

### ATYPICAL PRESENTATION OF DISSEMINATED TUBERCULOSIS – AN AUTOPSY CASE REPORT

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#### Abstract

Reporting a case of natural death where blind anti-tubercular treatment started late due to atypical presentation and conflicting laboratory reports. The deceased was a 25 year old male Indonesian rubber plantation worker initially diagnosed as Cryptococcal infection and had been treated on antifungal regime. Histological examination of various organs after post mortem examinations revealed disseminated tuberculosis.

**Key-words:** Atypical presentation, disseminated tuberculosis, autopsy.

#### Introduction

Tuberculosis (TB) is a disease caused by a bacterium called *Mycobacterium tuberculosis* that most often affect the lungs, but TB bacteria can attack any part of the body such as the kidney, spine, and brain. If not treated properly, TB disease can be fatal. Disseminated tuberculosis (TB) is a contagious bacterial infection in which TB bacteria has spread from the lungs to other parts of the body through the blood or lymph system<sup>1</sup>. TB spreads through the air when a person with TB of the lungs or throat coughs, sneezes, or talks. TB is a treatable and curable disease. Between 2000 and 2013, an estimated 37 million lives were saved through TB diagnosis and treatment<sup>2</sup>.

#### Case Report

A 25-year old Indonesian rubber plantation worker previously healthy was admitted in a General hospital with the complaints of headache, irregular fever, chills and rigor with vomiting for last 2 weeks. On examination, he was febrile and had signs of meningeal irritation. Laboratory investigations showed ESR 58mm in 1st hour, CSF obtained by lumbar puncture with

Indian ink preparation showed fungi which are consistent with *Cryptococcus neoformis*. CT scan of the brain revealed multiple ring enhancing lesions with cerebral oedema. X ray chest was normal. Serological tests for HIV/HCV/HBV were negative. All other tests done at the hospital were within normal limit. The deceased was treated with Amphoterecin B for two weeks but didn't show any improvement. His clinical condition was deteriorating and repeat CT scan showed increasing ventricular size. He was referred from general hospital to Hospital Universiti Sains Malaysia (HUSM). In the HUSM repeat CSF examination showed no cryptococcus, Serological test for cryptococcus was also negative.

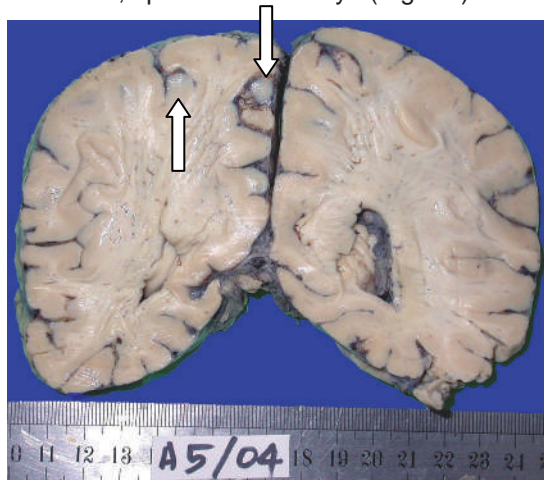
The clinical findings remained same. Extra Ventricular Drainage (EVD) was done to tackle raised Intracranial Pressure (ICP). Routine CSF examination showed TC 100/cmm, DC poly 92%, lymphocyte 8%, total protein 6.6gm, sugar 0.3m.mol. Hematological test showed an increased ESR. Repeat X-ray chest was normal. Blind anti-tubercular treatment was started while waiting for the *Mycobacterium* culture and sensitivity test results due to further deterioration of the patient in spite of anti-fungal therapy, general supportive therapy, procedure to reduce raised intracranial pressure, negative HIV, HBV, and HCV test. The common prevalence of tuberculosis in South East Asia as well as the poor socio-economical status of the patient was also considered. The patient died after 10 days of starting the treatment. An autopsy was advised to find out the cause of death. The cause of death was established after autopsy as disseminated tuberculosis involving brain, meninges, lungs, kidney and spleen. Atypical tuberculosis infection is noticed other than *Mycobacterium tuberculosis* or *Mycobacterium bovis*.

