Usefulness of Diffusion-weighted Magnetic Resonance Imaging-guided Biopsy: Pyothorax-associated Lymphoma

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Abstract

The relatively rare entity pyothorax-associated lymphoma (PAL) is an aggressive disease with a poor prognosis. Therefore, PAL should be diagnosed as soon as possible with minimal invasion. We herein report the case of an 81-year-old man with PAL that was successfully treated with chemotherapy. A computed tomography-guided tumor biopsy could not provide adequate specimens for pathological investigation, whereas a diffusion-weighted magnetic resonance imaging-guided tumor biopsy led to a diagnosis. Our findings suggest that diffusion-weighted image guidance for planning the biopsy of an intrathoracic mass, especially in cases of suspected PAL, is a highly accurate method because it provides information about cellularity and does not create calcification-related artifacts.

Key words: biopsy, diffuse large B-cell lymphoma, diffusion-weighted magnetic resonance imaging, Epstein-Barr virus, functional imaging, pyothorax-associated lymphoma

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Introduction

The relatively rare entity pyothorax-associated lymphoma (PAL) was first reported in Japan in 1987 (1). Almost all cases of PAL have occurred in Japan, with sporadic cases in Western countries. PAL is a distinct type of malignant lymphoproliferative disease, most commonly a diffuse large B-cell lymphoma associated with chronic inflammation and Epstein-Barr virus (EBV) infection (2). PAL develops in chronically inflamed tissue of the pyothorax after artificial pneumothorax for treatment of pulmonary tuberculosis and tuberculous pleurisy (2). Its duration of onset is long; the median interval between onset of pyothorax and diagnosis of PAL has been reported as 43 years (range 19-64 years) (3). Although a recent study showed that combination chemotherapy and radiation therapies were effective, the standard management strategy for PAL has not been established. The overall prognosis of PAL remains poor because of its aggressive nature and poor performance status and the advanced age and multiple comorbidities of PAL patients (2, 3). Therefore, to initiate appropriate treatment, we should diagnose PAL in a less invasive and more expeditious manner. We herein report the first case of a patient with PAL that was pathologically confirmed by diffusion-weighted magnetic resonance imaging (DW-MRI)-guided needle biopsy, suggesting the usefulness of DW-MRI guidance for biopsy.

Case Report

An 81-year-old Japanese man presented at the emergency department of our hospital because of a 12-month history of gradually worsening back pain despite several prescriptions of analgesic drugs from an outpatient clinic. His medical history included tuberculous pleurisy at 33 years of age, as well as hypertension, asymptomatic cerebral infarction, chronic kidney disease and depression, for which he took medication.

On admission, his vital signs were within the normal
ranges. A physical examination revealed dull to percussion and decreased vesicular breath sounds in the right lower posterior chest. There was no palpable lymphadenopathy or hepatosplenomegaly. Computed tomography (CT) scans of the chest revealed a large tumor adjacent to the pyothorax that was surrounded by calcification and directly invaded the vertebral bodies (Fig. 1). The laboratory tests revealed micrhythmic anemia, a red blood cell count of $363 \times 10^9/\mu L$, a hemoglobin level of 9.2 g/dL, a hematocrit level of 28.7% and elevated levels of lactate dehydrogenase (LDH, 288 IU/L), alkaline phosphatase (ALK, 1,683 IU/L), C-reactive protein (CRP, 15.49 mg/dL) and soluble interleukin-2 receptors (sIL-2Rs, 1,517 U/mL).

Guided by CT, a percutaneous needle biopsy was taken from the right lateral edge of the tumor on the day of admission (star).

Figure 1. A computed tomography scan of the chest on admission shows a large mass adjacent to the pyothorax that is surrounded by calcification and directly invades the vertebral bodies. An artifact caused by the calcification surrounding the pyothorax is seen in the lesion (black arrow). A percutaneous needle tumor biopsy was taken from the right lateral edge of the tumor on the day of admission (star).

In the present case, PAL associated with EBV latency type III infection was diagnosed on the basis of the histopathology and immunohistochemistry of DW-MRI-guided percutaneous needle biopsies. Latent infection with EBV, an oncogenic human herpesvirus, is known to be associated with various malignancies. There are three types of latent infection (types I-III) as categorized via viral latent gene expression patterns. EBV can transform B-cells into immortalized lymphoblastoid cells with type III latency, in which all latent genes are expressed, as in the present case. B-cell transformation and immortalization play a central role in EBV-associated lymphoproliferative disorders in immunocompromised individuals, including those with PAL.

