Sir,

Unilateral pleural effusions are common secondary to *Mycobacterium tuberculosis* infection in developing countries. However, new onset pleural effusion after start of anti-tuberculous therapy or recurrent pleural effusions are rare occurrences. We, hereby, present a young girl diagnosed to have tuberculous effusion developed recurrent pleural effusion on initiation of therapy and raised the possibility of other aetiology of pleural effusion.

A 16 year old girl presented with a week long history of fever with chills, malaise, anorexia, dyspnoea and left sided pleuritic chest pain. She had no past history of tuberculosis in her or history of any other significant chronic illness in family. On admission she had following vitals: pulse 126/min; blood pressure 96/70 mmHg; temperature 100.6°F; respiratory rate 24/min. Her oxygen saturation at room air was 99% by pulse oximetry. The general examination was unremarkable except mild pallor. Chest examination revealed reduced chest movements, stony dull note and absent breath sounds on left infrascapular region. Her haematological and biochemical profiles were within normal limits. Chest radiograph showed presence of pleural effusion on left side (Figure 1). Computed tomography of thorax was done to rule out any pneumonitis or space occupying lesion in the lung parenchyma. After hospitalisation, thoracocentesis was done and 600 ml straw colour fluid was aspirated out (Figure 2). The pleural fluid had pH 7.2, total leucocyte count 4600/cmm, polymorphs 12% and lymphocytes 88%, Proteins 5.6 gm/dl, lactic dehydrogenase 872 IU and glucose 14 mg/dl. Pleural fluid was negative for acid fast bacilli and gram staining. Pleural fluid culture was also sterile. However, adenosine deaminase (ADA) was positive (65 IL, normal < 40) in the pleural fluid. So she was diagnosed as a case of tuberculous pleural effusion and prescribed first line anti tuberculous therapy consisting of Isoniazid 300 mg, Rifampicin 450 mg, Pyrazinamide 1500 mg and Ethambutol 800 mg daily along with pyridoxine supplements. She noticed improvement in her symptoms for next few days but she reported back with recurrence of chest pain, dyspnoea and fever after 2 weeks. Skiagram chest showed collection of fluid again in left pleural cavity (Figure 3). This time there was minimal pericardial effusion as well. Aspirated pleural fluid was suggestive of exudative effusion and was negative for malignant cells (Figure 4). The pleural fluid and blood cultures were sterile. She was treated with empirical antimicrobials, (Piperacillin+Tazobactum combination and Linezulide) and oral prednisolone in addition to antituberculous therapy in view of possibility of parapneumonic effusion or immunological rebound. Skiagram chest showed refilling of pleural cavity (Figure 5). Thoracoscopy was planned but could not be done due to technical constraints.

The patient was re-evaluated to determine the cause of recurrent pleural effusion. Her ESR (62 mm FHR by Westergreen method) and CRP (20 u.g/dl) both were elevated while complements (C3, C4) levels were low. Antinuclear antibodies (ANA) titer was positive (1:320) in homogeneous pattern but rheumatoid factor was negative. On suspicion to have Isoniazid induced lupus she was further investigated for double stranded DNA antibodies and anti-histone antibodies. Both were found positive. Then Isoniazid was withdrawn. She improved with oral prednisolone along with antituberculous therapy and was discharged.
The appearance of recurrent pleural effusion could have been explained by paradoxical response well described in patients of tuberculosis and develops due to an effect between mycobacterial products and host immunity after initiation of antituberculous therapy. This was initially thought and steroid was added in the initial follow up visit but she did not improve.

Isoniazid (INH) is first line antituberculous drug used in treatment and prophylaxis of tuberculosis. INH has been implicated in drug induced lupus erythematosus which has been defined as lupus like syndrome related to continuous drug exposure and resolves after cessation of the offending drug. INH induced pleural effusion is exudative and usually occurs between 3-12 weeks of initiation of isoniazid. There have been few case reports of INH induced pleural effusion in the literature. INH is associated with ANA positivity in nearly 25% of patients and clinically apparent drug induced lupus in approximately 1% of patients. The non-specific serum elevation of ANA, double stranded deoxy ribonucleic acid (ds DNA) and anti-histone antibodies are consistent with it, followed by the pleural effusion resolution after removal of INH from the treatment regimen.

Young girl presented with recurrent pleural effusion could have been explained by immunological rebound but presence of antinuclear, dsDNA and anti-histone antibodies and response to Isoniazid withdrawal along with steroid makes possibility of INH induced lupus more likely in our patient.

References

