

Tuberculosis and “Sudden Death”

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Primary Tuberculosis

- 2 Primary pulmonary tuberculosis results from an initial infection with tubercle bacilli. In the majority of cases, the lesion heals spontaneously and may later be evident as a small calcified nodule (Ghon lesion). In severe cases, the primary site rapidly enlarges, its central portion undergoes necrosis, and acute cavitation develops (progressive primary tuberculosis) [18].

2 Secondary Tuberculosis

Also called postprimary disease, adult-type, or reactivation, secondary tuberculosis results from endogenous reactivation of latent infection and is usually localized to the apical and posterior segments of the upper lobes, where the high oxygen concentration favors mycobacterial growth [18].

Mycobacteria

- 4 Mycobacteria are slightly curved or straight, rod-shaped or coccoid bacilli traditionally identified by the property of acid-fastness: once stained, the organisms are not easily decolorized, even with acid-alcohol, because of the composition of their cell walls [12].

typical

Infection with bacteria from the *Mycobacterium tuberculosis* complex (consisting of *M. tuberculosis*, *M. bovis*, and *M. africanum*) [12].

atypical

Except for *Mycobacterium leprae*, the other mycobacteria (e.g. *M. avium*, *M. intracellulare*, *M. gordonae*, *M. kansasii*) are referred to as atypical mycobacteria, mycobacteria other than tuberculosis (MOTT), or nontuberculous mycobacteria (NTM) [12].

Silicosis

Most often, progressive pulmonary fibrosis (silicosis) occurs in a dose-response fashion after many years of exposure to free silica (SiO_2), or crystalline quartz. The major occupational exposures include mining, stonecutting, employment in abrasive industries, foundry work, packing of silica flour, and quarrying, particularly of granite [2][21].

Schlüsselwörter

Tuberkulose (TBC), primäre; TBC, sekundäre; HIV-Co-Infektion; Silikose; Plötzlicher Tod; Todesursache; Obduktion

Keywords

Tuberculosis (TB), primary, TB, secondary, HIV-Co-Infektion; Silikosis; Sudden Death; Cause of death; Post mortem examination

Glossary

Tuberculosis

Tuberculosis is caused by bacteria belonging to the *Mycobacterium tuberculosis* complex—consisting of *M. tuberculosis*, *M. bovis*, and *M. africanum* [12].

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1 Tuberculosis

1.1 Epidemiology

Mycobacteria are the most common human pathogen. A third of the world population is infected—luckily only a fraction of the infected show signs of the disease. 2 million people die every year from mycobacterial infection, mostly due to insufficient diagnosis and therapy [19].

The incidence of pulmonary tuberculosis is declining, with less than 10,000 new infections for 1999 in Germany [19]. Though the rate of non-pulmonary disease remains constant [1].

Two-thirds of the infected are male [19].

In Europe the main risk factors regarding a tuberculosis infection seem to be HIV-infection [4][20], recent immigration from the former Eastern-block [19], chronic alcohol abuse [11], insufficient diet, and homelessness [19]. Further risk factors are diabetes mellitus [18], substance abuse [7], and silicosis [2][21].

Unusual forms are particularly likely to occur in the elderly and immigrant populations [3].

In 1.3% of the autopsies residuals of an active tuberculosis or active tuberculosis itself was diagnosed [19]. In forensic autopsies the figure is 3%—at least in Hamburg [11]. Where a previously unknown active tuberculosis was diagnosed as cause of death in 0.03% of the autopsy cases (n=3, N=11483) [11]. The number seems to be an order of a magnitude higher in west London (0.24%, n=11, N=4600) [3].

In recent years the marked increase of antituberculosis-drug resistance is of growing concern limiting the number of tuberculosis cases with full remission [6][17].

1.2 Primary Disease

Tuberculosis is caused by bacteria belonging to the Mycobacterium tuberculosis complex. The disease usually affects the lungs, although in up to one-third of cases other organs are involved [18]. If properly treated, tuberculosis caused by drug-susceptible strains is curable in virtually all cases [8]. If untreated, the disease may be fatal within 5 years in more than half of cases. Transmission usually takes place through the airborne spread of droplet nuclei produced by patients with infectious pulmonary tuberculosis. It is much aided by modern ventilation systems [15][16].

