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Eosinophilic fasciitis triggered by nivolumab: a remarkable efficacy of the mTOR inhibitor Sirolimus

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To the Editor:

We previously reported in the JTO the case of a 56-year-old woman with a metastatic pulmonary adenocarcinoma in complete remission under Nivolumab, who developed a typical eosinophilic fasciitis with a concomitant immune cholangitis, both found considered as adverse events of the immune checkpoint inhibitor (ICI)¹.

Nonetheless, no improvement was observed after ICI discontinuation, and a dramatic worsening was noticed despite a combination of corticosteroids and methotrexate therapy, as the fasciitis extended to the whole body-involving the face- and causing a diffuse and painful stiffness.

Because the immune disease was still worsening, 9 months after Nivolumab withdrawal, and considering the absence of malignancy relapse on CT scan reassessment, methotrexate was switched for Sirolimus, a m-TOR inhibitor which had also shown efficacy in a case of idiopathic eosinophilic fasciitis².

A remarkable improvement was rapidly obtained, and after 6 months of therapy, the patient regained a close to normal range of motion of her large joints, with a clear improvement in skin thickening involving the fingers and the dorsum of the hands, which were previously stuck in flexion contracture, as illustrated in Figure 1. So far, the cancer is still in remission, despite the absence of antineoplastic agents.

Data regarding the management of steroid refractory idiopathic eosinophilic fasciitis are scarce. Concerning the specific situation of ICI-immune-mediated fasciitis, no practical guidelines are available, and especially in the case of fasciitis that are refractory to ICI cessation and classical corticosteroids therapy. Although considered as a rare affection, ICI-immune mediated fasciitis should deserve special attention to explore new therapeutic approaches, as the treatments that have

proven efficient in other rheumatic toxicities, e.g. in arthritis, might not be broadened to this specific ICI adverse event even if their pathophysiology share some similarities^{3,4}.

Hence, this observation suggests a noticeable efficacy of Sirolimus in Nivolumab related fasciitis, raising the question that the mTOR pathway could be a promising target in the field of ICI-immune-mediated diseases.

Captions

Figure 1. Clinical evolution after 6 months of Sirolimus therapy:

A (upper left picture), B (lower left picture): Skin thickening with contracture of the fingers

C (upper right picture), D (lower right picture): After 6 months of Sirolimus, marked improved mobility of the joints

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