



Letter to the Editor

Letter to the editor: Comments on ‘A case of pembrolizumab-induced autoimmune haemolytic anaemia with polymyalgia rheumatica’



David F.L. Liew^{a,b,c,*}, Claire E. Owen^{a,c}, Russell R.C. Buchanan^{a,c}

^a Department of Rheumatology, Austin Health, Melbourne, Australia

^b Department of Clinical Pharmacology and Therapeutics, Austin Health, Melbourne, Australia

^c Department of Medicine, University of Melbourne, Melbourne, Australia

Received 30 October 2018; accepted 11 November 2018

Available online 28 February 2019

Dear Editor,

We read with interest the report by Robilliard et al. [1] of a pembrolizumab-induced immune-related adverse event (irAE). We applaud them for bringing attention to polymyalgia rheumatica (PMR) as a rheumatic irAE after immune checkpoint inhibitor therapy and would like to add some comments and conclusions.

One point of note was the suggested approach to corticosteroid therapy for PMR. Classical PMR reliably responds to an initial corticosteroid dose of prednisone 15–25 mg daily, much lower than that suggested by the authors [2,3]. Although some patients experiencing PMR-like irAEs do require higher doses for symptomatic relief, in our experience, the majority respond as a patient with classical PMR would [4]. Indeed, it remains unclear whether the disease which afflicts non-responders represents *de novo* PMR or a different disease entity entirely [5]. We, therefore, suggest that

trials of prednisolone 15 mg daily rather than a higher dose in the first instance represents the most appropriate course of action for a patient presenting with a PMR-like irAE.

A careful approach to prescribing moderate doses of prednisone is important in light of evidence suggesting corticosteroids may diminish the efficacy of PD-1 inhibitor therapy [6]. In the case described by the authors, the therapeutic impetus was for a higher corticosteroid dose due to autoimmune haemolytic anaemia. By contrast, patients with PMR-like irAEs alone might be able to avoid higher doses of corticosteroids and any consequent impairment of antitumour response. Rheumatic irAEs may also be mimicked by non-inflammatory phenomena where corticosteroid use is not necessarily justified [7]. It is, therefore, imperative that suspected adverse events are clearly elucidated, so as to ensure that appropriate management can be instituted.

In differentiating phenomena, one potentially useful modality is whole-body positron-emission tomography/computed tomography (PET/CT) [8], where classical PMR exhibits a distinctive pattern of abnormal 18F-fluorodeoxyglucose (18F-FDG) uptake [9,10]. PMR-like irAEs may accordingly be detected on PET/CT scanning being performed for oncological staging purposes [11].

DOI of original article: <https://doi.org/10.1016/j.ejca.2018.07.318>.

* Corresponding author: Department of Rheumatology, Austin Health, Level 1, North Wing, 300 Waterdale Road, Heidelberg West, Victoria, 3081, Australia. Fax: +61 3 94964012.

E-mail address: david.liew@austin.org.au (D.F.L. Liew).

<https://doi.org/10.1016/j.ejca.2018.11.034>

0959-8049/© 2019 Elsevier Ltd. All rights reserved.

We consequently wonder whether the patient described in the case may have possessed characteristic features of PMR on the simultaneously performed PET.

In the context of these points, we cannot help but emphasise the sentiment from the authors that the emergence of irAEs increases the importance of collaboration between oncologists and other medical specialists. The involvement of rheumatologists in the assessment of rheumatic irAEs may help guide both diagnosis and therapy [12]. We would encourage oncologists to turn to their rheumatological colleagues for this purpose and for rheumatologists to likewise make themselves readily available to their oncology peers.

Author contributions

David Liew developed the initial manuscript and finalised for submission. All authors substantially contributed to revising the article, critically regarding important intellectual content, approving the final version and agreeing to be accountable for the integrity of the work.

Conflict of interest statement

None declared.

References

- [1] Robilliard B, Arnaud E, Gastaud L, Broner J. A case of pembrolizumab-induced autoimmune haemolytic anaemia with polymyalgia rheumatica. *Eur J Cancer* 2018;103:281–3.
- [2] DeJaco C, Singh YP, Perel P, Hutchings A, Camellino D, Mackie S, et al. 2015 recommendations for the management of polymyalgia rheumatica: a European league against rheumatism/American College of Rheumatology collaborative initiative. *Ann Rheum Dis* 2015;74(10):1799–807.
- [3] González-Gay MA, Matteson EL, Castañeda S. Polymyalgia rheumatica. *Lancet* 2017;390(10103):1700–12.
- [4] Calabrese LH, Calabrese C, Cappelli LC. Rheumatic immune-related adverse events from cancer immunotherapy. *Nat Rev Rheumatol* 2018;14(10):569–79.
- [5] Calabrese C, Kirchner E, Calabrese L. Polymyalgia rheumatica-like syndrome from checkpoint inhibitor therapy: case series and systematic review of the literature [abstract]. *Arthritis Rheumatol* 2018;70(suppl 10).
- [6] Arbour KC, Mezquita L, Long N, Rizvi H, Auclin E, Ni A, et al. Impact of baseline steroids on efficacy of programmed cell death-1 and programmed death-ligand 1 blockade in patients with non-small-cell lung cancer. *J Clin Oncol* 2018;36(28):2872–8.
- [7] Albayda J, Bingham CO, Shah AA, Kelly RJ, Cappelli L. Metastatic joint involvement or inflammatory arthritis? A conundrum with immune checkpoint inhibitor-related adverse events. *Rheumatology (Oxford)* 2018 Apr 1;57(4):760–2.
- [8] Mekki A, Derclé L, Lichtenstein P, Marabelle A, Michot J-M, Lambotte O, et al. Detection of immune-related adverse events by medical imaging in patients treated with anti-programmed cell death 1. *Eur J Cancer* 2018;96:91–104.
- [9] Henckaerts L, Gheysens O, Vanderschueren S, Goffin K, Blockmans D. Use of 18F-fluorodeoxyglucose positron emission tomography in the diagnosis of polymyalgia rheumatica—a prospective study of 99 patients. *Rheumatology* 2018;57(11):1908–16.
- [10] Sondag M, Guillot X, Verhoeven F, Blagosklonov O, Prati C, Boulahdour H, et al. Utility of 18F-fluoro-dexoxyglucose positron emission tomography for the diagnosis of polymyalgia rheumatica: a controlled study. *Rheumatology* 2016;55(8):1452–7.
- [11] Wong ANM, McArthur GA, Hofman MS, Hicks RJ. The advantages and challenges of using FDG PET/CT for response assessment in melanoma in the era of targeted agents and immunotherapy. *Eur J Nucl Med Mol Imaging* 2017;44(1):67–77.
- [12] Schaefferbeke T, Kostine M. Response to: ‘Checkpoint inhibitors and arthritis: seeking balance between victories and defeats’ by Moura and Moura. *Ann Rheum Dis* 2018 Aug 12. <https://doi.org/10.1136/annrheumdis-2018-213906>. pii: annrheumdis-2018-213906. [Epub ahead of print].