CLINICAL_IMPACT_OF_TUBERCULOUS_MENINGITIS_DISEASE__1_2.pdf

by

Submission date: 25-May-2021 01:37PM (UTC+0700)
Submission ID: 1593719643
File name: CLINICAL_IMPACT_OF_TUBERCULOUS_MENINGITIS_DISEASE__1_2.pdf (309.61K)
Word count: 3644
Character count: 20487

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, Pages. 13147- 13153
2021, Received 05 March 2021; Accepted 01 April 2021

CLINICAL IMPACT OF TUBERCULOUS MENINGITIS DISEASE: A CASE STUDY IN MAKASSAR REGIONAL HOSPITAL

Author
Jumraini Tammasse[1]
Lecturers Department of Neurology, Faculty of Medicine in Hasanuddin University, Makassar, Indonesia
Email: jumraini.tammasse@gmail.com

Abstract
One of the diseases that can be transmitted in the air through the bacteria Mycobacterium tuberculosis (M. tuberculosis) is an understanding of Tuberculosis (TB). The M. tuberculosis bacteria spreads to the human body with the help of droplet nuclei, which are 1 to 5 microns in size. Infectious nuclei droplets can be produced when an individual with pulmonary tuberculosis c larynx coughs. Transmission occurs when the individual inhales the bacteria and then crosses through the nasal passages or mouth, upper respiratory tract, and bronchi to reach the alveoli in the lungs. Tuberculous meningitis (TBM) is a subacute disease, resulting from extra-pulmonary complications of pulmonary tuberculosis and transmitting to the meninges. Symptoms can be found days before diagnosis. Initially the individual will experience a prodrome phase characterized by low-grade fever, malaise, headache, dizziness, vomiting, and personality changes that last for several weeks. Furthermore, the client will experience increasingly severe headaches, cranial neuropathy, stroke, hydrocephalus, changes in mental status, and other complications. The case involved in this research is a man aged 32 years at Wahidin Sudirohusodo Hospital. The initial symptoms of the patient begin to speak incoherently. There was also a history of fever since 5 days before admission and headaches without nausea or vomiting since two weeks before admission. His laboratory results reported an increase in white blood cell count (12,100 / μL) and hyponatremia (129 mmol / L). His cerebrospinal fluid analysis proved that there was a tuberculosis infection (low glucose levels, high protein levels, dominant mononuclear cells). Based on this information and examination, this client was diagnosed as having los consciousness with a positive meningeal sign and left lateralization due to tuberculosis meningitis. Tuberculous meningitis is an area of extra-pulmonary expansion of pulmonary tuberculosis that spreads to the meninges.

Keywords: Tuberculous meningitis, Positive meningeal, Left lateralization.

Introduction
According to Jullien, Ryan, Modi, and Bhatia (2016) Tuberculous meningitis (TBM) is the development of an extra-pulmonary disorder from pulmonary tubercu is (TB) which is characterized by chronic inflammation of the meninges caused by the spread of M. tuberculosis bacteria. The ratio of TBM disease in the TB group varies widely. However, in general, about 1% of TB cases are TBM. Ducomble (2013) states that around 10.4 million TB cases are reported each year. TBM in general can have very dangerous effects, despite treatment, so that chronic neurodisability can occur. Many of the fatal effects caused by TBM are due to the immune response, HIV coinfection, malnutrition, pathogen virulence, and other co-factors (Jullien, Ryan, Modi, & Bhatia, 2016).

Infection can occur due to the inhalation of M. tuberculosis containing aerosol droplets, followed by activation of neutrophils, alveolar macrophages, and dendritic cells that engulf mycobacteria in the terminal alveoli. Then the infected cells will move to lymphoid tissue, which ultimately leads to cell activation and production of pro-inflammatory cytokines, resulting in inflammatory changes in the lung parenchyma and blood vessels (O'Garra, 2013). If the bacteria reach the blood vessels, hematogenous expansion can occur, and will attack

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, Pages. 13147- 13153
2021, Received 05 March 2021; Accepted 01 April 2021

the CNS (Krishnan, Robertson, & Thwaites, 2010; Jain, et al., 2006; Donald, Schaaf, & Schoeman, 2005).