Unlike the risk of acquiring infection with *M. tuberculosis*, the risk of developing disease after being infected depends largely on endogenous factors, such as the individual's innate susceptibility to disease and level of function of cell-mediated immunity. Clinical illness directly following infection is classified as primary tuberculosis and is common among children up to 4 years of age. Although this form is often severe and disseminated, it is usually not transmissible. When infection is acquired later in life, the chance is greater that the immune system will contain it, at least temporarily. The majority of infected individuals who will ultimately develop tuberculosis do so within the first year or two after infection. Dormant bacilli, however, may persist for years before being reactivated to produce secondary tuberculosis, which is often infectious [18].

Overall, it is estimated that about 10 percent of infected persons will eventually develop active tuberculosis [5].

While up to one-third of untreated patients reportedly succumb to severe pulmonary tuberculosis within a few weeks or months after onset, others undergo a process of spontaneous remission or proceed along a chronic, progressively debilitating course (“consumption”) [18].

Up to one-third of cases of active tuberculosis in U.S. inner-city communities are due to recent transmission rather than to reactivation of latent infection [7][8]. Most European cases are found in elderly immigrants from the former Eastern block [11] with a marked increase in antituberculosis-drug resistance [6][17].

1.2.1 Clinical Symptoms [18]

Early in the course of disease, symptoms and signs are often nonspecific and insidious, consisting mainly of fever and night sweats, weight loss, anorexia, general malaise, and weakness. However, in the majority of cases, cough eventually develops—perhaps initially nonproductive and subsequently accompanied by the production of purulent sputum. Blood streaking of the sputum is frequently documented. Massive hemoptysis may ensue as a consequence of the erosion of a fully patent vessel located in the wall of a cavity. Pleuritic chest pain sometimes develops in patients with subpleural parenchymal lesions but can also be the consequence of muscle strain due to persistent coughing. Extensive disease may produce dyspnea and (occasionally) adult respiratory distress syndrome (ARDS). Physical findings are of limited use in pulmonary tuberculosis. Many patients have no abnormalities detectable by chest examination, while others have detectable rales in the involved areas during inspiration, especially after coughing. Occasionally, rhonchi due to partial bronchial obstruction and classical amphoric breath sounds in areas with large cavities may be heard. Systemic features include fever (often low-grade and intermittent) and wasting. In some cases, pallor and finger clubbing develop. The most common hematologic findings are mild anemia and leukocytosis.

1.3 Postprimary Disease [18]

Postprimary disease—also called secondary tuberculosis, adult-type, or reactivation tuberculosis—results from endogenous reactivation of latent infection. Thus the presence of old, self-healed, fibrotic tuberculous lesions constitutes a serious risk of active disease.

2 Extrapulmonary Tuberculosis

In order of frequency, the extrapulmonary sites most commonly involved in tuberculosis are the lymph nodes, pleura, genitourinary tract, bones and joints [14], meninges, and peritoneum. However, virtually all organ systems may be affected. As a result of hematogenous dissemination in HIV-infected individuals, extrapulmonary tuberculosis is seen more commonly today than in the past [4][18].

2.1 Pericardial Tuberculosis [4][18]

Due to direct progression of a primary focus within the pericardium, to reactivation of a latent focus, or to rupture of an adjacent lymph node, pericardial tuberculosis has often been a disease of the elderly in countries with low tuberculosis prevalence but develops frequently in HIV-infected patients. The onset may be subacute, although an acute presentation, with fever, dull retrosternal pain, and a friction rub, is possible. An effusion eventually develops in many cases; cardiovascular symptoms and signs of cardiac tamponade may ultimately appear. Without treatment, pericardial tuberculosis is usually fatal.

2.2 Myocardial Tuberculosis

The myocardium is usually affected by direct extension, or less often by retrograde lymphatic drainage, from tuberculous mediastinal nodes. Infection via the haematogenous route may develop in miliary disease and direct spread from tuberculous pericarditis can also occur [23].

Myocardial tuberculosis is rarely diagnosed during life. There are reports of some cases without any clinical symptoms. A myocardial tuberculosis should be suspected in patients with a history of tuberculosis if cardiac arrhythmia such as atrial fibrillation, paroxysmal ventricular tachycardia, ventricular fibrillation, or atrioventricular block occurs; if congestive heart failure supervenes; or if valve dysfunction or obstruction of the superior vena cava, right ventricular outflow tract, or pulmonary veins develops. Such obstructive lesions may be due to large nodular tubercles of the right atrium, right ventricle, and left atrium respectively [23].

