



Letter to the Editor

Allergic broncho-pulmonary aspergillosis following treatment with an anti-programmed cell death protein 1 monoclonal antibody therapy

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A 58-year-old patient was referred for evaluation of an acute onset of dyspnoea and cough four weeks after the initiation of an anti-program death 1 (PD-1) monoclonal antibody therapy. His past medical history included a nephrectomy for renal cell carcinoma, and a subsequent metastatic relapse in the lungs treated with sunitinib for six months. A progression of lung and pancreatic metastasis was then reported and led to the initiation of intra-venous anti-PD-1. He had no previous history of asthma and was an active 40-pack-year smoker. Cough, sputum plugs and dyspnoea were reported after two infusions. His oxygen saturation was 98% accompanied by expiratory wheezes. His blood tests showed a high eosinophil count at 1300/mm³. His chest X-ray was normal and a general workup led to the diagnosis of COPD exacerbation. The patient received ciprofloxacin and oral steroids for 7 and 21 days respectively. Anti-PD-1 therapy was initially interrupted and symptoms dramatically improved within three days. One month later, anti-PD-1 therapy was resumed, and similar respiratory symptoms were reported two weeks after

initiation. A thoracic CT scan demonstrated patterns of stable metastatic disease with central bronchiectasis, mucoid impactions, bronchial wall thickening and segmental atelectasis (Fig. 1). A bronchial endoscopy found mucus plugs with *Aspergillus fumigatus* on sputum culture. Elevated serum IgE up to 2514 kU/l and positive *A. fumigatus* IgE antibodies were consistent with the diagnosis of allergic bronchopulmonary aspergillosis (ABPA) [1]. No evidence of invasive aspergillosis was found based on blood or broncho-alveolar lavage fluid analyses. The patient was living in a damp house closed to a river. He was treated with itraconazole and corticosteroids, and his condition rapidly improved.

Interstitial pneumonitis is the most common form of pulmonary toxicity of anti-PD-1 immunotherapy with an estimated incidence around 5% [2]. Cases of organising pneumonia [3] and sarcoidosis-like syndrome [4] have additionally been described. Here, we report the first case of ABPA related to anti-PD-1 treatment, in the absence of any favouring condition including asthma. In addition, the causality assessment may be considered as nearly certain based on the time relationship between occurrence of ABPA and anti-PD1 treatment infusion, and recurrence of similar symptoms after

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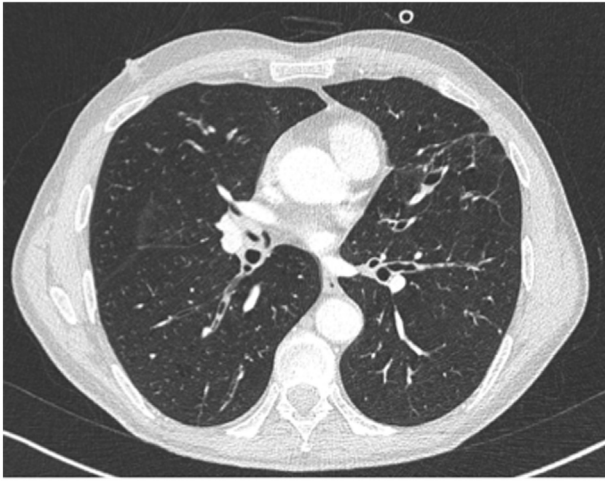


Fig. 1. Thoracic Computed Tomography scan showing proximal bronchiectasis with mucus plugs.

treatment rechallenge [5]. Of note, aspergillosis infection in immunocompromised patients from the oncology field is usually associated with an invasive form of the disease. However, in this case report, we describe a hypersensitivity reaction to aspergillosis that may have been triggered by anti-PD-1 therapy. The patient's damp environment further suggests that this complication may have been facilitated by an aspergillus respiratory tract precolonisation. Since anti-PD1 therapy may be involved in allergic responses [6], it could be proposed that this therapy may also have disrupted the tolerance balance between the host and aspergillus and triggered respiratory symptoms of allergic nature. In addition, this unusual case highlights that immune-related adverse events

due to novel immunotherapies could derive from close interactions between the patient's host background and his environment and support the need for biological documentation of immune-related adverse events. This first reported case of a respiratory immune-related adverse event potentiated by a respiratory pathogen colonisation highlights a new mechanism of immune-related adverse event physiopathology.

Conflict of interest statement

None declared.

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