DIAGNOSIS OF TUBERCULOUS PLEURAL EFFUSION

Essay

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ABSTRACT

Tuberculosis has troubled humankind throughout history, It has been a leading cause of death throughout the world, and still is in low-income and middle-income countries, especially those of sub-Saharan Africa where tuberculosis is an epidemic because of the increased susceptibility conferred by HIV infection **.** Tuberculosis defined as chronic necrotizing bacterial infection which is a specific disease caused by infection with ***Mycobacterium tuberculosis***, the tubercle bacillus, which can affect almost any tissue or organ of the body, the most common site of the disease being the lungs (Pulmonary) and extrapulmonary TBEPTB) is more commonly encountered in clinical practice. Primary TB is typically a mild or a symptomatic localpulmonary infection. Tuberculosis (TB) is a global burden and infection with human immunodeficiency virus is a growing epidemic. Prompt diagnosis and treatment can lead to control of tuberculosis in the world**.** A total of nine million new cases and approximately two million deaths from TB were reported in 2004. The most recent estimates of the worldwide epidemic of tuberculosis are for 2004.TB pleural effusion is the second most common form of EPTB, only less frequent than lymph node TB. Diagnosis of tuberculous (TB) pleural effusions is difficult and better diagnostic tools are needed. The definitive diagnosis of TB pleural effusions depends on the demonstration of ***M. tuberculosis*** insputum, pleural fluid, or pleural biopsy specimens. Diagnosis of tuberculous pleural effusion depend on clinical manifestations, tuberculin skin reaction, chest imaging, thoracocentesis with pleural fluid analysis by (biochemical analysis, cytological analysis, microbiological and molecular studies) and depend on also invasive studies like (closed needle biopsy and medical thoracoscopy).

Supportive evidence includes demonstration of classical TB granulomas in the pleura and elevated adenosine deaminase (ADA) and IFN-γ levels inpleural fluid. The first step in diagnosis is pleural fluid analysis. Immunological studies have only more recently been incorporated into the clinical diagnosis of tuberculous effusion. New diagnostic tests for diagnosis tuberculous pleural effusion founded now may helping improve Diagnosis of tuberculus effusion.

Key Words:

Tuberculosis, pathophysiology of tuberculosis, **pleural effusion diagnosis, diagnosis of tuberculous pleural effusion.**

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LIST OF ABBREVIATIONS

ADA	: Adenosine deaminase
AFB	: Acid fast bacilli
AFP	: Alpha fetoprotein
AgNOR	: Argyrophilic staining Nucleolar organiser regions
AMTDT	: Amplified mycobacterium tuberculosis direct test
ANA	: Antinuclear antibody
anti-ssDNA	: Anti single strand deoxy riboneuclic acid antibody
anti-dsDNA	: Anti double strand deoxy riboneuclic acid antibody
anti-Sm	: Anti smooth muscle antibody
ARI	: Annual Risk of Tuberculous Infection
ATS	: American Thoracic Society
BCG	: Bacille Calmette-Guérin
CDC	: Centre of Disease Control
CD4	: T-lymphocyte helper cell
CD8	: T-lymphocyte suppressor cell
CD30	: Cytokines –D 30
CEA	: Carcinoembryonic antigen
CFP-10	: culture filtrate protein antigen
CI	: Confidence interval
CMI	: Cell mediated immunity
CT	: Computed tomography
CXR	: Chest radiograph
DOTS	: Direct Observed Therapy
DNA	: Deoxyribonucleic acid
DN ab-T	: T-cell receptor double negative cells
ESAT-6	: Early secretory antigenic target- 6
GI	: Growth index
HIV	: Human immunodeficiency virus
HLA	: Human leukocyte antigen
HPLC	: High performance liquid chromatography
IFN-γ(IFN-c)	: Interferon-gamma
IL	: Interleukins
IL-4	: Interleukin-4
IL-4δ2	: Interleukin-4 sigma-2
IL-7	: Interleukin-7
IL-8	: Interleukin-8
IL-12 ß1	: Interleukin-12 beta 1 receptor
IS6110	: Insertion Sequence 6110
JVP	: Jugular venous pressure
LCR	: Ligand chain reaction

