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Images in Rheumatology

Simulated Rheumatoid Arthritis Induced by Immune Checkpoint Inhibitor

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The patient is a female, 46 years old, diagnosed with primary liver cancer with lung metastasis 2 years ago and was treated with Camrelizumab immunotherapy combined with targeted therapy with lenvatinib. After 3 months of drug treatment, the patient developed polyarticular swelling and pain in both wrists and fingers and was not treated with antirheumatic therapy. The patient's cancer improved and stabilized, but her arthritis gradually worsened, and she developed multiple joint deformities and dysfunctions. Physical examination revealed ankylosis of the left wrist joint and flexion deformity of the knuckles of both hands with claw hands (Figure 1A and B). Laboratory tests showed: RF (–); anti-CCP (–); ANA (–), ENA (–). Musculoskeletal ultrasonography suggested: bone erosion of the left wrist joint with narrowing of the joint space (Figure 2A and B). Bilateral synovitis of the third and fourth proximal interphalangeal joints, contracture of the finger flexor tendons, and joint misalignment (Figure 2C and D). She was diagnosed with simulated rheumatoid arthritis induced by immune checkpoint inhibitor (ICI). After treatment with methylprednisolone (8 mg/d) combined with triptolide, the joint pain was relieved, but the joint deformity did not improve.

This patient was treated with a combination of Camrelizumab and lenvatinib. Lenvatinib is a tyrosine kinase receptor inhibitor that inhibits tumor angiogenesis and is commonly used in the treatment of hepatocellular carcinoma. Clinical studies in China suggest that lenvatinib caused approximately 15% of musculoskeletal adverse reactions, characterized by joint and muscle pain, with no arthritis observed. Camrelizumab, a type of humanized PD-1 monoclonal antibody developed in China for the treatment of advanced hepatocellular carcinoma, has completed a global multicenter Phase III clinical study (CARES-310) with positive results.[1] Furthermore, it has achieved good results in immunotherapy for lung and esophageal cancer. An adverse reaction rate of 20% was observed for arthralgia.[2] Tumor cells can upregulate the expression of immune checkpoint molecules such as PD-1/PD-L1, inducing organismal immune tolerance and tumor immune escape. Immune checkpoint inhibitors can block immunosuppressive pathways and activate T cells to generate anti-tumor immune responses. This led to the development of tumor immunotherapy, which has revolutionized the treatment of malignant tumors.[3] However, a rapid rise in the use of ICIs is associated with a new group of immune-related adverse events (irAEs) in almost any organ system. The IrAEs can mimic many types of rheumatic diseases, with arthritis being the most common (1%-43%).[4] It is distinguished from primary rheumatoid arthritis mainly by prominent tendon involvement, early onset of bone erosion, and negative rheumatoid antibodies. As in this case, the above features are met. The precise pathophysiology of ICI-mediated irAEs is currently unknown. It may be due to attacks on healthy tissue by autoreactive T cells, autoantibodies, and/or pro-inflammatory cytokines. Additionally, immunotherapy may increase the levels of pre-existing autoreactive antibodies. The IrAEs are managed on a graded basis according to the severity of the disease, with glucocorticoids combined with immunosuppressants available for grades II and III.[5] Combination therapies including ICIs administered in combination with chemotherapy or targeted agents have the potential to enhance efficacy, but the combination regimen is observed to have more severe irAEs than monotherapy. This case suggests that we need to be alert to the occurrence of irAEs during tumor immunotherapy, especially combination therapy, and manage them promptly to avoid irreversible organ damage or malformation.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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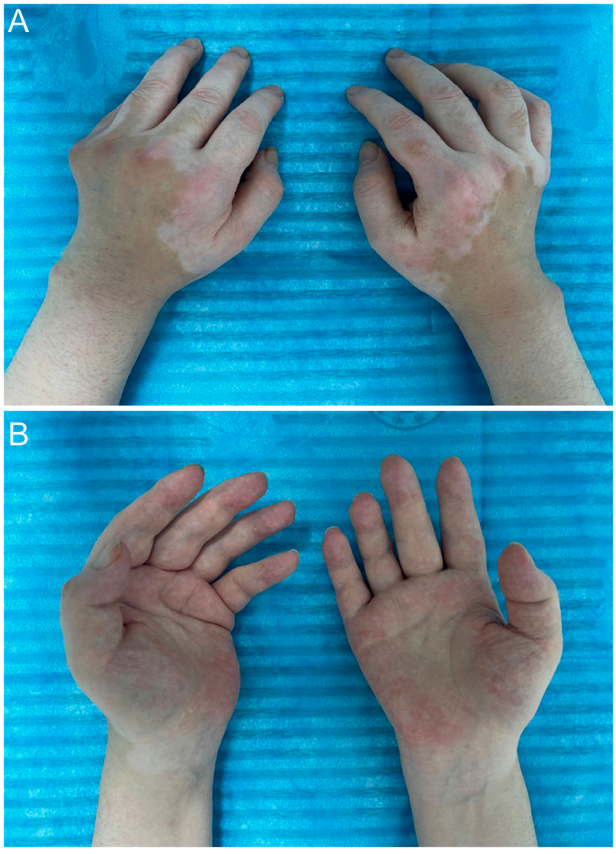

