The Problem of Geriatric Tuberculosis

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Abstract

Tuberculosis is emerging as a significant health problem in the elderly. The symptoms are often non-specific and may be attributed to changes related to age. This often leads to a delayed diagnosis and more advanced disease at presentation. The presence of other underlying diseases may also alter the clinical picture. The physicians need to have a high index of suspicion for the diagnosis of tuberculosis when elderly patients present with non-specific and vague symptoms, non-resolving pulmonary infiltrates on chest x-ray and laboratory abnormalities which remain unexplained. Special attention needs to be given to the monitoring for compliance with treatment, side effects of drugs and drug interactions.

Introduction

Tuberculosis has long been known as a disease with a predilection for young people. This pattern has persisted in countries with high prevalence of the disease including India. However, in countries like USA, where the disease showed a declining trend, several changes were observed in the epidemiological and clinical characteristics of tuberculosis. One of these was a concomitant increase in the proportion of older patients. According to the national figures in 1953, among those with newly reported tuberculosis the proportion of patients who were 65 years of age or more was 13.8%. By 1979, the figure had risen to 28.6%, a rise not explained by an increase in the proportion of elderly persons in the population from 8.7% to 11.2%1. By late 80’s, the elderly comprised the single largest group of patients with active tuberculosis and increasing proportion of deaths attributed to tuberculosis were in the elderly2. A similar age related trend has been reported from many other economically developed countries. A retrospective review of 411 patients of tuberculosis in U.K. showed that elderly were six times more likely to die from tuberculosis and over 20 times more likely than younger patients to have the diagnosis made at autopsy rather than during life3.

From India, not much data on the problem of tuberculosis in the elderly are available. With changing demography of the population, and increase in the number of elderly, more and more older individuals are being diagnosed as suffering from tuberculosis. However, the problem of geriatric tuberculosis has not received the attention it deserves. It is evident from the paucity of literature on this common problem affecting the elderly. An isolated study on the profile of disease in the elderly from Himachal Pradesh has been reported4. However, some of the observations that have been reported in the studies of geriatric tuberculosis from the West and South-East Asian countries could very well be applicable in our setting.

Pathogenesis

Mode of Infection

Tuberculosis in old people may be either exogenous or endogenous in origin. Over 90% of cases in the elderly represent endogenous tuberculosis, i.e., reactivation of dormant infection in the lungs or elsewhere in the body. In the remainder, it may be exogenous, i.e., acquired from an outside source, usually a sputum positive case. In individual cases, it is rarely possible to be sure which of these two mechanisms has been responsible, but there are theoretical reasons to
believe that in old people, endogenous reactivation is more important.5

Predisposing factors

Tuberculosis is the prototype of a disease in which cell-mediated immunity plays an important part in controlling the infection. It is well known that age related decline in the cell-mediated immunity influences reactivation of latent infection in the elderly. However, studies conducted on the immunoglobulin status in the geriatric pulmonary tuberculosis patients, have shown no deficiency in their humoral responses6. It has been observed that the cytokine production in response to stimulation with Mycobacterium tuberculosis is well preserved in old age7. In individual cases, presence of intercurrent illnesses like diabetes mellitus, chronic renal failure, malnutrition, alcohol abuse, certain malignancies and use of immunosuppressive drugs like corticosteroids further impair cell mediated immunity. These can thereby increase the risk of reactivation of the disease. Adverse social factors and poor living conditions also affect the elderly much more than the young.

Spectrum of the disease

Like any other infection, the pathogenesis of tuberculosis in the lungs and elsewhere in the body is determined by the virulence of the infecting strain and the immune response of the host8. At one end of the spectrum is the reactive form seen as a dormant focus wherein the infection is contained and localized as well formed granulomatous tubercles, i.e., there is an active immune response. When the immune response is sub-optimal, the lesions are exudative in which large number of organisms are found within areas of caseous necrosis surrounded by nonspecific inflammatory cells and few epithelioid and giant cells. At the other end of the spectrum are the lesions of non-reactive miliary tuberculosis when there are large concentrations of multiplying tubercle bacilli with minimal or no immune response. This form is common in elderly patients. Still more common is the cryptic or the chronic, indolent form of miliary tuberculosis when patients may just present with prolonged fever and no focal symptoms or signs.

