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Radiation

Efficacy of Low-Dose Nivolumab in Multiple Cancer Types

Dr. Ali Asgar Chowdhury[1*]

[1]Assistant Professor, Department of Clinical Oncology and Radiotherapy, Chattogram Medical College Hospital, Bangladesh

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***Corresponding author:** Dr. Ali Asgar Chowdhury
Assistant Professor, Department of Clinical Oncology and Radiotherapy, Chattogram Medical College Hospital, Bangladesh

Abstract **Case Report**

Introduction: Cancer is the uncontrolled growth and development of cells in the body, and is one of the foremost reasons of deaths throughout the world. Immunotherapy is a broad category of cancer therapies that triggers the body's immune system to fight cancer cells. Nivolumab, a monoclonal antibody, is used an immunotherapy drug that binds to the Programmed Cell Death protein (PD-1) to help immune cells kill cancer cells better and is used to treat many different types of cancer. This study is about two cancer patients, one being a case of Squamous Cell Carcinoma of the Right Lung, another being a case of metastatic Stage IV Renal Cell Carcinoma. They were treated with low-dose Nivolumab and resulted in remission of the malignancy without any significant complications. ***Case Presentation*:** The current study was conducted with 2 Bangladeshi male patients. The first patient, case of Carcinoma Lung, 55 years old, and the second patient, Renal Cell Carcinoma, 57 years old. They were treated with 6 cycles of Nivolumab at 40 mg dose for immunotherapy regimen. Both of them are clinically stable and no complications have been detected. ***Conclusion:*** Treatment with Nivolumab in such fatal cancers has demonstrated remarkable clinical response with significant remission of the disease. In addition, adverse effects are minimal compared to previous drug regimens.
Keywords: Immunotherapy; cancer; Nivolumab; carcinoma; malignancy.

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BACKGROUND

Cancer occurs due to the transformation of normal cells into tumor cells that takes place in a multi-stage process which generally progresses from a pre-cancerous lesion to a malignant tumor. The various changes that happen at cellular level are a result of interaction between the genetic structure of an individual along with certain external agents such as physical, chemical or biological carcinogens. Similar to most of the non-communicable diseases, tobacco, alcohol, unhealthy diet and lifestyle, air pollution is among some of the established risk factors of cancer. Exposure to some types of microorganisms is responsible for certain types of cancer. Cancer is a leading cause of death across the world. As of 2020, nearly 10 million deaths took place globally. The most common causes of cancer deaths were cancers of the lung, colon and rectum, liver, stomach and breast [1].

Among all adult malignancies, renal cell carcinoma accounts for 4%. As of 2020, about 270,000 cases are diagnosed per year across the world. Approximately 170,000 people die each year as a result of this disease. Renal cell carcinoma is the most common primary renal neoplasm and it originates from the renal pelvis. It is twice more common in males as compared to females and it occurs most frequently among the aged, mostly sixth to eighth decade of life with median age at diagnosis being 64 years. The commonest subtype appears to be clear cell carcinoma [2].

Regarding lung cancer, as of 2020, there were more than 2.2 million new cases diagnosed annually. In 2020, a total of 1,796,144 people lost their lives due to lung cancer. Average age at diagnosis is 71 years. Commonest cause of cancer-related death in both men and women is this disease. 85% of the lung cancers are non-small-cell cancers among which are adenocarcinomas, squamous-cell carcinomas, and large-cell carcinomas and around 15% are small-cell lung cancers [3].

Case Study I (the case of renal cell carcinoma)

A 57 years old, Bangladeshi male patient, hypertensive with the positive family history of renal cell carcinoma along with chief complaints of vertigo, anorexia and nausea for 1.5 months visited the out-patient department on 30.04.2022. Before that, the patient was diagnosed of stage IV renal cell carcinoma in Saudi Arabia. After that coming back to Bangladesh, patient was suggested to do some investigations such as

MRI which revealed Intra-cranial space occupying lesion at left cerebral hemisphere, suggestive features of hemorrhagic metastasis at 1.5.2022. His blood pressure was record high from the normal level. In routine examinations, serum creatinine was always increased (1.6mg/dl) and eGFR was recorded 55ml/min/1.73m^2. There was no significant finding in CBC and serum electrolytes report and the hemoglobin level was found normal. Patient was suggested to do chest X-ray and echocardiography at 6.06.2022, the echocardiography report was found normal. However, chest X-ray report indicated right consolidation with bilateral pulmonary nodules which was relevant to lung metastasis. The cortisol level was found high (0.226µg/dl). Patient had a history of bony metastasis, but, after starting treatment, there was no evidence of bony metastasis in whole body bone scan at 20.12.2022.