Figure 1. Joint deformity in immune checkpoint inhibitor–induced arthritis. (A): Flexion deformity of the metacarpophalangeal joints and interphalangeal joints of both hands (dorsal side of the hands). (B): Flexion deformity of the metacarpophalangeal joints and interphalangeal joints of both hands (palmar side of the hands).

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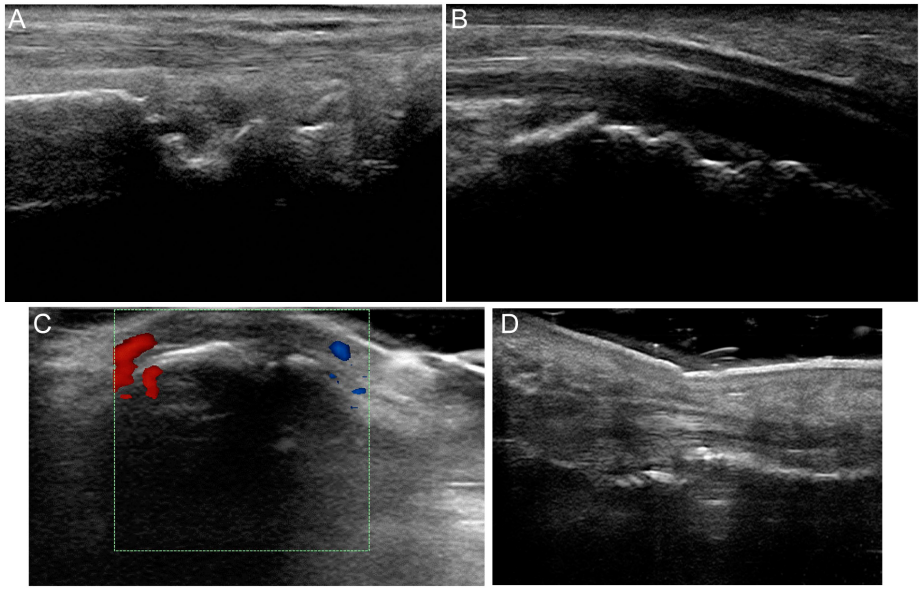

Figure 2. Arthritis revealed by ultrasonography. (A): Bone erosion of the left wrist joint shown by dorsal longitudinal scan. (B): Bone erosion of the left wrist joint shown by palmar longitudinal scan. (C): Synovitis of the left PIP4 joint shown by dorsal longitudinal scan. (D): Tendon contracture and joint misalignment of the left PIP4 joint shown by palmar longitudinal scan.