Optimizing management of immune checkpoint inhibitor-induced inflammatory arthritis: A case series and literature review

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Abstract. Immune checkpoint inhibitors (ICIs) are widely applied in the treatment of various malignant tumors, leading to notable improvements in patient prognosis. However, with their increased use, various immune-related adverse events (irAEs), including ICI-induced inflammatory arthritis (ICI-IA), may develop, affecting clinical evaluation and treatment decisions. The present report presents 3 cases of ICI-IA and reviews the literature on its clinical features, diagnosis and therapeutic approaches. The first patient, who had been diagnosed with metastatic bladder cancer, developed limb joint pain after undergoing combination therapy involving ICIs and chemotherapy. Laboratory tests showed elevated levels of C-reactive protein and interleukin (IL)-6. Bone scintigraphy excluded bone metastasis, and the symptoms of the patient improved following corticosteroid therapy. The second patient had advanced cervical cancer and a history of rheumatoid arthritis. Following multiple cycles of ICI combined with anti-angiogenic treatment, the patient experienced recurrent joint swelling and pain, accompanied by elevated IL-6 and IL-10 levels. Bone scintigraphy excluded bone metastasis, and the symptoms were controlled with corticosteroid therapy. The third patient had advanced lung cancer and developed persistent pain in the shoulders, knees and ankles during immunotherapy. Corticosteroid therapy effectively controlled the symptoms after bone metastases and autoimmune diseases were excluded. These cases illustrate that ICI-IA is a clinically relevant irAE. Early recognition and management are crucial for improving patient prognosis. A thorough understanding of the pathogenesis of ICI-IA is essential for optimizing treatment strategies and improving quality of life.

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Introduction

Immune checkpoint inhibitors (ICIs) enhance antitumor immunity by targeting inhibitory pathways that normally restrain T-cell activation and maintain peripheral immune tolerance, such as the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1)/programmed death ligand 1 (PD-L1) pathways. By boosting the ability of the immune system to recognize and eliminate cancer cells, ICIs effectively inhibit tumor progression and markedly improve survival outcomes in patients with cancer (1). This mechanism has demonstrated notable efficacy in various malignancies, including melanoma, non-small cell lung cancer and urothelial carcinoma (2). However, ICIs are also associated with a risk of immune-related adverse events (irAEs), primarily caused by excessive immune system activation leading to damage to normal tissues (3). The clinical manifestations of irAEs reflect abnormal activation of the immune system and can affect nearly all organ systems with variations in onset time, duration and severity. For example, dermatological toxicities such as rash and pruritus often present early and are usually mild, whereas endocrine irAEs such as thyroid dysfunction tend to present later and are often more persistent. Cardiac or neurological irAEs, although uncommon, can be severe and progress rapidly (4,5). These events can prolong hospitalization, increase healthcare costs and compromise the efficacy of cancer therapy, especially if treatment discontinuation is required. In severe cases, irAEs such as myocarditis, pneumonitis, encephalitis and myasthenia gravis-like syndromes can be life-threatening. According to published data from international studies, among patients receiving ICI therapy, the incidence of ICI-induced inflammatory arthritis (ICI-IA) has been reported to be 4-6%, and ~43% of patients experience an impaired quality of life due to arthralgia (6-8). However, systematic research specifically focusing on ICI-IA remains limited. In the present report, 3 cases of ICI-IA are presented and analyzed, discussing their clinical features, diagnosis and treatment strategies in

the context of existing literature. The aim of the current report is to provide clinicians with actionable insights and practical guidance in the recognition and management of this specific irAE.

Case report

Case 1. A 68-year-old woman with metastatic bladder cancer began treatment with tislelizumab (200 mg, day 1, every 21 days) plus gemcitabine (1.8 g, days 1 and 8, every 21 days) and nedaplatin (50 mg, days 1-3, every 21 days) in June 2020 at Renmin Hospital of Wuhan University (Wuhan, China). After two cycles, treatment response was evaluated by abdominal and pelvic MRI, and a partial response (PR) was documented. Follow-up MRI in September 2020 showed stable disease (SD), and subsequent assessments all showed SD. The last treatment was administered in November 2022. In total, ~4 months after stopping immunotherapy, in March 2023, the patient developed symmetric polyarticular swelling and pain predominantly affecting the bilateral shoulders, wrists, knees and ankles, with the wrists being the most severely involved. Physical examination revealed bilateral joint swelling and tenderness, without skin erythema or ulceration. Laboratory tests showed elevated levels of serum C-reactive protein (CRP) at 64.1 mg/l (normal range, 0-6 mg/l) and serum interleukin (IL)-6 at 57.73 pg/ml (normal range, 0-20 pg/ml), with negative rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibody results. Bone scintigraphy demonstrated symmetrically increased radiotracer uptake in multiple bilateral joints, predominantly involving the shoulders, wrists, knees and ankles, consistent with an IA pattern (Fig. 1). No focal areas of intense uptake suggestive of tumor metastasis were observed. The patient had no pre-existing joint symptoms or history of autoimmune conditions. Based on the clinical presentation, ICI exposure history and imaging findings, grade 2 ICI-IA was diagnosed according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 (9). The patient was initiated on a course of methylprednisolone (40 mg qd iv drip). After 9 days, joint pain and swelling had markedly improved. Follow-up laboratory tests showed decreased serum CRP at 6.21 mg/l and IL-6 at 16.12 pg/ml. On day 11, the dose was reduced (20 mg qd iv drip). From day 15 onwards, the patient was switched to oral methylprednisolone (20 mg qd), followed by gradual tapering. The arthritis symptoms continued to improve, and treatment was stopped after 48 days. The patient was followed up regularly thereafter for 23 months until May 2025, with clinical evaluation including symptom assessment, physical examination and restaging imaging. During the follow-up period, no recurrence of IA was observed.

Case 2. A 66-year-old female patient with recurrent advanced cervical cancer received second-line treatment with tislelizumab (100 mg, day 1, every 21 days) and anlotinib (8 mg, days 1-14, every 21 days) in June 2021 at Renmin Hospital of Wuhan University. Anlotinib was administered as anti-angiogenic therapy. Because the patient had a poor performance status (ECOG PS >2) and was unable to tolerate later-line chemotherapy after recurrence, a chemotherapy-free regimen of tislelizumab plus anlotinib was selected based on our institutional clinical experience and preliminary conference data suggesting potential efficacy and manageable toxicity of this combination in previously treated cervical cancer (10). Tumor response was first evaluated in August 2021 by chest and whole-abdominal CT together with pelvic MRI, and a PR was documented. Subsequent response assessments were performed every 3 months and consistently showed PR. In August 2022, ~13.3 months after starting immunotherapy, the patient developed polyarticular swelling and pain involving both the upper and lower limb joints. Laboratory tests revealed elevated serum IL-6 at 404.84 pg/ml and IL-10 at 11.16 pg/ml (normal range, 0-5.9 pg/ml). Bone scintigraphy revealed mildly increased radiotracer uptake in the right anterior fourth rib and right knee joint, with mild uptake in the dorsal aspects of both feet (Fig. 2A). No evidence of bone metastasis was observed. Based on the clinical presentation, history of prior ICI exposure and imaging findings, grade 3 ICI-IA was diagnosed according to the CTCAE version 5.0. Immunotherapy was suspended. The patient reported being diagnosed with rheumatoid arthritis (RA) at a community hospital 15 years earlier; however, they were unable to provide detailed medical records to support this, and they had discontinued RA treatment 13 years prior to recurrent cancer diagnosis. At the initiation of ICI therapy (in June 2021), the patient had no RA symptoms; therefore, their RA was considered to be in clinical remission. Given this history, further rheumatologic evaluation and additional examinations were recommended to exclude an RA flare-up. However, the patient declined further evaluation and escalation of therapy due to personal and financial constraints. The patient was started on methylprednisolone (30 mg qd iv drip). After 5 days, joint pain and swelling had notably improved. Follow-up laboratory tests showed decreased serum IL-6 at 30.43 pg/ml, whereas IL-10 remained mildly decreased at 11.03 pg/ml. On day 6, therapy was switched to oral methylprednisolone (20 mg qd), followed by gradual tapering. The arthritis symptoms continued to resolve. By day 10 after the initiation of anti-inflammatory therapy, the patient had no overt joint swelling or pain and only mild residual tenderness without limitation of daily activities, consistent with improvement to ≤ grade 1. Tislelizumab plus anlotinib was therefore resumed according to the original regimen. Methylprednisolone was gradually tapered and discontinued after 40 days.

