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Case Report

Pembrolizumab-Induced Optic Neuritis: A Case Report

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Abstract

Immune checkpoint inhibitors (ICIs) have transformed the treatment of relapsed and refractory Hodgkin's lymphoma, but they are associated with immune-related adverse effects (irAEs). Although rare, ocular irAEs can have a significant impact on vision. This is the case of a 29-year-old female with relapsed classical Hodgkin's lymphoma, who experienced unilateral, painless vision loss after two cycles of pembrolizumab-based therapy. The MRI revealed optic nerve inflammation and extensive investigations ruled out other causes. A diagnosis of immune-related optic neuropathy was made. Pembrolizumab was stopped, and high-dose intravenous methylprednisolone was immediately started, followed by a six-week prednisolone taper, which resulted in complete visual recovery within two weeks. The patient achieved remission with DHAP chemotherapy before receiving autologous stem cell transplantation. This case emphasises the necessity of early identification and prompt corticosteroid treatment for ocular immune-related adverse events, underscoring the requirement for meticulous surveillance and swift action to avert permanent vision impairment.

Key Words: Case Report, Optic Neuritis, Pembrolizumab

Background

Immune checkpoint inhibitor (ICI) treatment has established its relevance in refractory and relapsed Hodgkin's lymphoma.[1,2] ICIs are effective but can lead to immune-related adverse events (irAEs) due to overstimulation of the immune system.[3] Ocular irAEs are rare side effects but can have a major impact on the quality of life i.e., in the case of impaired vision or complete loss of vision.[3–7] Generally it appears with in few weeks of starting pembrolizumab but delay presentation also been recorded.[8] Ophthalmic irAEs are categorized by the affected area of the eye into ocular inflammation (e.g., uveitis, episcleritis, blepharitis, keratitis), orbitopathy (idiopathic or thyroid-induced orbitopathy), retinal/choroidal disease, and optic neuropathy.[4]

Patient Information

A 29-year-old female with a history of stage IV (Ann Arbor classification) Classical Hodgkin's Lymphoma (CHL) came to the emergency department with the complaint of painless loss of vision in the right eye since 7 days.

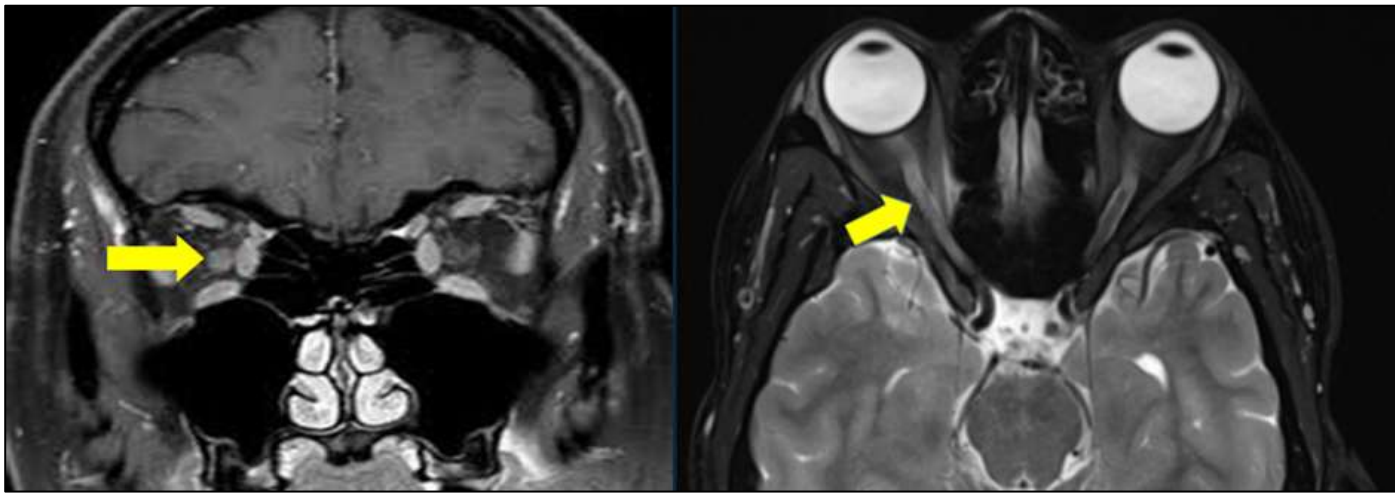
The patient was diagnosed with Stage IV CHL with bone marrow involvement in April 2021, and ABVD regime (Doxorubicin hydrochloride, Bleomycin sulphate, Vinblastine sulphate and Dacarbazine) followed by Escalated BEACOPP leading to remission and a 2-year disease-free survival. In January 2024, patients relapsed with the disease activity in bone marrow. For the same, 2 cycles of P-ICE (Pembrolizumab, Ifosfamide, Carboplatin, Etoposide) were given and the patient received a partial response. After the 7 days of the 2nd cycle, the patient presented with unilateral painless loss of vision.

On examination, no light perception in the right eye, fundus examination was unremarkable. MRI showed a bulky right optic nerve with inflammatory changes.[Figure 1] The CSF study was normal. Paraneoplastic panel (including anti-amphiphysin antibodies, anti-Hu/anti-Yo/anti-Ri/anti-Ma/anti-Tr antibodies, anti-SOX1 antibodies, anti-ZiC4 antibodies, anti-collapsin-responsive mediator protein 5 antibodies [CRMP 5], anti-glutamic acid decarboxylase antibodies [anti-GAD], antibodies) were negative.

Considering these diagnostic results, the patient was diagnosed with immune-related optic neuropathy due to PD-1 blockade with pembrolizumab.

High-dose steroid treatment was immediately initiated with intravenous methylprednisolone at a dose of 500 mg per day for three days, followed by tapering of prednisolone over six weeks. The patients showed dramatic improvement with complete recovery of vision within two weeks of steroid treatment. Due to favourable clinical outcome regarding binocular vision, additional treatment was not initiated. The treatment with pembrolizumab was discontinued permanently. Subsequently, the patient was treated with 2 cycles of Dexamethasone, High-dose Ara-C - cytarabine, and Cisplatin (DHAP). The patient achieved complete

Figure 1:
MRI Images- T2W hyperintensity is noted along Intra- orbital & intracanalicular segment of the right optic nerve



remission and was posted for an autologous stem cell transplant.

Discussion

To date, ocular adverse events (AEs) following immune checkpoint inhibitors (ICI) have been mostly described either in clinical trials or in retrospective case reports and small series, all of which are limited by small sample sizes.[6] Ocular side effects following ICI treatment are rare, occurring in approximately 3% of patients, as documented in the FDA Adverse Event Reporting System (FAERS) pharmacovigilance database.[3–7] This rare occurrence is thought to be primarily attributable to the immune-privileged location.[9]

The spectrum of ocular irAEs ranges from the most common ocular side effects, including uveitis & keratoconjunctivitis sicca (dry eye syndrome), to optic neuropathy which is much rarer (0.2%).[3–7,10] This case illustrates a rare but significant immune-related adverse event, pembrolizumab-induced optic neuritis, in a patient with relapsed classical Hodgkin's lymphoma (CHL).

Initiating treatment promptly after diagnosis is essential, with corticosteroids being the main method of therapy. This highlights the importance of being alert to irAEs and the vital role that rapid administration of corticosteroids plays in avoiding permanent loss of vision.

Options for further treatment are mainly based on case series and case reports. In the literature, the following additional interventions are described: plasmapheresis, intravenous immunoglobulin, infliximab, rituximab, and mycophenolate mofetil (MPA).[10–13]

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