Pembrolizumab Induced Bell's Palsy in Triple Negative Breast Cancer: A Case report

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Abstract

Pembrolizumab has been approved by the Food and Drug Administration (FDA) to treat multiple cancers one of which is triple-negative breast cancer positive for Programmed Cell Death Ligand 1 (PD-L1) protein. Multiple immune-related Adverse Drug Reactions (irADRs) have been reported with pembrolizumab affecting various organ systems. Bell's palsy is one such irADR that has been previously reported with Immune Checkpoint Inhibitors (ICI) use in other cancers, but it has not been reported in triple-negative breast cancer. We present a case of a 35-year-old woman with Bell's Palsy (lower motor neuron type), with a history of triple negative stage 2 invasive ductal carcinoma receiving neoadjuvant chemoimmunotherapy with pembrolizumab.

She presented with right-sided facial drooping affecting the upper and lower part with impaired sensation on the left side of the face. After an extensive workup, a diagnosis of Bell's Palsy was made which was attributed to treatment with pembrolizumab.. She was treated with high-dose steroids resulting in symptom resolution. We are reporting this case to emphasize that if anyone on ICI therapy for solid cancers has atypical presentation with non-focal symptoms, ICI induced Bell's Palsy should be kept high on differentials, even if there is no reported incidence in that particular cancer.

Keywords: Pembrolizumab • Bells palsy • Tripple Negative breast cancer

Introduction

Pembrolizumab is a monoclonal antibody approved by the Food and Drug Administration (FDA) to treat multiple cancers including triple-negative breast cancer. It binds to the Programmed Cell Death Protein 1 (PD-1) receptor on the surface of T cells, preventing immunosuppression.

Multiple Immune-Related Adverse Drug Reactions (IRADR) have been reported with pembrolizumab affecting gastrointestinal, cutaneous, pulmonary, endocrine, hematological, and neurological systems. Although neurological irADRs are rare with a prevalence of 1%-4%, it is important to be aware of the possible adverse effects which can be pivotal in guiding the therapy for the patient. Facial nerve palsy had been previously reported with Immune Checkpoint Inhibitors (ICI) use in other cancers, but it has not been reported with ICI use in triple-negative breast cancer. We report a case of triple-negative breast cancer patient who experienced bell's palsy on the right side of her face secondary to treatment with pembrolizumab.

Case Presentation

A 35-year-old African American woman, with a history of triple-negative stage 2 invasive ductal carcinoma receiving neoadjuvant chemoimmunotherapy presented to the emergency department with complaints of sudden onset numbness and tingling in her left arm and face for the past day. It was associated with difficulty speaking, and a documented fever of 103 degrees.

Additionally, she couldn't close her right eye or move the right side of her face and had difficulty chewing food. She denied any recent history of upper respiratory tract infections, chest pain, abdominal pain, dysuria, and palpitations. She had received 2 cycles of Carboplatin/Paclitaxel and Pembrolizumab with the last cycle being given to her 2 days before symptom onset. Her initial vital signs were significant for tachycardia (115 beats per minute) but remained afebrile. She was awake, alert, and oriented to time, place, and person. Neurological exam findings were notable for right-sided facial drooping affecting the upper and lower part of the face with impaired sensation on the left side of the face. Power was 5/5 in all four extremities with the absence of pronator drift, pinpoint pupil, and dysdiadochokinesia. Given the patient's presentation, she was evaluated for a stroke with a Non-Contrast Computed Tomography (CT) of the head and a CT angiogram of the head and neck which were unremarkable. Furthermore, an MRI head also revealed no acute intracranial abnormalities. A complete blood count revealed pancytopenia with a Hb of 9.6g/dL, platelets of 125,000/uL, WBC 2700/uL, and ANC of 1500/mL, secondary to the recent cycle of chemotherapy. Additionally, an ECHO with bubble study and ECG were also performed with results being unremarkable. Given these findings, a continuous EEG was done which ruled out focal seizure. She was initially started on Aspirin and Atorvastatin for stroke. After ruling out stroke, focal seizure, and metastasis, diagnosis of Pembrolizumab-induced Bell's Palsy was made. Following this, aspirin and atorvastatin were discontinued and she was started on oral prednisone (90mg) with supportive eye care with discontinuation of pembrolizumab.Subsequently, her right-sided facial palsy and left-sided numbness and tingling gradually improved. Her blood counts also started improving with new cell counts being Hb of 10.3g/dL, WBC of 6800/uL, and platelet of 351,000/mL. She was discharged with 80 mg of Prednisone with a weekly taper of 10 mg.

Discussion

Immune checkpoint inhibitor-related cranial nerve palsy has been reported in the literature as a rare side effect mostly seen in patients treated for solid cancers like melanomas. Given the rarity of this side effect, it was lower on the differential. A comprehensive workup was performed to pursue other potential causes of Bell's palsy like anatomic, viral infection, ischemia, inflammation, and exposure to cold. Additionally, having hypertension, diabetes mellitus, radiation exposure, migraine, and psychological factors can increase the risk of a patient developing Bell's palsy [1]. A retrospective study done at a tertiary center (facial nerve palsy center) looked at the cause of facial droop in patients who came to see them over 10 years.