In January 2024, after 30.2 months of immunotherapy, the patient experienced recurrent joint pain in the left ankle, right knee and bilateral sacroiliac joints, with the knee pain being exacerbated by walking. Physical examination revealed notable swelling and tenderness in the left index and ring finger joints, metacarpophalangeal joints, the lateral aspect of the left ankle and the right knee, without skin erythema or ulceration. Laboratory tests showed elevated serum IL-6 levels at 67.41 pg/ml. Repeat bone scintigraphy demonstrated diffuse polyarticular uptake involving the bilateral elbows, wrists, left interphalangeal joints, right knee and bilateral ankles, with perilesional uptake and central photopenia in the right hip, suggestive of active synovitis (Fig. 2B). A diagnosis of recurrent grade 3 ICI-IA was made according to the CTCAE version 5.0. Immunotherapy was suspended again, and the patient was started on methylprednisolone (40 mg qd iv drip).

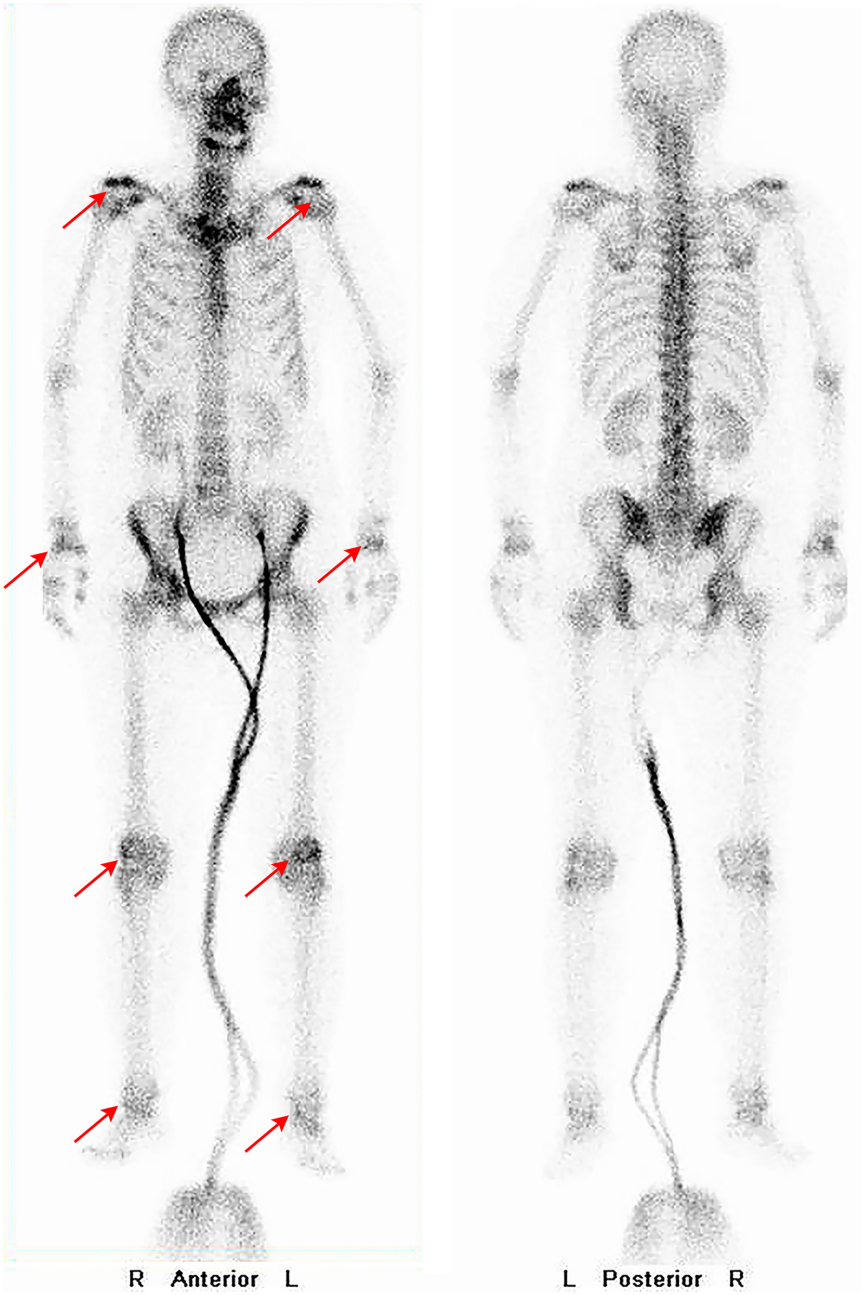

Figure 1. Whole-body bone scintigraphy of case 1. The anterior and posterior images show symmetrically increased radiotracer uptake in multiple bilateral joints, including the shoulders, wrists, knees and ankles (red arrows), consistent with immune checkpoint inhibitor-induced inflammatory arthritis. No focal areas of markedly intense uptake suggestive of bone metastases are identified. R, right; L, left.

After 6 days, the joint symptoms had markedly improved. Therapy was then switched to oral methylprednisolone (30 mg qd), followed by a gradual reduction to a maintenance dose (5 mg qd). Treatment was discontinued after 132 days. Cyclical immunotherapy was resumed according to the original regimen in March 2024 (day 64 of anti-inflammatory therapy). The patient's last immunotherapy administration was in April 2024. It should be noted that due to poor patient compliance and inadequate community healthcare capabilities, the patient experienced multiple instances of delayed dose reduction or missed doses during the post-discharge period of oral medication at home. After being guided and corrected by the doctor during follow-up visits, the patient resumed proper medication use and by day 132 had completely ceased taking methylprednisolone. The patient was followed up regularly thereafter for 19 months until December 2025, with clinical evaluation including symptom assessment, physical examination and restaging imaging, and no recurrence of IA was observed during the follow-up period.

Case 3. A 66-year-old man with recurrent lung adenocarcinoma complicated by brain metastasis began treatment with sintilimab (200 mg, day 1, every 21 days) plus pemetrexed disodium (0.8 g, day 1, every 21 days) and nedaplatin (60 mg on day 1 and 70 mg on day 2, every 21 days), in July 2020 at Renmin Hospital of Wuhan University. After completing five cycles, the best tumor response was assessed as PR by chest and whole-abdominal CT. Because the patient felt unable to

