

CLINICAL IMAGE

A Pitfall for Diffusion-weighted MR Imaging When Assessing the Response to Neoadjuvant Chemotherapy in Ewing Sarcoma

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Introduction

There is increasing interest to use MRI with diffusion-weighted imaging (DWI) as a non-invasive surrogate to histological response for the assessment of response to neoadjuvant chemotherapy in several cancers, including Ewing sarcoma. Despite the potential of DWI for tumor response assessment, an impeded diffusion can also be observed in benign marrow conditions, which may mimic progressive malignant disease.

An 18-year-old girl was diagnosed with Ewing sarcoma in the right proximal humerus (Fig. 1), with locoregional lymph node metastases and lung metastases. Neoadjuvant chemotherapy (vincristine, ifosfamide, doxorubicin, and etoposide [VIDE]) was started. After the fourth VIDE cycle, two packed red blood cells were administered because of symptomatic anemia (hemoglobin of 4.3 mmol/L). After the sixth and last VIDE cycle, the locoregional lymph nodes had normalized in size and the lung lesions had disappeared. The diffusion of the primary tumor location in the proximal humerus on MRI had markedly increased compared to baseline, suggestive of a good tumor response. However, there was a new area of impeded (lower) diffusion in the bone marrow of the humeral shaft distal to the primary tumor location (Fig. 2). The latter was initially interpreted as suggestive of local tumor progression.

A total humeral resection was performed, in combination with axillary lymph node dissection. Histopathological

examination after surgery showed an excellent tumor response in the proximal humerus (<1% focal microscopic residual tumor) and all 13 excised axillary lymph nodes proved to be tumor-free. Interestingly, there was an area of erythroid hyperplasia of bone marrow distal to the primary tumor location (Fig. 2), which corresponded to the area of impeded diffusion on the post neoadjuvant chemotherapy MRI. Therefore, the abnormal DWI signal could be attributed to erythroid hyperplasia of bone marrow and not tumor progression.

The presented case shows an important diagnostic potential pitfall on DWI, in that erythroid hyperplasia of bone marrow may mimic tumor tissue. DWI interpretation may become particularly challenging in the response assessment setting. A flip-flop appearance may develop, which refers to a change from lower diffusion to higher diffusion in successfully treated bone tumor, and a change from normal diffusion to lower diffusion in adjacent bone marrow that undergoes erythroid hyperplasia with previously noted areas of tumor-involved bone appearing with higher diffusion and adjacent erythroid hyperplasia of bone marrow appearing with lower diffusion. Note that fluorodeoxyglucose-positron emission tomography (FDG-PET) may suffer from the same pitfall, because hyperplastic red bone marrow may show increased FDG uptake, indiscriminable from viable tumor.¹ Ancillary clinical and MRI findings may help to differentiate erythroid hyperplasia of bone marrow from tumor. First, the patient developed symptomatic anemia during neoadjuvant chemotherapy, as a result of which red marrow stimulation may have been expected to occur. Second, erythroid hyperplasia also contains some amount of microscopic (intravoxel) fat, which exhibits signal loss on T₁-weighted out-of-phase images compared to in-phase images.^{2,3} Retrospective review of the T₁-weighted DIXON images indeed showed that this was also the case in the presented patient (Fig. 2).

In conclusion, erythroid hyperplasia of bone marrow may mimic progressive disease on DWI. DWI should be evaluated along with clinical information and other MRI sequences (particularly T₁-weighted in- and out-of-phase sequences) to avoid a false-positive bone marrow assessment.