Case Report

The patient, who is 32 years old with the male gender below by his family, went to the hospital because of a loss of consciousness that appeared two days before being treated at Wahidin Sudirohusodo Hospital. However, the day before, the patient began to have irregular conversations. Then, there is also a history of fever since five days before being rushed to the hospital and headaches without nausea or vomiting since the previous two weeks. However, there was no history of trauma and hypertension. In addition, there is also no history of using anti-tuberculosis drugs, the occurrence of weight loss, and there is a history of prolonged coughing since one month ago.

Physical examination results showed vital signs within normal limits. However, the client had a low-grade fever (37.5 ° Celsius) with tachycardia (105 times / minute), which refers to the Glasgow Coma Scale result is E3M5V3. Positive meningeal symptoms for nuchal stiffness and kernig signs were also present. Motor examination revealed left lateralization, increased all limb tone and all deep tendon reflexes, also positive for pathological reflexes in all extremities.

The results of the history and physical examination conducted by the researcher showed that the client was diagnosed with a loss of consciousness with positive meningeal signs and left lateralization caused by suspected tuberculous meningitis. The initial treatment given to patients is to provide a loading dose of dexamethasone 10 mg followed by paracetamol 1 gram / 8 hours / intravenously, 5 mg / 6 hours / intravenously, and ranitidine 50 mg / 12 hours / intravenously. At that time, several additional checks were carried out; including routine blood tests which reported an increase in the white blood cell count (12,100 / μL) and serum electrolytes which could be said to be hyponatremia (129 mmol / L). However, the results of HIV tests showed non-reactive results. Then the chest X-ray also showed bilateral pneumonia suspected as a specific process (Appendix 1) and a non-contrast CT scan of the head showed multiple hypodense lesions in the right caudate nucleus, right lentiform nucleus, right internal capsule, and right temporal lobe with ventriculomegaly, so it was suspected. there was a DD / Infarct cerebellum (Appendix 2). Furthermore, the results of cerebrospinal fluid analysis report tuberculosis infection which can be seen in the following table.

Table 1. Cerebrospinal Fluid Analysis

Parameters	Results
Color	Clear
Speed	Normal
Volume	15 cc
Molecular weight	1.010
pH	8.5
Quackendsted Test	Negative
Artificial Blood	Negative
Nonne-Pandy Test	Positive
LDH	216 u/L
Glucose	9 mg/dL
Protein	70 mg/dL
Leukocyte	75,
	Predominantly
	Monocyte
	90%
Mycobacterium	Negative
Staining	
Serum Glucose	117 mg/dL

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, Pages. 13147- 13153
2021, Received 05 March 2021; Accepted 01 April 2021

Based on the results of this information and examination, this patient was finally diagnosed as having a loss of consciousness with a positive meningeal sign and left lateralization due to tuberculosis meningitis. Researchers started giving 4 Fixed Drugs Combination, three tablets daily and Streptomycin 750 mg / 24 hours / intramuscularly for TB infection. Researchers also corrected hyponatremia with 3% sodium chloride 10 drops / minute (1500 cc per day). For follow-up analysis, the patient regained consciousness (GCS E4M6V5) after 3 days of initial treatment without cranial nerve deficits or limb weakness. In addition, plasma sodium levels also returned to normal limits (141 mmol / L). Finally, the patient was discharged after 15 days of hospitalization. However, researchers continued to provide 4 FDCs for up to 9 months of treatment duration.

Discussion

Disease that can be transmitted in the air through the bacteria Mycobacterium tuberculosis (M. tuberculosis) is an understanding of Tuberculosis (TB). The M. tuberculosis bacteria spreads to the human body with the help of droplet nuclei, which are 1 to 5 microns in size. Infectious nuclei droplets are produced when a patient has pulmonary TB disease or the larynx coughs and sneezes. M. tuberculosis is transmitted through the air, not through direct contact with individuals. Transmission occurs when individuals inhale droplet nuclei containing M. tuberculosis, then these droplet nuclei enter the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs.

TBM is usually a chronic disease that presents with symptoms for an average of ten days before diagnosis. Initially there is a prodromal phase of low-grade fever, malaise, dizziness, headache, vomiting, and personality changes that can last for several weeks. Eventually the patient may experience more severe headaches, stroke, hydrocephalus, cranial neuropathy, and altered mental status. Seizure behavior is an uncommon manifestation of TBM in adults and if it occurs, it is necessary to refer to a doctor to consider alternative diagnoses such as bacterial or viral meningitis or cerebral tuberculoma (Isabe, & Rogelio, 2014; Turgut, et al. , 2017). Based on this statement, patients who came to this hospital due to loss of consciousness and previous speech history were not clear one day before being admitted to the hospital, there was also a history of fever (occurred two days before admission to the hospital), also had a history of headaches (occurred two weeks before admission to hospital), and prolonged cough (occurring since one month before admission). On the chest X-ray, there was bilateral pneumonia which was suggested for a specific process. Then X-rays on his brain CT scan, which showed multiple hypodense lesions in the right caudate nucleus, right internal capsule, right lentiform nucleus, and right temporal lobe with ventriculomegaly. So it is advisable to use cerebritis DD / Infarct (Isabe, & Rogelio, 2014; Turgut, et al., 2017).