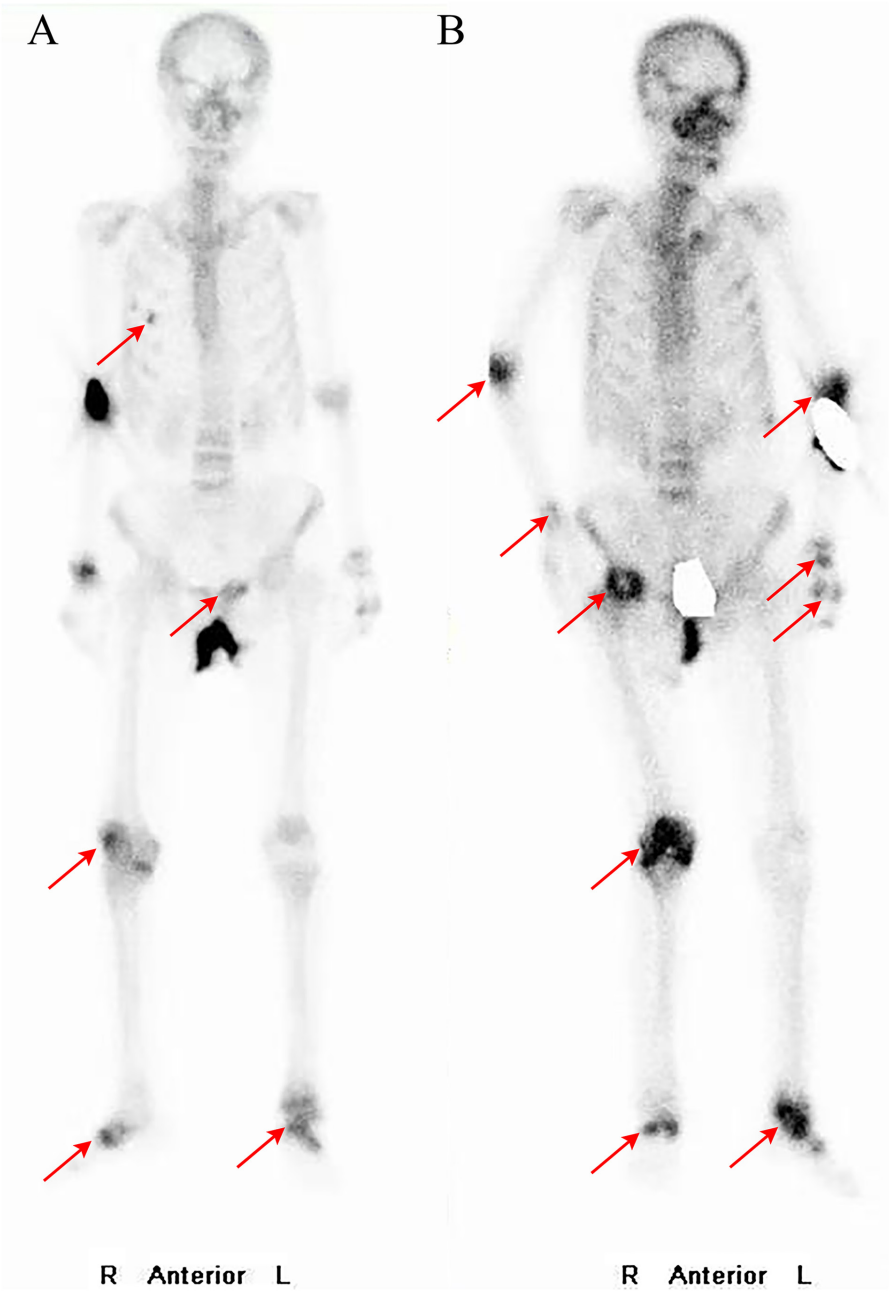

Figure 2. Two whole-body bone scintigraphy scans with anterior imaging of case 2. (A) First onset of ICI-IA: Mildly increased tracer uptake is observed in the right anterior fourth rib, the left pubic region (possibly due to contamination from a vesicovaginal fistula), right knee and dorsal aspect of bilateral feet (red arrows). (B) Recurrent ICI-IA: Recurrent episode demonstrating more extensive polyarticular uptake, involving the bilateral elbows, wrists, left interphalangeal joints, right knee and bilateral ankles, with perilesional uptake and central photopenia in the right hip, consistent with recurrent ICI-IA (red arrows). To highlight the abnormal joint metabolic activity, areas of physiological tracer accumulation in the bladder and tracer leakage at the left elbow have been digitally removed, resulting in white areas in the images. ICI-IA, immune checkpoint inhibitor-induced inflammatory arthritis; R, right; L, left.

tolerate further chemotherapy, the regimen was switched in December 2020 to a maintenance regimen with sintilimab (200 mg, day 1, every 21 days) plus bevacizumab (500 mg, day 1, every 21 days). Tumor response was re-evaluated in January 2021 by chest and whole-abdominal CT and showed SD; subsequent assessments also consistently showed SD. In June 2021, 11.2 months after starting immunotherapy, the patient developed pain in the bilateral shoulders, elbows, hips, knees and ankles, which severely affected their daily activities and self-care abilities. Physical examination revealed swelling and tenderness in these joints, without erythema or skin ulcers, with the left ankle being the most severely affected. Laboratory tests showed normal levels of RF, CRP, anti-CCP and antinuclear antibodies, effectively excluding underlying rheumatic diseases. Due to the severity of left ankle symptoms, an MRI scan of this joint was performed to evaluate the inflammatory changes. MRI revealed multiple findings consistent with IA, including tarsal sinus effusion, joint capsule and bursal effusions, subcutaneous soft tissue edema, posterior talar bursal enhancement, flexor tendon sheath enhancement and tarsal sinus enhancement (11) (Fig. 3). Subsequently, a whole-body 2-deoxy-2-[^{18}F]fluoro-D-glucose (FDG) positron

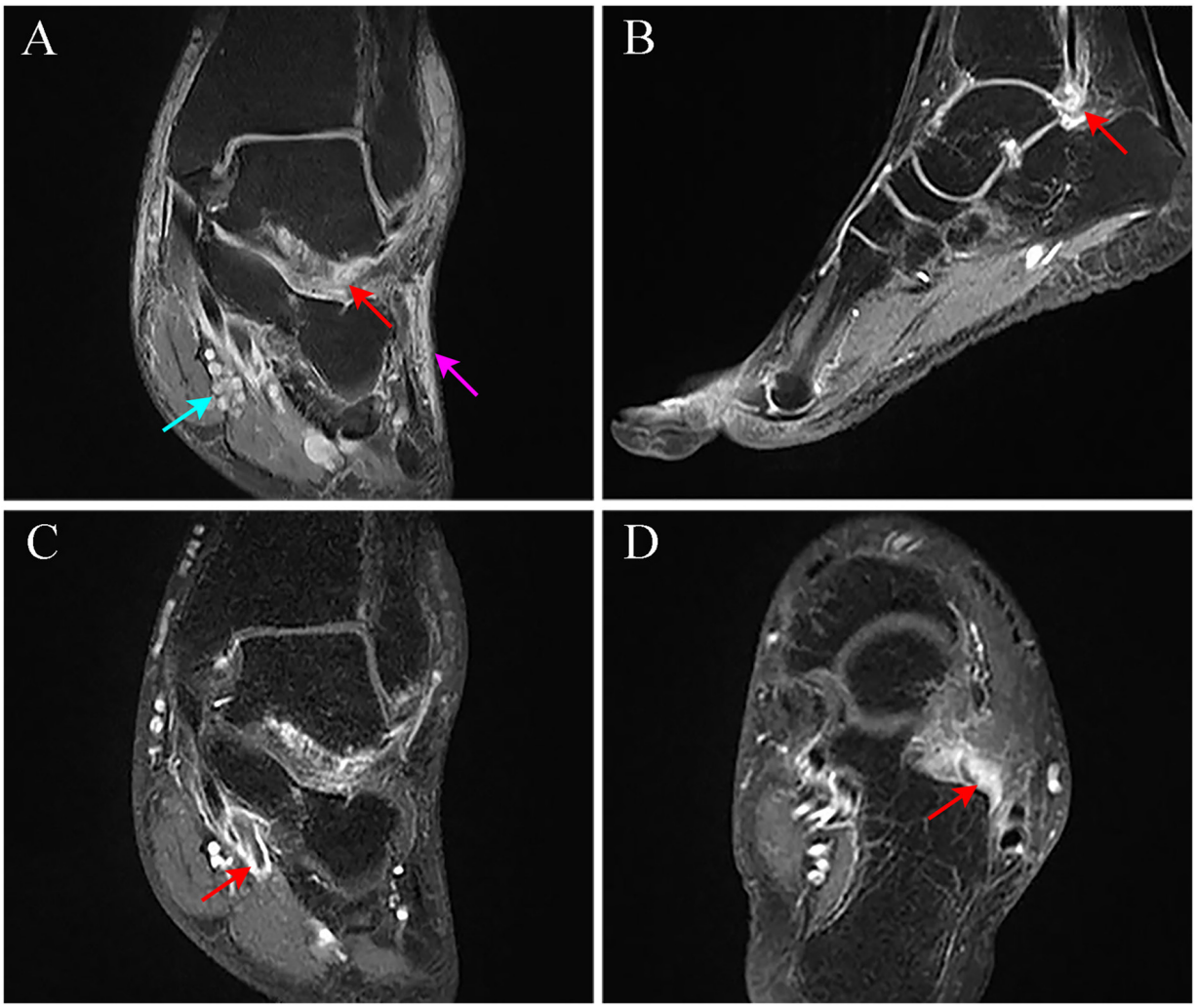

Figure 3. Magnetic resonance imaging of the left ankle in case 3. (A) Coronal T2-weighted fat-suppressed image shows tarsal sinus effusion (red arrow), subcutaneous soft tissue edema (purple arrow) and tibiotalar joint and bursal effusions (blue arrow), reflecting widespread intra-articular and periarticular inflammation. (B) Sagittal post-contrast T1-weighted fat-suppressed image demonstrates marked enhancement of the retrocalcaneal bursa (red arrow), indicating active inflammatory bursitis. (C) Coronal post-contrast T1-weighted fat-suppressed image reveals enhancement of the flexor tendon sheaths along the medial ankle (red arrow), consistent with active tenosynovitis. (D) Axial post-contrast T1-weighted fat-suppressed image shows diffuse synovial enhancement within the tarsal sinus (red arrow), an early indicator of inflammatory arthropathy in this region between the talus and calcaneus.

emission tomography-computed tomography (PET/CT) scan demonstrated symmetrical FDG uptake in the periarticular soft tissues of the affected joints, with knee joint effusion and periarticular edema of the ankles, suggesting ICI-IA (Fig. 4). No FDG-avid osseous lesions suggestive of metastases were identified. Based on the clinical presentation of the patient, history of ICI exposure and imaging results, the patient was diagnosed with grade 3 ICI-IA according to the CTCAE version 5.0. Anticancer treatment was suspended and the patient was started on methylprednisolone (40 mg qd iv drip). After 7 days, the symptoms of arthritis were relieved, and the dosage was adjusted to 30 mg once daily. From day 11 onwards, therapy was switched to oral methylprednisolone (16 mg qd), followed by gradual tapering to a maintenance dose (4 mg qd). The arthritic symptoms steadily improved, and the joint swelling resolved. Anticancer treatment was resumed on day 38 of anti-inflammatory therapy according to the maintenance regimen of sintilimab plus bevacizumab. The patient was followed up regularly thereafter for 47 months until July 2025, with clinical evaluation including symptom assessment, physical examination and restaging imaging, during which no recurrence of IA was observed. The clinical characteristics and management strategies of the 3 cases are summarized in Table I.

