Patients' blood counts including erythrocyte sedimentation rate were normal. Blood and sputum culture showed no growth.

A portable plain radiograph revealed bilateral reticular opacity. In view of skin rash, acute onset of breathlessness and infective causes were ruled out, drug toxicity was considered. A high-resolution computerized tomography (HRCT) along with expiratory scans was done (Figs. 1-3). A pulmonary function test was performed once patient stabilized and it showed moderate restrictive lung pattern.

In the background of recent initiation of specific drug therapy for proven liver disease the etiology was attributed to D-Penicillamine. The offending drug was stopped immediately, and patient was started on inhaled corticosteroids, N-acetyl cysteine 600 mg thrice a day and parenteral methyl prednisolone 60 mg thrice a day for a week with other symptomatic measures. Patient improved substantially with the treatment and symptoms subsided. A repeat chest plain radiograph was normal.

DISCUSSION

Drugs as etiological agents of ILD are confounding for two main reasons: One is that they offer a coherent explanation to a sizeable number of ILD cases seen in clinical practice [4]; and the second is that early withdrawal of the causative drug will often lead to improvement or even cure of the ILD.

DL lung injury has various patterns of pathogenesis in the presentation. The recognized ones are,
- Hypersensitivity reactions
- Non-cardiogenic pulmonary edema
- Interstitial pneumonitis
- Pleural and mediastinal disorders
- Pulmonary vascular disease
- DI Lupus
- DI bronchopasm

John Walde first described the use of penicillamine in Wilson's disease in 1956 [5]. He had discovered the compound in the urine of patients (including his own) who had taken penicillin, and experimentally confirmed that it increased urinary copper excretion by chelation.

Penicillamine is a drug of the chelator class. It is an alpha amino acid metabolite of penicillin although it has no antibiotic properties. Penicillamine is used as a form of immunosuppression to treat rheumatoid arthritis [6]. It works by reducing numbers of T-lymphocytes, inhibiting macrophage function, decreasing IL-1, decreasing rheumatoid factor, and preventing collagen from cross-linking. Other uses include in Rheumatoid arthritis, Lead poisoning, cystinuria.
In Wilson’s disease a dose of 500-1500 mg is indicated for initiation and titrated to achieve urinary copper levels of 0.5-1 mg per day. In our patient owing to psychiatric manifestations of the disease a higher dose was consumed by the patient inadvertently, which resulted in dose-dependent toxicity.

Adverse effects from drugs on the respiratory system have emerged as a significant topic in pulmonology and represent a sizeable proportion of patients seen in pulmonary practice in recent times. Under the impetus of a French study group on DI respiratory disease, known as the Grouped' Etudes de la Pathologie Pulmonaire Iatrogène, a comprehensive table of drugs initiating adverse respiratory reactions has been drawn up [7].

A major, but largely unresolved question is why, out of the treated population of patients, only some individuals will develop DI-ILD. A limiting dose has only been identified for a few drugs [9]. For most drugs, there is no apparent role of dosage or duration of treatment in relation to the likelihood of developing adverse effects, i.e., development remains largely unexpected and idiosyncratic.

Various histological patterns are recognized. Apart from conventional patterns of ILD as non-specific interstitial pneumonia (cellular or fibrotic), eosinophilic pneumonia [10], or pulmonary fibrosis, drugs can also elicit less usual patterns such as organizing pneumonia (OP, previously designated BOOP), or desquamative interstitial pneumonia [11].

Penicillamine has been attributed to cause few recognized patterns including acute and sub-acute pneumonitis, eosinophilic pneumonia, organizing pneumonia Adult Respiratory Distress Syndrome, diffuse alveolar hemorrhages and Goodpasture’s disease. A case of Goodpasture’s disease was reported in a patient with Wilsons Disease [12].

The primary goal of treatment in DI-ILD is to suppress the inflammatory response and prevent the deposition of fibrotic tissue. Treatment consists mainly of discontinuing the offending drug immediately, and supportive management of the pulmonary symptoms, e.g., inhaler therapy and oxygen if required until the drug-induced lung disease improves. Challenge tests (reintroducing the suspected medication to see if symptoms recur) are rarely performed.

Steroid therapy (such as prednisolone) is sometimes used to quickly reverse the lung inflammation caused by the offending drug [13]. Prognosis of acute drug-induced ILD is usually excellent. Symptoms will resolve within 24-48 hrs, with full recovery generally being achieved. Chronic syndromes may take longer to resolve but often leave significant scarring that may need long-term supportive therapy.

CONCLUSION

Penicillamine is not a very commonly cited drug as a cause of ILD. Since the drug is being used more widely in recent days for diverse conditions, clinicians should be aware of the possible toxic effects on the lung and also should have a high index of suspicion as drug-induced ILD is also masqueraded by the disease process and definitive diagnosis is generally not possible and is often by exclusion, by establishing a temporal relationship with the offending agent and assessing response after withdrawal of the offending drug.
REFERENCES