LCxMTB	: Ligand chain mycobacterium tuberculosis assay
LDH	: Lactic dehydrogenase
LE	: Lupus erythematosus cells
LTBI	: Latent TB infection
MDR-TB	: Multidrug Resistance Tuberculosis
MGIT	: Mycobacteria growth indicator tube system
MMP-1	: Matrix metalloproteinase-1
MMP-7	: Matrix metalloproteinase-7
MMPs	: Matrix metalloproteinases
mRNA	: Messenger ribonucleic acid
MTB	: Mycobacterium tuberculosis
Mtb72f	: Mycobacterium tuberculosis polyprotein vaccine-72F
MRI	: Magnetic resonance imaging
NAAT	: Nucleic acid amplification techniques
NAP	: P-nitro-α acetylamino-hydroxypropiophenone
NOR	: Nucleolar organiser regions
NRAMP-1	: Natural resistance-associated macrophage protein-1
NTM	: Non-tuberculous mycobacteria
NTP	: National Tuberculosis Control Programme
OR	: Odds ratio
plcA,B,C,D	: Phospholipase C-encoding genes
PCR	: Polymerase Chain Reaction
PE	: Pleural effusions
PMNLs	: Polymorphonuclear neutrophils
PPD	: Purified Protein Derivative
PPV	: Positive predictive value
RFLP	: Restriction fragment length polymorphism
ROC	: Receiver operating characteristic
SDA	: Strand displacement amplification
SLE	: Systemic lupus erythematosus
TB	: Tuberculosis
TGF-b	: Transforming growth factor
Th1	: T lymphocytes cell type-1
Th2	: T lymphocytes cell type- 2
TMA	: Transcription mediated amplification
TNF-α	: Tumor necrosis factor -alpha
TNF-γ	: Tumor necrosis factor gamma receptor
TST	: Tuberculin Skin Test
TU	: Tuberculin units
US	: Ultrasound
VATS	: Video-assisted surgical thoracoscopy
WBC	: White blood cell

INTRODUCTION AND AIM OF THE ESSAY

Tuberculosis has troubled humankind throughout history, It has been a leading cause of death throughout the world, and still is in low-income and middle-income countries, especially those of sub-Saharan Africa where tuberculosis is an epidemic because of the increased susceptibility conferred by HIV infection **(Maartens et al., 2007).**

Tuberculosis defined as chronic necrotizing bacterial infection which is A specific disease caused by infection with *Mycobacterium tuberculosis*, the tubercle bacillus, which can affect almost any tissue or organ of the body, the most common site of the disease being the lungs. Primary TB is typically a mild or asymptomatic local pulmonary infection. Regional lymph nodes may become involved, but in otherwise healthy people generalized disease does not immediately develop. A cell-mediated immune response arrests the spread of organisms and walls off the zone of infection. Infected tissues and lymph nodes may eventually calcify. The tuberculin skin test result becomes positive within a few weeks and remains positive throughout life. Organisms in a primary lesion remain viable and can become reactivated months or years later to initiate secondary TB. Progression to the secondary stage eventually occurs in 10–15% of people who have had primary TB; in one half of these, progression occurs within 2 years. The risk of reactivation is increased by diabetes mellitus, malnutrition, HIV infection, silicosis, and various systemic or malignant conditions, as well as in patients with alcoholism, IV drug abusers, nursing home residents, and those receiving adrenocortical steroid or immunosuppressive therapy. Secondary or reactivation TB usually results in a chronic, spreading lung infection, most often involving the upper lobes. Minute granulomas (tubercles), just visible to the naked eye, develop in involved lung tissue, each consisting of a zone of caseation necrosis surrounded by chronic inflammatory cells (epithelioid histiocytes and giant cells). These lesions, which give the disease its name, are also found in other tissues (lymph nodes, bowel, kidney, skin) to which the disease may spread.