Similar to TB disease in general, the spread of brain TB also begins with a respiratory tract infection followed by an earlier spread of hematogenous to extrapulmonary sites, including the CNS. Based on clinical and experimental observations that brain TB develops in two stages. The first is that it begins with a small tuberculous lesion that develops in the brain during the primary TB bacteremia stage. Tuberculosis lesions at this stage can be found on the meninges, subpial or subependymal surface of the brain, and may remain inactive for long periods of time. The second stage is marked by the completion of the dormancy period which produces CNS TB manifestations. TBM occurs with involvement of the meninges which is usually due to rupture of the focus into the subarachnoid or ventricular space and also occurs due to rupture of secondary blood vessels. Subsequently, the rupture of one or more small lesions results in the development of various types of CNS tuberculosis. Rupture of the subarachnoid space or into the ventricular system causes meningitis, which is a common form of cerebral TB (Marx, & Chan, 2011; Isabe, & Rogelio, 2014; Turgut, et al., 2017).

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, Pages. 13147- 13153
2021, Received 05 March 2021; Accepted 01 April 2021

The diagnosis of TBM disease is very difficult and is based solely on clinical findings of cerebrospinal fluid (CSF) without definitive microbiological confirmation. Certain clinical symptoms such as longer symptoms (more than six days), moderate CSF pleiocytosis, and the presence of a focal deficit may increase TBM (Isabe, & Rogelio, 2014; Turgut, et al., 2017). There are three clinical findings of cerebrospinal fluid which are characteristic of TBM, namely:

1. Lymphocytic predominant pleiocytosis. The total number of white blood cells is usually between 100 and 500 cells / uL. Early in the disease, a lower number and predominance of neutrophils can be found.
2. Increased protein levels, with a range of 1[illegible]to 500 mg / dL.
3. Low glucose levels, in the range less than 45 mg / dL or CSF, with a plasma ratio less than 0.5.

These characteristics are in line with the results of the CSF analysis of patients who report that pleiocytosis is dominated by monocytes (90%), increased protein cells (70 mg / dL), low glucose levels (9 mg / dl) and the ratio to serum, with glucose <0.5. (serum glucose: 117 mg / dL).

Researchers used neuroimaging to diagnose TBM, which showed an increase in basal meningeal and hydrocephalus. Hypodensity due to cerebral infarction, cerebral edema, and nodular enhancing lesions was also seen (Thwaites, et al., 2009; Turgut, et al., 2017). Radiological examination results reported ventriculomegaly without signs of hydrocephalus. This is because the onset of TBM in patients is too early to form hydrocephalus. However, there is some hypodense in the right hemisphere (Middle Cerebral Artery Area) which indicates vasculitis-induced infarction, thus supporting the diagnosis of TBM.

Lakshmi, Santhanam, and Chitralekha (2017) suggest that TBM can be classified into three levels, which can help researchers predict the prognosis of cases. Grade 1 includes Glasgow coma score (GCS) 15 without focal deficits, Grade 2 includes GCS 15 with focal neurological deficits or GCS 11-14 and TBM Grade 3 includes patients with GCS ≤ 10.Based on this level, the researchers diagnosed that the patient had tuberculous meningitis. Grade 2 (GCS 11).

The right treatment at an appropriate time can improve TBM results. Thus, empiric treatment is required if clinical features and CSF findings suggest TBM even before microbiological confirmation. Treatment that can be recommended for TBM that is suspected of being susceptible to drug consists of daily INH, pyrazinamide (PZA), rifampin (RIF) and / or ethambutol (EMB) or streptomycin (SM), with a span of seven to ten months. INH is considered the most critical first-line agent because of its excellent CSF penetration and high bactericidal activity.