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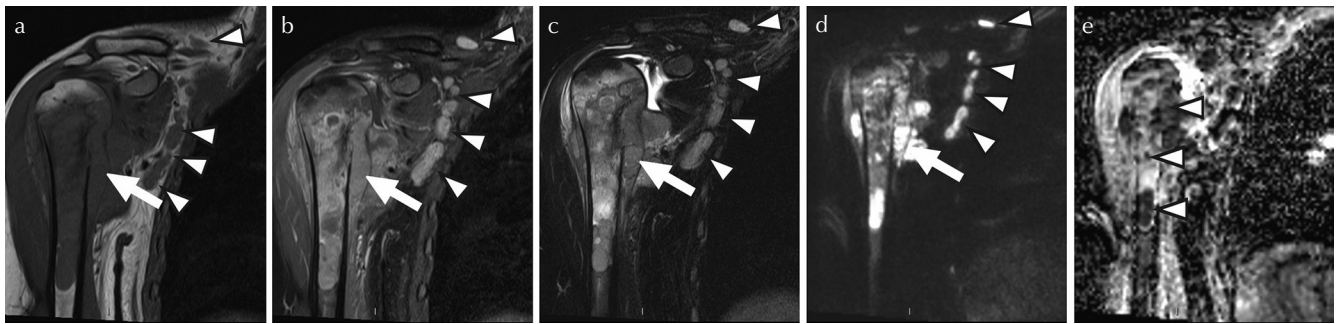


Fig. 1 Pretreatment MRI of the proximal right humerus. Coronal T₁-weighted (a), gadolinium-enhanced DIXON fat-suppressed T₁-weighted (b), DIXON fat-suppressed T₂-weighted (c), and diffusion weighted imaging (DWI) (*b* value of 800 s/mm²) (d) images show a tumor in the right proximal humerus with extension to the surrounding soft tissues (arrows) and several enlarged right axillary and supraclavicular lymph nodes (arrowheads). The coronal apparent diffusion coefficient (ADC) map (calculated with *b* values of 100 and 800 s/mm²) shows several locations with an impeded diffusion in the tumor (e, arrowheads). Tumor ADC in the proximal humerus was approximately 0.6×10^{-3} mm²/s.

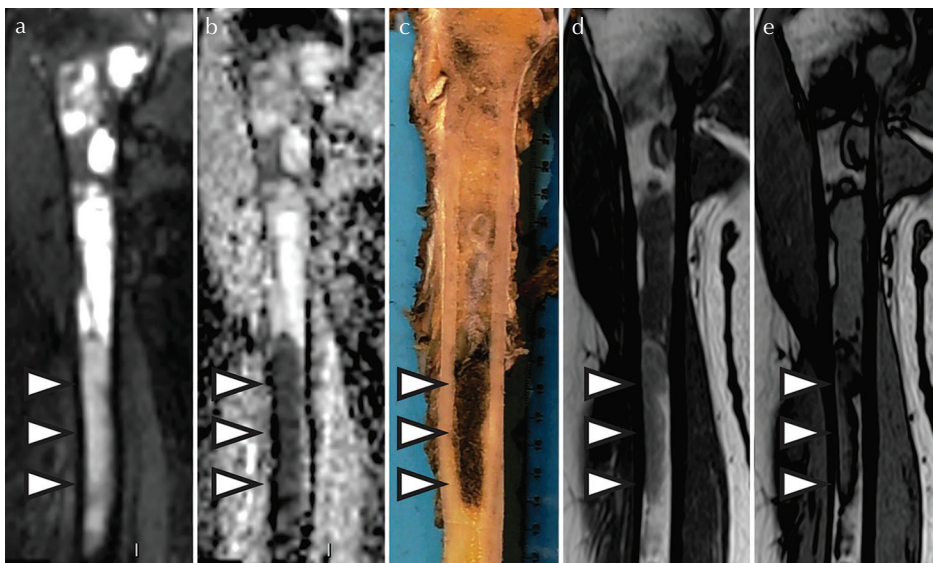


Fig. 2 Coronal diffusion weighted imaging (DWI) (*b* value of 800 s/mm²) (a) and apparent diffusion coefficient map (calculated with *b* values of 100 and 800 s/mm²) (b) show a new area of impeded diffusion in the bone marrow of the humeral shaft distal to the primary tumor location after neoadjuvant chemotherapy (arrowheads). Surgical cut demonstrates erythroid hyperplasia of bone marrow distal to the primary tumor location (c, arrowheads), corresponding to the area of impeded diffusion. Coronal DIXON in- (d) and out-of-phase (e) T₁-weighted images show some signal loss on out-of-phase images in the area of the erythroid hyperplasia of bone marrow (arrowheads).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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