

# Cocktail treatment of antibiotic, steroid, and analgesic in a tubercular case; the urgency to set up antimicrobial stewardship practices in the community

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### ABSTRACT

Tuberculosis is a well-known entity in India with many implemented policies to ensure the cost-effective early management. Missed, delayed, and complicated presentations do occur, requiring expensive tertiary level of health care. Among many contributing factors, lack of antibiotic stewardship is at the top. We report a case of 65-year-old man who presented with on and off fever for six months, receiving cocktail treatments of antibiotics, analgesics, and steroids from a local dispensary. Our initial investigations revealed microcytic anemia with high erythrocyte sedimentation rate, leukocytosis, and bilateral pleural effusion on chest X-ray. Contrast enhanced computer tomography of chest and abdomen suggested disseminated tuberculosis including bilateral empyema. Frank pus was drained on thoracentesis, which was negative for Gram stain, Ziehl-Neelsen stain, and bacterial culture, but positive CB-NAAT for tubercular bacilli with no resistance to rifampicin. Mantoux test and stool occult blood were positive. This case highlights an unusual presentation of tuberculosis and the ongoing lacunae in the society with importance to the primary care providers in the effective management of tuberculosis focusing on antimicrobial stewardship.

**Keywords:** Antibiotic stewardship, delayed diagnosis, empyema thoracis, primary care, tuberculosis

### Introduction

In addition to emphasizing the importance of considering tuberculosis in such chronic atypical presentations as a bilateral empyema thoracis (ET) in a primary care setting, we also like to throw some light on the social aspect of missing such well-known infectious condition, due to public dependence on inadequately trained personnel and availability and unsupervised issuing of antibiotics and steroids over the counter, which complicates the disease, and thereby increasing overall morbidity and mortality. This is basically due to lack of antimicrobial stewardship practice (ASP), which is defined as optimal utilization of the antimicrobials.<sup>[1,2]</sup>


Though ASP is the need of hour by all health-concerned individuals, practicing clinicians who prescribe the antibiotics, pharmacist who supplies it, and microbiologist who defines the role of the same are major contributors for the program in the society.<sup>[3,4]</sup> Physicians have been highly effective as stewardship program leaders.<sup>[3]</sup>

Furthermore, tubercular ET is a well-known entity especially in developing countries and accounts for a significant number of empyema cases.<sup>[5]</sup> Even though studies have shown a median age of 20–40 years and predominantly unilateral (usually right sided) involvement for tubercular empyema, elderly population presenting with chronic history of fever and/or cough and bilateral empyema should have tuberculosis in the differential diagnosis.<sup>[6-8]</sup>

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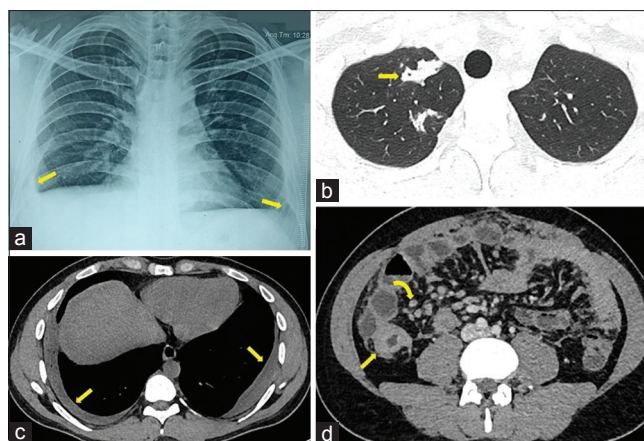
Hereby, we report a case of bilateral tubercular empyema with dissemination in a 65-year-old man where the diagnosis was overlooked and deferred for last six months at a local dispensary which could have prevented if ASP was practiced.

## Case Report

A 65-year-old man, non-alcoholic, non-smoker, presented with six-month history of intermittent high-grade fever with spikes occurring every 2–3 days in the initial few months and later continued to have persistently low-grade fever along with appetite loss and unintentional significant weight loss. The patient was advised a cocktail treatment of ciprofloxacin, prednisolone, and diclofenac intermittently on a weekly basis at a local dispensary. He denied any cough, shortness of breath, chest pain, rashes, myalgia, arthralgia, sore throat, dental caries, sexually transmitted diseases, jaundice, altered bowel habits, or past history or contact with tuberculosis.

