

TB episode following PD-1 blockade



Successful use of PD-1 blockade for cancer immunotherapy, has brought up the question as to whether this same therapy could be successful against infectious diseases such as tuberculosis (TB) and HIV. The fact that the role of PD-1 blockade has not yet been properly established shows that there is still great need to study about PD-1 in relation to TB and in cases where there is TB co-infection. Study by Barber et al., details the case reports of two patients that developed TB after cancer treatment using anti PD-1 therapy.

The first case is a 59-year-old man with metastatic nasopharyngeal carcinoma enrolled in a clinical trial evaluating an anti-PD-1 therapy, nivolumab. After the patient was found to have TB following a CT scan and sputum culture, the patient stopped treatment with nivolumab in June 2016 after three cycles and was started on anti-TB treatment but unfortunately passed away.

The second case is an 83 year old man with Merkel cell carcinoma participated in a clinical trial evaluating pembrolizumab as an anti-PD1 therapy. The patient was also found to have pulmonary nodules in the right lower lobe present on the CT scan, as well as sputum positive for acid fast bacilli (*Mycobacterium tuberculosis*, *Mtb*). The patient was initially non-responsive to anti-TB treatment, it was only after the patient had been taken off the anti-PD1 treatment that they became more responsive to the TB drugs. This in

turn caused the patient's mass to increase forcing them to be put back on Pembrolizumab infusions. This patient managed to complete 9 months of TB therapy and was able to carry out their normal physical activity. PPD-stimulated PBMCs were analyzed from the patient before and after treatment. Researchers observed an increase in antigen-specific Th1 cells post-treatment. This treatment, however, did not result in an increase in PPD-specific Th17, mycobacteria-specific CD8+ T-cells or regulatory T-cells expressing PD-1. They did not observe any significant change in *Mtb*-specific antibody responses before treatment and after the development of pulmonary lesions which shows that antibodies may not have played a significant role in the development of TB.

There are tremendous efforts to develop host-directed therapies for TB, in light of this we have to pay close attention to the kind of immune responses present when these therapies are being evaluated. This is to ensure that benefits of therapy out weigh the detrimental effects in the long run. These data support exercising caution when treating TB with pro-inflammatory strategies in general and with PD-1 blockade in particular. This work also suggests that TB screening before checkpoint therapy may be warranted.

Journal Article: Barber *et al.*, 2019. [Tuberculosis following PD-1 blockade for cancer immunotherapy](#). Sci. Transl. Med.

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