RHEUMATIC IMMUNE RELATED ADVERSE EVENTS ASSOCIATED WITH CANCER IMMUNOTHERAPY: A NATIONWIDE MULTI-CENTER CANADIAN COHORT FROM THE CANADIAN RESEARCH GROUP OF RHEUMATOLOGY IN IMMUNO-ONCLOGY (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 genitourinary cancer (n=19, 16.1%). ICI included nivolumab (n=30, 25.6%), pembrolizumab (n=38, 32.5%), ipilimumab (n=1, 0.9%), durvalumab (n=4, 3.2%), atezolizumab (n=4, 3.4%) or combination therapy (n=29, 24.8%). Common Rh-irAE included symmetric polyarthritis (n=45, 35%), 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-rirAE. 53% experienced at least one other non-rheumatic irAE (O-rirAE) (n=63). Mean time from first ICI exposure to onset of Rh-irAE was 6.8 months. In 65% ICI was held or discontinued (n=77). Despite this, 68.6% (n=81) had favorable tumor response, while 12% (n=14) had tumor progression. There were no deaths related to Rh-irAE.

Conclusion: This is the largest multi-centered cohort of Rh-irAE described to date. Seronegative inflammatory polyarthritids 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 NSAID and intra-articular steroid injections. Prednisone was effective, however higher doses were required. Disease-modifying antirheumatic drugs (DMARD) and biologic therapy were well tolerated and effective, with 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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