While RIF penetrates less of the CSF, the high mortality of TBM due to strains that are resistant to RIF has emphasized its importance. PZA has excellent penetration into CSF and is a key drug in reducing the total treatment time for drug-susceptible TB. If PZA cannot be tolerated, the treatment period for TBM should be extended to eighteen months. While SM or EMB is traditionally used as the fourth anti-TB agent in TBM, neither penetrates CSF well in the absence of inflammation and both can produce significant toxicity with long-term use. It should be emphasized that not only the selection of antimicrobials, but also the dosage used and the duration of treatment are the keys to success in overcoming TBM and are largely based on pulmonary TB treatment (Thwaites, 2002; Yasar, Pehlivanoglu, & Sengoz, 2009; Turgut, et al., 2017; Lakshmi, Santhanam, & Chitralekha, 2017).

Table 2. Recommended daily doses of each drug for adults and children

Essential TB drug (abbreviation)	Dose mg/kg	Dose range mg/kg
Rifampicin (R)	12	8-12
Isoniazid (H)	5	4-6

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, Pages. 13147- 13153
2021, Received 05 March 2021; Accepted 01 April 2021

Pyrazinamide (Z)	25	20-30
Ethambutol (E)	15	15-20
Streptomycin (S)	15	12-18

Source: National Tuberculosis Management Guidelines - WHO 2014

There are many neurological sequelae of TBM found characterized by excessive host inflammatory response leading to tissue injury and brain edema. Since the mid-20th century, systemic corticosteroids have been used as an adjunct treatment for TBM, on the basis that suppressing the inflammatory response reduces morbidity and mortality. The assumptions made make sense because the brain is limited to a fixed space. In an effort to determine the cell types associated with triggering the inflammatory response, investigators found that co-incubation of TB-infected microglial cells with dexamethasone significantly inhibited the production of inflammatory mediators. For patients with more severe TBM levels, intravenous dexamethasone is given for four weeks (1 week, 0.4 mg / kg / day, 0.3 mg / kg / day, 0.2 mg / kg / day, and 0, respectively. , 1 mg / kg / day) followed by four weeks of oral tapering dexamethasone therapy (Thwaites, 2002; Yasar, Pehlivanoglu, & Sengoz, 2009; Turgut, et al., 2017). This statement, shows that it is appropriate for this patient to receive four drugs in combination with anti-tuberculosis for 2 months as initial therapy. Then the patient also received intramuscular streptomycin 750 mg / day and intravenous dexamethasone loading 10 mg, followed by 5 mg / 6 hours / day, tappering off per week.

In patients with TBM, there is non-osmotic stimulation of antidiuretic hormone (ADH) expression, resulting in inappropriate ADH release syndrome (SIADH). While ADH itself may not worsen cerebral edema, the acute development of significant hypoosmotic hyponatremia can exacerbate cerebral edema as water shifts from the intravascular compartment to the extravascular (intracellular and extracellular) spaces of the brain. Hyponatremia (plasma sodium <135 mmol / l) occurs in about 40-50% of TBM patients. Management difficulties stem from the incompletely characterized pathogenesis of hyponatraemia, combined with scanty data detailing optimal treatment. SIADH (Improper Antidiuretic Hormone Secretion Syndrome) and CSWS (Cerebral Salt Removal Syndrome), which may occur due to secretion of atrial natriuretic peptides, are conventionally thought to be the cause of hyponatremia in TBM, with results from a 2016 study conducted in India suggesting waste brain salt is the most common cause.

However, differentiating the two conditions can be difficult. By convention, SIADH is managed by fluid restriction, and wasting of brain salt with fluid administration. Many argue that both conditions can be treated with hypertonic saline, while others argue that fluid restriction, the traditional treatment for SIADH, has little benefit in meningitis and may even exacerbate hypovolemia. Hydrocephalus is a common complication of TBM; prevalence has been documented in 75% of patients in several published series. The insertion of a ventriculoperitoneal shunt and a third endoscopic ventriculostomy is a surgical technique that has been proven to relieve increased intracranial pressure (ICP) in TBM patients, leading to better neurological outcomes (Yasar, Pehlivanoglu, & Sengoz, 2009; Wilkinson, & Rohlwink, 2009) . The statement is in accordance with patients with complications of Hyponatremia. It is treated with IVFD Sodium Chloride 3% (1500 cc) at 10 drops / minute. After correction occurred by treating the clinical symptoms of Hyponatremia, it was concluded that low serum sodium levels were caused by Cerebral Salt Wasting Syndrome (CSWS).

