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Gene-Xpert: Diagnosis of Pulmonary Tuberculosis in a Sputum Smear Negative Patient

Oshna Pandey,[1] Buddhi Paudyal,[1] Buddha Basnyat[2]

[1]Patan Academy of Health Sciences, Lagankhel, Lalitpur, Nepal, [2]Oxford University Clinical Research Unit, Patan Academy of Health Sciences, Lagankhel, Lalitpur, Nepal.

ABSTRACT

This case report has tried to highlight the ease and benefit of Gene-Xpert testing in difficult to diagnose patient with sputum smear negative pulmonary tuberculosis. Early treatment of tuberculosis is usually delayed by lack of rapid and accurate diagnostic modalities, especially in resource-limited settings like ours. Gene-Xpert is a rapid test based on real time PCR assay and molecular technology for the detection of Mycobacterium tuberculosis. It is highly sensitive tool and enables simultaneous detection of rifampicin resistance within short period of time i,e. <2hrs. It has distinct advantage of providing same-day diagnosis which could potentially limit loss to follow up during diagnostic evaluation of smear negative tuberculosis patients.

Keywords: Gene-Xpert; pulmonary tuberculosis; sputum microscopy.

INTRODUCTION

Tuberculosis (TB) is an infectious disease and a major public health problem in Nepal. It particularly affects lungs (pulmonary TB) but can also affect other sites (extra-pulmonary TB). Overall, a relatively small proportion of people infected with *Mycobacterium tuberculosis* will develop TB.[1] it mainly affects adults in the most economically productive age groups. The most common and widely used method for diagnosing TB is sputum smear microscopy. Following recent advances in TB diagnostics, the use of Gene-Xpert is being offered from 22 national centers to diagnose TB and drug-resistant TB in Nepal.[2] Here, we highlight a case of sputum smear negative pulmonary tuberculosis which was diagnosed and treated on basis of Gene-Xpert test.

CASE REPORT

A 48 year old male was presented with intermittent fever, sweating, headache, decreased appetite, myalgia and generalized weakness for 3 weeks. There was some cough with occasional whitish sputum. There was no contact exposure or past history of tuberculosis (TB).

After 3 weeks of illness, the patient went to nearby medical clinic where he was treated with combination of amoxicillin-clavulinate and azithromycin. As his fever was persistent, he attended Patan Hospital outpatient clinic, where he was again treated with a course of cepfodoxime. However, his fever did not subside. Thus, on the 3rd day of this antibiotic, he was admitted to Patan hospital.

On admission, he was febrile (100°F), with pulse 102 bpm, RR 22/min, and BP 100/70 mm of Hg. There was no significant lymphadenopathy and his systemic examination was unremarkable.

Investigation revealed WBC of 14000/cumm with 83% neutrophil and 17 % lymphocyte. Chest X-ray (Fig 1) showed increased bronchovascular markings in right perihilar and lower zones. Sputum smear for acid fast bacilli (AFB) for 3 consecutive days was negative. CT chest (Fig 2) revealed fibrotic changes and nodular opacities in right middle and lower lobes and minimal bronchiectasis and segmental collapse/consolidation in right middle lobe with mediastinal lymphadenopathy. Serological tests for brucellosis, leptospirosis and malaria were negative.

As the patient's condition didn't improve even after 7 days of intravenous antibiotics, and there was right middle lobe involvement probably due to tuberculosis, bronchoscopy was planned which revealed purulent secretions in right middle lobe bronchus. Bronchoalveolar lavage sample (purulent secretions) was sent for culture and Gene-Xpert testing. The sample was positive for *Mycobacterium tuberculosis* on Gene-Xpert test (reporting on same day) and on culture (reporting on

Correspondence: **Oshna Pandey, Patan Academy of Health Sciences, Lagenkhel, Lalitpur, Nepal, Email: oshnapandey@gmail.com, oshnapandey@pahs.com, Phone: +9779841934576/ +9779808788451.**

follow-up). He was started on standard antitubercular therapy (ATT); interestingly, his fever was down by second day of ATT. He was on regular follow-up then after and was doing well.

