Reversible Bleomycin Toxicity

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Introduction

Pulmonary drug toxicity is an important cause of acute and chronic lung disease and is often under diagnosed. All forms of interstitial pneumonia have been reported to occur as a result of pulmonary drug toxicity with non specific interstitial pneumonia (NSIP) being the most common entity. Bleomycin is a chemotherapeutic agent used in the treatment of several tumours, including lymphoma, seminomatous and nonseminomatous germ cell tumours of the testes. Bleomycin-induced pulmonary toxicity occurs in 3-5% of treated patients and is the major factor that limits its dosage. Diffuse alveolar damage (DAD) is the most common manifestation of bleomycin-induced lung disease [1], with NSIP and bronchiolitis obliterans organizing pneumonia (BOOP) being less common. We report a case of reversible bleomycin induced pulmonary toxicity, in a patient of non-seminomatous germ cell tumour of testis, resembling usual interstitial pneumonia (UIP) on high resolution computed tomography (HRCT). Such an imaging feature of bleomycin induced pulmonary toxicity has not been described previously.

Case Report

A 52 year old man with non-seminomatous germ cell tumour (mixed pattern) of testis was treated with orchiectomy followed by three cycles of a combination chemotherapy including bleomycin, etoposide and cisplatin at 21-day intervals. Bleomycin 30 IU was given intravenous (IV) bolus on days 1, 8 and 15 of each cycle. At the end of three cycles, he started having dry cough and dyspnea on exertion. On examination, his vital parameters were found within normal limits. On auscultation, he was found to have inspiratory crackles bilaterally, especially at the lung bases. A chest radiograph (Fig. 1) revealed peripheral based reticulonodular opacities predominantly involving middle and lower zones of both lung

fields. His previous chest radiograph at the time of starting of chemotherapy schedule was reviewed and was found to be normal. A pulmonary function test was carried out which revealed moderate restrictive defect with impaired gas exchange. He underwent HRCT scan of chest in a 16 slice multi-detector computed tomography (MDCT) machine. The HRCT revealed nearly symmetrical subpleural irregular reticular opacities and honeycombing involving all zones with a predominant basal distribution (Fig. 2). In addition, there were multiple sub-centimeter sized mediastinal lymph nodes. Based on the clinical profile, chest radiograph and HRCT findings, possibility of bleomycin induced pulmonary toxicity was considered. Bleomycin was stopped and the chemotherapeutic regime was modified accordingly. He showed a gradual improvement over next few months. At the last review, which was approximately six months after stoppage of bleomycin, he was asymptomatic. A chest radiograph did not reveal any significant abnormality. A repeat HRCT chest revealed near complete resolution of the previous lung lesions with a few residual fibrotic lesions bilaterally (Fig. 3). A repeat pulmonary function test was normal.

Discussion

A wide range of cytotoxic and non cytotoxic drugs have the potential to cause pulmonary toxicity. The most common cytotoxic drugs resulting in lung toxicity are bleomycin, methotrexate, carmustine, busulfan, and cyclophosphamide [2]. Clinical, radiologic and histologic findings of pulmonary drug toxicity are nonspecific and hence it is difficult to recognize this entity. The underlying histopathologic processes include DAD, NSIP, BOOP, eosinophilic pneumonia, obliterative bronchiolitis, pulmonary haemorrhage, edema or hypertension [1].

Bleomycin is an effective antitumour agent for treatment of lymphoma, testicular tumours and squamous cell carcinomas. Pulmonary toxicity of bleomycin is well

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Fig. 1 : Chest radiograph (PA view) shows reticulonodular opacities (white arrows) predominantly involving middle and lower zones bilaterally.

Fig. 2 : HRCT (section thickness = 1mm, Lung window) at various levels shows presence of nearly symmetrical sub-pleural irregular reticular opacities (white arrows) and occasional honeycombing involving all zones with a predominant basal distribution.

Fig. 3 : Follow up HRCT (section thickness = 1mm, Lung window) sections at the same levels as in Fig 2 showing near complete resolution of the lesions with a few residual fibrotic lesions (white arrows).

known and includes pulmonary edema, diffuse alveolar damage, and chronic pneumonitis with fibrosis, BOOP and hypersensitivity reactions [3]. Clinically, pulmonary toxicity is manifested by cough, dyspnea, tachypnea and fine rales, decreased breath sounds or pleural friction rubs on auscultation. At times, bleomycin pulmonary toxicity can be rapidly fatal [4]. Important risk factors for bleomycin pulmonary toxicity include elderly age (>70 years), cumulative dose of bleomycin >400 IU, pre-existing pulmonary disease, coexisting renal failure, prior or concomitant thoracic irradiation, high-dose oxygen exposure, smoking or previous exposure to bleomycin within six months.

In a patient with testicular tumour, bleomycin toxicity and pulmonary metastases may coexist making it extremely difficult to differentiate between these two conditions. Therefore, in the appropriate clinical setting, a high index of suspicion and knowledge of the typical radiologic manifestations of bleomycin toxicity is essential. Plain radiography is known to be less sensitive and specific in the detection of early changes of pulmonary drug toxicity [2]. In a study of 100 patients treated with bleomycin, Bellamy et al [5] found CT evidence of lung damage due to bleomycin in 38%, where as damage was detected in only 15% by radiography. HRCT provides a very sensitive and reasonably specific means of diagnosing early lung changes of drug toxicity. Needless to say that the most important component of management of pulmonary drug toxicity is to suspect, diagnose the condition at the earliest and stop the offending agent immediately. Hence HRCT plays a crucial role in the management of pulmonary drug toxicity.

Our patient showed several unusual features. He was middle aged and developed bleomycin toxicity at a

relatively lower dosage of 270 IU. He demonstrated HRCT features resembling usual interstitial pneumonia as a part of bleomycin toxicity. A follow up HRCT scan, six months after stoppage of bleomycin showed near complete resolution of the lesions, an observation which emphasizes that the lesions observed in earlier HRCT scans were due to bleomycin toxicity. Bleomycin toxicity resembling UIP on HRCT has not been described in the literature. Moreover, a follow up HRCT documenting near complete resolution of the lesions has been rarely described. This highlights the importance of knowing atypical HRCT features of bleomycin toxicity so as to stop the medication immediately. Our case also shows HRCT documentation of reversibility of the lesions when diagnosed early in the course of the disease.

Conflicts of Interest

None identified

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