Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

The diagnostic value of FDG–PET cannot be judged by iliac bone marrow biopsy: Author response

The Editor,

We read with interest the letter entitled “The diagnostic value of FDG–PET cannot be judged by iliac bone marrow biopsy” by Cheng [1], which was written in response to our paper “Clinical utility of 18F FDG–PET/CT in the detection of bone marrow disease in Hodgkin’s lymphoma” [2]. Prior to the introduction of 18-fluorodeoxyglucose–positron emission tomography (FDG–PET)/CT, bone marrow biopsy (BMB)—with all its limitations, which were mentioned in our paper and also highlighted by Cheng—was the gold standard for assigning bone marrow involvement (BMI) status to a lymphoma patient. Against this background, our study presented the first comparison between FDG uptake and BMB findings in Pakistani patients with Hodgkin’s lymphoma (HL). Our study highlighted, in conclusion, the complementary role of FDG–PET/CT with BMB in detecting BMI in HL, with BMB as the reference standard. We agree that BMB has a high false-negative rate and cannot accurately reflect the status of lymphoma in bone marrow. In our study, we found that of 122 patients who had negative BMBs, PET/CT was negative for BMI in 85, with no false-negatives noted; this indicates that routine BMB might be unnecessary when FDG–PET/CT is negative. The remaining 37 patients showed abnormal FDG uptake (diffuse, unifocal and multifocal). PET/CT was performed as a baseline scan followed by a mid-treatment or end-of-therapy scan to evaluate response to therapy, and the resolution of PET-positive foci during chemotherapy was considered as an additional indication of malignancy. Diffuse uptake was seen in 11 of the 37 patients; interestingly, 2 of these patients also had positive BMBs and were treated as having stage IV disease by oncologists. We agree that a diffuse homogeneous axial and appendicular skeleton often reflects benign enhancement owing to inflammation or cytokine release, and that would have accounted for resolved uptake in 9 of the 11 patients and remains non-specific in nature. However, considering the long-standing role of BMB in lymphoma staging, a lack of universal availability of FDG–PET/CT for all HL patients and occurrences such as when 2 of our 11 patients showed diffuse uptake with positive BMB, it is still too early to ignore BMB findings in lymphoma patients entirely.

In ideal circumstances, PET/CT showing unifocal or multifocal sites of FDG uptake with negative BMBs should be subjected to biopsy and characterised histologically; however, this was beyond the scope of our study. We correlated unifocal and multifocal sites of uptake with corresponding CT images and were able to identify bony lesions in 17 of 37 (46%) patients with abnormal FDG uptake. However, routine CT has a low yield in detecting bone/bone marrow disease.

Our study indicated a high negative predictive value (76.57%) of PET/CT in the evaluation of bone/bone marrow disease and further supported the emerging evidence that normal bone/bone marrow FDG uptake may eventually obviate the need for BMB [3–6]. The spectrum of abnormal FDG uptake from diffuse to unifocal to multifocal represents an increasing likelihood of disease involvement; however, further characterisation of patterns is needed with studies involving FDG-directed biopsies or correlative MRI [7].

We agree that the positive predictive value (PPV) of 29.72% in our study is low compared with other studies. The reason for this was that, given the retrospective nature of the disease, not all the focal lesions noted on PET/CT were biopsied; however, all patients underwent a follow-up PET/CT scan to check their response, and clinical follow-up ranging from 3 to 12 months was also taken into account. It was noted that on follow-up PET/CT, 34 of the 37 patients showed complete metabolic response with the resolution of both nodal and bony disease. These patients remained in complete remission on clinical follow-up, suggesting the true-positive nature of the lesions. 3 of the 37 patients showed progressive disease on follow-up PET/CT, of whom 1 died and the 2 others were switched to second-line chemotherapy. Because we used conventional BMB as the reference standard, this led to a low PPV. However, the follow-up PET/CT scan did show the true-positive nature of the bone lesions identified on PET/CT which were missed on BMB. We agree that BMB has long been regarded as the gold standard in diagnosing BMI, and its role needs to be re-evaluated with a biopsy of the affected sites seen on PET/CT to increase the diagnostic yield [4]. This raises the need to take PET/CT as the initial imaging tool in diagnosing bone marrow disease; however, further prospective studies are required to validate this.

Yours etc.,

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