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Case Report

TRASTUZUMAB-INDUCED RESPIRATORY DISTRESS: A CASE REPORT

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ABSTRACT

Trastuzumab is a monoclonal antibody effective in treating metastatic breast carcinomas. Cardiotoxicity is the most commonly reported adverse event occurring when used in combination with anthracycline derivatives. Even though pulmonary toxicities are uncommon, immediate withdrawal of the drug is recommended and only reinitiates after the vitals of the patient have become normal. Here, we discuss the case of an 81-year-old female patient who was treated with Injection Trastuzumab for the treatment of breast cancer with metastasis to lungs and received 6 cycles without any major complications. However, 24 h post the last dose; the patient developed a sudden onset of breathlessness and desaturation and was intubated in view of severe metabolic and respiratory acidosis. Blood investigations revealed elevated brain natriuretic peptide, aspartate transaminase, and alkaline phosphatase. Her blood and urine cultures were found to be sterile. She was managed with IV antibiotics, nebulizations, IV fluids, and other supportive medications and had improved considerably. However, on the 11th day, her condition had deteriorated and developed bradycardia. The patient could not be revived and died. Review of the patient's medication did not reveal the presence of any other possible drugs capable of producing pulmonary toxicity. Trastuzumab should be avoided in patients with underlying respiratory or cardiac issues.

Keywords: Trastuzumab, Pulmonary toxicity, Breast cancer.

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INTRODUCTION

Trastuzumab is a monoclonal antibody used for the treating women with metastatic breast carcinoma whose tumors overexpress human epidermal growth factor receptor 2 (HER2)/Neu protein along with other chemotherapeutic drugs as well as for the adjuvant therapy of node-positive cancer [1,2]. The growth factor receptor HER2 is encoded by the HER2 gene, which is amplified and overexpressed in 25–30% of breast cancers, increasing the aggressiveness of the tumor [3]. A study on 1 year of adjuvant Trastuzumab showed a significantly improved disease-free and survival rates among women with HER2-positive breast cancer [4,5]. However, cardiotoxicity of trastuzumab when used in combination with anthracyclines is a well-established adverse effect including a wide spectrum of adverse pulmonary reactions such as eosinophilic infiltrates, lipoproteinosis, organizing pneumonia (OP), fibrosis, and respiratory distress syndrome are also reported [2,6].

CASE REPORT

An 81-year-old postmenopausal multiparous woman, who had come with complaints of a painless lump in her left breast for 2 weeks, was diagnosed with invasive ductal carcinoma on the basis of her histopathological examination and immunohistochemistry testing. The patient underwent a left modified radical mastectomy along with adjuvant chemotherapy of cyclophosphamide, methotrexate, and 5-fluorouracil regimen and completed 6 cycles of chemotherapy without any major complaints and was on regular follow-up. Later patient complained of pain over the surgical site and left arm and computed tomography chest was done which showed metastasis of carcinoma following which the patient received palliative radiotherapy and Injection Herceptin 440 mg once in 3 weeks for carcinoma of the breast with lung metastasis. Before the initiation of trastuzumab treatment, a two-dimensional echo was done which showed Grade I diastolic dysfunction. She received 6 cycles without major complaints. Within 24 h of the last dose, the patient developed an acute onset of breathlessness and desaturation for which she was intubated in view of severe metabolic and respiratory acidosis. Her blood examinations showed an elevated brain natriuretic peptide (750.4 pg/ml), SGOT (118 IU/L), and alkaline phosphatase (173 IU/L) indicating cardiotoxicity and hepatotoxicity. All her blood cultures and urine cultures were found to be sterile. Despite aggressive supportive treatment with antibiotics, nebulizations and IV fluids and other supportive medications, the patient developed bradycardia and succumbed to death.

DISCUSSION

Over the years, there have been many promising data over the efficacy of Trastuzumab as a standard drug for the management of (HER2+)-over expressing breast cancers with metastasis [7]. Trastuzumab is given in conjunction with anthracycline derivatives, and hence there is a significant improvement in the overall survival rates of HER2 positive breast cancer patients. However, there are many reports confirming cardiotoxicity due to this combination therapy since neuralgin-1 signaling pathway is present in the cardiomyocytes which are inhibited by trastuzumab [8]. 15% of patients have infusion-related events such as hypotension, angioedema, bronchospasm, dyspnea, fever, chills, and urticaria which are common at the time of initiating the treatment whereas these reactions were not seen in our patient [9-11]. Trastuzumab can also cause serious and fatal pulmonary toxicities such as dyspnea, interstitial pneumonitis, pulmonary infiltrates, pleural effusions, non-cardiogenic pulmonary edema, pulmonary insufficiency and hypoxia, acute respiratory distress syndrome, and pulmonary fibrosis. Patients with pre-existing intrinsic lung disease or extensive tumor involvement in lungs are at a higher risk for pulmonary toxicity [12-14]. Discontinuation of the drug at the earliest can improve the condition of the patient with subsequent corticosteroid therapy [15]. Bronchospasm was the only pulmonary adverse event identified when 25,000 patients were treated with Trastuzumab in an analysis performed and usually occurred within 2.5 h of administration. However, our patient developed an acute onset of breathlessness and desaturation 24 h post last dose due to development of pneumonia. There have been some rare reports of a patient with organizing pneumonia and another with pneumonitis, both probably induced by Trastuzumab [6,16,17]. Two mechanisms have been proposed for drug-induced lung injury resulting from apoptosis or impaired cell and tissue repair sequence. Anticancer agents can expose the cells to apoptosis

by generating an apoptotic stimulus which causes the activation of proapoptotic proteins that increase the permeability of the outer membrane of mitochondria which ultimately leads to the cell [8,9].

In our case, the patient had an underlying cardiac issue but due to the oncologic condition of the patient; Trastuzumab injection was administered. The patient died ultimately due to pneumonia probably due to Trastuzumab.

CONCLUSION

Cardiotoxicity of traustuzumab is when used in combination with anthracyclins is a well established adverse effect. In our case, patient had an underlying cardiac issue but owing to oncologic condition of the patient, Trastuzumab injection was administered. The patient died ultimately due to pneumonia probably due to Trastuzumab.

AUTHOR'S CONTRIBUTIONS

Acquisition of Data: Nithu M Kumar, Analysis of case report: Nithu M Kumar, Akhila Sivadas, Drafting of Case Report: Nithu M Kumar, Critical Revision: Lakshmi R, Nithu M Kumar.

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