IMAGE OF THE ISSUE

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Drug Induced Liver Injury to Immune Checkpoint Inhibitors Detected by F18-Fluorodeoxyglucose PET/CT

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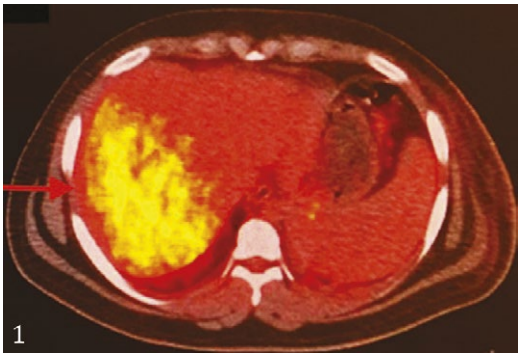

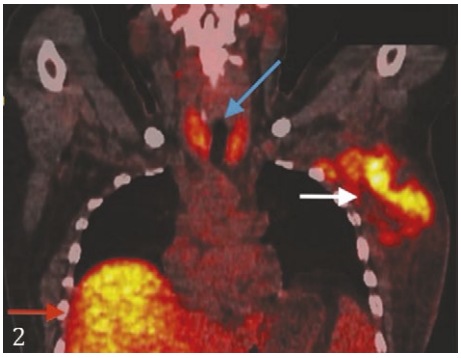

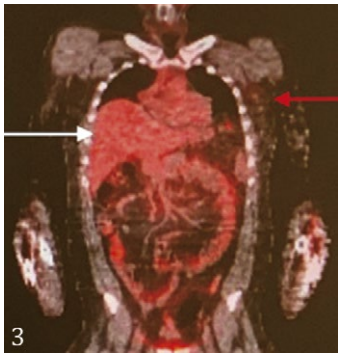

A 23-year-old male diagnosed with metastatic malignant melanoma originating on the left arm, started the immunotherapy with a combination of Ipilimumab for 4 cycles and Nivolumab every two weeks in maintenance, targeting the checkpoint inhibitors cytotoxic T-lymphocyte-associated protein 4 (CTLA4) and programmed death-ligand 1 (PD-L1), respectively. At the follow up visit, 6 weeks after starting the therapy, the patient reported mild symptoms of nausea and fatigue; face edema was noted on physical examination. The blood analyses revealed increased liver aminotransferases 2.5x upper limit of normal (ULN), mild cholestasis, increased anti-thyroglobulin antibodies 5xULN and thyroid stimulating hormone 9xULN. The patient was submitted to 2-[18F]-fluoro-2-deoxy-d-glucose (F18-FDG) positron emission tomography/computed tomography (PET/CT) for treatment efficacy assessment. An important pathologic F18-FDG uptake was detected in the liver (Fig. 1, axial section), in the thyroid and the lymph nodes of the left axilla (Fig. 2, coronal section). Viral, autoimmune and metabolic causes of liver injury were excluded. These results were interpreted as drug induced liver injury (DILI) and thyroiditis with hypothyroidism, developed as immunotherapy related adverse effects (IRAE). Hepatoprotective drugs and substitutive thyroid hormonal therapy were initiated, the immunotherapy being delayed for 2 weeks. A second F18-FDG PET/CT, after 3 months of surveillance revealed important metabolic response of more than 87% in the target lesions of axilla and normal liver and thyroid uptake (Fig. 3, coronal section), suggesting remission of the DILI and of the drug induced thyroiditis. There was also a rapid normalization of serologic results both for liver and thyroid function.

Immune checkpoint inhibitors induced liver toxicity is a rare complication of immunotherapy, being heterogeneous in its onset, presentation and severity [1]. Patients treated with anti-CTLA-4 (with or without anti-PD-1) experience a median interval of 3 (1–7) weeks between immunotherapy initiation and hepatic IRAE development [2]. Early development of DILI and thyroiditis may represent an early response indicator to immunotherapy efficacy [3, 4]. In this context, as illustrated by our case, PET-detectable IRAE might be an essential tool for prediction of a favorable outcome [4, 5].

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Conflicts of interest: None to declare.

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