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LETTER

Safe use of tocilizumab in rheumatic patients with Kaposi's sarcoma

Dear Editor,

Viral reactivation is a frequent adverse event of immunosuppressive agents, that can be very severe in patients with a history of human herpes virus type 8 (HHV8)-related disease, including Kaposi's sarcoma (KS) and multicentric Castelman disease. We report two cases of rheumatic patients who developed or worsened classic KS during anti-TNF-α or steroid therapies and who were subsequently safely treated for their rheumatic conditions with tocilizumab, a monoclonal antibody directed against interleukin-6 receptor.

Patient 1: A 68-year-old man with rheumatoid arthritis developed purple nodules on his right sole 3 months after the initiation of infliximab at a dose of 3 mg/kg every 6 weeks. The patient consulted 6 months later because of the extension of lesions to both feet. A skin biopsy specimen showed the presence of spindle-shaped cells and positive human herpesvirus 8 (HHV8) staining, confirming the diagnosis of iatrogenic KS. The 18-FDG-PET showed multiple cutaneous lesions without lymph node or visceral involvement (Figure 1A). Infliximab was discontinued and switched to tocilizumab (8 mg/kg, monthly), leading to the remission of rheumatoid arthritis as well as the near complete regression of skin lesions, which remained stable after 2 years of treatment (Figure 1B).

Patient 2: An 83-year-old man with a history of paucilesional classic KS located to the inferior limbs presented with severe exacerbation of skin lesions associated with bilateral lymphedema (Figure 1C). The worsening of KS occurred one month after the initiation of prednisone at a dose of 1 mg/kg for giant cell arteritis (GCA). The patient received bleomycin during 3 months and steroids were rapidly tapered, allowing a significant reduction of KS lesions, but also resulting in severe GCA relapse. In order to limit the risk of KS recurrence, it was decided to maintain steroids at a low dose of 5 mg prednisone and to initiate tocilizumab at 8 mg/kg monthly as a steroid-sparing agent. This treatment regimen allowed a rapid remission of GCA, and was associated with the complete stability of the remaining KS lesions, persistent after 6 months of treatment (Figure 1D).

The management of auto-immune or auto-inflammatory diseases in patients with KS is very challenging because of the frequent occurrence of KS flare following the introduction of corticosteroids[1] or other immunosuppressive agents, especially anti-TNF-α agents.[2] In our two patients, we aimed to select a treatment that could be efficient on the rheumatic conditions without impacting KS. Among the available immunomodulatory treatments,

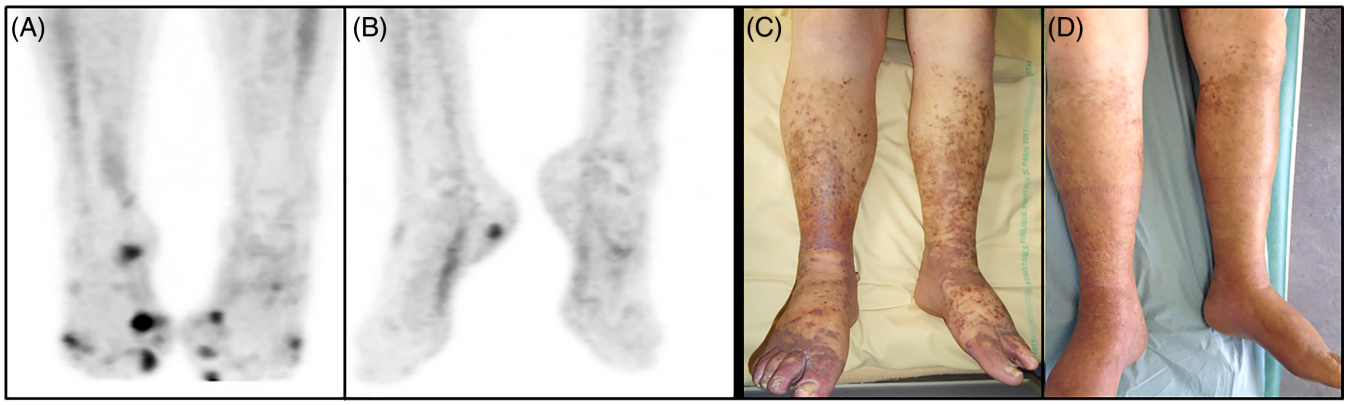

FIGURE 1 Patient 1 (A) 18-FDG-PET images centered on the feet showing intense focal uptake in KS lesions SUV max = 9.1 before TCZ initiation. (B) Near complete regression of KS lesions, persistent two years after TCZ initiation. Patient 2 (C) KS flare following the initiation of prednisone at a dose of 1 mg/kg/day. (D) Stability of the remaining KS lesions during TCZ treatment

tocilizumab has demonstrated efficacy in various inflammatory diseases[3] and is approved for the treatment of several rheumatic diseases including rheumatoid arthritis, systemic juvenile idiopathic arthritis and GCA. Our therapeutic choice was based on the fact that tocilizumab was less likely to worsen KS because it targets IL-6 which is strongly implicated in the pathogenesis of KS. Indeed, HHV8 induces the secretion of IL-6 which in turn enhances tumor cell proliferation in a positive paracrine feedback loop.[4] Moreover, IL-6 is considered a promising target for HHV8-related diseases, with recent reports of tocilizumab efficacy in treating multicentric Castleman's disease.[5]

To our knowledge there is only one case similar to ours reported in the literature, that concerns a man with rheumatoid arthritis who developed iatrogenic KS induced by methotrexate and prednisone, and was therefore switched to tocilizumab, enabling a complete remission of skin lesions.[6] In addition to the available data of the literature, our observations suggest that tocilizumab, when indicated, could be a safer alternative to steroids or anti-TNF-α agents for rheumatic patients with a history of KS.

AUTHOR CONTRIBUTIONS

Sarah Demouche and Florence Brunet-Possenti wrote the manuscript. Pierre-Antoine Juge, Pierre Charles and Vincent Descamps treated the patient. Khadija Benali performed the nuclear imaging. All authors contributed to revising the work and approved the final version.

CONFLICT OF INTEREST

The authors have no conflict of interest to report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Written informed consent was obtained from the patient for publication of their case.

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