After what time interval are we justified to diagnose immune checkpoint inhibitor-mediated polymyalgia rheumatica?

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Dear Editor,

The number of cases of cancer patients diagnosed as having immune checkpoint inhibitor-mediated polymyalgia rheumatica (ICI-PMR) is increasing. However, the lack of a validated scale or algorithm is still a relevant methodological limit in diagnosing this nosologic entity. A recent systematic literature review well illustrates this diagnostic limitation. The authors found a wide onset range – from 1 day to 213 weeks (about 4 years) – after the initiation of ICI treatment [mean time of onset ± standard deviation (range): 15.40±10.54 weeks]. The diagnosis of ICI-PMR was never based on validated algorithms. Clinical judgment only was preferred. Several articles included in this review were published after 2021 (1). In 2021, a European Alliance of Associations for Rheumatology task force suggested the use of validated scales or algorithms (such as the so-called Naranjo scale) for assessing the causal link between immune-mediated adverse events and ICI therapy (2). The Naranjo scale is based on a list of 10 weighted questions and classifies the probability that an event is related to drug therapy as an adverse drug reaction. The higher the score (the range is from -4 to +13), the higher the probability that an adverse event is related to the drug itself. According to Naranjo's algorithm, the time between drug administration and event occurrence must be plausible for the specific event (3). The pathogenesis of ICI-PMR is still a matter of more or less fascinating speculations. It could be hypothesized that in ICI-PMR, the first trigger is represented by an antigenic stimulus (potentially activated by the primary or metastatic tumor mass) recognized by the antigen-presenting macrophages. Subsequent activation of T-lymphocytes induced by ICIs could favor their infiltration in the anatomical sites where PMR starts (4). Could the variability of these steps, if confirmed, justify a temporal unpredictability of ICI-PMR? As of today, what is the "plausible time interval" that can justify the diagnosis of ICI-PMR seems entirely subjective (5). The duration of this time interval should instead be defined, as it cannot be dilated *ad libitum*. Are we willing to accept the diagnosis of ICI-PMR when PMR manifestations occur after several months or even years of ICI treatment?

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