

Interstitial Pneumonitis in a Patient with Occult Sarcoidosis Treated with Pembrolizumab for Advanced Melanoma

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Abstract

We report on a case of a 68-year-old man with metastatic melanoma presenting with interstitial pneumonitis following initiation of pembrolizumab, in the setting of occult sarcoidosis. There have been no previous reports on pembrolizumab inducing a flare of sarcoidosis. This patient was managed with high dose steroids with improvement in his respiratory symptoms. The use of immunotherapy in the management of various solid tumours is increasing and clinicians from different specialities need to be aware of the potential toxicities associated with this class of drugs that can affect multiple organs.

Keywords: Pembrolizumab; Immunotherapy; Adverse event; Pneumonitis; Sarcoidosis

Key Message

This case highlights the prompt recognition and management of immune-related adverse events associated with immune checkpoint inhibitors used in the management of solid tumours.

Case Report

A 68-year-old man was started on pembrolizumab for the management of metastatic melanoma. No BRAF mutation was identified on tumour mutational analysis but he was found to have rare c-KIT mutations (exon 11 mutation c.1733A>G [Y578C] and exon 17 c.2447A>T [D816V]). Computed tomography (CT) staging one-month prior had found hypermetabolic skin lesions in the torso, ground glass changes in lung fields with mediastinum and hilar lymphadenopathy, in keeping with stage II sarcoidosis (Figure 1a). He did not have any previous diagnosis of sarcoidosis.



Figure 1a: Initial staging CT chest indicating nodular and ground glass opacities at baseline.

One week after the first dose, he presented to hospital with a dry cough, worsening dyspnoea over the last week and oxygen desaturation to 84%. The patient was afebrile, inflammatory markers were not raised and respiratory serology was unremarkable. A CT chest done during this admission (Figure 1b) showed an interstitial pattern of lung disease characterised by extensive subpleural reticular changes, most marked at lung bases and diffuse widespread centrilobular nodules. When compared to the baseline CT scan (Figure 1a), there was increased nodular opacities and worsening of the pre-existing ground-glass opacities in the lower lobes bilaterally. Bronchoscopy identified endobronchial melanoma metastases that were cauterised. Transbronchial biopsy was attempted that did not confirm sarcoidosis or melanoma but contained multiple reactive cells. Serum ACE levels were normal.



Figure 1b: CT chest at presentation showing subpleural reticular changes.

The patient subsequently received three doses of intravenous methylprednisolone and six-week prednisolone oral taper, with near complete resolution of his symptoms and improvement of radiological findings on CT chest (Figure 1c). He subsequently received two further cycles of pembrolizumab with low dose maintenance steroid cover. However he continued to have moderate dyspnoea and developed multiple new cutaneous metastases consistent with disease

progression. He declined further treatment and pursued alternative therapy.

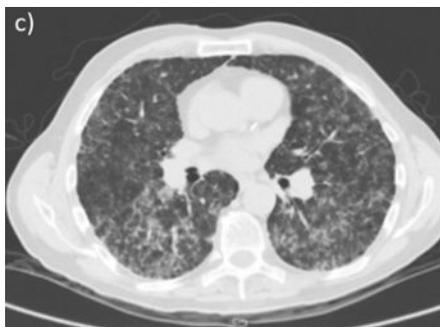


Figure 1c: CT chest following course of intravenous and six week oral corticosteroid taper showing improvement to interstitial disease.

Discussion

Given the clinical picture and radiological findings, it is likely that our patient had interstitial pneumonitis triggered by pembrolizumab therapy in the setting of occult sarcoidosis. Alternate diagnosis that should also be considered includes progression of disease or interstitial pneumonitis due to pembrolizumab, as this is a known side effect of this drug. However given there were radiological changes on pre-treatment CT chest, it is highly likely he experienced exacerbation of his underlying occult autoimmune condition.

Prompt initiation of steroids led to improvement of the patient's symptoms. This highlights the need to educate general practitioners and junior doctors in emergency department about the toxicities associated with this class of drugs as any delay in initiation of treatment can lead to serious patient morbidity and mortality. We were also faced with the challenging issue of either continuing the treatment risking sarcoidosis flare or treatment cessation leading to disease

progression after the first cycle. Following discussion with the patient, the decision was made to continue immunotherapy with oral corticosteroid cover.

This patient also had rare c-KIT mutations. There is no data to support the use of c-KIT inhibitors like imatinib or immunotherapy in the management of these rare mutations. Baseline bloods samples were taken for circulating tumour cells and circulating tumour DNA for PDL1 expression to evaluate its predictive value but follow up samples could not be taken.

Traditionally patients with pre-existing autoimmune conditions have been excluded from clinical trials of immunotherapy. Cousin et al. [1] reported on the first reported case of pulmonary sarcoidosis induced by pembrolizumab in a patient with uterine leiomyosarcoma. However as discussed by Paydas [2] in her letter to the editor, the more appropriate terminology may be post-immunotherapy granulomatous reaction. To date, there have been no published reports of pembrolizumab use in the setting of pre-existing sarcoidosis. This case highlights the diagnostic conundrum of immunotherapy-related adverse reactions, in particular in the setting of pre-existing autoimmune conditions.

Conclusion

As pembrolizumab therapy, and indeed immunotherapies as a whole, becomes more widely utilised in the management of advanced cancers, we should expect to see more cases of immune-related adverse events and thus a wide range of differential diagnosis must always be considered and appropriately managed.

References

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