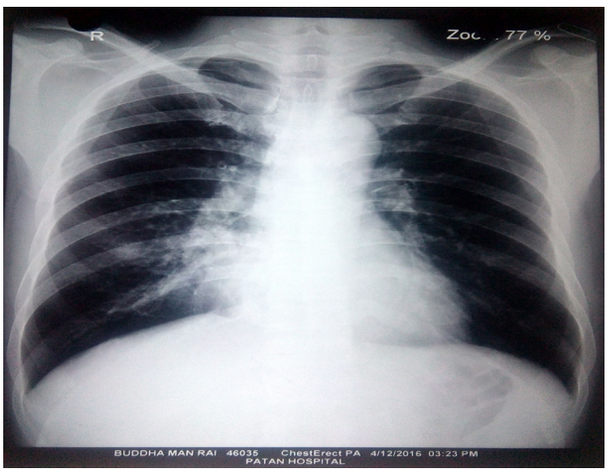

Figure 1. Chest Xray showing increased bronchovascular markings in right perihilar and lower zone.

Figure 2. CT scan of chest showing fibrotic changes and nodular opacities and minimal bronchiectasis in right middle and lower lobes.

DISCUSSION

The earliest chest radiographic findings of reactivated TB consist of one or more ill-defined patchy opacities, occurring in the posterior segments of the upper lobes in the majority of patients and in the superior segment of the lower lobes in most of the remainder of patients.[2] This distribution of disease is very helpful in suggesting the diagnosis of reactivated TB. However, Chest X-ray in this case showed increased bronchovascular markings in right perihilar and right lower zone. Though he had prolong fever and cough - features suggestive for tuberculosis, the radiological finding was not typical for TB and the sputum AFB was also negative, so there was delay in reaching the diagnosis.

Early treatment of tuberculosis is usually delayed by the lack of rapid and accurate diagnostic modalities, especially in resource-limited settings. Sputum smear microscopy remains common and inexpensive way to diagnose pulmonary TB.[3] However, it has significant limitations because it can only be used to diagnose TB when sputum has sufficient bacillary load, and moreover it cannot detect drug resistance. Thus, the diagnosis of TB often goes undetected especially in those with low load of bacilli, as in our case. In addition, when the chest X-ray findings are not seen in the upper lobes but confined to other areas as in our patient, many treating physicians in Nepal may fail to consider tuberculosis as a possible differential diagnosis, even in setting of tuberculosis endemicity. We were fortunate at Patan Hospital to have bronchoscopy performed in this patient to obtain bronchoalveolar lavage samples from the middle lobe for a proper diagnosis.[4] Furthermore, facility of mycobacterial culture is limited and where available results are often delayed by several days. Gene-Xpert is new molecular test in routine TB diagnosis and its use is increasing in developing countries. It has much higher sensitivity than sputum smears microscopy and enables simultaneous detection of rifampicin resistance.[1]

Gene-Xpert test has distinct advantage of providing same-day diagnosis which could potentially limit loss to follow up during diagnostic evaluation of smear negative TB patients. Moreover this test could potentially reduce the time required for subsequent bacteriological investigations. Through this case, we have tried to highlight the ease and benefit of Gene-Xpert testing in difficult to diagnose patient with pulmonary tuberculosis.

CONCLUSIONS

Compared to sputum smear microscopy, Gene-Xpert is rapid and highly sensitive diagnostic tool for tuberculosis detection. Although culture remains the gold standard method for diagnosis of tuberculosis, it takes days to show the results. Hence, Gene-Xpert can be a useful modality for early diagnosis of a patient with suspected tuberculosis due to its rapidity and simultaneous detection of Rifampicin resistance in the same setting.

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