Rarely, reactivation results in widespread dissemination of tubercles throughout the body (miliary TB). The symptoms of active pulmonary TB are fatigue, anorexia, weight loss, low-grade fever, night sweats, chronic cough, and hemoptysis. Local symptoms depend on the parts affected. Active pulmonary TB is relentlessly chronic and, if untreated, leads to progressive destruction of lung tissue. Cavities form in the lungs, and erosion into pulmonary blood vessels can result in life-threatening hemorrhage. Gradual deterioration of nutritional status and general health culminates in death due to wasting, infection, or multiple organ failure. Variant syndromes (tuberculous lymphadenitis in children, severe systemic disease in persons with AIDS) are caused by organisms of the ***Mycobacterium avium-intracellulare*** complex (MAIC). The diagnosis of TB is based on tuberculin skin testing (negative in 20% of people with active TB), imaging studies (computed tomography is more sensitive than standard chest radiography in detecting pleural effusion, miliary disease, and cavitation), and the finding of the causative organism in sputum or tissue specimens by acid-fast or fluorochrome staining, nucleic acid amplificatin, or culture **(Maartens et al., 2007**).

The effectiveness of the Bacille Calmette Guérin (BCG) vaccine is partial, and that of treatment of latent tuberculosis is unclear in high-incidence settings **(Maartens et al., 2007).**

The routine diagnostic methods that are used in many parts of the world are still very similar to those used 100 years ago **(Maartens et al., 2007**).

Nevertheless, the duration of treatment needed reduces its effectiveness, as does the emergence of multidrug-resistant and extensively drug-resistant disease; the latter has recently become widespread **(Maartens et al., 2007)**.

The rapid expansion of basic, clinical, and operational research, in addition to increasing knowledge of tuberculosis, is providing new diagnostic, treatment, and preventive measures **(Maartens et al., 2007**).

The challenge is to apply these advances to the populations most at risk. The development of a comprehensive worldwide plan to stop tuberculosis might facilitate this process by coordinating the work of health agencies. However, massive effort, political will, and resources are needed for this plan to succeed **(Maartens et al., 2007)**.

The limitations of existing methods of prevention, diagnosis, and treatment of tuberculosis have been emphasised by the increased susceptibility of HIV-infected people to develop the disease, and by the emergence of drug-resistant strains **(Maartens et al., 2007)**.

Overall, the worldwide burden of tuberculosis is still growing, Improvement in the control of the disease in many regions of the world is off set by the effect of HIV in the resource-poor health systems of sub-Saharan Africa. The challenge is to apply advances tothe populations most at risk **(Maartens et al., 2007)**.

The most recent estimates of the worldwide epidemic of tuberculosis are for 2004, when there were 8·9 million new cases and 1.7 million deaths. **(WHO Global tuberculosis Control Geneva et al., 2006)**.

The worldwide annual incidence continues to increase in Africa because of the HIV epidemic, whereas it is stable or falling in all other regions. The risk of tuberculosis increases shortly after HIV seroconversion, doubling within the first year **(Sonnenberg et al., 2005)**.

The annual incidence of tuberculosis is about 10% in HIV-infected individuals from high-burden communities in both industrialised and developing countries, with reported rates of 7·6 per 100 person years in US users of intravenous drugs who are tuberculin skin test (TST) positive **(Selwyn et al., 1989)**, and 10·4 per 100 person years in South Africans of unknown TST status **(Wood et al., 2000)**.

This risk increases further with serious immunosuppression; a incidence as high as 30% has been reported in South African patients with clinically advanced HIV **(Wood et al., 2000**).

HIV infection predisposes to the reactivation of latent tuberculosis **(Selwyn et al., 1989)**.

Which is the basis for the provision of preventive therapy in HIV-infected individuals at risk **(Woldehanna et al., 2004)**.

HIV infection is also strongly associated with the transmission of tuberculosis between adults in sub-Saharan Africa **(Glynn et al., 2005)**.

High transmission rates of tuberculosis cause large numbers of children tobe infected, which is concerning not least because of the rapid disease progression and the difficulties with diagnosis in this group **(Marais et al., 2006)**.

TB pleural effusion, considered as a form of extrapulmonary TB (EPTB), constitutes a frequent clinical problem and is particularly important in the present era of HIV infection, when EPTB is more commonly encountered in clinical practice **(Sharma, Mohan et al., 2004)**.

