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Title: Progression or response: new liver lesions in a patient with responding Hodgkin lymphoma

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Case

A 29-year-old woman with relapsed Hodgkin lymphoma was being assessed for response to ifosfamide, carboplatin and etoposide therapy. ^{18}F-Fluorodeoxyglucose (^{18}F-FDG) PET/CT showed progressive hypermetabolic mediastinal lymphadenopathy (A-dashed-arrow) with diffuse hypermetabolism in the bone-marrow, likely secondary to marrow stimulation by Granulocyte-Colony Stimulating Factor therapy. Treatment was escalated to Gemcitabine, Vinorelbine, Doxorubicin (GVD), and Pembrolizumab. ^{18}F-FDG PET/CT performed six weeks later, showed near complete metabolic resolution of prior mediastinal lymphadenopathy. However, interval development of hepatomegaly with multifocal hypermetabolic lesions throughout the liver was noted (B-solid-arrows). In view of favorable response at the primary site, the new hepatic lesions were favored to represent immune-related hepatitis over progressive lymphomatous involvement of the liver. The patient's laboratory results obtained within four days of the PET/CT showed elevated levels of aspartate transaminase - 115 U/L, and alanine transaminase - 151 U/L (11 U/L, and 15 U/L respectively, one month prior). Based on the suggestion of immune-related hepatitis, Pembrolizumab was discontinued and Prednisone 40 mg daily was started, tapering by 10 mg weekly over four weeks. GVD regimen was continued. Re-assessment ^{18}F-FDG PET/CT performed five weeks later showed continued remission of the mediastinal disease with marked anatomic and metabolic improvement of the liver lesions (C-solid-arrow). The patient received autologous stem cell transplant two weeks later and a re-assessment ^{18}F-FDG PET/CT (D) showed continued response in the mediastinal disease and complete resolution of the liver lesions.

Immune-related adverse events (irAE), such as hepatitis are known to occur in patients treated with immune-checkpoint inhibitors. However, the presentation of immune-related hepatitis as multi-focal involvement of the liver is uncommon and can mimic the appearance of progressive disease. In such cases, a re-assessment ^{18}F-FDG PET/CT performed at least four weeks after

discontinuation of immunotherapy can help improve the diagnostic accuracy. The detection of irAE on PET/CT is critical, as patients with severe irAEs require cessation of immunotherapy and initiation of corticosteroids.

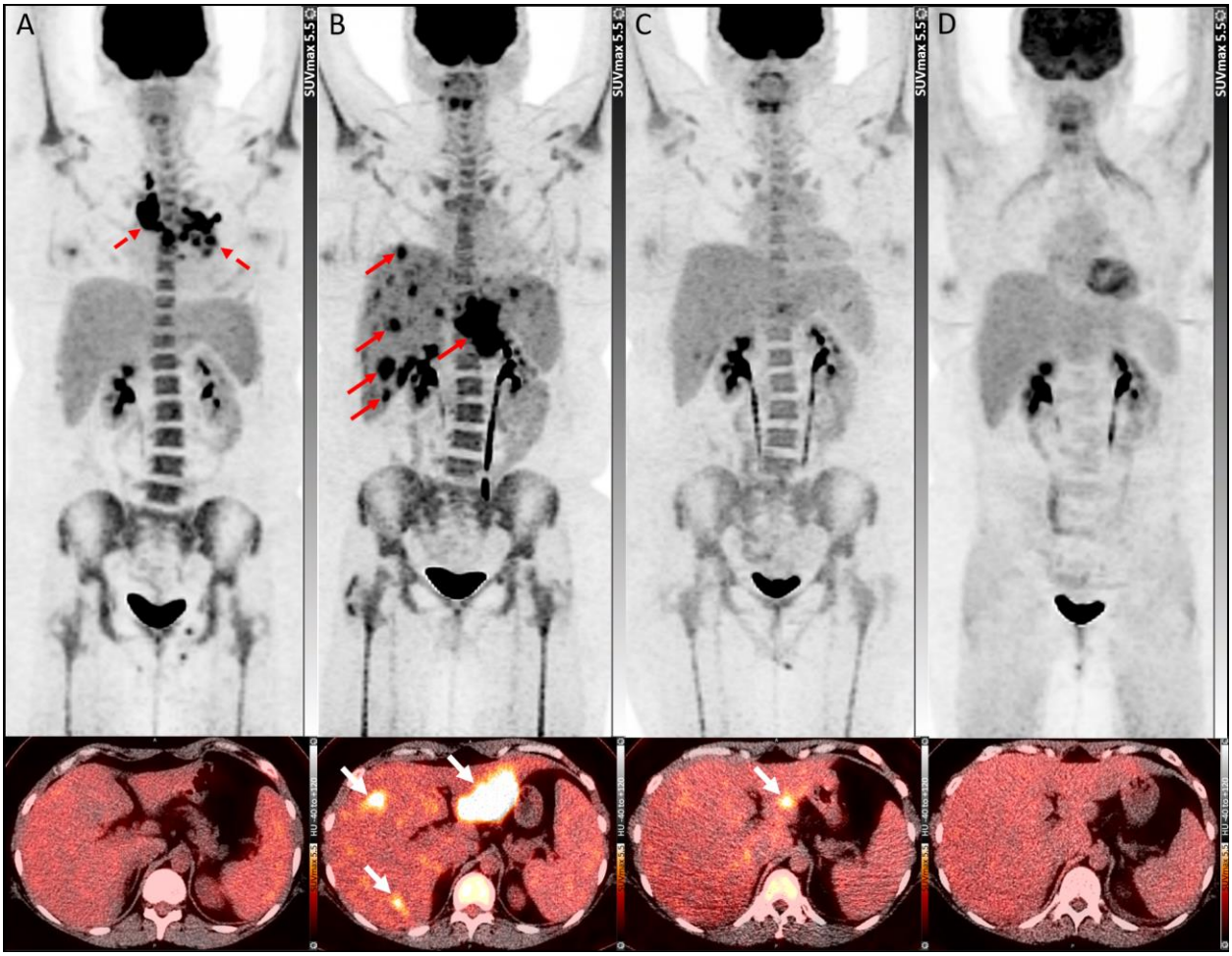

Figure: ^{18}F-FDG PET/CT maximum intensity projection (top) and fused PET/CT transaxial images (bottom) at baseline (A) show hypermetabolic mediastinal lymphadenopathy (dashed-arrow). ^{18}F-FDG PET/CT performed at six weeks after treatment with Pembrolizumab (B) shows metabolic resolution of the mediastinal lymphadenopathy and interval development of multiple discrete hypermetabolic lesions in the liver (solid-arrows). ^{18}F-FDG PET/CT performed five weeks after discontinuation of Pembrolizumab and treatment with Prednisone shows significant improvement in the liver lesions (C) which resolved completely at eight weeks (D).