Complete remission in an elderly patient of advanced-stage squamous cell carcinoma lung with nivolumab: An exceptional case study from India

Shyam Aggarwal, Sachin Minhas, Shrinivas Shinde, Madhusudan Ganvir

ABSTRACT

Introduction: Recent research of immunotherapy on non-small cell lung cancer (NSCLC) has initiated a change in the management of this disease with offering a potential for prolonged responses and survival. However, the treatment options for advanced stage lung squamous cell carcinoma (SCC) remain limited. In recent times a fully human IgG4 programmed death one immune checkpoint inhibitor antibody Nivolumab was approved by Drug Controller General of India to treat patients with advanced stage, relapsed or refractory lung SCC.

Case Report: In this case report, we have discussed about an elderly patient of NSCLC who showed complete remission with Nivolumab in short duration of treatment without any significant adverse event. To date, this is the first case of complete remission in relapsed advanced stage SCC lung with Nivolumab in India and contributes to the exceptional cases of Nivolumab in SCC in the world.

Conclusion: This report suggests exceptional safety and efficacy of Nivolumab in elderly patients with NSCLC. Further research in larger sample size in Asian countries is needed to test the safety and efficacy of Nivolumab immunotherapy for elderly patients with NSCLC.
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Keywords: Immunotherapy, Lung squamous cell carcinoma, Nivolumab, Oncology, PD-L1

INTRODUCTION

Lung cancer is the second most common cancer in the world. The estimates of American Cancer Society for lung cancer of year 2016 were about 224,390 (men: 117,920 and women: 106,470) new cases, and in the United States, total deaths from lung cancer were about 158,080 (men: 85,920 and women: 72,160) [1]. In India, it constitutes 6.9% of all new cancer cases as well as 9.3% of all deaths related to cancer [2]. As per the published reports, the incidence of lung cancer is increasing every year in metropolitan cities like Delhi, Chennai and Bengaluru [2]. Treatment options for advanced non-small cell lung cancer (NSCLC) are rapidly growing and advancement in chemotherapy or molecular targeted therapy have improved outcomes in the advanced setting but survival remains poor with a five-year overall survival of 4–5% [3]. Medical treatment of NSCLC includes third generation platinum doublets, epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) in EGFR mutation-positive lung cancer, anaplastic lymphoma kinase (ALK) TKIs in ALK rearrangement-
positive disease, maintenance systemic therapy, and second- or third-line treatment [4].

Recently immunotherapy has brought a major change in the management of this disease while offering a potential for prolonged responses and survival. Nivolumab is the first immune checkpoint inhibitor approved by the Drug Controller General of India for the treatment of patients with advanced-stage squamous and non-squamous NSCLC following progression on or after platinum-based chemotherapy.

We studied published reports of phase III clinical trial (checkmate 057), phase III clinical study (checkmate 017) and phase II clinical study (checkmate 063) where Nivolumab treatment showed unpredictable survival in lung cancer patient in terms of overall survival, median survival, response rate and disease progression [5, 6]. Huang et al. (2016), published meta-analysis report of nine clinical trials of Nivolumab [7]. They suggest that it is a promising drug for previously treated advanced NSCLC patients with positive PD-L1 expression.

We reviewed many published case studies of SCC lung with Nivolumab and till date very few cases of complete remission have been reported worldwide [8]. This case study contributes to the reported exceptional cases in the world of complete remission of SCC lung with Nivolumab. Although published literature has shown complete remission or durable tumor remission in different malignancies with Nivolumab like indolent Hodgkin’s lymphoma, melanoma, advanced renal-cell carcinoma and squamous cell carcinoma of the anal canal (SCCA) [9–12]; according to the collected information this is the first case of NSCLC from India. In this case study, we will discuss the role of Nivolumab in the treatment of SCC lung in an elderly Indian patient and its complete remission in a short duration of time.

CASE REPORT

A 66-years-old male with past history of chronic smoker was presented in July 2016 with chief complaints of dull aching pain in upper chest, cough with scanty, white mucoid expectoration and loss of weight for one month duration. He had no history of high grade fever, hemoptysis, exertional dyspnea and orthopnea. He had no history of tuberculosis, asthma, diabetes and hypertension. He was chronic renal failure since 2014 with creatinine around 2.3 mg/dl. His medical and surgical histories were unremarkable.

