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Original Research Paper

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DOCETAXEL INDUCED LUNG INJURY (PNEUMONITIS): A CASE REPORT

Dr. Javeriya Anjum	Pharm D, Department of Pharmacy Practice, Al-Ameen College of Pharmacy, Bengaluru, India
Dr. Rahul Saha	Pharm D, Department of Pharmacy Practice, Al-Ameen College of Pharmacy, Bengaluru, India
Dr. T Vithya*	HOD, Department of Pharmacy Practice, Al-Ameen College of Pharmacy, Bengaluru, India *Corresponding Author
Dr. Sumi Laurence	Head Clinical Pharmacologist, Cytecare Hospital, Yelahanka, India

ABSTRACT Docetaxel is a chemotherapy drug commonly used to treat cancers such as head and neck, prostate, gastric, breast, and non-small cell lung cancer (NSCLC). The treatment demonstrates a 41% pulmonary response rate, while interstitial lung disease (ILD) remains a rare but serious adverse effect, occuring in less than 1- 5% of patients. Despite its rarity, docetaxel-induced ILD can lead to significant lung damage and has a high mortality rate. In this article we report a case of a 55-year-old female who developed pulmonary toxicity after three cycles of docetaxel (75 mg/m^2, 120 mg IV). The adverse drug reaction (ADR) was evaluated using the WHO-UMC causality assessment scale, indicating a probable association. The patient responded well to steroid treatment after discontinuing docetaxel. This case underscores the importance of vigilant monitoring of pulmonary function in patients undergoing docetaxel treatment, as early detection and intervention can improve outcomes.

KEYWORDS : Docetaxel, ILD (pneumonitis), Naranjo ADR probability scale, Breast Cancer

INTRODUCTION

Docetaxel is a taxane chemotherapeutic agent used to treat solid tumors, including breast, prostate, gastric, head and neck, and non-small cell lung cancers, improving outcomes in metastatic, adjuvant, and neoadjuvant settings.[1,2]

Despite its therapeutic benefits, docetaxel can cause a range of acute and long term adverse effects, particularly pulmonary toxicity.[1,3]

Common adverse effects of docetaxel (occurring in more than 10% of patients) include fluid retention, hair loss (alopecia), central nervous system effects (such as neuropathy), dermatological reactions, stomatitis, nausea, vomiting, diarrhea, elevated serum transaminases, hematologic changes like neutropenia, thrombocytopenia, leukopenia, and anemia, as well as myalgia, neuromuscular reactions, nail issues, and pulmonary complications. Pulmonary reactions occur in approximately 41% of patients receiving docetaxel, but interstitial lung disease (ILD) is a rare event, affecting less than 1%-5% of patients receiving Docetaxel, it remains an important event that carries a high mortality up to 40%.[4]

In this report, we present a case of Interstitial lung disease (ILD), an immune response mediated lung injury following three cycles of docetaxel chemotherapy, a rare but notable adverse effect of the drug.

Interstitial lung disease (ILD) refers to a group of disorders that affect the interstitium, the thin, delicate tissue lining the lung alveoli, where blood vessels are located for gas exchange.

Pneumonitis/ILD: Docetaxel can rarely cause interstitial pneumonitis, presenting as dyspnea, dry cough, malaise, and fever, often dose-dependent and more frequent with weekly regimens or in combination with gemcitabine or radiation. Patients with preexisting lung disease are at higher risk. Management includes discontinuing docetaxel, supportive care, and glucocorticoids for severe cases. Most cases resolve with appropriate treatment.[1]

Mechanisms of Lung Injury

The mechanism of action involves cellular mitosis inhibition by antagonizing the microtubule proteins disassembly.[6]

Although DILD generally affects the lung parenchyma, it can also involve the airways, giving rise to a variety of clinical and histological patterns, including hypersensitivity reaction, pulmonary fibrosis, bronchospasm, pneumonitis, and noncardiogenic pulmonary edema.7 The interaction between individual factors, such as genetics and previous or current exposures, may predispose individuals to pulmonary toxicity. In Japanese patients, for instance, the presence of HLA-DRB1*04:05 and HLA-B*15:01 alleles has been linked to pulmonary toxicity.2,8 In contrast, the presence of the HLA-A*3101 allele has been associated with drug-induced hypersensitivity reactions in individuals of European descent.[7]

Clinical Implications

Symptoms: Patients may exhibit cough, dyspnea, fever, and chest pain, which can mimic other respiratory disorders. Timely recognition is crucial for effective intervention.[8]

Diagnosis: Diagnosis involves clinical evaluation, imaging (such as chest CT), and pulmonary function tests. It is important to differentiate between drug-induced pneumonitis and other etiologies.[9,10]

Incidence and Risk Factors: The incidence of lung injury ranges from mild to severe, with risk factors including high doses of docetaxel and pre-existing lung disease. [10]

As a result, Docetaxel's enhanced solubility (compared to the insolubility of paclitaxel) increases its cytotoxicity against cancer cells in ovarian, endometrial, colon, and breast cancers.