The prognosis for TBM is strongly influenced by the neurological status at the time of presentation, and the time to start treatment. The spread of TBM is generally not as rapid as meningitis due to pyogenic bacteria, so empiric treatment should be started as soon as the diagnosis is suspected because delaying treatment could worsen the outcome. Case series shows that the mortality rate ranges from 7% to 65% in developed countries, and up to 69%

in disadvantaged areas. The risk of death is highest in patients with comorbidities, severe neurological involvement, rapid disease progression, and elderly people who are very prone to death (Thwaites, 2002; Yasar, Pehlivanoglu, & Sengoz, 2009; Wilkinson, & Rohlwink, 2009; Raviglione, 2014).

Conclusion

CNS TB is a dangerous disease with a very deadly impact that requires long-term treatment. Early treatment can reduce the high death rate associated with this disease. Although there is ongoing debate about treatment modalities and in terms of timing. However, the most important factor in achieving the success rate of treatment is early initiation of therapy. Treatment time is indicated as nine to twelve months. In reducing mortality and the risk of developing neurological morbidity, it is necessary to use corticosteroids in CNS TB patients. Resistance to anti-TB therapy is a very important matter which must be managed properly. Furthermore, we expect more studies related to the evaluation of CSF penetration of the most recent TB agents to facilitate the development of better treatment regimens in susceptible and drug-resistant TBMs.

References

Ducomble, T., Tolksdorf, K., Karagiannis, I., Hauer, B., Brodhun, B., Haas, W., & Fiebig, L. (2013). The burden of extrapulmonary and meningitis tuberculosis: an investigation of national surveillance data, Germany, 2002 to 2009. *Eurosurveillance*, *18*(12), 1-9.

Donald, P. R., Schaaf, H. S., & Schoeman, J. F. (2005). Tuberculous meningitis and miliary tuberculosis: the Rich focus revisited. *Journal of Infection*, *50*(3), 193-195.

Isabe, B. E., & Rogelio, H. P. (2014). Pathogenesis and immune response in tuberculous meningitis. *The Malaysian journal of medical sciences: MJMS*, *21*(1), 1-7.

Jain, S. K., Paul-Satyaseela, M., Lamichhane, G., Kim, K. S., & Bishai, W. R. (2006). Mycobacterium tuberculosis invasion and traversal across an in vitro human blood-brain barrier as a pathogenic mechanism for central nervous system tuberculosis. *The Journal of infectious diseases*, *193*(9), 1287-1295.

Jullien, S., Ryan, H., Modi, M., & Bhatia, R. (2016). Six months therapy for tuberculous meningitis. *Cochrane Database of Systematic Reviews*, *9 (CD012091)*, 1-105.

Krishnan, N., Robertson, B. D., & Thwaites, G. (2010). The mechanisms and consequences of the extra-pulmonary dissemination of Mycobacterium tuberculosis. *Tuberculosis*, *90*(6), 361-366.

Lakshmi, K., Santhanam, R., & Chitralekha, S. (2017). Management of Tuberculous meningitis–A review. *Indian Journal of Microbiology Research*, *4*(1), 1-6.

Marx, G. E., & Chan, E. D. (2011). Tuberculous meningitis: diagnosis and treatment overview. *Hindawi Publishing Corporation : Tuberculosis Research and Treatment,* 1-9.

O'Garra, A., Redford, P. S., McNab, F. W., Bloom, C. I., Wilkinson, R. J., & Berry, M. P. (2013). The immune response in tuberculosis. *Annual review of immunology*, *31*, 475-527.

Raviglione, M. (2014). Treatment of Tuberculosis Guidelines. *World Health Organization,* 1-160.

Thwaites, E. G. (2002). The Diagnosis and Management of Tuberculous Meningitis. *Practical Neurology, Blackwell Science : British Medical Journal*, 250-261.

Thwaites, G., Fisher, M., Hemingway, C., Scott, G., Solomon, T., & Innes, J. (2009). British Infection Society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. *Journal of infection*, *59*(3), 167-187.

Turgut, M., Akhaddar, A., Turgut, A. T., & Garg, R. K. (Eds.). (2017). *Tuberculosis of the central nervous system: pathogenesis, imaging, and management*. Springer.

Wilkinson, J. R., & Rohlwink U. (2009). Tuberculous Meningitis. *Nature Reviews Neurology, Advanced Online Publication,* 1-18.