Diagnostic difficulties

Some of the problems that are encountered in the diagnosis of tuberculosis apply to any disease in old people. Perhaps the biggest problem is their inability to give an accurate account of their symptoms. The contributory factors may be poor memory, deafness, mental confusion or impairment of speech. Old people, and sometimes also their family members wrongly attribute their symptoms to the effect of old age. The presence of other chronic diseases may confuse the clinical picture, both for the patient and the doctor. In particular, concomitant malignant disease can mask the symptoms of tuberculosis since the two conditions may coexist at this age.

Besides the general problems of diagnosis there are special difficulties in relation with the recognition of tuberculosis affecting various sites. The basis of this problem is that in old age the body’s reaction to tuberculosis as also to other infections is often diminished. The patient may appear unwell without showing any specific focal signs. The likely reasons for failure of recognition of pulmonary tuberculosis are a paucity of respiratory symptoms, the presence of significant underlying diseases like chronic obstructive airway disease (COAD) and inability to produce sputum and above all, atypical radiographic findings like solitary nodules, mass like densities, extensive broncho-pneumonia and lower lobe infiltrates.

Clinical features and atypical presentation in the elderly

The clinical presentation of tuberculosis in the elderly is variable. The various types of pulmonary tuberculosis which can be seen are:

Primary infection - Though more common in childhood and adolescence, primary infection is occasionally observed in old age. Some such outbreaks have been reported in the elderly living
in nursing homes\textsuperscript{9}. Middle and lower lung field infiltrates like those occurring in younger patients with progressive primary infection have been reported to occur with this type of tuberculosis in the elderly\textsuperscript{10}.

\textit{Pleurisy with effusion} - caused by rupture of a subpleural caseous focus into the pleural space which occurs usually within first few months following the exposure is being reported more frequently in older individuals. Older patients may have a more insidious onset than the young adults. Pleural biopsy is the most accurate means of diagnosis.

\textit{Reactivation or post-primary form of pulmonary tuberculosis} - is the most common form of pulmonary tuberculosis in older adults. Failure to recognize this problem early contributes to an increased morbidity and mortality in the elderly. It has been noted that elderly patients with pulmonary tuberculosis may present with symptoms different from younger patients\textsuperscript{11-13}. They present more commonly with non-specific complaints. Therefore, the diagnosis of tuberculosis may not be suspected initially and there may be considerable delay before the diagnosis is made. In some cases, the diagnosis of tuberculosis is made only at postmortem examination\textsuperscript{14-15}. Many elderly patients present at an advanced stage of the disease and with multiple other medical problems. Even if they are given adequate antituberculous therapy (ATT), the mortality rate during treatment may still be high because of associated problems.

Clinical features of pulmonary tuberculosis in the young and the elderly patients have been compared\textsuperscript{16}. The classic symptoms of tuberculosis like fever, night sweats, weight loss, sputum production and haemoptysis were noted in a significantly lower proportion of elderly group as compared to the young. Abnormal mentation was more common in the elderly. Radiographic findings were similar in the two groups. The mortality related to tuberculosis was 20 percent in the elderly versus 3 percent in the younger group.

However, Katz \textit{et al} found no significant differences in the presentation with symptoms of fever, anorexia, cough and weight loss among the young and the elderly\textsuperscript{17}. They observed that the elderly were significantly less likely to present with haemoptysis or have cavitary lesions on radiographs. They were more likely to present with complaints of dyspnoea and right lower lobe infiltrates. Although the treatment was delayed in the elderly, there were no age-related differences in the mortality.

Chan \textit{et al} studied the effect of age on the presentation of patients with tuberculosis\textsuperscript{18}. They included all patients diagnosed as tuberculosis over a period of two years. There were 78 young and 94 elderly (> 65 years) patients. The elderly patients had lower body weight, less haemoptysis but more non-specific complaints. The symptoms of cough, fever, dyspnoea, weight loss, anorexia, malaise and chest pain were not significantly different between the two groups. Co-existing medical illnesses and past history of tuberculosis were much more common in the elderly. The chest radiographs in the elderly patients were less likely to have upper lobe infiltration. The elderly patients however, tended to have more extensive disease involving both lungs though cavitation was much more common in the younger adults. The outcome of the disease in terms of mortality was much poorer amongst the elderly as compared to younger patients. In a prospective study of hematological and biochemical abnormalities in elderly patients with pulmonary tuberculosis, the occurrence of anaemia, hypoalbuminaemia, hyponatraemia, hypokalaemia and deranged liver function tests (LFTs) have been seen much more commonly in the elderly as compared to younger patients, signifying that there may be clinically silent extrapulmonary involvement\textsuperscript{19}.

