

## Isoniazid and Pulmonary Fibrosis

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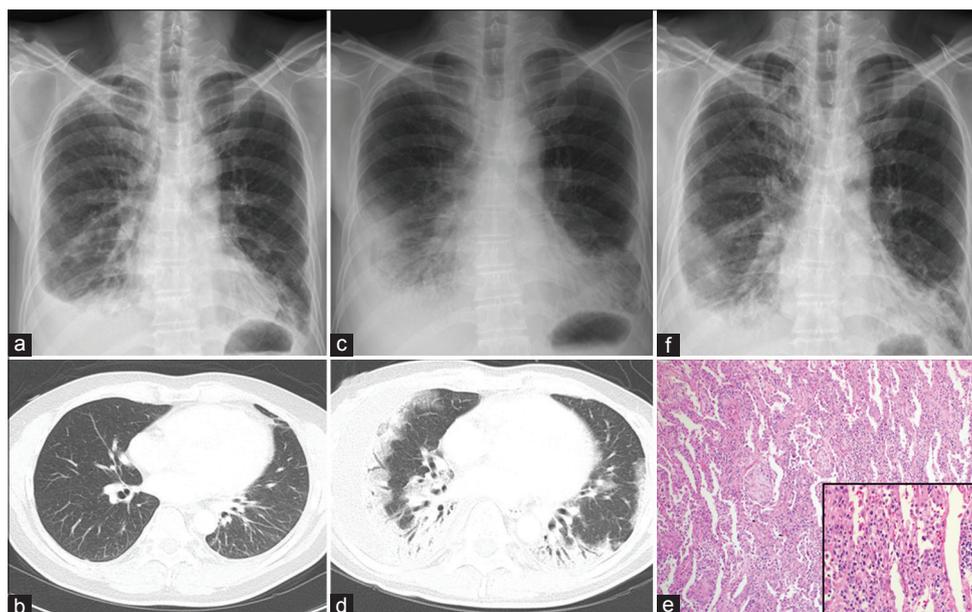
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To the Editor: The anti-tuberculosis (TB) therapy can cause various drug adverse effects including hepatotoxicity, nephrotoxicity and skin rash.<sup>[1,2]</sup> There are some case reports about interstitial lung disease (ILD) such as pneumonitis caused by isoniazid (INH), rifampin (RFP), ethambutol (EMB).<sup>[3,4]</sup> The causative drug was discontinued permanently or re-administrated after desensitization therapy. But the pulmonary fibrosis induced by short anti-TB medication was very rare. We herein report a case of pulmonary fibrosis due probably to INH, which was developed after 3 weeks of anti-TB treatment.

A 42-year-old man was admitted to hospital due to continuous fever, night sweating, and weight loss for 1-month and exacerbated dyspnea on exercise (DOE) for 2 weeks. Chest posterioranterior showed right side pleural effusion [Figure 1a and b]. Although pleural biopsy showed chronic inflammation, the effusion was

exudates dominantly with lymphocyte cells and adenosine deaminase was 136.2 IU/L, highly suggesting TB pleurisy. Overall, he was diagnosed as TB pleurisy. INH, RFP, EMB, and pyrazinamide were administered, and the pleural effusion was drained with chest catheter. After taking anti-TB medication, symptoms diminished gradually but intermittent fever above 38°C occurred. After 3 weeks of anti-TB medication, he complained of DOE and cough again, and the symptoms got worsened. The arterial gas blood analysis gave PaO<sub>2</sub> 41 mmHg, PaCO<sub>2</sub> 49 mmHg, and SaO<sub>2</sub> 86% on room air. Chest images showed no increase of pleural effusion but newly developed bilateral lung infiltrations including glass ground opacity, consolidation, and the reticular opacity [Figure 1c and 1d]. Because ILD induced by anti-TB medication was mostly suspected, all drugs were discontinued. To define the diagnosis



**Figure 1:** (a) Before initiation of anti-tuberculosis (TB) medication, chest posterioranterior (PA) showed right side pleural effusion; (b) Chest computed tomography (CT) scan before anti-TB medication; (c) After 3 weeks of anti-TB therapy, chest PA exhibited newly developed bilateral lung infiltrations; (d) After 3 weeks of anti-TB therapy, chest CT scan showed glass ground opacity, consolidation, and reticular opacity on both lower lobe; (e) Histological examination revealed chronic interstitial inflammation with fibrosis (H and E, original magnification  $\times 100$  and  $\times 400$ ); (f) Chest PA after 2 months of steroid therapy.

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of lung lesion, open lung biopsy was promptly performed. Biopsy at right lower lobe revealed chronic interstitial inflammation with fibrosis [Figure 1e]. We considered provocation test confirming the causative drug, but we thought that drug challenge could aggravate the lung injury. Many references suggested that INH is most common cause of pneumonitis.<sup>[2,4,5]</sup> At postoperation days 5, anti-TB medication except INH was started with prednisolone 60 mg and tapered. At 2 months after open lung biopsy, follow-up chest images showed combined pulmonary fibrosis and emphysema [Figure 1f].

The frequency of ILD caused by anti-TB medication is relatively rare, about 2%. The most frequently causative drug is INH and other drugs such as RFP and EMB also cause ILD.<sup>[4]</sup> But there is no case report of the patient with INH-induced lung fibrosis. Pneumonitis induced by anti-TB medication causes some symptoms including fever, dyspnea, rash, and even chest pain. Among them, fever is the most common symptom.<sup>[4,5]</sup> In this case, the patients complained of intermittent fever above 38°C within first 10 days of TB treatment, the fever might be an early sign of pneumonitis. In this case, the lung fibrosis was developed very rapidly in 3 weeks of anti-TB medication, and the causative drug is probably INH. This case emphasizes that the clinician should consider the possibility of drug-induced pneumonitis or lung fibrosis even at initial phase of

anti-TB treatment when the patient shows fever and complains of worsening of DOE.

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