Acute cardiogenic shock with paclitaxel use in a lung carcinoma patient

Sir,

Paclitaxel is a taxane group of anticancer drug, widely used in the treatment of ovarian, breast, lung, and genitourinary carcinomas. In advanced non-small cell lung carcinomas, paclitaxel is indicated at a dose of ≥175 mg/m^2 in combination with a platinum compound. Toxicities of paclitaxel are commonly bone marrow suppression, hypersensitivity reaction, peripheral neuropathy, and rarely cardiac toxicity. Spectrum of cardiotoxicity varies from asymptomatic bradycardia, AV conduction block, bundle branch block, and ventricular arrhythmia to fatal myocardial ischemia.[1] We are highlighting a case of acute cardiogenic shock shortly after paclitaxel infusion in a patient of squamous cell lung carcinoma in the first cycle of chemotherapy, to emphasize the importance of this rare yet serious, life-threatening cardiac adverse event to improve awareness among clinicians.

A 54-year-old male nondiabetic, nonhypertensive, patient was admitted with stage IV squamous cell right lung carcinoma with left hip metastasis. The baseline vitals as blood pressure, pulse rate, hemogram, and blood biochemistry including blood sugar, urea, creatinine, electrolytes, liver, and renal function tests, electrocardiogram (ECG) were within normal range.

The patient was advised chemotherapy regimen of paclitaxel (175 mg/m^2) injection followed by carboplatin (AUC-5) injection at a dose of 450mg. Carboplatin maximum dose capping is based on target area under the curve (AUC) using Calvert formula to avoid toxicity due to overdosing. The first cycle was initiated with the requisite premedications (intravenous ondansetron 8 mg; ranitidine 50 mg; and dexamethasone 8 mg). Within 20 min of initiating paclitaxel infusion (260 mg diluted in 300 ml normal saline), the patient developed profuse sweating, feeble pulse and unrecordable blood pressure, cold extremities, and impaired consciousness without chest pain. The patient did not have any features of any hypersensitivity reaction (angioedema, bronchospasm, and urticaria) or any neurological deficits. Paclitaxel infusion was stopped immediately, and cardiopulmonary resuscitation was given. ECG revealed tachycardia with multiple ventricular ectopics [Figure 1]. In order to rule out acute myocardial infarction as the underlying cause, cardiac enzymes were normal, and serial Troponin-T tests were negative. The SpO_2 was 93%, and random blood sugar levels were within the normal range. The patient was treated with vasopressor agents as noradrenaline, dopamine and hydrocortisone, and moist oxygen inhalation. Echocardiography report showed no regional wall motion defect, the left ventricular ejection fraction was 58% with no other significant abnormalities.

He responded well to conservative treatment and was stabilized hemodynamically within the next 36–48 h. The patient had to be discharged as he refused to give consent for any further chemotherapy.

Although some drugs which were used for premedication (ondansetron and ranitidine) may rarely cause cardiac adverse events, the possibility of any interaction with paclitaxel though not documented cannot be ruled out with certainty. Therefore, the diagnosis of paclitaxel-induced acute cardiogenic shock was made based on clinical suspicion, temporal association, absence of other causes, and previous reports of the pharmacological plausibility of paclitaxel and the observed cardiac adverse event. The positive dechallenge information was also noted.

Causality assessment was done by the WHO UMC causality assessment scale shows "*probable*," by the Naranjo's scale shows "*possible*" association and Hartwig's adverse drug

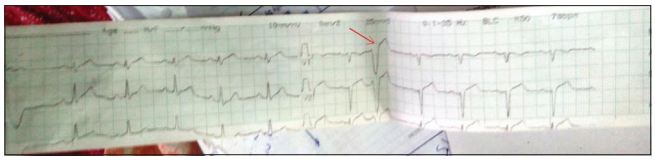

Figure 1: Electrocardiograph showing tachycardia with ventricular ectopic

reaction (ADR) severity assessment scale shows "moderate" severity ADR. The ADR was reported in the prescribed form of the Pharmacovigilance Program of India (individual case safety reports [ICSR] number2017-15512).

The most common reported cardiac adverse event is paclitaxel-induced bradycardia (0.1%–31%), while myocardial ischemia is relatively rare (1%–5%). Several formulations of paclitaxel contain *CremophorELP* as the vehicle. Some published reports have suggested that some cardiac effects could be due to cremophor which stimulates histamine release.[2-4]

The underlying mechanism of the cardiac adverse events is yet to be well understood. Some studies on isolated myocytes have suggested that polymerization of microtubules in myocytes leads to reduced calcium release from sarcoplasmic reticulum resulting in negative inotropic effects or due to its effects on the His-Purkinje system or autonomic control.[5]

There are no published reports of acute cardiogenic shock without associated acute myocardial infarction.

We also undertook a search for reports of suspected paclitaxel-induced cardiogenic shock in *Vigibase*, the WHO global drug safety database using *vigiLyze* on April 13, 2017, using the following search criteria: "*Paclitaxel*" (substance) in the WHO Drug Dictionary and "cardiogenic shock" as "*Preferred term*" of the Medical Dictionary for Regulatory activities terminology. The search revealed 34 ICSR with reports, from America (18), Europe (12), Asia (2), and one each from Africa and Oceania. There was only one report from India. Data mining report generated from the search shows reports from 10 countries with information component (IC) value of 1.17 and IC_{025} value of 0.64. However, information from each ICSR in the *vigibase* comes from a variety of sources, and the likelihood that the suspect ADR is drug related is not the same in all cases.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. Bovelli D, Plataniotis G, Roila F; ESMO Guidelines Working Group. Cardiotoxicity of chemotherapeutic agents and radiotherapy-related heart disease: ESMO clinical practice guidelines. Ann Oncol 2010;21 Suppl 5:v277-82.
2. Berardi R, Caramanti M, Savini A, Chiorrini S, Pierantoni C, Onofri A, *et al*. State of the art for cardiotoxicity due to chemotherapy and to targeted therapies: A literature review. Crit Rev Oncol Hematol 2013;88:75-86.
3. Schrader C, Keussen C, Bewig B, von Freier A, Lins M. Symptoms and signs of an acute myocardial ischemia caused by chemotherapy with paclitaxel (Taxol) in a patient with metastatic ovarian carcinoma. Eur J Med Res 2005;10:498-501.
4. Shah K, Gupta S, Ghosh J, Bajpai J, Maheshwari A. Acute non-ST elevation myocardial infarction following paclitaxel administration for ovarian carcinoma: A case report and review of literature. J Cancer Res Ther 2012;8:442-4.
5. Howarth FC, Calaghan SC, Boyett MR, White E. Effect of the microtubule polymerizing agent taxol on contraction, Ca^{2+} transient and L-type Ca^{2+} current in rat ventricular myocytes. J Physiol 1999;516 (Pt 2):409-19.

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