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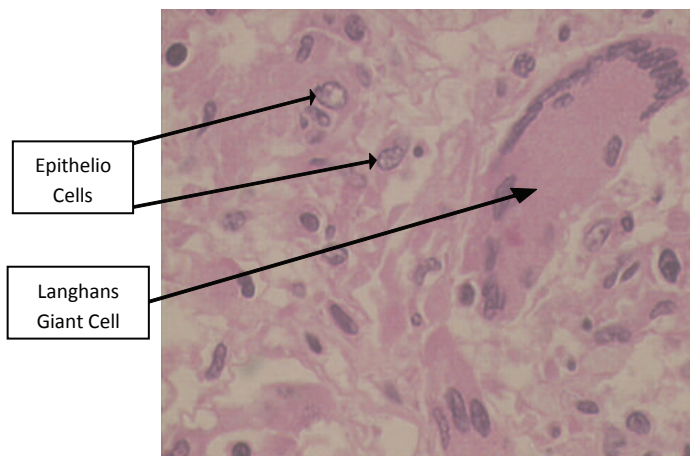
Most of them are opportunistic pathogens such as Mycobacterium avium complex (MAC)/avium intracellulare(MAIM). The atypical mycobacteriums are normally identified based on their speed of growth, production of pigments as well as DNA probes. They are well known to infect the immuno compromised patients such as HIV and present with non specific symptoms such as fever, night sweat, abdominal pain, diarrhoea and weight loss. These infections are usually treated with Clarithromycin or Azithromycin and Ethambutal but multiple drug combination are often been used.

### Autopsy findings

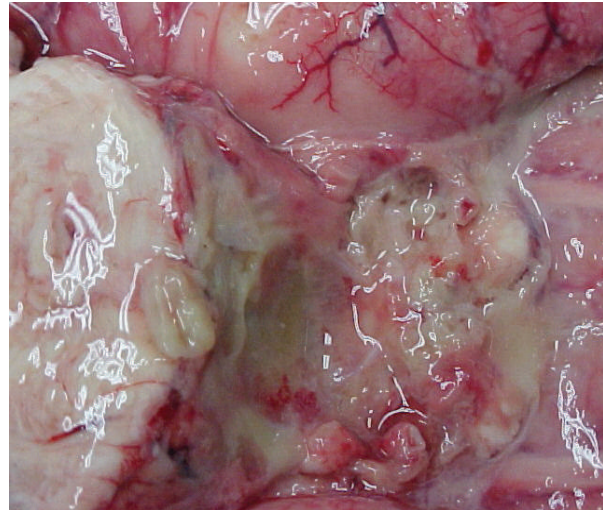
Overall, the external examination showed no emaciation and found healthy. In gross examination of brain, tuberculoma, basal meningitis and tonsillar herniation were evident. Multiple granulomas were seen at the lungs with pleural thickening. Focal granulomas were also seen in liver, spleen and kidneys (Fig.1-6).



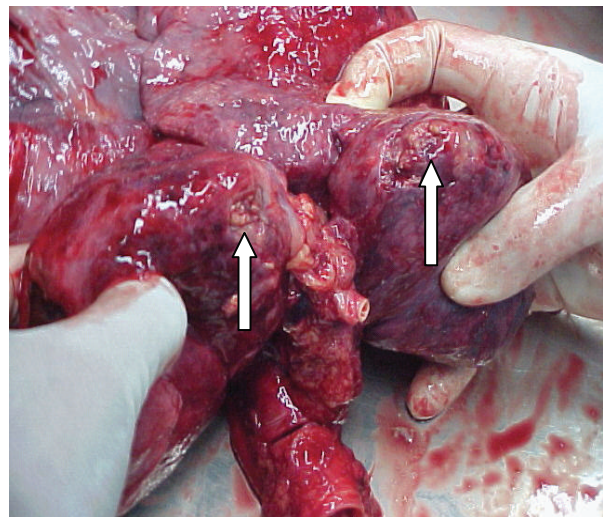
**Fig-1:** Gross picture of brain showing tuberculoma.



**Fig-2:** Microphotograph of brain showing granuloma H&E x 40.



**Fig-3:** Gross picture of brain showing Basal Meningitis.



**Fig-4:** Gross picture of lungs showing Apical Granuloma.



**Fig-5:** Gross picture showing Hepatic granuloma.



**Fig-6:** Gross picture showing renal granuloma.



Other organs were apparently healthy by looking at their gross appearance. Histological examinations later confirmed the Epithelioid Granulomas in brain, lung, liver and spleen. Imprint cytology from smear of brain and lung revealed numerous Acid Fast Bacillus (AFB).