Myocardial tuberculosis can be separated into three histological types [13]:

- nodular tubercles (tuberculomas) of the myocardium tuberculomas varying in size from “pea to egg” with central caseation usually affecting the right side of the heart, particularly the right atrium.
- miliary tubercles of the myocardium a complication of the generalized miliary disease.
- diffuse infiltrative tuberculosis of the myocardium uncommon variant usually associated with tuberculous pericarditis, in which the myocardium is diffusely infiltrated by granulation tissue containing giant cells, endothelial cells, and lymphocytes.

2.3 Miliary Tuberculosis [8][18]

Miliary or disseminated tuberculosis is due to hematogenous spread of tubercle bacilli. While in children it is often the consequence of a recent primary infection, in adults it may be due to either recent infection or reactivation of old disseminated foci. If it goes unrecognized, miliary tuberculosis is lethal; with proper treatment, however, it is amenable to cure.

It should be noted that central caseation of the miliary tubercles is often absent in the early stages of development.

2.3.1 Clinical Symptoms [18]

Clinical manifestations are nonspecific and protean, depending on the predominant site of involvement. Fever, night sweats, anorexia, weakness, and weight loss are presenting symptoms in the majority of cases. At times, patients have a cough and other respiratory symptoms due to pulmonary involvement as well as abdominal symptoms. Physical findings include hepatomegaly, splenomegaly, and lymphadenopathy. Eye examination may reveal choroidal tubercles, which are pathognomonic of miliary tuberculosis, in up to 30 percent of cases. Meningismus occurs in fewer than 10 percent of cases. No radiographic abnormality may be evident early in the course.

2.4 Tuberculous Meningitis [22]

Tuberculosis of the central nervous system accounts for about 5 percent of extrapulmonary cases. It is seen most often in young children but also develops in adults, especially those who are infected with HIV [18]. Tuberculous meningitis results from the hematogenous spread of primary or postprimary pulmonary disease or from the rupture of a subependymal tubercle into the subarachnoid space. In more than half of cases, evidence of old pulmonary lesions or a miliary pattern is found on chest radiography.

2.4.1 Clinical Symptoms [18]

The disease may present subtly as headache and mental changes or acutely as confusion, lethargy, altered sensorium, and neck rigidity. Typically, the disease evolves over 1 or 2 weeks—a course longer than that of bacterial meningitis. Paresis of cranial nerves (ocular nerves in particular) is a frequent finding, and the involvement of cerebral arteries may produce focal ischemia, hydrocephalus is common.

2.5 HIV-Associated Tuberculosis

The most common endogenous factor favouring tuberculosis infection is a HIV infection. Extrapulmonary tuberculosis is an AIDS-qualifying diagnosis in HIV-infected patients [4][20]. In various series studied in the United States and many developing countries, extrapulmonary tuberculosis—alone or in association with pulmonary disease—has been documented in 40 to 60 percent of all HIV-infected patients [?]. The most common forms are lymph nodal, disseminated, pleural, and pericardial. Mycobacteremia and meningitis are also frequent, particularly in advanced HIV disease [4].

In the last stages of a HIV infection it is typical to find an increased frequency of negative sputum-smears, atypical radiographic findings, a lack of classic granuloma formation as well as negative results in PPD skin tests despite a tuberculosis infection [4][10].

In HIV-infected patients no radiographic abnormality may be evident even in cases of miliary tuberculosis [18].

Delays in treatment may prove fatal. Due to their delicate health HIV positive substance abusers are at an even greater risk of a fatal tuberculosis infection [7][20].

3 TB-Infection Diagnosis [3][18]

The diagnosis can easily be missed in an elderly nursing-home resident or a teenager with a focal infiltrate. The key to the diagnosis of tuberculosis is a high index of suspicion. A missed tuberculosis infection can easily be fatal and in cases of secondary tuberculosis even unexpectedly.