Discussion

ICI-IA encompasses a range of clinical phenotypes, most commonly presenting as inflammatory polyarthritis (12), but it may also manifest as oligoarthritis or monoarthritis and, in some cases, resemble psoriatic, reactive, remitting seronegative symmetrical synovitis with pitting edema or axial spondyloarthritis-like disease (13). The wrists, hands, shoulders and knees are the most frequently affected joints (14). These symptoms are temporally associated with ICI therapy (6). Published international studies have reported that 4-6% of patients receiving ICI therapy develop IA (6-8). The median time to the onset of ICI-IA is ~124 days (interquartile range, 56-252 days) after the initiation of ICI therapy (6). Other studies suggest that 60% of ICI-IA cases occur within the first 2-3 months of treatment

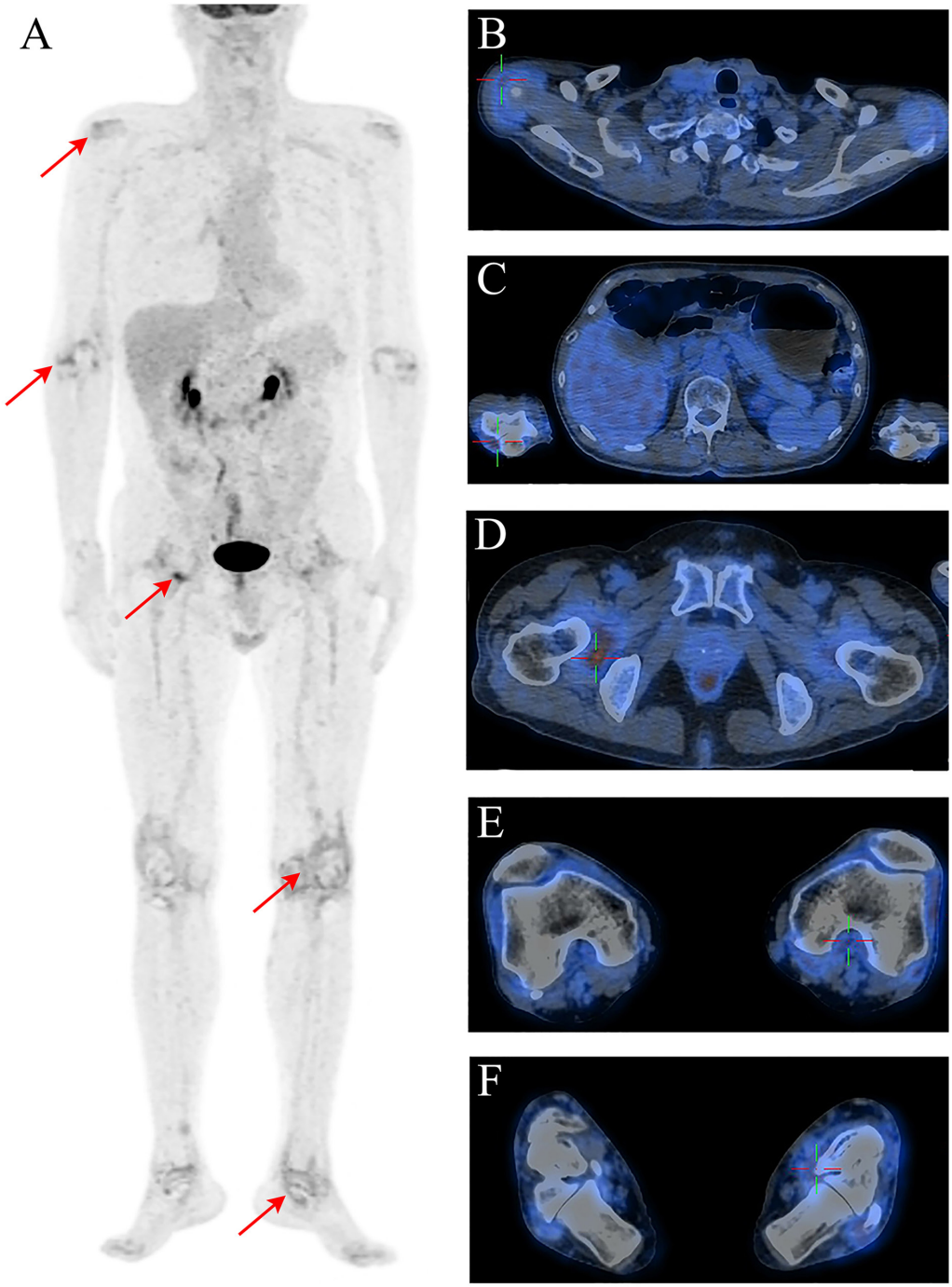

Figure 4. FDG PET/CT scan of case 3 and representative fused PET/CT images showing polyarticular and periarticular FDG uptake, consistent with immune checkpoint inhibitor-induced inflammatory arthritis. (A) Whole-body musculoskeletal FDG uptake imaging. (B) Bilateral shoulder joints and periarticular soft tissues. (C) Bilateral elbow joints. (D) Bilateral hip joints. (E) Bilateral knees and surrounding soft tissues, depicting a small amount of joint effusion within the knee cavities. (F) Bilateral ankle joints and periarticular soft tissues, showing swelling. In panel A, the red arrows indicate representative sites of abnormal periarticular FDG uptake. In panels B-F, the crosses indicate the representative joints/regions shown on the corresponding fused PET/CT images. FDG, 2-deoxy-2-[^{18}F]fluoro-D-glucose; PET/CT, positron emission tomography-computed tomography.

and often present as a delayed-onset condition that may persist even after discontinuation of ICI therapy (15-18). In the present case series, two clinically important patterns of ICI-IA were highlighted that warrant heightened clinical attention: i) IA presenting after discontinuation of ICI therapy; and ii) recurrent IA following ICI rechallenge. Although these patterns have been previously described, they remain under-recognized in current clinical practice and the existing literature, and may influence management decisions and patient counseling. Therefore, sustained long-term vigilance is required, even after immunotherapy has been discontinued.

Evidence indicates that the type of ICI therapy may influence both the clinical presentation and persistence of ICI-IA (19,20). Combined CTLA-4 and PD-1 inhibition is more commonly associated with chronic inflammation involving large joints, particularly the knees, whereas PD-1/PD-L1 inhibitor monotherapy tends to affect small joints such as the wrists, metacarpophalangeal joints and proximal interphalangeal

Table I. Clinical characteristics and management of 3 cases with ICI-IA.

