Unusual presentations of tuberculosis: let the clinician beware

The cases of extrapulmonary tuberculosis published in this issue of *Hospital Medicine* show what a difficult problem tuberculosis can be for both patient and doctor. Tuberculosis can occur in virtually any organ in the body and is protean in its manifestations.

Among the white population of the UK extrapulmonary disease occurs in about 15% of cases, but in the ethnic minorities, primarily African or South Asian, extrapulmonary sites are present in up to 50% of cases. Data from national surveys showed that extrapulmonary disease in England and Wales increased from 33% in 1988 to 38% in 1998 and 40% in 2002; a reflection of the increased proportion presenting with tuberculosis from ethnic minorities (Rosen et al, 2001; Health Protection Agency, 2004a).

Extrapulmonary disease is usually a complication of primary infection. Miliary and meningeal tuberculosis usually presents within a year of the initial infection but bone and joint or genitourinary disease may present many years later (Davies, 2003).

DIAGNOSIS

Diagnosis is always more difficult in extrapulmonary than pulmonary disease. Symptoms are usually insidious and it may be weeks or months from the first symptom to presentation. Confirmation by culturing *Mycobacterium tuberculosis* from a specimen is more problematic. A report on cases in England, Wales and Northern Ireland in 2001 showed that only 49% of extrapulmonary cases were culture confirmed compared with 63% of pulmonary cases (Health Protection Agency, 2004b). In other words less than half of all extrapulmonary cases are confirmed.

The case of tuberculous meningitis (p. 436) particularly illustrates how difficult the diagnosis can be to make. The patient only had symptoms for about a month. With relatively little delay treatment was started but despite this the patient died. Mortality from tuberculous meningitis is higher than from pulmonary disease (Martineau et al, 2004). The diagnosis should be considered in anyone with a 'viral' pattern of CSF results, i.e. a low white count, high protein and low glucose. It should be strongly suspected in anyone from an ethnic minority group with these results who has had symptoms for more than a few days. Treatment should be started as soon as specimens have been sent off for smear and culture. A negative smear or culture dose not exclude disease. The value of the polymerase chain reaction in such cases is still being evaluated.

Tuberculosis at other sites such as lymph glands, bone and joints or the genitourinary system is usually less urgent to treat but delay can result in unnecessary complications such as pain, deformity, fibrosis causing obstruction to hollow tubes or disfigurement. Specimens taken from these sites such as pus or urine are almost always smear negative and often sterile because the bacteria reside and are active in the walls of the cavities they cause rather than the cavities themselves. Biopsy should therefore include the wall of the cavity, be it lymph gland, bone or duct, and be sent for bacteriological culture as well as histology.

TREATMENT

Treatment should be started with the four first-line drugs isoniazid, rifampicin, pyrazinamide and ethambutol. The increasing incidence of drug resistance emphasizes how important obtaining specimens for culture and sensitivity is becoming, even for extrapulmonary disease. Randomized controlled trials suggest that 6 months of chemotherapy is sufficient for all sites except tuberculous meningitis when treatment should be continued for a year (Yew, 2003).

EPIDEMIOLOGY

The question arises as to why extrapulmonary tuberculosis is so much more common in those whose ethnic origin is South Asian or black African than in the white endogenous population. Greatly increased incidence of extrapulmonary tuberculosis is well described in those suffering from human immunodeficiency virus (HIV) infection. In this infection the virus targets the CD4 cell, initially destroying specific immunity to organisms defended by cell-mediated rather than humoral immunity (Pozniac, 2003).

For this reason, where tuberculosis is rife, such as in Southern Africa, the earliest presenting feature of acquired immunodeficiency syndrome (AIDS) is usually tuberculosis.

But in the HIV seronegative population why is extrapulmonary disease so prevalent? The explanation which the author favours is the hypothesis of acquired immunodeficiency of migration as a result of vitamin D deficiency. The potential patient is infected with *M. tuberculosis* in the country of origin where tuberculosis is very prevalent. Sunlight is plentiful and the macrophage, which is vitamin D sensitive, is activated to contain the infection. The individual then moves to the UK where sunlight is scarce, vitamin D concentrations fall and the macrophage is weakened. The previously contained infection then breaks out into overt disease with a high incidence of extrapulmonary disease, in a

pattern resembling those who are HIV infected (Davies, 1985).

To date very few South Asians presenting with tuberculosis in the UK are HIV infected although the number of black Africans presenting with HIV-associated tuberculosis is probably increasing. HM

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KEY POINTS

- Tuberculosis can occur at virtually any organ in the body and is protean in its manifestations.
- In ethnic minorities, primarily African or South Asian, extrapulmonary sites are present in up to 50% of cases.
- Symptoms are usually insidious and it may be weeks or months from the first symptom to presentation.
- Biopsy should include the wall of the cavity, be it lymph gland, bone or duct, and be sent for bacteriological culture as well as histology.
- Treatment should be started with the four first-line drugs isoniazid, rifampicin, pyrazinamide and ethambutol.
- Greatly increased incidence of extrapulmonary tuberculosis is well described in those suffering from human immunodeficiency virus (HIV) infection.