MB, Spunt SL, Pappo AS. Rhabdomyosarcoma in pediatric patients: The good, the bad, and the unusual. *AJR Am J Roentgenol* 2001;176:1563-9.
5. Bellah R, Suzuki-Bordalo L, Brecher E, Ginsberg JP, Maris J, Pawel BR. Desmoplastic small round cell tumor in the abdomen and pelvis: Report of CT findings in 11 affected children and young adults. *AJR Am J Roentgenol* 2005;184:1910-4.
6. Tateishi U, Hasegawa T, Kusumoto M, Oyama T, Ishikawa H, Moriyama N. Desmoplastic small round cell tumor: Imaging findings associated with clinicopathologic features. *J Comput Assist Tomogr* 2002;26:579-83.
7. Hayashi M, Ueda K, Tanaka T, Enoki T, Tanaka N, Gondo T, et al. Mucosa-associated lymphoid tissue (MALT) lymphoma arising in the esophagus, stomach, and lung. *Gen Thorac Cardiovasc Surg* 2011;59:826-30.
8. Ahmed S, Kussick SJ, Siddiqui AK, Bhuiya TA, Khan A, Sarewitz S, et al. Bronchial-associated lymphoid tissue lymphoma: A clinical study of a rare disease. *Eur J Cancer* 2004;40:1320-6.
9. Borhani AA, Hosseinzadeh K, Almusa O, Furlan A, Nalesnik M. Imaging of posttransplantation lymphoproliferative disorder after solid organ transplantation. *Radiographics* 2009;29:981-1000.