Management Strategies

Evaluating lung function prior to chemotherapy and monitoring during treatment can help identify at-risk patients. Dose adjustments may be necessary for those with compromised pulmonary function.

Although the occurrence of docetaxel-related ILD is rare, it will lead to respiratory failure if treatment is delayed. ILD responds well to steroid treatment, it can be prevented or

delayed by the administration of oral dexamethasone before and after infusion of docetaxel and discontinuation of docetaxel administration to prevent further complications.[11,12]

Discussions about alternative therapies should be conducted with patients. Collaboration among oncologists, pulmonologists, and primary care providers is vital for comprehensive management of affected patients.

Case Report

Case Study: Docetaxel-Induced Interstitial Pneumonitis in a Patient with Breast Cancer

Patient Information:

A 54-year-old female with a history of hypertension, currently on Metoprolol XL 25 mg OD and Telmisartan 40 mg OD, presented to the hospital with a lump in her left breast. Upon evaluation, several diagnostic tests, including a Positron Emission Tomography (PET) scan, confirmed the diagnosis of primary carcinoma of the left breast (stage PT2N0M0) with involvement of the left axillary lymph node.

Initial Treatment:

The patient underwent breast conservation surgery with sentinel lymph node biopsy on February 15, 2023. Following surgery, she was referred to the Medical Oncology Department for adjuvant chemotherapy. The planned treatment regimen included six cycles of TC chemotherapy (Docetaxel 75 mg/m^2 and Cyclophosphamide 600 mg/m^2) (combined chemotherapy) every three weeks, along with adjuvant radiation therapy (RT) and hormonal therapy (HT) for 5 years.

The first cycle of chemotherapy was administered on March 18, 2023, at higher doses than initially planned (Docetaxel 120 mg and Cyclophosphamide 1000 mg).

Development of Pulmonary Symptoms

By the third cycle, on April 29, 2023, the patient developed symptoms of cough and breathlessness. A pulmonary evaluation was conducted on May 15, 2023, which included a Computed Tomography (CT) chest scan. The scan revealed bilateral ground glass opacities (GGO), which were suggestive of drug-induced interstitial pneumonitis, a known but rare side effect of docetaxel.

The adverse drug reaction (ADR) was evaluated using the WHO-UMC causality assessment scale, indicating a probable association.

Management and Modification of Treatment

In light of the pulmonary findings and the patient's symptoms, it was decided to modify her treatment plan. Options included switching the chemotherapy regimen to either AC (Doxorubicin + Cyclophosphamide) or EC (Epirubicin + Cyclophosphamide), or discontinuing chemotherapy altogether. Keeping the severity of the symptoms in mind, the decision was made to discontinue the current chemotherapy regimen and initiate appropriate management for the pulmonary toxicity.

The patient was started on the following medications to manage her pulmonary symptoms:

1. Acetylcysteine 600 mg twice daily for 10 days to help reduce the mucus viscosity and support lung function.
2. Levocloperastine Fendizoate (2 tsp BD for 20 days), an anti-tussive and bronchodilator, to help manage the cough and reduce airway irritation.
3. Levosalbutamol MDI (Metered Dose Inhaler) 50 mcg, 2 puffs twice daily to alleviate breathlessness and provide bronchodilation.
4. Prednisolone:
   - 40 mg once daily for 5 days after food.
   - 20 mg once daily for the next 5 days.
   - 10 mg once daily for 5 days.
   - 10 mg on alternate days for the final 5 days, after which the steroidal treatment was stopped.

Outcome

The patient's symptoms like cough and breathlessness gradually improved following the initiation of corticosteroid therapy, and the pulmonary toxicity appeared to resolve. There were no further complications related to lung function, and the steroid regimen was successfully tapered off as per the plan.

CONCLUSION

This case highlights the rare but serious side effect of docetaxel-induced interstitial pneumonitis in a patient undergoing chemotherapy for breast cancer. Early recognition of pulmonary symptoms, along with prompt radiological and clinical evaluation, is critical in managing such adverse reactions. In this case, the timely intervention with steroids and the modification of the chemotherapy regimen led to a favorable outcome. This underscores the importance of close monitoring and individualized management in patients receiving chemotherapy with known pulmonary toxicity risks.

Docetaxel-induced lung injury is a significant complication that can impact treatment outcomes in cancer patients. Increased awareness of its mechanisms, risk factors, and management strategies is essential for healthcare providers. Further research is needed to better understand this phenomenon and improve preventive measures and treatment protocols.

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