Steroid Responsive Acute Inflammatory Demyelinating Polyneuropathy Induced by an Immune Check Point Inhibitor

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Key words: acute inflammatory demyelinating polyneuropathy, nerve conduction study, intravenous immunoglobulin, steroids, immune check point inhibitors.

Abbreviations:
AIDP, acute inflammatory demyelinating polyneuropathy, ICPs, immune check point inhibitors, NSCLC, non-small cell lung cancer, NCS, nerve conduction study, EMG, electromyography, IVIg, intravenous immunoglobulin.

Introduction

Lung cancer is the second most commonly diagnosed cancer and the leading cause of death worldwide,[1] with most cases presenting at an advanced, inoperable stage of the disease.

Platinum-based chemotherapy is the standard first line therapy for advanced non-small cell lung cancer (NSCLC), however immune check point inhibitors (ICPIs) are considered a major breakthrough in cancer treatment in the last decade. Pembrolizumab, a highly selective anti-PD-1 humanized monoclonal antibody, was approved by the United States Food and Drug Administration (US FDA) in October 2016 for previously untreated metastatic NSCLC patients whose tumors have high PD-L1 expression, as well as for metastatic NSCLC patients progressing on or after platinum-based chemotherapy.[2]

There is a greater focus on side effects of ICPIs [3] as well guidelines by the American Society of Clinical oncology to guide physicians in the management of side effects of ICPIs.[4] There are few case reports describing acute onset inflammatory demyelinating polyneuropathy with use of ICPIs.[5,6,7]

Case Presentation

We report a case of acute inflammatory demyelinating polyneuropathy (AIDP) that developed during platinum-based chemotherapy and pembrolizumab for NSCLC which raised diagnostic dilemma in regards to the cause of the neuropathy in the context of recent diagnosis of cancer, initiation of chemotherapy and ICPIs and a dramatic response to offered therapy.

A 60-year-old gentleman who was diagnosed with stage IV adenocarcinoma of the lung (PD-L1 expression 100%) with extensive infiltrative lymphadenopathy in the mediastinum, supraclavicular region and upper abdomen. He was started on carboplatin/pemetrexed/pembrolizumab on a 21-day cycle. He reported acute onset tingling and numbness in both feet about 10 days after his second cycle; he noted that his symptoms were slowly getting worse and reported them to his treating oncologist who attributed it to side effects of chemotherapy. When he came for his third cycle, it was noted that his symptoms continued to get worse and he started to experience lower extremity weakness and difficulty walking, which necessitated admission for further evaluation.

During his admission he was due for his third cycle which was given but without carboplatin and pemetrexed. Neurology service was consulted for evaluation of his progressive worsening of his symptoms. His neurological examination revealed normal mental status and cranial nerve examination. He had weakness of long forearm flexor muscles MRC grad 4/5, intrinsic hand muscle weakness 3/5, hip flexors 3/5, knee flexion/extension, dorsiflexion and plantar flexion 3/5. Deep tendon reflexes were absent and sensory examination showed reduced light touch and prick up to the level of his knees.

A nerve conduction study (NCS) was done and showed absent right median and ulnar sensory responses with reduced right superficial peroneal sensory nerve action potential (SNAP) amplitude and normal sural sensory study (sural sparring pattern). A motor nerve conduction study showed reduced right median, ulnar, and bilateral peroneal and tibial compound nerve action potential (CMAP) amplitudes with more than 50% partial conduction block of the right ulnar nerve in the forearm segment and tibial nerve in the popliteal fossa with more than 60% temporal dispersion. Distal motor latencies were prolonged along with reduced conduction velocity. Right median and ulnar minimum F-wave latencies were significantly prolonged and bilateral tibial F-waves were absent. Needle electromyography (EMG) showed active denervation changes and reduced recruitment in the leg muscles and the right abductor pollicis brevis with reduced recruitment only noted in the proximal muscles. Based on this study, it was concluded that findings are highly suggestive of acute inflammatory demyelinating polyneuropathy (AIDP). He had extensive blood tests which included a negative paraneoplastic panel and a magnetic resonance imaging (MRI) of the brain and spine with contrast which was negative for metastasis or leptomeningeal enhancement. Lumbar puncture was recommended, however, the patient declined.

He was started on intravenous immunoglobulin (IVIg) 0.4 g/kg/day for 5 days. Initially he had stabilization of his weakness and was discharged to acute rehabilitation center. However, after two weeks, he continued to have worsening of his lower extremity weakness with progression to involve the upper extremity. At this point it was decided to maintain the patient on biweekly IVIg infusion at dose of 1g/kg/day along with IV methylprednisolone 1g with every infusion. After receiving 2 cycles of IVIg and IV methylprednisolone, he had significant improvement of his deficit, as patient started to ambulate with help of a walker.

Discussion

In this case we postulate that AIDP was induced by pembrolizumab, and response to treatment was different than usual cases of AIDP, suggesting the possible role of steroids in such cases to improve prognosis and recovery.

This case also highlights the importance of clinical history in guiding diagnostic work up. Platinum-based chemotherapy is well known to cause neuropathy in a dose-dependent pattern and tends to be predominantly sensory neuropathy caused by damage of the dorsal root ganglion or its axons causing a sensory neuronopathy.[8] Electrodiagnostic study, in this case, played a major role in characterizing the type of neuropathy, as well as guiding the appropriate treatment.

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