On examination, the patient was pale and thin-built with normal vitals. Chest examination demonstrated a central trachea, decreased chest expansion, non-tender dull note to percussion, and decreased air entry in lower hemithorax of both sides. Rest of the systemic examinations were unremarkable except for a wide-fixed split S2 and an ejection systolic murmur in the pulmonary area. Considering the findings, few differentials were considered, such as valvular heart disease with infective endocarditis, partially treated chronic infective diseases, disseminated malignancy, and connective tissue diseases.

Blood picture revealed moderate anemia, neutrophilic leukocytosis, elevated erythrocyte sedimentation rate, reversed A:G ratio, and negative viral markers. Chest X-ray suggested bilateral minimal pleural effusion [Figure 1a]. Ultrasound-guided pleurocentesis demonstrated frank pus of about 10 ml from the right side and 30 ml from the left. Bilateral ET was diagnosed and analysis of pus showed negative for Gram staining, Ziehl–Neelsen staining, and KOH mount, but cell counts and biochemistry studies could not be done due to the thick nature of pus. Transthoracic echocardiography and serial blood cultures did not show any evidence of infective endocarditis or structural abnormality. Meanwhile, anemia work-up revealed microcytic hypochromic RBCs, reticulocyte index – 1%, serum ferritin – 39.2 ng/ml, and a positive stool occult blood. These findings pointed towards iron deficiency anemia (IDA) from chronic gastrointestinal (GI) blood loss possibly from prolonged steroid and analgesic use. Upper GI endoscopy was deferred due to the denial consent. Mantoux test was positive ( $12 \times 10 \text{ mm}^2$ ). Repeat chest ultrasound did not show drainable pus. Contrast-enhanced computer tomography (CT) of abdomen and chest revealed bilateral upper lobe patches, minimal bilateral empyema (post pleurocentesis), multiple intraabdominal lymph nodes (non-necrotic), and omental and bowel wall thickening which were consistent with disseminated tuberculosis [Figure 1b-d]. Pus CB-NAAT came out to be positive for tubercular bacilli with no rifampicin resistance detected. However, bacterial cultures (aerobic,



**Figure 1:** Radiological images of thorax and abdomen. Frontal radiograph (a) in standing position shows bilateral pleural effusion (R > L); computer tomography images through the lung apex shows fibrotic (b) changes (arrow) of both lungs with mild surrounding ground glass changes in the left anterior segment (not shown), bilateral empyema with subtle enhancing walls (c), short segment enhancing (d) mural thickening at the ileocecal junction (arrow) and multiple discrete enhancing lymph nodes in right iliac fossa and mesentery of central abdomen (curved arrow)

anaerobic, and tubercular) were negative. Hence, a final diagnosis of disseminated pulmonary and abdominal tuberculosis with bilateral ET and IDA due to chronic GI blood loss was made.

He was started on daily weight-based anti-tubercular treatment (ATT) regimen as per WHO recommendation along with proton pump inhibitors and iron supplements. The patient responded well to the treatment and tolerated ATT with minimal side effects after three months of follow-up.

## Discussion

This case represents a delayed diagnosis and wrong treatment of smear and culture negative disseminated tuberculosis by first-contact health care providers. As primary care physicians are one of the initial points of contact, it is crucial for them to know about the rare presentations of common diseases like this case and their right approach.

In low resource setting like India, people prefer to approach the local dispensaries or pharmacy stores, run by inadequately trained personnel and facilities. The common practice of giving ‘cocktail’ treatment with antibiotic, steroid, and analgesic as in our case is seen very rampantly, contributing to the misdiagnosis, delay in right treatment, leading to late presentation at higher center with complications, and development of antibiotic resistance, in turn leading to high morbidity and mortality. The primary target in such setting by the first contact/pharmacists should be to identify the cases, which need referral to higher level of care for optimal selection of drugs, and to restrict use of antibiotics unless prescribed by the registered practitioners (part of ASP).<sup>[4]</sup> Physicians should prescribe antibiotics cautiously as per ASP, refer to higher center when necessary, and counsel patients against overconsumption.

Tuberculosis is a very common infectious disease in developing countries and always needs a higher priority in the list of differentials.<sup>[9]</sup> Similar to our case of bilateral ET, atypical presentations often get overlooked due to lack of facilities for further investigations, economical constraints, and preference of people to obtain symptomatic treatment from local unregistered practitioners, despite existence of the national policies. This can be solved if all of us shall follow ASP.

A case report is only a tip of the iceberg where vast majority of such cases are undiagnosed/missed. This calls for a check on the actual use of existing facilities, monitoring of national programs, need to make CB-NAAT easily available at primary care setting as many cases are smear negative, educating bilateral tubercular ET, and ultimately practicing ASP by all health concerned individuals.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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