Tofacitinib and subacute pneumonitis, don't hold your breath

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IBD-related lung diseases encompass different entities (e.g. interstitial lung diseases [ILD]) which can be drug or non-drug related.¹ Although extremely rare, case-series did associate drug-related lung diseases with several approved IBD therapies.¹ Nevertheless, a diagnosis of drug-related lung disease remains challenging, and can only be made after extensive investigations to exclude other causes.^{2,3} Early recognition is therefore critical, with discontinuation of the causal compound being the key principle. The use of “Pneumotox” website (www.pneumotox.com) can be of outstanding value in this etiological approach.

Recently, tofacitinib was approved as first-in-class Janus kinase (JAK)-inhibitor for ulcerative colitis (UC). A recent meta-analysis on pulmonary adverse events of JAK inhibitors in autoimmune diseases concluded that JAK-inhibitors have an equally low pulmonary risk as anti-TNF agents.⁴

We here report the case of a 76-year old woman who was diagnosed with UC back in 2002. Ever since, she was treated with 5-aminosalicylates, corticosteroids, adalimumab, thiopurines and vedolizumab. In April 2019 tofacitinib 10mg BID was initiated, which resulted in endoscopic and histologic remission. Therapy was tapered (tofacitinib 5mg BID) and successfully maintained. Six months later she was admitted with recurring fever for 4 weeks, associated with night sweating, dry cough and dyspnea on exertion. GI symptoms were well controlled. There was no recent travelling, nor any exposure to animals/molds. Two courses of antibiotics did not improve her symptoms. She did not have any signs of hypoxia. Clinical examination was unremarkable. Blood tests demonstrated mild inflammation. Blood and urinary cultures, and swabs of the upper respiratory tract were negative, as well as auto-immune and infectious screening. Urine analysis was unremarkable.

Computer tomography revealed limited ground-glass opacities in both lungs, without adenopathy (**Figure 1**). Long-standing history of recurrent fever for 4 weeks before the start of the COVID-19 crisis further argued against SARS-CoV-2, which was afterwards also confirmed by absence of SARS-CoV-2 antibodies. Pulmonary function tests revealed a reduced diffusion capacity (DLCO 41%), without evidence for obstructive/restrictive lung disease. Broncho-alveolar lavage ruled out infection, with normal eosinophils and lymphocyte counts. PET-CT did only show hypermetabolic regions in both lungs. Because of suspicion of tofacitinib-induced ILD, tofacitinib was discontinued.

Fever spontaneously disappeared, with normalization of diffusion capacity and improvement of the ground-glass opacities in both lungs in the next weeks-months, associated with clinical improvement without any steroid exposure.

As it might take years before rare, serious, and meaningful adverse effects become apparent, post-marketing surveillance strategies and adverse event reporting remain critical to recognize a drug's safety profile.⁵ Overall, we would recommend clinicians initiating tofacitinib to be vigilant and monitor the respiratory status. Furthermore, we aim to increase awareness of drug-induced ILD after initiation of any novel compound.

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Figures

Figure 1: Computed tomography (CT) of the chest on admission (**A**), and 3 weeks (**B**), 2 months (**C**) and 5 months (**D**) after tofacitinib discontinuation.

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Author contributions

BV wrote the manuscript. LP and PB were involved in the daily care of the described patient. All authors reviewed and agreed on the final manuscript.

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Conflicts of interest

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Data availability statement

The data underlying this article are available in the article and in its online supplementary material.

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Figure 1