32 Tuberculosis of the Central Nervous System

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32.1 History

Tuberculosis (TB) has affected humans since antiquity. References to what is believed to be tuberculous infection were made in some writings from ancient Egypt and Babylonia. Typical spine deformity of Pott’s disease appear in numerous drawings of hunchbacks on the walls of ancient Egyptian tombs. By morbid anatomy, spinal TB can be traced back to about 2000 B.C., as was shown by psoas abscess found in a mummy.

Microscopically, Zimmerman demonstrated the tuberculous bacillus in a mummy of a child (Cave 1939; Zimmerman 1979). Symptoms of TB were recognized

by Hippocrates (460–377 B.C.). Aristotle (384–322 B.C.) observed that persons associated with a person affected by “phthisis” may contract the disease, thereby alluding to the possibility of its contagious nature.

Avicenna (Ibn Sina, 980–1037) described the cerebral involvement by hot or cold swelling (inflammation). The latter is thought to represent chronic meningitis (most likely tuberculous) that frequently led to death as he noted.

With the industrial revolution in Europe, a massive population shift toward inner cities resulted in crowding and created conditions that favored the spread of infection. Consequently, TB became a major cause of death between the late 17th and early 20th centuries. Schoenlein (1793–1864) coined the term tuberculosis to highlight the gross pathological appearance of small lumps caused by granulomata and the word “phthisis” fell into disfavor. Laennec (1781–1826), who was credited with the invention of the stethoscope, described in detail the auscultative findings in pulmonary TB.

Following on the research done by Villemin (1827–1892) to show that TB was transmissible, Koch (1843–1910) described the necessary postulates for the proof of a contagious nature of any illness. The conditions he described were widely accepted as classical teachings and were as follows: finding the pathogen in every lesion in the body, being able to culture the pathogen outside the patient’s body and reproducing the disease by inoculation into animals. By applying the aforementioned postulates to TB he was able to establish the infectious nature of the Bacillus tuberculosis. The glory of his discovery, however, was tarnished by the tuberculin blunder. He touted a prepared glycerin extract of the bacillus as a secret cure for TB. In fact, the extract injected in large quantities to patients with TB did cause many deaths. By the turn of the last century, Osler noted that in 1911, “in a population of one million, seventeen hundred persons died from TB” (Osler 1921). At the Pasteur Institute, Calmette and Guérin (1921) produced a live vaccine prepared by successive subculturing of a strain of Mycobacterium bovis. This was what came to be known later as BCG vaccine.
Until the middle of the last century, treatment remained generally supportive—aimed at boosting the innate defenses of the body to overcome the infection. It was not until 1943 that specific treatment against the causative organism was started. Chemotherapy began in earnest with the advent of streptomycin followed by PAS in 1946 and then isoniazid (INH) in 1951; the latter heralded the era of modern effective anti-tuberculous chemotherapy.

32.2 Epidemiology

It is estimated that one billion people are infected with \textit{M. tuberculosis} worldwide. Active TB claims nearly 8 million new victims each year (Barnes and Barrows 1993) Among them, 15% will develop extrapulmonary infection and 6% of that is meningeal (Kochi 1991). Therefore, we can estimate that there are approximately 70,000 new victims of TB meningitis per annum. Most initial infections with \textit{M. tuberculosis} remain clinically silent. The lifetime risk of developing a clinical case of TB after an initial silent infection has been estimated at 10%. TB of the central nervous system (CNS) is the most serious form of extrapulmonary TB, and about 10% of immuno-competent patients who develop clinical TB manifest CNS involvement (Udani et al. 1971). TB of the CNS has a higher incidence in children with no particular gender predilection.

Prior to the acquired immune deficiency syndrome (AIDS) epidemic, good steps were made in the prevention and treatment of TB and its CNS complications. In a review of a large number of autopsies done in Germany from 1955 to 1969, there was a statistically significant decrease in frequency of TB meningitis to about 1/7 when compared with the data from 1924 to 1938. This difference was attributed to the BCG vaccination and to the effective anti-tuberculous medications (Weigel 1976).

In spite of the advances made in the fight against infectious diseases, the overall prevalence of TB is again on the increase worldwide. The AIDS epidemic created circumstances favoring the spread of TB both in the developing and developed countries alike. Extrapulmonary TB is considered an AIDS-defining condition. The likelihood of contracting clinical TB is much higher in the AIDS population (Selwyn et al. 1992). The proportion of AIDS patients who develop TB is estimated at 5–9% (Sanchez-Portocarrero et al. 1999). The importance of this observation is highlighted by the fact that TB in a human Immunodeficiency virus (HIV)-infected patient may present as an overwhelming systemic disease (Gachot et al. 1990). CNS TB may be the initial presentation of AIDS and has a high mortality among such affected individuals. Tuberculous meningitis is the most frequent meningeal infection in the HIV patients living in areas with high prevalence of TB (Berenguer et al. 1992). Infection with HIV may increase the risk of developing TB meningitis five-fold from 2% of patients to 10% (Tagliati et al. 1994).

Another growing at-risk population is the medically compromised patients with systemic diseases or organ failure who are kept alive with modern management techniques.

32.3 Microbiology

The predominant organism in human infections is \textit{M. tuberculosis}. The organism \textit{M. tuberculosis} is considered a gram-positive bacterium, though it is difficult to stain by the standard method. Its growth is very slow in culture, which clinically correlates with the slow infection it causes in vivo. Similarly, a long treatment course with anti-tuberculous medications is necessary to eradicate infection and to insure non-resurgence. The genome of \textit{M. tuberculosis} has been sequenced and it includes approximately 4000 genes in a circular chromosome consisting of over 4 million base pairs (Cole et al. 1998).

32.4 Pathogenesis

The microorganism reaches the CNS in the course of dissemination following a primary infection. Entry into the host is most frequently airborne. The lung tissue is infected first along with a regional lymph node. Several factors determine the clinical picture and outcome of CNS TB. These include age, nutritional status, load and virulence of infecting organism, immune deficiency and prior immunization with BCG. The density of bacilli in a unit volume of inspired air is dependent on severity of disease in the infecting person and the effectiveness of air circulation in the environment. The longer the exposure to contaminated air, the more likely the infection is to take place. Acid-fast bacilli do not produce toxins, therefore, they cause no initial tissue reaction or