FDG-PET in bleomycin-induced pneumonitis following ABVD chemotherapy for Hodgkin's disease-a useful tool for monitoring pulmonary toxicity and disease activity

Bleomycin-related pneumonitis (BIP) has recently emerged as one of the main causes of death in Hodgkin's disease treated with standard chemotherapy ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine). We used 18-fluorodeoxyglucose (FDG) positron emission tomography (PET) scanning in a patient with Hodgkin's disease who developed bleomycin lung toxicity following the 4th cycle of chemotherapy. The PET scan done two month after the acute presentation with BIP showed uptake of FDG in the lungs. Following treatment with corticosteroids, the FDG avidity in the lungs disappeared. Corticosteroids were tapered off subsequently, without recurrence of the respiratory symptoms. Conventional CT scanning was not able to distinguish between residual changes and active inflammation. Thus PET represents a useful diagnostic tool and, independently of CT, indicates the resolution of disease activity, even in the presence of residual pulmonary scarring

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Case report

A 47-year-old woman with stage IIIb Hodgkin's disease (HD) presented with progressive shortness of breath and dizziness after cycle 4b of chemotherapy with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD). She was afebrile and haemodynamically stable, but hypoxic with oxygen saturation of 79% on room air. There were crepitations over the lower and middle lung fields. Blood gas analysis showed pO_2 of 7.05 with mild, compensated respiratory alkalosis. The chest X-ray revealed bilateral shadowing to the midzone lung fields. Diagnosis of bleomycin-induced pneumonitis (BIP) was made on clinical grounds based on characteristic presentation, X-ray and high-resolution CT scan findings, and exclusion of infection by septic screen. Lung biopsy was not undertaken as it was not deemed specific and sensitive enough for the investigation of suspected BIP. Treatment with prednisolone 30 mg daily was commenced. Her symptoms improved and she was restarted on the same chemotherapy regimen without bleomycin (AVD) after a 3-week break. She continued to suffer from exertional dyspnoea and dry cough.

Two months later, after 6 cycles of chemotherapy (4x ABVD and 2x AVD), a restaging PET-CT scan was performed (Figure 1 c,d). While the nodal FDG uptake visible on pre-treatment PET-CT scan (Figure 1 a,b) had resolved, there was FDG avid diffuse uptake noted in the lung. On the nonenhanced CT scan, there was a reticular pattern, predominantly in subpleural areas. At this time the patient was taking reduced dose prednisolone (10 mg daily) because of significant weight gain, anxiety and insomnia symptoms associated with high dose prednisolone. The PET-CT scan finding in this clinical setting and in the absence of infection this strongly suggested persistent active BIP and we increased her prednisolone treatment to 30mg daily. The patient went on to receive a further 2 cycles of AVD chemotherapy and the treatment with corticosteroids was continued. A PET-CT scan performed six months after her admission for BIP showed normal uptake in the lungs as well as complete remission of HD (Figure 1 e,f). The parenchymal changes were still seen on the unenhanced CT scans and were only marginally improved despite the resolution of FDG uptake in the lungs. The improvement in FDG uptake in the lungs coincided with marked improvement in forced vital capacity (FVC) as well as carbon monoxide lung transfer (TLCO), and her prednisolone treatment was tailed off slowly over 4 weeks without any exacerbation of her pulmonary symptoms.

The incidence of BIP and bleomycin-related fibrosis is substantial following standard ABVD treatment for patients with Hodgkin's Disease.[1,2] Duggan et al reported pulmonary toxicity in 28% of their HD patients (224 of 814 patients) when treated with ABVD or its variant.[1] More recently Martin et al reported a BIP incidence rate of 18% when treated with ABVD (25 of 141 patients) and one-quarter of their BIP patients all died from pulmonary toxicity within 9 months of their HD diagnosis.[2] The total dose of administered bleomycin, the age of the patient, and impaired renal function are important risk factors in predicting BIP.[2,3] Although late deaths have been described, most patients die in the acute inflamma-

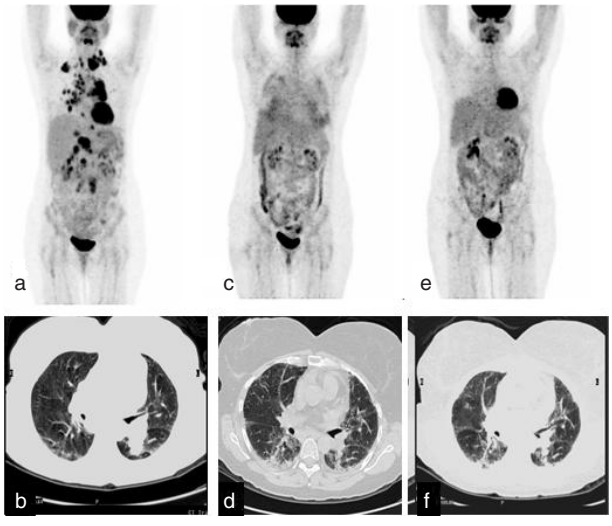

Figure 1. Pre-treatment PET-CT scan shows extensive FDG-avid lymphadenopathy but no FDG uptake in lung parenchyma (a, b). PET-CT three months after the acute presentation of pneumonitis shows diffuse FDG uptake in the lungs consistent with bilateral inflammatory process and reticular pattern predominantly in subpleural areas (c,d). The uptake in the lungs normalised after further four months of treatment with corticosteroids but the parenchymal changes persist (e,f).

tory phase.[2] Currently there is no diagnostic tool available to monitor the effects of corticosteroid treatment for BIP or a screening tool to detect early asymptomatic BIP before patients develop pulmonary symptoms and bilateral interstitial infiltrates on chest x-ray or CT scan. Although there is no standard approach, withholding bleomycin, treatment with high-dose corticosteroids, and continuing with a non-bleomycin chemotherapy regimen is the most common management of patients who develop BIP. Also, there are ongoing trials looking into the possibility of omitting bleomycin altogether from HD treatment protocols, to prevent short-term and long-term pulmonary toxicity without compromising the treatment outcome.[4]

FDG uptake in BIP has been reported previously.[5-7] In a report by von Rohr et al PET scan and CT scan both became negative after a brief treatment with corticosteroids.[7] Our report extends these observations in that we show that the FDG uptake disappears after successful immunosuppressive treatment even if CT scan still shows abnormalities (Figure 1). Thus, our experience highlights the potential of PET scanning to distinguish between active inflammation and residual lung damage. Lung function testing and conventional CT scans do not give any information about the activity of the bleomycin-induced inflammation. As BIP is reversible only in the inflammatory phase and not in the fibrotic stage, PET might be useful to for deciding whether to initiate/continue treatment with anti-inflammatory agents.

As PET-CT is increasingly used for staging in HD, it would be interesting to explore whether it could pick up BIP early after ABVD chemotherapy before clinical symptoms and radiological changes occur. Clinical trials examining early PET to predict disease outcome and retrospective analyses in centres where PET is routinely performed for restaging, e.g. after 2 cycles of ABVD, may provide interesting answers to this question.

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