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Pembrolizumab-Induced Vasculitis and its Implications for Treatment

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Introduction:

Immune checkpoints are inhibitory receptors expressed on T-cells that control activation and dampen inflammatory responses to prevent tissue injury. Cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) and Programmed Cell Death 1 Receptor (PD-1) are two such immune checkpoints with key roles in regulating immune responses. Over-activity of PD-1 and CTLA-4 signalling can be induced by cancer cells to avoid immunosurveillance. Targeting these receptors with monoclonal antibodies that block their interaction with their natural ligands takes the brake off anti-tumour immunity, allowing T cells to identify and destroy malignant cells. This approach has demonstrated striking therapeutic potential across a range of cancer types. However, it has also led to a new class of drug side effect referred to as Immune Related Adverse Events (IRAEs), as blockade of these natural checkpoints can also unleash the immune system to attack healthy tissues.

Pembrolizumab is a therapeutic antibody that blocks the receptor PD-1 and is licenced for the management of non-small cell lung cancer and melanoma.

Case Study:

A 68-year-old female with a diagnosis of metastatic lung cancer was managed with Pembrolizumab immunotherapy. Her GP noted a gradual decline in her renal function since starting Pembrolizumab, and referred her for a renal ultrasound scan. Her urine dip was positive for blood only. She denied any urinary symptoms. A glomerulonephritis screen was sent and renal biopsy arranged.

Results:

Her renal USS showed complex cystic lesions. Blood tests indicated high titres of myeloperoxidase (MPO). Since stopping Pembrolizumab, her renal function improved in a week, from an eGFR of 23 ml/min to 32 ml/min, and a creatinine from 185 µmol/L to 144 µmol/L.

Discussion:

Previous case reports have highlighted the implication of immunotherapy in the development of autoimmune disease. Our case demonstrates a relationship between treatment with Pembrolizumab and the onset of MPO positive vasculitis, whereby the cessation of treatment led to an improvement in renal function. A similar case study proposed that Pembrolizumab had contributed to the development of antineutrophilic cytoplasmic antibody (ANCA) positive vasculitis. Indeed, aberrant expression of PD-1 has been referenced in the literature in the pathogenesis of Granulomatosis with Polyangiitis.

Conclusion:

Over-stimulation of T-cells can lead to a predisposition to autoimmune disease. In this case report, we have seen a temporal relationship between the start of treatment with Pembrolizumab and renal decline

associated with high MPO titres. MPO positivity is commonly seen with a number of malignancies. In our patient, a decline in function and high MPO titres were seen after initiation of treatment, with a resolution in renal function when immunotherapy was discontinued.

This case has identified a possible correlation between treatment with Pembrolizumab and a decline in renal function associated with high MPO titres. This may suggest a link between immune checkpoint inhibitors and the development of drug-induced vasculitis.