Feature	Case 1	Case 2		Case 3
		First onset	Recurrence	
Age, years	68	66	66	66
Sex	Female	Female	Female	Male
Cancer type	Metastatic bladder cancer	Advanced cervical cancer	Advanced cervical cancer	Advanced lung adenocarcinoma
ICI regimen	Tislelizumab (200 mg, day 1, every 21 days) + gemcitabine (1.8 g, days 1 and 8, every 21 days) + nedaplatin (50 mg, days 1-3, every 21 days)	Tislelizumab (100 mg, day 1, every 21 days) + anlotinib (8 mg, days 1-14, every 21 days)	Rechallenge with tislelizumab (100 mg, day 1, every 21 days) + anlotinib (8 mg, days 1-14, every 21 days)	Sintilimab (200 mg, day 1, every 21 days) + pemetrexed disodium (0.8 g, day 1, every 21 days) + nedaplatin (60 mg on day 1 and 70 mg on day 2, every 21 days), followed by maintenance sintilimab (200 mg, day 1, every 21 days) + bevacizumab (500 mg, day 1, every 21 days) from December 2020.
Time to IA onset	4 months after ICI discontinuation	13.3 months after ICI initiation	30.2 months after ICI initiation	11.2 months after ICI initiation
Joints involved	Bilateral shoulders, wrists, knees and ankles	Polyarticular joints of both upper and lower limbs	Left ankle, right knee, bilateral sacroiliac joints, left fingers	Bilateral shoulders, elbows, hips, knees and ankles
Laboratory findings	Serum CRP, 64.1 mg/l; serum IL-6, 57.73 pg/ml; RF/anti-CCP, negative	Serum IL-6, 404.84 pg/ml; Serum IL-10, 11.16 pg/ml	Serum IL-6, 67.41 pg/ml	RF, CRP, anti-CCP and ANA within normal ranges
Key imaging findings	Bone scintigraphy: Symmetric increased uptake in bilateral shoulders, wrists, knees and ankles	Bone scintigraphy: Increased uptake in the right fourth rib, right knee and bilateral feet	Bone scintigraphy: Diffuse polyarticular uptake, right hip perilesional uptake with central photopenia	MRI: Tenosynovitis, bursitis, synovial enhancement; PET/CT: Symmetric periarticular FDG uptake
Management	Methylprednisolone (40 mg qd iv drip) followed by oral tapering over 48 days	Methylprednisolone (30 mg qd iv drip) followed by oral tapering over 40 days; ICI resumed on day 10	Methylprednisolone (40 mg qd iv drip) followed by oral tapering over 132 days, ICI resumed on day 64	Methylprednisolone (40 mg qd iv drip) followed by oral tapering to maintenance dose (4 mg qd); anticancer treatment resumed on day 38
Outcome	Complete resolution; no recurrence through last follow-up in May 2025	Symptoms controlled; ICI successfully resumed according to the original regimen	Controlled after compliance correction; no further recurrence through last follow-up in December 2025	Complete resolution; no recurrence through last follow-up in July 2025
Disease pattern	Delayed-onset ICI-IA after treatment discontinuation	Classic ICI-IA during active treatment	Recurrent ICI-IA upon ICI rechallenge	Classic ICI-IA during active treatment

ICI, immune checkpoint inhibitor; IA, inflammatory arthritis; CRP, C-reactive protein; IL, interleukin; RF, rheumatoid factor; anti-CCP, anti-cyclic citrullinated peptide; ANA, antinuclear antibody; PET/CT, positron emission tomography-computed tomography; FDG, 2-deoxy-2-[^{18}F]fluoro-D-glucose; MRI, magnetic resonance imaging.

joints (20). Importantly, ICI-IA may persist after ICI discontinuation. Longer ICI exposure, combined CTLA-4/PD-1 blockade therapy and multiple concomitant irAEs have all been associated with more persistent arthritis after ICI discontinuation (18). In addition, arthritis symptoms tend to be more persistent in patients achieving a complete response or PR compared with those with SD or progressive disease (18). Pre-existing osteoarthritis (OA) has been recognized as an independent risk factor for ICI-IA, alongside higher body mass index and smoking (21). In a cohort of ICI-treated patients, OA was markedly more prevalent in those who developed ICI-IA compared with patients experiencing non-arthritic irAEs or no irAEs, indicating that OA may serve as a clinically relevant predictor and support baseline risk stratification before ICI therapy. In addition, higher serum levels of vascular endothelial growth factor A (VEGF-A) and tumor necrosis factor α (TNF-α) have been reported in patients with ICI-IA compared with ICI-treated patients who did not develop IA (22). These elevations are associated with more severe arthritis, persistent disease activity and an increased need for systemic corticosteroids or disease-modifying antirheumatic drugs (DMARDs), independent of cancer type or ICI regimen. Consequently, VEGF-A and TNF-α show promise as prognostic biomarkers, and may help guide precision medicine-oriented targeted interventions, including anti-TNF or anti-VEGF therapies, in selected patients.

The pathogenesis of ICI-IA involves immune system activation, the participation of specific immune cell subsets and the formation of an inflammatory micro-environment. It is generally accepted that ICIs relieve T-cell inhibition by blocking immune checkpoint pathways such as PD-1/PD-L1, thereby enhancing antitumor immune responses. However, this may also enable autoreactive T cells to attack joint tissues (23). A previous study has identified a cytotoxic $CD38^{high}/CD127^{-}/CD8^{+}$ T-cell subset in the synovial fluid and peripheral blood of patients with ICI-IA, which expresses high levels of effector molecules, such as perforin and granzyme B, exhibits proliferative activity and can contribute directly to arthritic damage (24). Upon antigenic stimulation, exhausted $CD8^{+}$ T cells in the synovial fluid lose their regulatory function, releasing pro-inflammatory cytokines, such as interferon-γ and TNF-α. These cytokines act synergistically with IL-1β^{high} macrophages to promote synovitis and cartilage destruction (24,25). Additionally, the expansion of $CD21^{low}$ B cells, a subset associated with enhanced autoreactivity and antigen presentation, in the circulation has been linked to a higher risk of severe irAEs, particularly after combined CTLA-4 and PD-1 blockade, whereas such changes were not significant with anti-PD-1 monotherapy in the reported cohort (26,27). More specifically, elevated levels of transitional $CD19^{+}/CD10^{+}/CD24^{high}/CD38^{high}$ B cells have been observed in patients who develop ICI-IA compared with ICI-treated patients who did not develop arthritis. Notably, this increase can precede clinical symptom onset, suggesting its potential as an early predictive biomarker for arthritis development (28). Together, these specific cytotoxic T-cell and atypical B-cell signatures delineate the immune-driven pathophysiology of ICI-IA, while also highlighting promising options for risk stratification and precise future interventions aimed at these aberrant pathways.

Currently, no unified diagnostic criteria for ICI-IA have been established. In clinical practice, diagnosis relies on a comprehensive assessment integrating symptom characteristics, treatment history, laboratory findings and imaging results, while excluding alternative causes such as pre-existing rheumatic diseases or bone metastases. Existing frameworks proposed by Naidoo *et al* (29) and Choi and Lee (30), along with grading systems from the CTCAE version 5.0 (9) and international oncology guidelines [European Society for Medical Oncology (ESMO) and American Society of Clinical Oncology (ASCO)] (31,32), provide a practical reference for clinical evaluation and severity assessment. Furthermore, for high-risk patients (such as those with a history of autoimmune diseases), a comprehensive baseline joint function assessment should be conducted, and joint symptoms should be closely monitored throughout the treatment process to enable early detection and intervention (4). For patients suspected of having myositis, assessing muscle weakness or myocarditis symptoms is critical, as these conditions often co-occur with other irAEs (33,34).

In the present cases, the diagnosis was primarily based on the following features: i) A clear temporal association between ICI therapy and the onset of arthritic symptoms; ii) physical examination revealing a characteristic pattern of joint involvement without overlying skin erythema or ulceration; iii) laboratory tests ruling out rheumatic diseases; iv) imaging findings showing abnormal joint metabolic activity; and v) a favorable response to corticosteroid therapy. In case 2, the diagnosis of pre-existing RA could not be definitively verified. Although the patient reported a prior history of RA, detailed medical records were unavailable and they declined further rheumatologic evaluation, including MRI/ultrasound imaging and RA-related serological testing (RF and anti-CCP); therefore, diagnostic uncertainty regarding the presence of existing RA or an underlying autoimmune background must be acknowledged. Despite this limitation, several features favor ICI-IA over a flare-up of conventional RA: i) The patient had been asymptomatic and untreated for several years before ICI initiation, consistent with stable remission if RA had existed; ii) arthritis onset showed a clear temporal association with ICI exposure, whereas RA has no established causal relationship with immune checkpoint blockade; iii) the distribution of joint involvement, including the ankle, knee, lumbar spine and sacroiliac joints, does not conform to the typical pattern of RA, which predominantly affects symmetric small joints, but is more compatible with reported ICI-IA phenotypes (35); iv) arthritis showed a rapid and marked response to systemic corticosteroids, and the prolonged treatment course during the second episode was largely attributable to poor medication adherence rather than steroid refractoriness, whereas active RA typically requires sustained DMARD therapy for adequate disease control; v) objective serological evidence supporting RA, such as RF or anti-CCP positivity, was lacking; and vi) markedly elevated inflammatory cytokines, particularly IL-6 and IL-10, are consistent with previously described irAEs (36). Taken together, although underlying RA cannot be entirely excluded, the clinical course, joint distribution, temporal relationship to immunotherapy, treatment response and cytokine profile collectively support the diagnosis of ICI-IA in this case.