In recent years, due to the establishment of personalized medicine, oncological management and treatment have been advanced and become individualized along with the development of numerous anti-cancer agents based on molecular profiles and targeted therapy. Therefore, it is important to collect adequate amounts of tumor cells and/or tissue for histopathological and molecular biological assessment. Im-

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aging studies using CT and ultrasound sonography play an
important role in determining the sites for biopsies of chest
lesions. Today, a percutaneous needle biopsy is commonly
guided by CT or ultrasound, and its safety and usefulness
are widely recognized.

Until very recently, DW-MRI was only used to evaluate
intracranial diseases. Its application to extracranial, espe-
cially intrathoracic, lesions was technically problematic and
not always practicable because of the high number of arti-
facts resulting from physiologic motions such as breathing
and heart pulsation (4). However, with advances in MRI
techniques, DW-MRI can currently be applied to extracranial
lesions such as those located in the trunk and especially in
the abdomen and pelvis (5). To date, this technique has been
used to characterize, grade and stage intrathoracic lesions
such as lung tumors and mediastinal masses, as well as to
differentiate central tumors from post-obstructive atelecta-
sis (6). It is beginning to be used for the staging and re-
sponse assessment of lymphomas (7-10). Because DW-MRI
of extracranial lesions has only just begun, there are only a


Figure 2. The second tumor biopsy was guided by the fusion image of T2-weighted and diffusion-
weighted image sequences. (A) A fusion image of axial T2-weighted and diffusion-weighted image
sequences shows a high signal intensity area in the tumor close to the posterior surface of the body. It
suggests that the rest of the tumor is less cellular because of necrosis. (B) The second tumor biopsy
was directed to the high signal intensity area with the patient in a prone position. This image is upside
down.


Figure 3. Diagnosis of diffuse large B-cell lymphoma associated with Epstein-Barr virus (EBV) in-
fecion. (A) Histopathological examination of the second tumor biopsy shows a diffuse proliferation
of medium to large atypical lymphoid cells with round to ovoid, sometimes irregularly shaped, large
nucleoli (Hematoxylin and Eosin staining). The lymphocytic cells expressed CD79a (B) and paired
box gene-5 (PAX-5) (C), but not CD20 (D) or CD3 (E). In situ hybridization showed robust expression
of EBV-encoded small mRNA (F). Expression of CD79a, PAX-5, CD3 and CD20 was determined via
immunohistochemistry. The magnification of all microphotographs is × 400.
few reports about its usefulness for evaluating pleural disease (11, 12) and identifying appropriate areas for biopsies of intrathoracic lesions (13, 14). There are no reports about its usefulness for determining optimum biopsy sites of pleural disease.

In the present case, tumor biopsies were performed in two different areas, the first selected by CT and the second by DW-MRI. The first biopsy was uninformative because the specimens contained only necrotic tissue. Retrospectively, the first biopsied area had a lower signal intensity in DW-MRI than did other areas of the lesion. Conversely, the second biopsy was taken from an area with a high signal intensity in DW-MRI, and it provided adequate specimens for analysis. This finding suggests that DW-MRI has some advantages over other modalities for evaluating lesions and selecting optimum biopsy areas in PAL patients.

DW-MRI can detect anatomical and morphological differences between soft tissues and organs in detail. DW-MRI can provide additional information about the degree of tissue cellularity and the integrity of cellular membranes (15). Many malignant tumors, including lymphomas, often consist of tissues with a high density of atypical cells with intact membranes (15). As shown in our study, DW-MRI can distinguish cell-rich, high activity regions from regions with low cellularity in necrotic areas of the tumor and surrounding normal tissue. Therefore, the areas showing high signal intensity on DW-MRI should be biopsied for high diagnostic accuracy.

Contrast-enhanced CT provides image contrast dependent on tissue vascularity and can indicate areas inappropriate for biopsy, such as intratumoral necrotic areas. However, it is not a functional imaging method and cannot select the areas with the highest cellularity. Additional disadvantages are radiation exposure, calcification artifacts and the need to use contrast media, which is discouraged in elderly populations where the prevalence of diabetes is high.

Compared with FDG PET-CT and contrast-enhanced CT, the advantages of DW-MRI are the readily accessible equipment, the affordability of equipment, a shorter procedure and the elimination of calcification artifacts, the risks of radiation exposure and the use of contrast media. Therefore, in the initial assessment of pleural masses with minimum invasiveness, CT, DW-MRI and FDG PET-CT provide different information: tumor presence, the optimum biopsy areas and the initial clinical stage after the diagnosis of malignant disease, respectively.

In conclusion, DW-MRI is a useful technique for the planning of the biopsy of intrathoracic pleural masses, especially in cases of suspected PAL. It provides high diagnostic accuracy based on cellularity and does not create calcification artifacts. At the dawn of a new era in DW-MRI application to extracranial lesions, further research is needed to confirm its efficacy in practical use.

The authors state that they have no Conflict of Interest (COI).
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