The forms of \textit{extrapulmonary tuberculosis} that may be seen in the elderly are miliary or disseminated tuberculosis, gastrointestinal tuberculosis, bone and joint tuberculosis, genitourinary tuberculosis and tuberculous meningitis.
Miliary tuberculosis in the elderly can be particularly difficult to recognize. Patients over 60 years make up the majority of both undiagnosed and fatal cases of miliary tuberculosis. The classical acute or subacute pattern of high intermittent fever and early onset of complicating meningitis or serositis is often absent in the elderly. Instead, the more chronic form of slowly progressive, protracted and wasting illness with absent or low grade fever and without any localizing symptoms or signs may be present. Examination may reveal only anaemia and hepatosplenomegaly. A normal chest x-ray is quite compatible with miliary tuberculosis.

Tuberculous meningitis is more commonly seen in the elderly as a result of reactivation of dormant foci of infection in the central nervous system or as part of miliary disease. Clinical features are often subacute or chronic and atypical in the elderly. These may include a change in personality, an altered or abnormal behaviour, loss of memory, urinary incontinence, social withdrawal or just mental confusion. Many of these symptoms may be attributed to the effects of aging by the relatives and medical attention may not be sought in time. Typical history of headache, vomiting and fever and the classical meningeal signs are often absent. Examination may reveal just a confused individual. Blood chemistry may show electrolyte abnormalities like hyponatraemia which often co-exist. The clinical picture may be attributed to these and specific investigations may not be sought. The diagnosis should be considered in any elderly patient with obtundation or dementia of recent onset and a CSF examination must be performed.

The diagnosis of gastrointestinal tuberculosis is difficult even in the young adults since the symptoms are often non-specific and vague. The problem is further compounded in the elderly as the symptoms are often attributed to motility disorders which are common in the elderly. Fever is often absent. Abdominal tuberculosis remains underdiagnosed in the elderly.

Genitourinary tuberculosis, the result of reactivation of dormant haematogenous foci in the kidneys, is seen in a significant proportion of elderly patients. Except in patients with miliary disease, systemic symptoms are unusual. Most common symptoms are dysuria and frequency. These symptoms in the elderly men are often attributed to enlargement of prostate since benign prostate hyperplasia is so common and the necessary investigations may be delayed. Less frequent symptoms are flank pain and gross haematuria. About 20% of patients are asymptomatic and their disease is recognized only because of an abnormal urinary sediment. Sterile pyuria should lead the clinician to suspect genitourinary tuberculosis. Onset of the tuberculosis of the female genitourinary tract is uncommon in old age.

Bone and joint tuberculosis - The age at diagnosis of patients with osteo-articular tuberculosis also seems to be increasing. The pathologic lesion is a combination of osteomyelitis and arthritis, usually occurring as a result of reactivation of dormant foci. The most common sites are the vertebrae and the weight bearing joints such as hip and knee. Diagnosis is often delayed because both the patient and the doctor may attribute the symptoms to age related osteoarthritis, which also tends to occur in weight bearing joints and spine. Absence of fever and systemic symptoms may be misleading. The diagnosis should be suspected in any elderly patient with unexplained unifocal inflammation or destruction of bone or joint.

What should be done to prevent a delay in the diagnosis of TB in the elderly?

It is suggested that tuberculosis should be included in the differential diagnosis of any elderly patient presenting with vague pleuro-pulmonary symptoms or unexplained fever, anorexia, weight loss, change in behaviour or mentation or organ dysfunction. Physical findings are often non-specific. Laboratory abnormalities, e.g., abnormal chest radiograph, anaemia, pyuria, etc., without a definite cause should prompt a search for tuberculosis. Elderly with tuberculosis are more
likely to have hypoalbuminaemia, abnormal LFTs, hypokalaemia and hyponatraemia.

Early use of specific investigations should be sought\textsuperscript{24}. If patients with suspected pulmonary infiltrates are unable to produce sputum, induced spuota or fasting gastric aspirates should be tested. Tuberculosis should be actively sought in the elderly with pneumonic infiltrates on chest X-ray which do not clear with antibiotics. In elderly patients with suspicious infiltrates where sputum is negative, fibreoptic bronchoscopy should be performed. Definitive diagnosis of miliary tuberculosis depends upon isolation of the organism from histologically documented miliary foci of tuberculous infection in various organs. However, this may take time and therapy may have to be initiated for the critically ill elderly patient on the basis of presumptive evidence of infection, which must be aggressively sought. In patients with a miliary pattern on chest X-ray and negative sputum smears for AFB, fibreoptic bronchoscopy with transbronchial biopsy may be useful. In patients without miliary infiltrates, bone marrow and/or liver biopsies should be done if there is a strong suspicion of miliary tuberculosis. The yield is likely to be higher if there are prominent haematologic or LFT abnormalities respectively.