In case 3, MRI revealed early inflammatory changes (tenosynovitis, bursitis and synovial enhancement) with superior soft tissue resolution, while PET/CT demonstrated systemic polyarticular involvement. The PET/CT pattern of large joint FDG uptake with periarticular inflammation and shoulder-hip girdle involvement resembled IA rather than the typical small joint pattern of RA, supporting ICI-IA diagnosis (37-41). This multimodal approach aligns with the literature, which shows that MRI detects early ICI-IA changes before radiographic abnormalities, thereby guiding therapeutic decisions (11). These cases emphasize the critical role of comprehensive evaluation, multimodal imaging and differential diagnosis in ICI-IA recognition. Notably, data on ultrasound or MRI examinations were lacking in cases 1 and 2. This was primarily due to patients prioritizing cancer management over joint symptoms, refusing to invest time and financial resources into further arthritis diagnostic evaluations. This also reflects a common reality among patients with advanced malignant tumors, who often focus on managing life-threatening diseases while underestimating the importance of immune-related musculoskeletal complications.

According to current international guidelines, including those from the National Comprehensive Cancer Network, ASCO, ESMO, Society for Immunotherapy of Cancer and European Alliance of Associations for Rheumatology, corticosteroids remain the first-line treatment for patients with grade ≥2 ICI-IA (31,32,42-44). Treatment intensity is guided by symptom severity, with escalation to conventional synthetic DMARDs or biologic agents reserved for patients with corticosteroid-refractory or recurrent disease. In the present case series, all patients achieved meaningful symptom control with systemic corticosteroid therapy, although treatment duration and tapering strategies varied. Notably, case 2 required prolonged corticosteroid exposure following arthritis recurrence after ICI rechallenge, highlighting the importance of individualized treatment planning and close follow-up rather than rigid adherence to standardized dosing algorithms.

For patients with severe symptoms (grade ≥3) who show no improvement after 2 weeks of corticosteroid therapy, early use of DMARDs or biologics should be considered. Given that traditional synthetic DMARDs (such as methotrexate) have been demonstrated to be effective and well-tolerated, they are often the first-line treatment. For example, studies have shown that methotrexate can effectively control ICI-IA with minimal impact on tumor control (45,46). When additional treatment is required, biologics should be considered. IL-6 receptor antagonists (such as tocilizumab and sarilumab) can rapidly alleviate IA (47,48). Not only does tocilizumab treat ICI-IA effectively, but it may also serve as a secondary prophylactic agent, notably reducing the risk of recurrence and prolonging the duration of ICI rechallenge (47). TNF-α inhibitors can also quickly improve arthritis symptoms, but it has been suggested that they may accelerate cancer progression (46); therefore, caution is advised when administering TNF-α inhibitors. Ma *et al* (49) reported that treatment with secukinumab, an anti-IL-17A inhibitor, effectively managed ICI-IA in two patients with melanoma without leading to tumor progression.

Emerging treatment strategies for ICI-IA include targeted small-molecule drugs and advanced delivery systems. Janus kinase inhibitors (such as tofacitinib) have demonstrated good efficacy in severe corticosteroid-resistant irAEs (50). In the largest multicenter observational study to date, clinical remission rates were 54.5% in life-threatening irAE cases, 96.7% in steroid-resistant cases and 100% in steroid-taper-failure cases, with a median overall survival of 16.1 months from ICI initiation, suggesting no obvious short-term compromise in antitumor outcomes (50). More specifically for articular disease, tofacitinib induced rapid and sustained remission in a reported case of ICI-IA (51). Nevertheless, as the multicenter data were dominated by myocarditis, myositis and hepatitis rather than arthritis, and the arthritis-specific evidence is currently limited to case reports, the role of JAK inhibitors in ICI-IA remains investigational and warrants further validation. Bruton's tyrosine kinase (BTK) inhibitors can regulate B-cell activation and reduce the secretion of cytokines such as IL-1β, IL-6 and IL-17. Through precise immune modulation, BTK inhibitors may exert both anti-inflammatory and antitumor effects, although their application in ICI-IA remains in the experimental stage (52). Additionally, engineered extracellular vesicles, particularly exosomes, are being studied as novel anti-inflammatory drug delivery systems, enabling targeted, efficient and low-immunogenicity interventions (53). Although these strategies hold promise, further clinical validation is required before they can be routinely incorporated into ICI-IA management.

Clinical observations suggest a potential link between the development of rheumatic irAEs, including ICI-IA, and enhanced antitumor immune responses. In a prospective cohort, patients with rheumatic irAEs had a higher tumour response rate than patients without irAEs (85.7 vs. 35.3%) (54). Similarly, in another single-centre analysis, the tumour response rate was 94.4% in patients with rheumatic irAEs, compared with 43.5% in patients without rheumatic irAEs, and the median progression-free survival was 20 months in the rheumatic irAE cohort vs. 2 months in patients without irAEs (55). In a longitudinal ICI-IA cohort, 53.3% of patients continued to have active arthritis at the most recent follow-up, and persistent IA was associated with a trend toward better tumour response, while immunosuppressive treatment did not appear to adversely affect tumour outcomes (18,56). These findings are consistent with the treatment responses and survival outcomes observed in the present cases.

International guidelines recommend that most irAEs can be managed by temporarily discontinuing ICI therapy ± corticosteroid treatment, except for severe or life-threatening irAEs requiring permanent discontinuation (57). Clinical data indicate that ICI rechallenge following adjustments to the treatment regimen, such as changing from combination to monotherapy, generally has a favorable safety profile and remains effective (58). Among patients experiencing ICI-IA for the first time, spontaneous symptom resolution during continued ICI treatment is rare (~16%), and most patients require temporary discontinuation until symptoms resolve before rechallenging with ICI therapy (56). However, a study has shown that ~52% of patients experienced arthritis recurrence upon rechallenge, often with a severity similar to that of the initial episode, with the median time to recurrence being only 1 month (59). In the present case series, the patient in case 2 maintained PR after two ICI treatment interruptions, confirming that short-term discontinuation does not compromise long-term antitumor

efficacy. However, close monitoring for joint symptom recurrence is essential.

In conclusion, through the analysis of 3 cases and a literature review, the present report highlighted key clinical patterns of ICI-IA, particularly delayed onset after therapy cessation and recurrence upon rechallenge, and discussed their diagnostic and therapeutic implications. The current study found that ICI-IA is characterized by typical symptoms, delayed onset and a prolonged disease course, while its clinical manifestations are influenced by treatment regimens and host-related factors. A comprehensive diagnosis approach is required, incorporating treatment history, exclusionary laboratory tests and multimodal imaging. The response to corticosteroids provides notable diagnostic value. Graded management strategies can effectively control ICI-IA symptoms; however, multidisciplinary team consultation and long-term follow-up are essential for patients with recurrent, persistent or complex symptoms. Moreover, the pathogenesis of ICI-IA may be linked to enhanced antitumor immunity, and appropriate ICI rechallenge is safe and feasible in most patients. Nevertheless, the limitations of the present study should be acknowledged. Firstly, the findings are based on a small number of cases from a single center. Secondly, imaging examinations, such as ultrasound or MRI, were not performed on all patients, which may limit the generalizability and comprehensiveness of the evaluation. Additionally, the retrospective nature of the study and the limited availability of certain laboratory and serological data, such as serial cytokine measurements, complete autoantibody testing including RF, anti-CCP and ANA, prevented a more in-depth exploration of the underlying immunological mechanisms. Further multicenter prospective studies involving larger cohorts are required to clarify the clinical spectrum, pathogenesis and optimal management strategies of ICI-IA more effectively.

