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ORAL PRESENTATIONS

LARGE VESSEL VASCULITIS

16. CHECKING IN WITH NOVEL CANCER THERAPIES: A CASE OF IMMUNOTHERAPY-RELATED LARGE VESSEL VASCULITIS

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Introduction: Immune checkpoint inhibition has revolutionised the management of patients with cancer. However, many immunotherapy-related adverse events have been recognised, such as colitis and dermatitis. We are increasingly aware of patients presenting to rheumatology with musculoskeletal complaints including polymyalgia-like symptoms or an inflammatory arthritis. More uncommonly, patients can present with large vessel vasculitis. We present a case of immunotherapy-related large vessel vasculitis following treatment with a combination of ipilimumab and nivolumab.

Case description: A 67-year-old man has been known to the oncology team with prostate cancer since 2014. He developed osteoblastic metastases despite androgen deprivation therapy and he was subsequently enrolled onto the NEPTUNE study which involved a combination of ipilimumab and nivolumab. Three weeks after his first cycle of immunotherapy, he developed fevers, diarrhoea and a macular rash. He was admitted for a flexible sigmoidoscopy and biopsies demonstrated inflammation in keeping with immunotherapy-related colitis. It was also noted that his thyroxine level was 64.7pmol/L with a TSH of 0.02mIU/L and this was thought to be immunotherapy-related thyroiditis. His immunotherapy was discontinued and he was on a weaning course of prednisolone with a good response.

Five months after his single cycle of immunotherapy, he began reporting generalised aches which were worse in his chest and radiated to his right scapula. He also had bilateral shoulder pain but no specific stiffness. This pain was more noticeable as he weaned off the prednisolone. He had no claudication, headaches or constitutional symptoms. A CT pulmonary angiogram showed no evidence of pulmonary emboli, but there was an incidental finding of circumferential thickening of the aorta suggestive of a vasculitis. Inflammatory markers were notably raised - ESR 127mm/h and CRP 199mg/L. There was no evidence of infection on cultures.

He was referred to the rheumatology team. Examination was unremarkable with no evidence of weak pulses or bruits. Immunology tests were all negative. An urgent PET-CT was organised which demonstrated extensive active large vessel vasculitis involving the aorta, subclavian, axillary, carotid and vertebral arteries. He was given one dose of methylprednisolone (1mg/kg) which resulted in a marked improvement in his pain overnight. He received two further doses of methylprednisolone and his CRP improved to 38mg/L. He continues to improve on a weaning course of prednisolone.

Discussion: Ipilimumab was the first checkpoint inhibitor approved for cancer in 2010. Immune checkpoint inhibitors have since become an expanding field in oncology, particularly in resistant or advanced cases of melanoma and lung cancer. There are currently six checkpoint inhibitors licensed by the US Food and Drug Administration. These are monoclonal antibodies targeting the checkpoint pathway including CTLA4, PD-1 and PDL-1. There are well documented case series with regard to immunotherapy-related toxicities including colitis, dermatitis and endocrinopathies. More relevant to rheumatologists, checkpoint inhibitors have also been associated with rheumatic presentations including inflammatory arthritis, polymyalgia rheumatica, sicca symptoms, myositis and vasculitis. A review of the literature in 2018 found 53 cases of vasculitis associated with checkpoint inhibition, of which 20 were confirmed. All these cases were resolved by withholding the immune checkpoint inhibitor and where necessary, giving steroid therapy. On the whole, immunotherapy-related vasculitis is not as common as arthritis or polymyalgia. As the use of checkpoint inhibitors becomes more widespread, it is important that as rheumatologists, we are aware of the various rheumatic conditions that they can trigger and how to manage them.

Key learning points: This single case highlights the wide range of immunotherapy-related adverse events associated with immune checkpoint inhibition. Their use in clinical practice will likely become more widespread owing to their success in treating a variety of advanced or resistant malignancies. Apart from being familiar with the various rheumatic complaints, we should also be aware of the other systems that can become involved, so that the patient is managed holistically. Symptoms will usually improve with termination of the checkpoint inhibitor but steroid therapy is often required. The addition of disease modifying antirheumatic drugs should be considered in cases where there are relapsing symptoms whilst weaning steroids. However, this is a decision that requires a multidisciplinary approach since it could affect the prognosis of the underlying malignancy. With more research into this area, there will a better understanding of the true incidence of immunotherapy-related adverse events in these patients and how to reduce these in the future.

Conflict of interest: The authors declare no conflicts of interest.