### Discussion

In recent years the diagnosis of tuberculosis has become more difficult since number of classic cases has declined and more patients present now with occult or atypical symptoms. Atypical presentations are more common in elderly patients, HIV infected cases and immuno compromised patients<sup>3,4</sup>. But the present case is a young healthy man and without immuno compromised as evident from the negative serological tests. Thus, it is possible for young healthy patients with atypical symptoms of tuberculosis. Conventional and routine laboratory reports are sometimes confusing and cannot give a definite diagnosis of tuberculosis like Hb, TC, DC, ESR, negative sputum for AFB, negative X ray chest<sup>5,6,7,8</sup>. In the present case only ESR was mildly increased while other tests were normal. It is advocated that advance test PCR should be used along with conventional tests to come to a rapid and accurate diagnosis due to its sensitivity and specificity of detection even in a very diminutive amount. Superadded fungal infection may complicate the diagnosis of tuberculosis as occurred in the present case, where initial diagnosis of cryptococcosis was made on India ink preparation of the CSF.

However after antifungal therapy and repeated CSF examination for cryptococcosis including serology were negative. This has worsened the condition of the patient and delayed the starting of the antituberculous treatment and ultimately leading to death of this patient.

Postmortem examination is an important tool in establishing the accurate diagnosis of suspected cases dying of different common diseases with atypical presentation and uncommon clinical conditions as happened in the present case<sup>9</sup>. It speaks for the dead to protect the living, helps identification of the underlying purpose of obtaining knowledge about deaths, investigates suspicious, obscure, unnatural, litigious or criminal deaths<sup>10</sup>. Autopsy also helps to demonstrate all external and internal abnormalities, malformations and diseases. Many researches and studies had indeed able to conclude that errors in diagnosis are no longer unusual phenomena and most of this could be only determined during autopsy<sup>11</sup>. Most doctors are very certain that their diagnosis was correct and neglected this important manner, which could be wrong in up to 45% most of the time. Only by autopsy which proves to be the best method for doctors to discover whether the effectiveness of current treatment and understand more of the evolvement of disease. These in turn helps us to define and improvise better strategies, advise appropriate investigations and management of the patient to reduce morbidity and mortality.

### Conclusion

Exact diagnosis of tuberculosis is particularly important in starting the anti tubercular treatment. Atypical presentations and conflicting results may lead to undue delay in starting the treatment and leading to death. Any patient presenting with irregular fever, symptoms of raised intra cranial pressure should be investigated meticulously to exclude tuberculosis. In addition to the routine and conventional investigations like hematological tests, sputum for AFB for 3 consecutive samples, X-ray some more sensitive tests like PCR should be constituted for early diagnosis of tuberculosis. Post mortem examination is essential and advocated in any case of hospital death to establish the cause of death.

## References

1. Ellner JJ. Tuberculosis. In: Goldman L, Schafer AI, eds. *Goldman's Cecil Medicine*. 24th ed. Philadelphia, PA: Elsevier Saunders; 2011:chap 332.
2. World Health Organization: Tuberculosis (TB); Fact Sheet N° 104, Updated October 2014. Available at <http://www.who.int/mediacentre/factsheets/fs104/en>.
3. Cotran, Kumar, Collin, Robbins Pathologic basis of disease, 6th ed, WB Saunders,1999, p378-81.
4. Souza RD, Franklin D, Simpson J, Kerr F. Atypical presentation of tuberculous meningitis. *Scott Med J*. 2002 Feb; 47(1):14-5.
5. Palmieri F, Giardi E, Pellicelli AM, Rianda A, Bordi E, Rizzi EB, Petro N, Ippolito G. Pulmonary tuberculosis in HIV-infected patients presenting with normal chest radiograph and negative sputum smear. *Infection*. 2002 Apr; 30(2):68-74.
6. Prasad R, Saini JK, Gupta R, Kannaujia RK, Sarin S, Suryakant, Kulshreshth R, Nag VL, Tripathi AK. A comparative study of clinico-radiological spectrum of tuberculosis among HIV seropositive and HIV seronegative patients. *Indian J Chest Dis Allied Sci*. 2004 Apr-Jun;46(2):99-103.
7. Kiyani E, Kilicaslan Z, Gurgan M, Tunaci A, Yildiz A. Clinical and radiographic features of pulmonary tuberculosis in non-AIDS immuno compromised patients. *Int J Tuberc Lung Dis*. 2003 Aug;7(8):764-70.
8. Shaikh MA, Singla R, Khan NB, Sharif NS, Saigh MO. Does diabetes alter the radiological presentation of pulmonary tuberculosis. *Saudi Med J*. 2003 Mar;24(3):278-81.
9. Saukko P, Knight B, Knight Forensic Pathology, 3rd edition, Arnold, London, 2004, p1-17.
10. James JP, Busuttill A, Smock W, Forensic Medicine Clinical & Pahtological aspects, 1st ed, London, GMM:2003, P73-9.
11. Kingford D.P.W. A review of Diagnostic Inaccuracy. *Med Sci. Law*. 1995;35(4):347-51.