Literatur

- [1] Ananko J, Burska I (1981) Diagnostic and Legal aspects of clinical unrecognised adrenal tuberculosis. *Wiadomości Lekarski* 34:1393
- [2] Chan ACL, Dickens P (1992) Tuberculous Myocarditis Presenting as Sudden Cardiac Death. *For Sci Int* 57:45-50
- [3] Chapman RC; Claydon SM (1992) Mycobacterium tuberculosis: a continuing cause of sudden and unexpected death in west London. *Journal of Clinical Pathology* 45(8):713-5
- [4] CDC/Center for Disease Control and Prevention (1998) Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR* 47(No. RR-20):1-25
- [5] CDC/Center for Disease Control and Prevention (1998) Use of Short-Course Tuberculosis Preventive Therapy Regimens in HIV-Seronegative Persons. *MMWR* 47(42):911-2
- [6] Espinal MA, Laszlo A, Simonsen L, Boulahbal F, Kim SJ, Reniero A, Hoffner S, Rieder HL, Binkin N, Dye C, Williams R, Raviglione MC (2001) Global Trends in Resistance to Antituberculosis Drugs. *N Engl J Med* 344 (17):1294-1303
- [7] Friedman LN, Williams MT, Singh TP, Frieden TR (1996) Tuberculosis, AIDS, and Death among Substance Abusers on Welfare in New York City *N Engl J Med* 334 (13):828-33
- [8] Gasner MR, Maw KL, Feldman GE, Fujiwara PI, Frieden TR (1999) The Use of Legal Action in New York City to Ensure Treatment of Tuberculosis. *N Engl J Med* 340 (5):359-66
- [9] Braunwald E, Fauci A, Hauser S, Jameson J, Kasper D, Longo D (2001) *Harrison's Principles of Internal Medicine*. McGraw-Hill, New York 2001, 15th edition, ISBN 0-07-007272-8
- [10] Havlir DV, Barnes PF (1999) Current Concepts: Tuberculosis in Patients with Human Immunodeficiency Virus Infection *N Engl J Med* 340 (5):367-73
- [11] Heinemann A, (1995) Tuberkulose-Manifestation im rechtsmedizinischen Obduktionsgut in den Jahren 1984-1994 Vortrag, 4. Frühjahrstagung der Deutschen Gesellschaft für Rechtsmedizin – Region Nord, Mai 1995, Rostock
- [12] Hirschel, B (2001) Infections Due To Nontuberculous Mycobacteria. Chapter 173. In: [9]
- [13] Horn H, Saphir O (1935) The involvement of the myocardium in tuberculosis: a review of the literature and report of three cases. *Am Rev Tuberc* 32:492-506
- [14] Jenks PJ, Stewart B (1998) Vertebral Tuberculosis (Images in Clinical Medicine). 338 (23):1677
- [15] Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG (1996) Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. *N Engl J Med* 334(15):933-8
- [16] Kline SE, Hedemark LL, Davies SF (1995) Outbreak of Tuberculosis among Regular Patrons of a Neighborhood Bar. *N Engl J Med* 333 (4):222-7
- [17] Pablos-Méndez A, Raviglione MC, Laszlo A, Binkin N, Rieder HL, Bustreo F, Cohn DL, Lambregts-van Weezenbeek CSB, Kim SJ, Chaulet P, Nunn P, The World Health Organization-International Union against Tuberculosis and Lung Disease Working Group on Anti-Tuberculosis Drug Resistance Surveillance (1998) Global Surveillance for Antituberculosis-Drug Resistance, 1994-1997. *N Engl J Med* 338:1641-9
- [18] Raviglione MC, O'Brien R (2001) Tuberculosis. Chapter 171. In: [9]
- [19] RKI/Robert Koch Institut (2001) Zur Struktur der Tuberkulosemorbidität in Deutschland *Epidemiologisches Bulletin* 2001(11):78-80
- [20] Selwyn PA, Hartel D, Lewis VA, Schoenbaum EE, Vermund SH, Klein RS, Walker AT, Friedland GH (1989) A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection *N Engl J Med* 320(9):545-50
- [21] Speizer FM (2001) Environmental Lung Diseases, Silicosis. Chapter 253. In: [9]
- [22] Viallard JF, Blanco P (1999) Tuberculous Meningitis (Images in Clinical Medicine). *N Engl J Med* 341 (16):1197
- [23] Wallis, PJW, Branfoot AC, Emerson PA (1984) Sudden Death due to Myocardial Tuberculosis. *Thorax* 39:155-6
- [24] Ward S, Evans CC (1985) Sudden Death due to isolated adrenal tuberculosis. *Postgraduate Medical Journal* 61:635-6