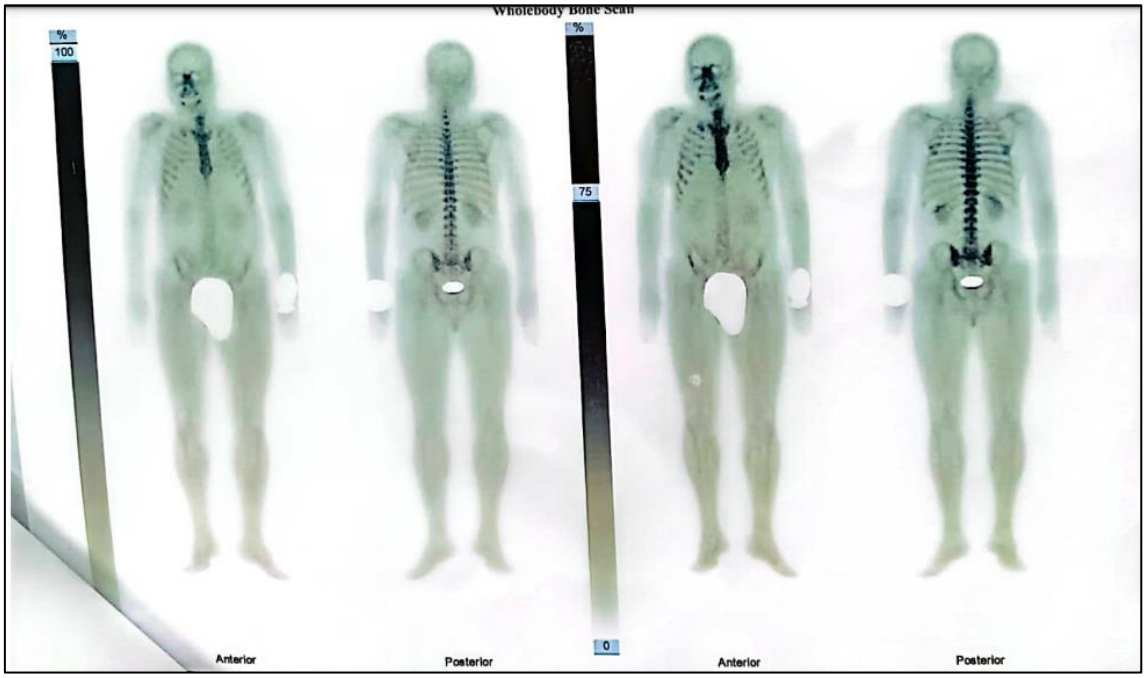

Figure 1: Whole body bone scan (21.12.22) of Case I. Whole body scan showed no metastasis

Treatment Details

After diagnosis, treatment started from 30.04.2022 followed by radiotherapy. 1st chemotherapy started on 4.07.2022. In the whole treatment journey, patient received 6 cycles of chemotherapy. The drug regimen contained low dose Nivolumab which was 40 mg and Lenvatinib 8 mg along with conservative treatments. The last cycle was given on 26.10.2022. During treatment with these regimens, no major side effect was recorded.

Patient outcome

After immunotherapy treatment with Nivolumab along with Lenvatinib, the patient was clinically stable. As a result of the treatment, bony metastasis was totally resolved.

Case Study II (Lung Cancer)

A 55 years old patient with history of Chronic obstructive pulmonary disease with complaints o of chest pain came to outdoor department on 31.01.2022. In routine examination, CBC report revealed anemia, lowest hemoglobin was recorded 9gm/dl. Serum creatinine and serum electrolyte was normal. Patient was suggested to do CT scan. CT scan report on 31.1.22 illustrated multiple satellite nodules in ipsilateral lung, that might be metastatic. After receiving 8 cycles of chemotherapy, CT scan report showed K/C of carcinoma-lung (right), there is internal progression of primary lung tumor with stable satellite nodule, mediastinal lymphadenopathy with right adrenal mass with hepatic invasion (new), overall features, suggested disease progression. In the meantime, immunotherapy started and CT scan was done on 29.9.2022 that showed a positive change that was, overall features suggesting, partial response of the disease. Partial response was also found in the last CT scan which was done on 18.11.2022.

Treatment details

After the diagnosis of the disease, patients received 8 cycles of chemotherapy with supportive treatment. However, the prognosis was poor. Patient received his 1st cycle of immunotherapy on 16.08.2022 and the regimens were low dose of Nivolumab 40 mg along with Docetaxel 100mg. Patient received his last cycle on 22.11.2022.

Patient outcome

After immunotherapy treatment with Nivolumab along with Docetaxel, the patient was clinically stable. Patient was not improved after

receiving 8 cycles of chemotherapy. However, after receiving immunotherapy, CT scan showed partial response of the disease. The hemoglobin level was also raised after receiving immunotherapy.

Nivolumab neoadjuvant immunotherapy

In recent times, the most promising treatment modality for cancer patients is targeted immunotherapy. A human immunoglobulin G4 PD-1 immune checkpoint inhibitor antibody, which is responsible for blocking PD-1 as well as enhancing antitumor immunity, Nivolumab, and it functions for the treatment of non-small-cell lung cancer (NSCLC), melanoma, renal cell carcinoma (RCC) and other cancers. The anti-PD-1 antibody nivolumab was approved by the US Food and Drug Administration (FDA) for the treatment of melanoma in 2014 and renal cell carcinoma in 2015. Nivolumab also gained the FDA approval in March 2015 for the management of squamous cell carcinoma of the lung, and on October 9, 2015, the FDA expanded the Nivolumab for metastatic non-small-cell lung cancers [4].

DISCUSSION

A trial conducted in 2013 revealed, Nivolumab produced sustainable survival and responses in a subset of heavily pretreated metastatic RCC patients, with a significant safety profile. Overall survival appeared to be promising for this mass of patients [5].

During 2012 to 2013, a trial performed demonstrated that, 117 patients who were enrolled in the trial, had an effective response. Median time taken for response was 3·3 months. Certain number of patients suffered from some treatment-related adverse reactions such as, fatigue, diarrhoea and pneumonitis. Overall, this drug showed significant response in terms of treatment and the safety profile is also remarkable [6].

With regards to adverse effects, the most commonly recorded ones being fatigue, decreased appetite, diarrhea, nausea, cough, dyspnea, constipation, vomiting, rash, pyrexia, and headache. Adverse events of special interest were pneumonitis, vitiligo, colitis, hepatitis, hypophysitis, and thyroiditis. Pneumonitis is a serious adverse effect and is a great matter of anxiety for sufferers of lung cancer [4].

CONCLUSION

Both the patients showed remarkable recovery with treatment by low-dose nivolumab. The adverse effects were minimal with comparison to previously established drug regimens. Patients are now clinically stable and continuing their regular life in a healthy manner.

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Conflict of interest: None declared.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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