Tuberculin test is valuable and reliable in elderly if a few precautions are kept in mind. Tuberculin sensitivity is known to wane with old age. Advancing age, malnutrition, extensive infection can all be associated with non-reactive tuberculin, despite active disease. It is difficult to separate the effects of advanced or extensive infection in the elderly patients from the effects of advancing age alone. The booster effect occurs at all ages but is more frequent in the elderly. There are data to suggest that the negative tuberculin reaction, which is often found in the elderly mainly due to failing immune response to tuberculin antigen can be restored progressively by repeated administrations\textsuperscript{25}. A two stage TB skin testing is recommended in the elderly initially classified as negative reactors\textsuperscript{26}. Utilization of such a ‘test-retest’ procedure in elderly patients may enhance the recall of waning cell-mediated immunity to the tuberculin antigen and may detect more tuberculin positive individuals. It needs to be emphasized that especially in the elderly, care should be taken not to interpret a boosting reaction as a conversion.

Therapeutic difficulties

Old people with tuberculosis present problems not only of the diagnosis but also of treatment. The key problems are a poor compliance with treatment, poor tolerance of therapy and the presence of underlying or associated diseases\textsuperscript{14,23}.

The main cause of failure of treatment in tuberculosis, whatever the age, is poor patient compliance, and in the elderly this problem is accentuated. Old people especially the very old are unreliable about taking tablets regularly, at the right time or in the right dose, particularly if several drugs are to be taken concurrently. Poor memory, poor eyesight and mental confusion may be contributory factors. Old people often become apathetic about their treatment and lack the determination required to complete a course of treatment of six months. Many countries, therefore, prefer to use supervised intermittent chemotherapy for such patients. Side effects of certain drugs may also lead to poor compliance with the treatment.

A careful watch must be kept for the side effects of drug treatment because the old persons, particularly the very old, cannot be relied upon to recognize their significance. Doses of drugs must be carefully monitored and special care taken if there is evidence of hepatic or renal failure. In a retrospective review, it has been reported that elderly people were nearly three times more likely to have reactions to antituberculous drugs as compared to younger patients\textsuperscript{3}. Various studies including those from India have definitely shown advancing age as an important predictor of hepatotoxicity due to INH and rifampicin\textsuperscript{2,27}. Rifampicin combined with INH has an additive but not synergistic hepatotoxic effect. Monthly monitoring of serum transaminases is advisable in such patients.
Ethambutol can cause diminution of visual acuity, central scotomas and disturbance of red-green vision attributable to optic neuritis. Since some visual impairment is common in elderly, a careful examination that includes testing of visual acuity and color discrimination should be performed before initiating ethambutol therapy. In elderly patients with significant renal dysfunction associated with retinopathy, or cataracts, in whom evaluation of visual changes may be difficult, the benefits of ethambutol administration must be carefully weighed against the risks. The nephrotoxicity and ototoxicity due to streptomycin is more frequent in patients with pre-existing renal impairment and is generally irreversible. Since with normal aging, renal function declines, hearing acuity diminishes, and vestibular disturbances are more incapacitating, elderly patients have increased risks of suffering from renal toxicity and ototoxicity and of being severely impaired by them. As with ethambutol, the benefits of streptomycin therapy must be weighed against its risks in the elderly patient and dose adjusted accordingly.

Drug interactions must also be considered in old people who are likely to be on treatment for other diseases at the same time: e.g., INH can reduce the anticonvulsant action of phenytoin; rifampicin can interfere with the action of digoxin, tolbutamide and corticosteroids. In most cases, all that is needed to overcome the unwanted effects of drug interactions is an adjustment of dosage.

Conclusion

Tuberculosis in the elderly is a serious disorder. Unlike many other diseases seen in the elderly, tuberculosis is potentially curable if treated early. It is, therefore, extremely important that all those who care for the elderly are alert to the special problems of diagnosis and treatment which they present.

References


Flavedon 20
3 TABLETS DAILY

A major antianginal for all patients

- As first line treatment
- Uncontrolled on conventional drugs
- To replace a poorly tolerated antianginal
- At risk (elderly, diabetic CAD patients)

When it comes to the heart do not compromise on quality