Tuberculosis – Barriers to Early Diagnosis

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“In its beginning the malady (tuberculosis) is easier to cure but difficult to detect, but later it becomes easy to detect but difficult to cure”.

Niccolo Machiavelli (1469-1527)

Tuberculosis is prevalent in this part of the world. It is a disease associated with poverty, overcrowding, debilitating diseases, drug abuse, alcoholism, homelessness and immunodeficiency. It has become more important with the advent of the HIV epidemic, presenting in less familiar ways and pursuing a more aggressive and relentless course(1). Outbreaks of drug-resistant tuberculosis have occurred usually in HIV-infected persons, due to nosocomial transmission of infection in congregate settings. To halt the advance of tuberculosis, an important first step is to suspect and diagnose the disease early so that treatment and other control measures can be undertaken.

Tuberculosis is a disease with protean manifestation. It is therefore not surprising that diagnosis can elude the most astute physician. This is well illustrated in a recent article on the final illness of the late Eleanor Roosevelt published in the December 2001 issue of the International Journal of Tuberculosis and Lung Disease(2). Eleanor Roosevelt died of a very severe form of miliary tuberculosis. There was a suspicion after her death that the diagnosis of miliary tuberculosis was missed. This prompted the author to review in greater detail the case records and autopsy findings which had been made available to historians in 1990.

Eleanor Roosevelt was initially diagnosed to have aplastic anaemia in June 1960 at the age of 75 years. She developed recurrent episodes of fever over a period of 18 months with no weight loss or night sweats. This was followed by fever due to blood transfusion reaction whenever she was given blood for anaemia. Prednisone was added in April 1962 to stimulate the bone marrow. When she was admitted in August 1962 for fever and night sweats, reactivation of acid fast bacilli in the lungs was considered but excluded because the chest x-ray on admission was normal except for old scars suggestive of previous exposure to tuberculosis. Bone marrow aspiration showed no change compared with previous findings. She continued to have fever and by September 1962, a generalised ill-defined nodularity appeared in both lung fields. Bone marrow aspiration was done which showed no AFB on the smear. However culture subsequently grew tubercle bacilli. She was treated empirically for tuberculosis for six weeks with two drugs, streptomycin and isoniazid, but her condition deteriorated and she died on 7 November 1962. Autopsy showed involvement of the lungs, liver, spleen, kidneys and bone marrow. The extensive involvement led the
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pathologists to use the term disseminated tuberculosis acutissima, signifying overwhelming infection in an immunocompromised person. In the case of Eleanor Roosevelt, immunosuppression was due to long standing bone marrow failure and therapy with prednisone. Although the postmortem diagnosis was aplastic anaemia and miliary tuberculosis, it was speculated that the aplastic anaemia could also be due to tuberculosis. Disseminated tuberculosis can give rise to haematological abnormalities such as leukemoid reaction, pancytopenia, aplastic anaemia, and thrombocytopenia. In retrospect, the diagnosis of miliary tuberculosis could have been diagnosed in July 1962 or earlier if bone marrow biopsy or AFB culture of the marrow had been done.

TB is a disease with diverse manifestations which can mimic other diseases. The clinical presentation can be typical or atypical depending on the immune status of the patient. Examples of atypical lung presentation include lower lung field disease, diffuse infiltrates, pleural effusion, tuberculoma and endobronchial involvement associated with airway stenosis. Tuberculosis can masquerade as a bacterial pneumonia, bronchogenic carcinoma, lymphoma, sarcoidosis, fungal infection, pneumoconiosis and asthma. When the presentation is acute e.g. acute respiratory distress syndrome, tuberculosis tends to be forgotten and the clinical picture is ascribed to a severe form of bacterial or necrotising pneumonia. Diagnostic complacency can also occur when tuberculosis coexists with another disease (e.g. malignancy) or the finding of a normal chest x-ray in the presence of disseminated disease. This can occur in HIV infected patients or older patients with cryptic miliary tuberculosis. Diagnostic difficulties can also occur with extrapulmonary tuberculosis which is diagnosed usually by an invasive procedure. Unusual sites may be involved, especially in patients with HIV infection, e.g. brain tuberculoma, brain abscess, meningitis, skin and solid organ abscesses, pericardium, etc. Thus it is not surprising that patients with undiagnosed tuberculosis during life are detected only at autopsy.

Delayed diagnosis leads to delayed treatment and prolongs the transmission of infection in the community. Late treatment can also jeopardise recovery and cure of the patient. Delays can occur at the patient level or at the level of the health care system. While it is easy to attribute delay to patients, this may not be true, as shown in an article published in this issue of the journal.

The author highlighted the problem of missed diagnosis by doctors. The patients presented with features highly suggestive of tuberculosis and had consulted many doctors, general practitioners as well as specialists. However, the diagnosis of tuberculosis was not considered in many cases and in 40% of patients, no investigations for tuberculosis were done. When sputum smear examination was done (usually of a single specimen), a negative result was considered to have excluded the diagnosis of tuberculosis. Sputum smear examination is not highly sensitive and should not be used to exclude a diagnosis of pulmonary tuberculosis. A minimum of two good quality specimens should be collected to obtain a reliable diagnosis of smear positive pulmonary tuberculosis.

A previous study in Kuala Lumpur, Malaysia also found that tuberculosis was not considered in most patients when they consulted their private practitioners and essential investigations such as sputum examination and chest x-ray were often not done. This was attributed to the lack of x-ray facilities in the general practitioners’ clinics and the small
number of laboratories which can perform reliable sputum examination. Furthermore, patients have to pay a higher fee if the diagnostic tests are ordered.

In many countries, the doctor of first contact is the general practitioner. Thus the general practitioner plays an important role in the battle against tuberculosis. All primary health care doctors in the private or public sector, should be constantly updated on the diagnosis and treatment of tuberculosis. This can take the form of lunch talks, conferences, film shows and distribution of printed materials on tuberculosis e.g. guidelines on diagnosis and treatment. Information on tuberculosis can also be disseminated through radio and the Internet. Private practitioners should have easy access to good quality laboratories and x-ray facilities. When cost is a problem, doctors should be able to refer patients for free consultation and treatment in government tuberculosis or chest clinics.

The problem of patient delay is important. Causes of patient delay include factors such as language difficulty, immigration status of patients, homelessness, female sex, and patients living in rural areas. Knowledge of the causes will complement efforts to combat the disease. Patients may be ignorant of the symptoms and signs of tuberculosis attributing them to other chest diseases and seeking help from traditional healers. They may also not be aware of the diagnostic and treatment facilities available. Dissemination of information on tuberculosis to the public is important as it will encourage patients to seek medical consultation earlier and make better use of health care facilities.

Doctors should be familiar with the varied manifestations of tuberculosis and be highly suspicious of tuberculosis in any patient with respiratory symptoms. They should not hesitate to order tests which are found to be cost effective such as sputum examination (smear and culture) and chest x-ray. Additional investigations may be necessary for problem cases, such as sputum smear negative cases and patients with extrapulmonary tuberculosis e.g. bronchoscopy, tissue biopsy and culture, examination of body fluids for adenosine deaminase, CT scan and endoscopy for gastrointestinal involvement. There is a place for empirical therapy when there is a strong clinical suspicion of tuberculosis in the absence of bacteriological or histological confirmation.

REFERENCES