RHEUMATIC IMMUNE RELATED ADVERSE EVENTS ASSOCIATED WITH CANCER IMMUNOTHERAPY: A NATIONWIDE MULTI-CENTER CANADIAN COHORT FROM THE CANADIAN RESEARCH GROUP OF RHEUMATOLOGY IN IMMUNO-ONCOLOGY (CANRIO)

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Background: Immune checkpoint inhibitors (ICI) have revolutionized cancer therapy by harnessing the immune system to fight cancer. As the indications for ICI continue to expand, their success in advanced stage malignancies is tempered by the development of autoimmune toxicities, referred to as immune-related adverse events (irAE). Rheumatic irAE (Rh-irAE), particularly arthralgias and arthritis are common and optimal management remains unknown.

Objectives: The Canadian Research Group of Rheumatology in Immunology-Oncology (CanRIO) is an emerging network of Canadian rheumatologists with an interest in Rh-irAE secondary to ICI. We describe the clinical presentation and management of Rh-irAE associated with ICI in patients seen at 9 CanRIO sites.

Methods: Patients presenting with rheumatic symptoms associated with ICI therapy between 2013 and January 2019 at participating CanRIO sites were identified. Cases were stratified based on the presence or absence of pre-existing autoimmune disease (PAD). Standardized data were extracted by chart review. The data were pooled and analyzed descriptively.

Results: 118 patients without PAD who developed 140 Rh-irAE were identified, 59% were male with a mean age of 62 years. Common indications for ICI were melanoma (n=57, 48.3%), lung (n=30, 25.4%), and gastrointestinal cancer (n=19, 16.1%). ICI included nivolumab (n=30, 25.6%), pembrolizumab (n=38, 32.5%), ipilimumab (n=1, 0.9%), durvalumab (n=3, 2.6%), atezolizumab (n=4, 3.4%) or combination therapy (n=29, 24.8%). Common Rh-irAE included symmetric polyarthritis (n=45, 32%), arthralgias/myalgias or acute flare of osteoarthritis (n=20, 14.3%), polymyalgia rheumatica-like presentation (n=17, 12%), tenosynovitis/enthesitis (n=17, 12%), sicca syndrome (n=11, 7.9%) and myositis (n=9, 6.4%). 20 patients with PAD were identified, 70% of whom were in remission prior to starting ICI. 50% (n=10) had flares, 15% (n=3) developed a new Rh-irAE and 20% (n=4) developed O-irAE. 53% experienced at least one other non-rheumatic irAE (O-irAE) (n=63).

Conclusion: This is the largest multi-centered cohort of Rh-irAE described to date. Seronegative inflammatory polyarthritis was the most common Rh-irAE although a broad range of conditions were identified. The most common first-line treatment was systemic corticosteroids followed by hydroxychloroquine being the most commonly used DMARD. Despite moderate to high doses of immunosuppression, the majority of patients had favorable tumor responses.

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