Although ICI-IA is increasingly recognized in clinical practice, future efforts should focus on elucidating its immunological mechanisms and validating predictive biomarkers, such as specific immune-cell subsets, VEGF-A and TNF-α, to facilitate early identification of high-risk populations and guide preventive strategies. Simultaneously, the establishment of prospective multicenter clinical trials is essential to delineate the full disease spectrum and generate robust real-world evidence, which will underpin the development of standardized diagnostic and therapeutic guidelines. These advances are expected to optimize long-term management, refine ICI rechallenge protocols and strengthen multidisciplinary care. Collectively, such initiatives will enhance the understanding of ICI-IA and ultimately support the dual goals of maximizing antitumor efficacy while preserving patient quality of life.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YWa made substantial contributions to the acquisition, analysis and interpretation of data, and wrote the initial draft of the manuscript and subsequent revised versions. YWe and JX participated in the follow-up examination of the patients and the collection of clinical material. HF, FW, DY and YG treated the patients. QL and YY provided guidance on patient management, participated in the manuscript preparation, assisted with data analysis and interpretation, and revised the manuscript for important intellectual content. DY and QL confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patients for the publication of the present case series and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

References

1. Zhang Y and Zhang Z: The history and advances in cancer immunotherapy: Understanding the characteristics of tumor-infiltrating immune cells and their therapeutic implications. Cell Mol Immunol 17: 807-821, 2020.
2. Singh S, Hassan D, Aldawsari HM, Molugulu N, Shukla R and Kesharwani P: Immune checkpoint inhibitors: A promising anticancer therapy. Drug Discov Today 25: 223-229, 2020.
3. Yin Q, Wu L, Han L, Zheng X, Tong R, Li L, Bai L and Bian Y: Immune-related adverse events of immune checkpoint inhibitors: A review. Front Immunol 14: 1167975, 2023.
4. Martins F, Sofiya L, Sykiotis GP, Lamine F, Maillard M, Fraga M, Shabafrouz K, Ribi C, Cairoli A and Guex-Crosier Y: Adverse effects of Immune-checkpoint inhibitors: Epidemiology, management and surveillance. Nat Rev Clin Oncol 16: 563-580, 2019.
5. Poto R, Troiani T, Criscuolo G, Marone G, Ciardiello F, Tocchetti CG and Varricchi G: Holistic approach to immune checkpoint inhibitor-related adverse events. Front Immunol 13: 804597, 2022.
6. Bass AR, Xie FL, Jannat-Khah D, Ghosh N, Chan KK, Saxena A and Curtis JR: Incidence of checkpoint inhibitor-associated inflammatory arthritis, immunomodulation and mortality in cancer patients on immunotherapy: A retrospective cohort study. Rheumatology 64: 1637-1642, 2024.
7. Cappelli LC, Gutierrez AK, Bingham CO III and Shah AA: Rheumatic and musculoskeletal immune-related adverse events due to immune checkpoint inhibitors: A systematic review of the literature. Arthritis Care Res 69: 1751-1763, 2017.
8. Xie RX, Xue YB, Ci XY and Zhang MJ: Immune checkpoint inhibitor induced colitis and arthritis: A case report. Medicine 102: e36334, 2023.
9. US Department of Health and Human Services: Common terminology criteria for adverse events (CTCAE) version 5.0, 2017.

10. Zheng M, Zhou Y, Zhou J and Jiang Y: 564P Efficacy and safety of tislelizumab plus anlotinib in the treatment of cervical cancer resistant to standard therapy: A prospective, single-arm, open labelled phase II clinical trial. Ann Oncol 33 (Suppl): S806, 2022.
11. Subedi A, Williams SG, Yao L, Maharjan S, Strauss J, Sharon E, Thomas A, Apolo AB, Gourh P, Hasni SA, *et al*: Use of magnetic resonance imaging to identify immune checkpoint inhibitor-induced inflammatory arthritis. JAMA Netw Open 3: e200032, 2020.
12. Abdel-Wahab N and Suarez-Almazor ME: Frequency and distribution of various rheumatic disorders associated with checkpoint inhibitor therapy. Rheumatology 58 (Suppl 7): vii40-vii48, 2019.
13. Melissaropoulos K, Klavdianou K, Filippopoulou A, Kalofonou F, Kalofonos H and Daoussis D: Rheumatic manifestations in patients treated with immune checkpoint inhibitors. Int J Mol Sci 21: 3389, 2020.
14. Kostine M, Truchetet ME and Schaeverbeke T: Clinical characteristics of rheumatic syndromes associated with checkpoint inhibitors therapy. Rheumatology (Oxford) 58 (Suppl 7): vii68-vii74, 2019.
15. Smith MH and Bass AR: Arthritis after cancer immunotherapy: Symptom duration and treatment response. Arthritis Care Res 71: 362-366, 2019.
16. Richter MD, Crowson C, Kottschade LA, Finnes HD, Markovic SN and Thanarajasingam U: Rheumatic syndromes associated with immune checkpoint inhibitors: A single-center cohort of sixty-one patients. Arthritis Rheumatol 71: 468-475, 2019.
17. Johnson DB, Nebhan CA, Moslehi JJ and Balko JM: Immune-checkpoint inhibitors: Long-term implications of toxicity. Nat Rev Clin Oncol 19: 254-267, 2022.
18. Braaten TJ, Brahmer JR, Forde PM, Le D, Lipson EJ, Naidoo J, Schollenberger M, Zheng L, Bingham CO III and Shah AA: Immune checkpoint inhibitor-induced inflammatory arthritis persists after immunotherapy cessation. Ann Rheum Dis 79: 332-338, 2020.
19. Gómez-Puerta JA, Lobo-Prat D, Perez-García C, Ponce A, Frade-Sosa B, Millán Arciniegas AM, Ojeda F, Ruiz-Esquide V and Corominas H: Clinical patterns and follow-up of inflammatory arthritis and other immune-related adverse events induced by checkpoint inhibitors. A multicenter study. Front Med (Lausanne) 9: 888377, 2022.
20. Cappelli LC, Brahmer JR, Forde PM, Le DT, Lipson EJ, Naidoo J, Zheng L, Bingham CO III and Shah AA: Clinical presentation of immune checkpoint inhibitor-induced inflammatory arthritis differs by immunotherapy regimen. Semin Arthritis Rheum 48: 553-557, 2018.
21. Paiola M, Portnoy DM, Hao LY, Bukhari S, Winchester RJ, Henick BS, Mor A and Gartshteyn Y: Osteoarthritis increases the risk of inflammatory arthritis due to immune checkpoint inhibitors associated with tissue-resident memory T cells. J Immunother Cancer 13: e010758, 2025.
22. Gray-Gaillard EF, Shah AA, Bingham CO III, Elisseeff JH, Murray J, Brahmer J, Forde P, Anagnostou V, Mammen J and Cappelli LC: Higher levels of VEGF-A and TNFα in patients with immune checkpoint inhibitor-induced inflammatory arthritis. Arthritis Res Ther 27: 74, 2025.
23. Chen M, Li H, Qu B and Huang X: The roles of T cells in immune checkpoint inhibitor-induced arthritis. Aging Dis 16: 2100-2119, 2024.
24. Wang RC, Singaraju A, Marks K, Shakib L, Dunlap G, Adejoorin I, Greisen SR, Chen L, Tirpack AK, Aude C, *et al*: Clonally expanded CD38hi cytotoxic CD8 T cells define the T cell infiltrate in checkpoint inhibitor-associated arthritis. Sci Immunol 8: eadd1591, 2023.
25. Zhou ZY, Zhou XX, Jiang X, Yang B, Lu X, Fei YY, Zhao LD, Chen H, Zhang L, Si XY, *et al*: Single-cell profiling identifies IL1Bhi macrophages associated with inflammation in PD-1 inhibitor-induced inflammatory arthritis. Nat Commun 15: 2107, 2024.
26. Reincke ME, Payne KJ, Harder I, Strohmeier V, Voll RE, Warnatz K and Keller B: The antigen presenting potential of CD21low B cells. Front Immunol 11: 535784, 2020.
27. Das R, Bar N, Ferreira M, Newman AM, Zhang L, Bailur JK, Bacchiocchi A, Kluger H, Wei W and Halaban R: Early B cell changes predict autoimmunity following combination immune checkpoint blockade. J Clin Invest 128: 715-720, 2018.
28. Gatto M, Bjursten S, Jonsson CA, Agelii ML, Jonell C, McGrath S, Lönnblom E, Sareila O, Holmdahl R and Rudin A: Early increase of circulating transitional B Cells and autoantibodies to joint-related proteins in patients with metastatic melanoma developing checkpoint inhibitor-induced inflammatory arthritis. Arthritis Rheumatol 75: 856-863, 2023.
29. Naidoo J, Cappelli LC, Forde PM, Marrone KA, Lipson EJ, Hammers HJ, Sharfman WH, Le DT, Baer AN and Shah AA: Inflammatory arthritis: A newly recognized adverse event of immune checkpoint blockade. Oncologist 22: 627-630, 2017.
30. Choi J and Lee SY: Clinical characteristics and treatment of immune-related adverse events of immune checkpoint inhibitors. Immune Netw 20: e9, 2020.
31. Haanen J, Obeid M, Spain L, Carbonnel F, Wang Y, Robert C, Lyon A, Wick W, Kostine M and Peters S: Management of toxicities from immunotherapy: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol 33: 1217-1238, 2022.
32. Schneider BJ, Naidoo J, Santomasso BD, Lacchetti C, Adkins S, Anadkat M, Atkins MB, Brassil KJ, Caterino JM and Chau I: Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: ASCO guideline update. J Clin Oncol 39: 4073-4126, 2021.
33. Matas-García A, Milisenda JC, Selva-O'Callaghan A, Prieto-González S, Padrosa J, Cabrera C, Reguart N, Castrejón N, Solé M and Ros J: Emerging PD-1 and PD-1L inhibitors-associated myopathy with a characteristic histopathological pattern. Autoimmun Rev 19: 102455, 2020.
34. Jeyakumar N, Etchegaray M, Henry J, Lelenwa L, Zhao B, Segura A and Buja LM: The terrible triad of checkpoint inhibition: A case report of myasthenia gravis, myocarditis, and myositis induced by cemiplimab in a patient with metastatic cutaneous squamous cell carcinoma. Case Reports Immunol 2020: 5126717, 2020.
35. Georgios I, Fani S, Dmitrios B, David L and Dimitrios D: Immune checkpoint inhibitor-induced inflammatory arthritis vs rheumatoid arthritis: A comparative review. Autoimmun Rev 25: 103943, 2025.
36. Kao CJ, Charmsaz S, Alden SL, Brancati M, Li HL, Balaji A, Munjal K, Howe K, Mitchell S and Leatherman J: Immune-related events in individuals with solid tumors on immunotherapy associate with Th17 and Th2 signatures. J Clin Invest 134: e176567, 2025.
37. Kwok TSH and Bell MJ: Immune checkpoint inhibitor-induced rheumatoid arthritis: Insights into an increasingly common aetiology of polyarthritis. BMJ Case Rep 12: e227995, 2019.
38. Gosangi B, McIntosh L, Keraliya A, Irugu DVK, Baheti A, Khandelwal A, Thomas R and Braschi-Amirfarzan M: Imaging features of toxicities associated with immune checkpoint inhibitors. Eur J Radiol Open 9: 100434, 2022.
39. Liu Y, Jaquith JM, Mccarthy-Fruin K, Zhu X, Zhou X, Li Y, Crowson C, Davis JM III, Thanarajasingam U and Zeng H: Immune checkpoint inhibitor-induced inflammatory arthritis: A novel clinical entity with striking similarities to seronegative rheumatoid arthritis. Clin Rheumatol 39: 3631-3637, 2020.
40. Ponce A, Frade-Sosa B, Sarmiento-Monroy JC, Sapena N, Ramírez J, Azuaga AB, Morlà R, Ruiz-Esquide V, Cañete JD and Sanmartí R: Imaging findings in patients with immune checkpoint inhibitor-induced arthritis. Diagnostics 12: 1961, 2022.
41. Karlsen W, Akily L, Mierzejewska M, Teodorczyk J, Bandura A, Zaucha R and Cytawa W: Is 18F-FDG-PET/CT an optimal imaging modality for detecting immune-related adverse events after immune-checkpoint inhibitor therapy? Cancers (Basel) 16: 1990, 2024.
42. Brahmer JR, Abu-Sbeih H, Ascierto PA, Brufsky J, Cappelli LC, Cortazar FB, Gerber DE, Hamad L, Hansen E and Johnson DB: Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immune checkpoint inhibitor-related adverse events. J Immunother Cancer 9: e002435, 2021.
43. Thompson JA, Schneider BJ, Brahmer J, Achufusi A, Armand P, Berkenstock MK, Bhatia S, Budde LE, Chokshi S and Davies M: Management of immunotherapy-related toxicities, version 1.2022, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 20: 387-405, 2022.
44. Kostine M, Finckh A, Bingham CO, Visser K, Leipe J, Schulze-Koops H, Choy EH, Benesova K, Radstake TR and Cope AP: EULAR points to consider for the diagnosis and management of rheumatic immune-related adverse events due to cancer immunotherapy with checkpoint inhibitors. Ann Rheum Dis 80: 36-48, 2021.