Yasar, K. K., Pehlivanoglu, F., & Sengoz, G (2009). Analysis of Diagnostic Scorings of Thwaites and Marais in Two Groups of Definite and Probable Tuberculous Meningitis Cases. *Department of Infectious Disease and Clinical Microbiology Haseki Training and Research Hospital*.

Appendix

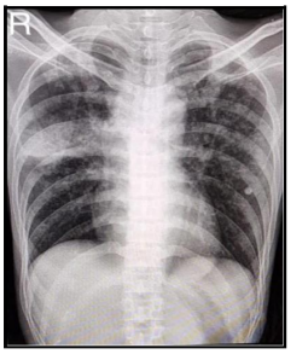
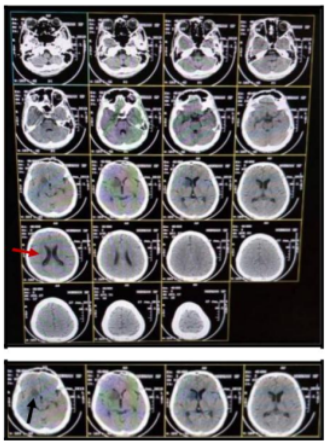


Figure 1. Plain chest radiograph. This indicates the presence of bilateral pneumonia which is thought to occur in a specific process (tuberculosis infection) and aortic extension.



7gure 2.Non-contrast Head Computed Tomography scan showing multiple hypodense lesions of the right caudate nucleus, right internal capsule, right lentiform nucleus, and right temporal lobe (black arrow) with ventriculomegaly (red arrow), suspected cerebritical DD / Infarction.

CLINICAL_IMPACT_OF_TUBERCULOUS_MENINGITIS_DISEASE_...

ORIGINALITY REPORT

22%	14%	13%	9%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.mdpi.com Internet Source	2%
2	docplayer.net Internet Source	2%
3	stacks.cdc.gov Internet Source	2%
4	wellcomeopenresearch.org Internet Source	1%
5	link.springer.com Internet Source	1%
6	Submitted to International Medical University Student Paper	1%
7	Sturm, W.. "On the Functional Neuroanatomy of Intrinsic and Phasic Alertness", Neuroimage, 200107 Publication	1%
8	Angharad Davis, Graeme Meintjes, Robert J. Wilkinson. "Treatment of Tuberculous Meningitis and Its Complications in Adults",	1%

	Current Treatment Options in Neurology, 2018 Publication	
9	"Textbook of Pediatric Neurosurgery", Springer Science and Business Media LLC, 2020 Publication	1 %
10	Şule T. Gülen, Mehmet Turgut, Güliz U. Güleç, Ahmet T. Turgut, Ali Akhaddar. "Chapter 27 Medical Therapy", Springer Science and Business Media LLC, 2017 Publication	1 %
11	Submitted to Tikrit University Student Paper	1 %
12	Submitted to Monash University Student Paper	1 %
13	Submitted to University of KwaZulu-Natal Student Paper	1 %
14	aidsfree.usaid.gov Internet Source	1 %
15	Submitted to October University for Modern Sciences and Arts (MSA) Student Paper	1 %
16	dailymed.nlm.nih.gov Internet Source	1 %

17	Submitted to Rochester Institute of Technology Student Paper	<1%
18	Charles M. Manyelo, Regan S. Solomons, Gerhard Walzl, Novel N. Chegou. "Tuberculous Meningitis: Pathogenesis, Immune Responses, Diagnostic Challenges, and the Potential of Biomarker-Based Approaches", Journal of Clinical Microbiology, 2021 Publication	<1%
19	Submitted to Panjab University Student Paper	<1%
20	www.clinicalguidelines.scot.nhs.uk Internet Source	<1%
21	Submitted to National Institute of Mental Health and Neuro Sciences Student Paper	<1%
22	Submitted to University of Glamorgan Student Paper	<1%
23	"Extrapulmonary Tuberculosis", Springer Science and Business Media LLC, 2019 Publication	<1%
24	Submitted to Bridgepoint Education Student Paper	<1%
25	Submitted to Fiji National University	

	Student Paper	<1%
26	www.mjhid.org Internet Source	<1%
27	doktori.bibl.u-szeged.hu Internet Source	<1%
28	www.gssrr.org Internet Source	<1%
29	R. K. Garg. "Classic diseases revisited: Tuberculosis of the central nervous system", Postgraduate Medical Journal, 1999 Publication	<1%

Exclude quotes	On	Exclude matches	< 5 words
Exclude bibliography	On		