Chest X-ray (posteroanterior view) of the patient showed a left sided opacity in the region occupying the area of left upper lobe. Bronchoscopy and transbronchial lung biopsy were done and histopathology findings reported poorly differentiated squamous cell carcinoma of lung.

Positron emission tomography computed tomography (PET-CT) (Figure 1) of the patient was done which revealed a soft tissue density mass in the left suprahilar region (measuring about 34 mm (AP) x 36 mm (TR) x 32 mm (CC)) and a large parenchymal nodule (measuring about 25 mm in longest dimension) in the anterior segment of the left lung upper lobe. We also noted FDG avid lymph nodes at portacaval and periportal station which were likely metastasis (Figure 2). Other organs and musculoskeletal system were normal.

The patient was treated with weekly chemotherapy comprising paclitaxel 80 mg and gemcitabine 800 mg, (D1, D8, and D15 for four weeks). After two cycles he presented in casualty with severe breathlessness, left side chest pain and generalized weakness. On evaluation he was found to have evidence of gross amount of pericardial effusion with maximum thickness of approximately 3.7 cm with compression over cardiac chamber (Figure 3). These findings were indicative of progressive disease. His eastern cooperative oncology group (ECOG) status was 2.

The patient underwent urgent pericardiocentesis for gross pericardial effusion and 1200 ml fluid was drained. After being confirmed with disease progression, he was treated with second line therapy with immune checkpoint inhibitor Nivolumab at the dose of 3 mg/kg every two weeks. After two courses, the general condition of the patient became better. He was followed-up with a PET CT scan (Figure 4) which showed absence of FDG activity as well as reduction in size of lung lesions and...
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no new lesion were found in PET-CT scan. Thus, we achieved complete remission within one and half month in this patient after Nivolumab therapy. There were no significant adverse events noted during the Nivolumab therapy treatment.

DISCUSSION

Squamous cell carcinoma (SCC) lung account for 20–30% of all type of lung cancers and represent a significant health burden [1]. Until recently, single agent Docetaxel chemotherapy was available as a standard second-line treatment for the relapsed or refractory lung SCC and the median overall survival with this therapy was approximately seven months. A major problem associated with the use of Docetaxel was its severe adverse reactions. So there was an urgent need of novel therapeutic drugs to replace Docetaxel as second-line therapy in elderly because of its toxicity. Nivolumab is one such drug which has showed lesser toxicity in elderly patients as compared to Docetaxel in conducted research and clinical trials [13–15].

CheckMate 017 trial was conducted by Brahmer et al. to evaluate the efficacy and safety of Nivolumab as compared with docetaxel in advanced squamous cell non-small cell lung cancer [14]. The researchers concluded that overall survival, response rate, and progression-free survival were significantly better with Nivolumab than with docetaxel, regardless of PD-L1 expression level. Rizvi et al. conducted a phase 2, single-arm clinical trial (CheckMate 063) at 27 sites in France, Germany, Italy, and USA [15]. They concluded that Nivolumab has clinically meaningful activity and a manageable safety profile in previously treated patients with advanced, refractory, squamous non-small cell lung cancer [15]. We reviewed the median time to response of Nivolumab in published clinical reports which was found to be 2.1 months in the Nivolumab group compared to 2.6 months in the Docetaxel group [13], 2.2 months in the Nivolumab group compared to 2.1 months in the Docetaxel group [14] and 3.3 months with Nivolumab [15]. In this case study, the time to response of Nivolumab was almost equivalent to published clinical reports and complete remission was achieved in 1.5 months after initiation of Nivolumab therapy. This kind of response is exceptional since in previously published reports complete response towards Nivolumab therapy was reported to be only about 1% (n = 4 out of 292 and n = 1 out of 135) [13, 15].

In a published research report in European Society for Medical Oncology (ESMO) (2016) Forde et al. shared their finding related to complete response (n = 1 out of 18) in NSCLC [8].

Studies suggest that there are very few adverse events associated with Nivolumab treatment. Most of these adverse effects are mediated by the immune system. We found no significant adverse drug reactions with Nivolumab which showed better safety profile as compared to Docetaxel.

CONCLUSION

This report suggests exceptional efficacy and safety in an elderly patient with advanced-stage lung squamous cell carcinoma in response towards short-term Nivolumab treatment. Further clinical trials in Asian countries are needed to evaluate the safety and efficacy of Nivolumab immunotherapy for elderly patients with lung squamous cell carcinoma.

REFERENCES


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