They found that out of 1989 people that came - 38 % had bells palsy, 10 percent had acoustic neuroma resections, 7 percent had it secondary to either cancer/ VZV/ iatrogenic, 4% secondary to Lyme's disease, 5 percent each because of congenital reasons or benign causes and 17 percent were because of other causes [2]. Stroke and transient ischemic attack were the first suspects as the facial palsy was associated with left hand and foot tingling and headache in addition to the hypercoagulable state due to her malignancy. CT and MRI imaging following guidelines did not reveal any acute ischemic abnormality thereby eliminating stroke as well as intracranial metastases. There were no complaints of ipsilateral facial pain as well as bullous rash or hearing loss eliminating VZV reactivation from the

differentials. The patient did not have any significant comorbid conditions like HIV, hepatitis B, hepatitis C, diabetes mellitus, or hypertension indicating an infectious or ischemic etiology. The patient had normal vitamin B1, B6, and B12 levels thereby excluding the reversible causes of cranial neuropathies. Other differentials included a focal seizure which was eliminated by normal results on continuous
video EEG monitoring. Immune-related neurological adverse effects are quite rarely observed in patients receiving Immune Checkpoint Inhibitor (ICI) therapy. It has a prevalence of 1%-4% in all patients receiving ICI therapy [3]. Within neurological adverse events, the peripheral nervous system is twice as likely to be involved compared to the central nervous system. The incidence of facial palsy is 0.2% among ICI-treated patients in a study reported by Zhu J *et al* [4]. In the same study, ICI drugs were associated with an increased risk of facial palsy in patients receiving treatment for melanoma, gastro-esophageal cancer, renal or urothelial cancer, and malignant mesothelioma. Neurological ADRs associated with ICI drugs include myositis, GBS and other peripheral neuropathies, myasthenic syndromes, encephalitis, cranial neuropathies, meningitis, CNS demyelinating diseases, and myelitis in the decreasing order of frequency respectively [5]. These are summarized in the table below. In cranial neuropathies, usually affected cranial nerves include: Optic [II], trigeminal (V), vestibulocochlear (VIII), oculomotor (III), and facial(VII) with facial nerve being affected in 39% of cases. The side effects of ICI are not seen until 2 months after its introduction and help with ICI imputability [6]. This favors our diagnosis since the facial droop occurred 2 days after our patient received her second dose of pembrolizumab. Upon diagnosis of Bell's palsy as an adverse effect of pembrolizumab, guidelines state that the offending agent should be withheld and supportive therapy must be administered to treat the ADR. Subsequently, she was initiated on a high-dose prednisone (1 mg/kg). Although her symptoms improved after receiving high-dose steroids, she continued to have dysarthria. She was discharged from the hospital on 80 mg prednisone with 10 mg taper per week with recommendations for home speech therapy. At a follow-up visit 1.5 months later, her right-sided facial palsy and dysarthria had completely resolved. However, she had residual left-sided facial numbness and was on 20 mg of prednisone as per the taper. We increased the dose to 30 mg and decided to slow down the taper to completely alleviate her symptoms. Isolated facial palsy has a good prognosis given that 70 % of patients have a complete recovery within a median of 41 days, remaining have a partial recovery [6,7]. Rehabilitation strategies like exercise, electrical stimulation, facial neuromuscular retraining, and biofeedback are used in those patients who do not have a complete recovery [8]. A study conducted by Pepys J *et al*, summarized that the currently available data suggest ICI rechallenge after complete ADR resolution factoring in the severity of the side effects and patient characteristics [9]. A lower risk of relapse is seen with the switch of the ICI subtype in non- neurological irAEs but no such evidence is available for the neurological irAEs [10]. We did not rechallenge pembrolizumab for our patient as she had residual numbness. This raised high suspicion for a recurrence of facial palsy or a new immune-related ADR resulting in noncompliance to the chemotherapy. We also did not switch to a different ICI class because of the lack of specific guidelines. We are reporting this case to emphasize that if anyone on ICI therapy for solid cancers has facial droop, pembrolizumab should be kept high on differentials, even if there is no reported incidence in that particular cancer. Since pembrolizumab can affect any cranial nerve, atypical presentation with non-focal symptoms should also raise suspicion for the same. Monitoring and follow-up are also an important factor in assessing the recurrence or development of new neurological ir-ADR and ensuring response to treatment.

Table 1. Follow up of patient through homeopathic treatment.

Immune-associated neurological ADRs	**Frequency**
Myositis	32%
GBS and other peripheral neuropathies	22%
Myasthenic syndromes	14%
Encephalitis	13%
Cranial neuropathies	7%
Meningitis	3%
CNS demyelinating diseases	2%
Myelitis	2%

Conclusion

In conclusion, this case report highlights the rare occurrence of Bell's palsy as an immune-related adverse reaction to pembrolizumab in a patient with triple-negative breast cancer. The case emphasizes the need for clinicians to consider immune checkpoint inhibitors as a potential cause when patients on these therapies present with atypical neurological symptoms. Early identification and prompt intervention with high-dose steroids were key in managing the adverse event, resulting in symptom resolution. This case underscores the importance of monitoring patients on pembrolizumab for any neurological complications, even those not commonly associated with specific cancers.

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Note: The Publisher and Editor regretfully retract the article titled "Pembrolizumab Induced Bell's Palsy in Triple Negative Breast Cancer: A Case Report" "Oncology and Cancer Case Reports" Volume 10, Issue 04, and Page no. 01-03. Following an investigation which found that the author violated the Journal's policy and putting false allegations towards to the journal. This is contrary to the ethical standards of the journal and unacceptable. The author denied to support open access. The authors have been notified of this decision. The Publisher and Editor apologize to the readers of the journal for any inconvenience this may cause.

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