



# Patient Impact and Clinical Presentation on Immune Checkpoint Inhibitor-Associated Joint Disorders

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## ABOUT THE STUDY

Immune Checkpoint Inhibitors (ICIs) have revolutionized cancer therapy, offering new hope for patients with various malignancies. These therapies, such as pembrolizumab, nivolumab, and atezolizumab, harness the body's immune system to attack cancer cells by blocking immune checkpoint proteins like PD-1, PD-L1, and CTLA-4. While these agents are highly effective, their use has been associated with a range of immune-related Adverse Events (irAEs), including joint disorders that can significantly impact patients' quality of life.

### Clinical presentation of joint disorders

Joint disorders associated with ICIs manifest as a spectrum of symptoms that may include joint pain, stiffness, swelling, and, in severe cases, joint deformity. These conditions can present in different ways, ranging from mild, self-limiting arthralgia to more severe forms that may mirror autoimmune joint diseases. Patients may report discomfort in large joints like the knees, hips, and shoulders or experience pain in smaller joints such as those in the hands and feet. Symptoms may develop gradually or emerge suddenly, depending on the individual response to ICIs.

One common manifestation is immune checkpoint inhibitorassociated arthritis, which can sometimes lead to joint effusion, warmth, and tenderness. Patients may describe morning stiffness that lasts longer than 30 minutes, an indicator of inflammatory joint conditions. This symptom profile can overlap with that of rheumatoid arthritis, contributing to diagnostic challenges. In addition to joint pain, musculoskeletal symptoms may include myalgia and, less frequently, muscle weakness.

### Impact on patient health

Joint disorders linked to ICIs can have a profound impact on a patient's physical and psychological well-being. Pain and reduced joint function can lead to decreased mobility, which affects daily activities and overall quality of life. The physical limitations imposed by these disorders may result in social isolation, depression, and a decrease in adherence to cancer treatment protocols.

The psychological toll of these musculoskeletal symptoms should not be underestimated. Many patients are already dealing with the stress and emotional burden of a cancer diagnosis and treatment. The added challenges of joint pain and stiffness can exacerbate feelings of anxiety and hopelessness, complicating the management of their overall health.

#### Diagnostic considerations

Accurately diagnosing immune checkpoint inhibitor-associated joint disorders requires a detailed clinical evaluation. Physicians should consider the patient's treatment history, including the type and duration of ICIs administered. A thorough history and physical examination should be conducted to assess joint function, range of motion, and the presence of any signs of inflammation.

Imaging modalities such as X-rays, ultrasound, and MRI can be employed to evaluate joint integrity and identify any structural changes or signs of synovitis. Although these tests can provide valuable information, they should be interpreted in the context of the patient's clinical presentation and ICI treatment history.

#### Patient impact

Joint disorders resulting from ICIs often lead to a significant decline in quality of life. Patients may experience a reduction in physical activity, which can contribute to muscle wasting, joint deformity, and chronic pain. The ongoing struggle with these symptoms can limit their ability to maintain normal routines, including work, recreational activities, and other aspects of daily living.

Furthermore, the need for ongoing medical appointments, assessments, and treatments can create a sense of instability and increased stress for patients. The uncertainty about the future progression of symptoms can add to the emotional burden, emphasizing the need for holistic approaches that consider both physical and mental health.

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#### Multidisciplinary approach to care

Managing immune checkpoint inhibitor-associated joint disorders requires a collaborative approach involving oncologists, rheumatologists, physical therapists, and primary care providers. Regular communication among healthcare professionals can ensure that a patient's symptoms are effectively monitored and managed. Physical therapy can play a need role in maintaining joint mobility, reducing stiffness, and preventing muscle atrophy, while occupational therapy can help patients adapt their daily activities to accommodate joint limitations.

### Key considerations for physicians

Physicians need to maintain a high index of suspicion for immune-related joint disorders when evaluating patients undergoing ICI treatment, especially those presenting with unexplained joint pain or stiffness. Early intervention is critical to prevent the progression of symptoms that can lead to longterm functional impairment. Regular follow-ups and patient education on the potential side effects of ICIs are need components of patient care.

Clinicians should also be aware of the potential overlap of ICIrelated joint disorders with other autoimmune or inflammatory conditions. For instance, patients may present with symptoms that resemble rheumatoid arthritis, but they may not meet the diagnostic criteria for such a condition. Proper documentation and clear communication with the patient are important for managing expectations and guiding treatment plans.

Immune checkpoint inhibitors have undoubtedly transformed the landscape of cancer treatment, offering promising outcomes for patients facing various types of cancer. However, their association with joint disorders poses a significant challenge that can impact both the physical and mental health of patients. Comprehensive care that includes early detection, multidisciplinary management, and patient education is need to mitigate the effects of these musculoskeletal symptoms.