45. Hysa E, Casabella A, Iandolino N, Gotelli E, Genova C, Tanda ET, Pizzorni C, Smith V, Sulli A and Cutolo M: Clinical outcomes in cancer patients with immune checkpoint inhibitor-induced arthritis treated with methotrexate: A retrospective longitudinal monocentric pilot study. Clin Exp Rheumatol 43: 867-873, 2025.
46. Bass AR, Abdel-Wahab N, Reid PD, Sparks JA, Calabrese C, Jannat-Khah DP, Ghosh N, Rajesh D, Aude CA and Gedmintas L: Comparative safety and effectiveness of TNF inhibitors, IL6 inhibitors and methotrexate for the treatment of immune checkpoint inhibitor-associated arthritis. Ann Rheum Dis 82: 920-926, 2023.
47. Petit PF, Daoudlarian D, Latifyan S, Bouchaab H, Mederos N, Doms J, Abdelhamid K, Ferahta N, Mencarelli L and Joo V: Tocilizumab provides dual benefits in treating immune checkpoint inhibitor-associated arthritis and preventing relapse during ICI rechallenge: The TAPIR study. Ann Oncol 36: 43-53, 2025.
48. Abe K, Ishikawa Y, Fujiwara M, Yukawa H, Yanagihara T, Takei S, Arioka H and Kita Y: Immune checkpoint inhibitor-induced refractory polyarthritis rapidly improved by sarilumab and monitoring with joint ultrasonography: A case report. Medicine (Baltimore) 101: e28428, 2022.
49. Ma VT, Lao CD, Fecher LA and Schiopu E: Successful use of secukinumab in two melanoma patients with immune checkpoint inhibitor-induced inflammatory arthropathy. Immunotherapy 14: 593-598, 2022.
50. Liu Q, Liu M, Zou Z, Lin J, Zhang N, Zhao L, Zhou J, Zhou H, Zhou X and Jiao X: Tofacitinib for the treatment of immune-related adverse events in cancer immunotherapy: A multi-center observational study. J Transl Med 22: 803, 2024.
51. Murray K, Floudas A, Murray C, Fabre A, Crown J, Fearon U and Veale D: First use of tofacitinib to treat an immune checkpoint inhibitor-induced arthritis. BMJ Case Rep 14: e238851, 2021.
52. Berg MHH, Del Rincón SV and Miller WH: Potential therapies for immune-related adverse events associated with immune checkpoint inhibition: From monoclonal antibodies to kinase inhibition. J Immunother Cancer 10: e003551, 2022.
53. Ma X, Liu B, Fan L, Liu Y, Zhao Y, Ren T, Li Y and Li Y: Native and engineered exosomes for inflammatory disease. Nano Res 16: 6991-7006, 2023.
54. Kostine M, Rouxel L, Barnetche T, Veillon R, Martin F, Dutriaux C, Dousset L, Pham-Ledard A, Prey S and Beylot-Barry M: Rheumatic disorders associated with immune checkpoint inhibitors in patients with cancer-clinical aspects and relationship with tumour response: A single-centre prospective cohort study. Ann Rheum Dis 77: 393-398, 2018.
55. Verspohl SH, Holderried T, Behning C, Brossart P and Schäfer VS: Prevalence, therapy and tumour response in patients with rheumatic immune-related adverse events following immune checkpoint inhibitor therapy: A single-centre analysis. Ther Adv Musculoskelet Dis 13: 1759720X211006963, 2021.
56. Ladouceur A, Barnetche T, Prey S, Dutriaux C, Gerard É, Pham-Ledard A, Beylot-Barry M, Zysman M, Veillon R and Domblides C: Resolution of immune checkpoint inhibitors-induced inflammatory arthritis while maintaining active treatment with checkpoint inhibitors and after its discontinuation: An observational study. Joint Bone Spine 92: 105795, 2025.
57. Thompson JA, Schneider BJ, Brahmer J, Andrews S, Armand P, Bhatia S, Budde LE, Costa L, Davies M, Dunnington D, *et al*: NCCN guidelines insights: Management of immunotherapy-related toxicities, version 1.2020. J Natl Compr Canc Netw 18: 230-241, 2020.
58. Park R, Lopes L and Saeed A: Outcomes following immunotherapy re-challenge after immune-related adverse event: Systematic review and meta-analysis. Immunotherapy 12: 1183-1193, 2020.
59. Ladouceur A, Barnetche T, Mouterde G, Tison A, Bitoun S, Prey S, Dutriaux C, Gerard E, Pham-Ledard A, Beylot-Barry M, *et al*: Immune checkpoint inhibitor rechallenge in patients who previously experienced immune-related inflammatory arthritis: A multicentre observational study. RMD Open 9: e003795, 2023.