RHEUMATIC COMPLICATIONS OF IMMUNE CHECKPOINT INHIBITOR THERAPY: A CASE SERIES

Benedict Moore1, Matthew Ho2, Jochen Schaller3, Emily Des Fleurs4, Pascal Claudepierre1, Laure Gossec2, Laurent Capron4,5, Marco Garrido-Cumberna3,8,9, Emilie Des Fleurs4, Francesca Aliotti Launais10, René-Marc Flipo11,12

1 Imperial College School of Medicine, London, United Kingdom; 2 Chelsea and Westminster Hospital, London, United Kingdom

Background: Immune checkpoint inhibitor therapy reduces negative signals of T cell activation and enables tumour-specific T cells to mount a more effective response. Use of these drugs in management of malignancy has been associated with the development of autoimmune disease. There are few published studies describing immune-related adverse events affecting the musculoskeletal system.

Objectives: This study aimed to describe the spectrum of musculoskeletal complications in patients treated with immune checkpoint death (PD)-1 and/or cytotoxic T lymphocyte associated antigen (CTLA)-4 blockade.

Methods: 16 patients were identified by retrospective review of records. All patients had received treatment with monoclonal antibodies specific for PD-1, PD ligand-1 and/or CTLA4 and had been referred for rheumatology assessment of musculoskeletal complications. We assessed clinical presentation, results of blood tests for C-reactive protein (CRP), anti-nuclear antibody (ANA), rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) antibody, and response to treatment.

Results: Seven males and nine females, with mean age of 56 years were evaluated. 13 patients had melanoma, two renal cell carcinoma and one triple negative breast cancer. Patients presented with a spectrum of musculoskeletal symptoms. Five patients displayed features most consistent with polymyalgia rheumatica (PMR), five had peripheral spondyloarthritis (SPA) features with lower limb oligoarthritis or plantar fasciitis, four had rheumatoid arthritis (RA) features with small joint polyarthritis, one had myositis with raised creatine kinase and one had new onset of gout. Only one of 16 patients was positive for RF. All patients were seronegative for ANA, anti-cyclic citrullinated peptide (anti-CCP) antibodies and ANA. One patient with RA presentation had a high CRP of 39mg/L. Five patients had a mildly elevated CRP of 5-10mg/L. Other patients did not show an acute phase response. All patients received treatment with corticosteroid with benefit. Intra-articular and soft-tissue corticosteroid injections were also effective. One of two patients with RA presentation responded to sulfasalazine and the other responded to methotrexate. One patient with RA presentation and one with SPA presentation responded to tumour necrosis factor (TNF)-alpha blockade.

Conclusion: Attenuating inhibitory signals of T cell activation using immune checkpoint inhibitor therapy is associated with a range of rheumatic complications, including PMR-like as well as RA- and peripheral SPA-like presentations. The majority of patients were seronegative for RF, CCP and ANA, and had low or borderline elevated CRP. All patients showed a response to prednisolone. TNF-alpha blockade was effective for RA and SPA presentations.

REFERENCES:

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