Response to: ‘Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) induced by immune checkpoint inhibitors’ by Delyon et al

We thank Delyon et al for their interest in our original paper and for reporting on a patient with immune checkpoint inhibitors (ICI)-induced eosinophilic granulomatosis with polyangiitis (EGPA). Since the first description in 2014 of giant cell arthritis (GCA) following treatment with ipilimumab (anti-CTLA-4 agent) in two patients with melanoma, several vasculitis cases have been reported, as recently highlighted by Daxini et al in a systematic literature review. Overall, they compiled 20 cases of confirmed ICI-induced vasculitis, which were classified using the revised International Chapel Hill Consensus Conference nomenclature. The most commonly reported types of vasculitis were large vessel vasculitis and vasculitis of the nervous system, with a median exposure time to ICI of 3 months. The majority of patients received oral or intravenous corticosteroids and ICI was discontinued. Of note, a granulomatosis with polyangiitis occurred 1 week following anti-programmed cell death 1 (PD-1) agent for advanced melanoma, requiring methylprednisolone and oral daily cyclophosphamide. Unfortunately, data on cancer and vasculitis outcomes are often missing.

By adding the first case report of EGPA, Delyon et al complete the unique and expanding list of ICI-related adverse events (irAEs). Interestingly, antineutrophil cytoplasmic antibodies were negative, similar with findings in other rheumatic irAEs such as myositis and inflammatory arthritis where autoantibodies are often negative, which should not exclude the diagnosis. Therefore, rheumatologists as well as other organ specialists involved in the diagnosis and management of irAEs have to consider vasculitis when evaluating patients receiving ICI. Notably, since polymyalgia rheumatica-like syndrome is frequently reported with anti-PD-(L)1 therapies, we should pay particular attention to GCA symptoms.

On the other hand, Zhang et al reported an insufficient negative signalling by the immune checkpoint PD-1/PD-L1 in the pathogenesis of GCA. Indeed, they demonstrated low expression of PD-L1 in GCA dendritic cells compared with healthy arteries, unleashing PD-1high T cells to infiltrate and damage the walls of large arteries. These data shed light on the association between vasculitis and the downregulation of PD-1/PD-L1 pathway, either spontaneous or induced by ICI, and may suggest future therapeutic immunomodulatory approaches in our classical vasculitis.

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