Pegylated-Interferon Induced Interstitial Pneumonitis

Sir,

Pulmonary toxicity is a rare but serious side effect of interferon. Its spectrum can range from gross parenchymal disease to subtle obstruction of airways and sometimes interstitial involvement. Chest X-ray, high resolution computed tomography (HRCT), spirometry, bronchoalveolar lavage and tissue biopsy are the key investigations used to define the type of lung injury.1-3 It has been a few years since interferon was globally recognized as a cause of interstitial pneumonitis and only a handful of cases have been described so far.4 However, no consensus guidelines regarding the diagnosis and management of interferon induced interstitial pneumonitis (IIP) have been published so far. Through this report, we aim to describe the first case of IIP from Pakistan and seventeenth in the world with further elaboration of its salient features from literature to suggest possible formulation of guidelines for IIP.

A 53 years old gentleman with chronic liver disease secondary to HCV presented at our clinic with active viremia. He did not have any respiratory symptoms to start with and his chest X-ray was also normal. Patient was given 180 µg of pegylated interferon α-2a once weekly plus 1200 mg of oral ribavirin daily. He was followed fortnightly and evaluated for side effects. After 12 weeks of treatment, he developed dyspnea with bilateral crepitations all over the chest. There was gradual worsening of dyspnea on Medical Research Council (MRC) scale, restrictive pattern on spirometry, progressively worsening 6 minutes walk test and appearance of bilateral reticulonodular shadowing with ground glass attenuation (Figure 1A). HRCT showed diffused involvement of both lungs with randomly distributed nodules, patchy infiltrates, septal thickening, bronchiectasis and ground glass attenuation (Figure 1B-D). Bronchoscopy and broncoalveolar lavage (BAL) were normal.

Based on the above, list of differential diagnosis was made namely (1) pulmonary sarcoidosis, (2) cryptogenic fibrosing alveolitis, (3) hypersensitivity pneumonitis, (4) drug induced interstitial pneumonitis and (5) infective/neoplastic lung infiltrates.3 Interferon combination therapy was immediately stopped but the patient did not show clinical recovery. A lung biopsy was arranged, which showed varying degree of fibrosis with plugs of granular tissue, cell infiltrates and focal honey combing with proliferation of peri-bronchiolar and para-alveolar smooth muscle (Figure 1E). There was no eosinophilia or raised IgE in serum. Considering the above, diagnosis of interferon induced interstitial pneumonitis was made and patient was immediately put on oral prednisolone. He made good clinical recovery with complete resolution of symptoms and clearance of chest X-ray with 8 weeks of treatment with 1 mg/kg prednisolone; gradually tapered off thereafter (Figure 1F).

By a comprehensive review of earlier case reports and our own experience, we made the conclusion that diagnosis and management of IIP can be both tricky and difficult but if done before the onset of permanent lung damage, can yield excellent patient outcomes.1,4 It mostly presents in the first 12 weeks of starting interferon with symptoms of cough, dyspnea, fever or fine inspiratory crackles in chest. Chest radiographs usually show bilateral patchy infiltrates or opacifications, and HRCT shows bilateral patchy consolidation and ground-glass attenuation.2,4 Definitive diagnosis, however,
needs tissue biopsy. Possible treatment options include stopping the drug, use of adjuvant steroids or immunosuppressants; based on severity, type and extent of lung injury as well as clinical response. As there are no consensus guidelines on the diagnosis and management of IIP, we suggest following recommendations based on the above:  

1. All patients planned to receive interferon therapy should be evaluated for pulmonary pathologies before starting treatment both clinically and radiologically (i.e., chest X-ray).

2. All patients on interferon therapy should visit their treating physician at least monthly for the first 12 weeks of treatment and at least 3 monthly thereafter for evaluation of pulmonary status.

3. Physicians should evaluate their patients for new onset or worsening symptoms like cough, dyspnea, fever and should auscultate them for chest crepitations with the perspective of keeping low threshold for diagnosing IIP.

4. All patients presenting with respiratory symptoms should at least have a chest X-ray performed on the same visit and evaluated for new or expanding opacities/infiltrates.

5. Patients with suspicious findings on chest X-ray should be referred to chest physician who should then offer CT/HRCT for proper evaluation of X-ray findings.

6. Bronchoscopy with BAL or tissue diagnosis via pulmonary biopsy should be considered earlier in difficult cases.

7. Threshold for discontinuation of therapy should be low for individuals with moderate to severe chest symptoms and steroids or immunosuppressants should be considered for resistant cases.

The use of above mentioned formulation might help to diagnose and manage IIP in a more comprehensive and systematic way. It should be critically reviewed by experts in future studies to develop proper guidelines for IIP.

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**REFERENCES**


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