Tuberculous (TB) pleural effusion occurs in approximately 5% of patients with *Mycobacterius tuberculosis* infection **(Arun Gopi et al., 2007)**.

The HIV pandemic has been associated with a doubling of the incidence of extrapulmonary TB, which has resulted in increased recognition of TB pleural effusions even in developed nations **(Arun Gopi et al., 2007)**.

The definitive diagnosis of TB pleural effusions depends on the demonstration of acid-fast bacilli in the sputum, pleural fluid, or pleural biopsy specimens **(Arun Gopi et al., 2007)**.

The diagnosis can be established in a majority of patients from the clinical features, pleural fluid examination, including cytology, biochemistry, and bacteriology, and pleural biopsy **(Arun Gopi et al., 2007).**

Aim of the Essay:

The **aim** of essay to study diagnosis of tuberculous pleural effusion and methods used in diagnosis.

EPIDEMIOLOGY OF TUBERCULOSIS

The Centers for Disease Control and Prevention recently published the trends in tuberculosis (TB) incidence in the UnitedStates In 2006, a total of 13,767 TB cases were reported inthe United States, at a rate of 4.6 per 100,000, representing a 3.2% decline from 2005. The incidence of TB in 2006 was the lowest recorded since 1953, but the rate of decline has slowed since 2000. Foreign-born persons and racial/ethnic minority populations continued to be affected disproportionately. TheTB rate among the former was 9.5 times that of United States–born persons. The slowing of decline in the overall national TB rate and the inability to effectively address persistent disparities in TB rates between United States–born and foreign-born persons, and betweenwhites and racial/ethnic minority populations, may hamper progress toward the goal of TB elimination in the United States **(CDC et al., 2006)**.

About 9 million people around the world developed tuberculosis (TB) for the first time in 2004, and nearly 2 million people died with or from the disease. Globally, TB is currently responsible for more years of healthy life lost (2.5 percent of all disability-adjusted life years, or DALYs) than any other infectious disease, bar AIDS and malaria **(Corbett et al. 2003; WHO 2002; WHO 2006).**

Only AIDS is responsible for more deaths. The full cost of the worldwide TB epidemic is rarely appreciated. The direct monetary costs of diagnosis and treatment are borne by health services and by patients and their families. Added to these are the indirect costs of lost income and production, incurred when TB patients are too sick to work and when young adults often parents and householders die prematurely **(Christopher Dye et al., 2006**).

Beyond these losses, baldly expressed in DALYs and dollars, enormous psychological and social costs are associated with TB. These extra costs are less easily quantified, but they are nonetheless real.A decade ago the problem of TB in Africa attracted little attention, a. Part of the reason was that TB

incidence was low and falling in most parts of the continent **(Cauthen, Pio, and ten Dam, 2002).**

About one-third of the population of Sub-Saharan Africa is infected with ***M. tuberculosis*** **(Dye et al. 1999).**

In the year 2000, an estimated 17 million people in Sub-Saharan Africa were infected with both ***M. tuberculosis*** and HIV 70 percent of all people co-infected worldwide **(Corbett et al. 2003).**

As more people have become infected and coinfected with HIV, especially in eastern and southern Africa, the incidence of TB has been driven upward, as reflected in estimates derived from population-based surveys and from routine TB surveillance data **(Maher et al., WHO 2002, 2006).**

In 2004, the incidence rate of TB in the WHO African region was growing at approximately 3 percent per year, and at 4 percent per year in eastern and southern Africa (the areas most affected by HIV), faster than on any other continent, and considerably faster than the 1 percent per year global increase **(Harries et al., WHO 2004, 2006).**

In several African countries, including those with well-organized control programs, annual TB case-notification rates have risen more than fivefold since the mid-1980s, reaching more than 400 cases per 100,000 people **(Harries et al., WHO, 2004, 2006).**

HIV infection is the most important single predictor of TB incidence across the African continent. Despite the emphasis placed on finding smear-positive cases under DOTS and the new WHO Stop TB Strategy, the proportion of cases reported to be smear-positive has fallen in recent years in several African countries with high rates of HIV. Although there are uncertainties about diagnosis, these data conform with the expectation that there will be more smear-negative TB where there is more HIV. Because HIV