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Central Nervous System Manifestations of Tuberculosis: A Review Article

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Abstract

Tuberculosis can involve almost any organ of the body. In the central nervous system (CNS) it can cause meningitis, tuberculoma, abscess, or other manifestations. Around 10% of all patients with tuberculosis have CNS involvement. Tuberculosis is rampant in the developing world and has reemerged as a major public health menace with the HIV pandemic. Compared with HIV-negative individuals, HIV-positive individuals with TB are 5 times more likely to have CNS involvement. We review the CNS manifestations of tuberculosis here in this article.

Keywords: Tuberculoma; Meningitis; Alcoholism; Vessels

Introduction

In about 1% of individuals with *Mycobacterium tuberculosis* infection, central nervous system (CNS) involvement develops, including meningitis, tuberculoma, abscess, or other manifestations [1]. The incidence of tuberculosis varies from 9 cases per 100 000 population per year in the US to 110–165 cases per 100 000 population in the developing countries of Asia and Africa [2-4]. Tuberculous involvement of the central nervous system (CNS) is an important and serious type of extra-pulmonary involvement. It has been estimated that approximately 10% of all patients with tuberculosis have CNS involvement [5]. In the largest prospective epidemiological study on CNS tuberculosis, the chance of developing CNS tuberculosis was 1.0% among 82,764 tuberculosis cases from 1970 to 2001 in a Canadian cohort [1]. Several risk factors for CNS tuberculosis have been identified. Both children [6] and HIV co infected patients [7-9] are at high risk for developing CNS tuberculosis. Other risk factors include malnutrition and recent measles in children [10] and alcoholism, malignancies, and the use of immunosuppressive agents in adults [11-13]. Studies conducted in developed countries have also identified that foreign-born individuals (individuals born outside of developed countries are overrepresented among CNS tuberculosis cases [14,1]. Extra pulmonary manifestations appear in ~40% of HIV-infected patients with TB [15]. Compared with HIV-negative individuals, HIV-positive individuals with TB are 5 times more likely to have CNS involvement [16].

Tuberculous meningitis

In tuberculous meningitis there is a thick, gelatinous exudate around the sylvian fissures, basal cisterns, brainstem, and cerebellum. Hydrocephalus may occur as a consequence of obstruction of the basal cisterns, outflow of the fourth ventricle, or occlusion of the cerebral aqueduct. Hydrocephalus frequently develops in children and is associated with a poor prognosis. The basal exudates of tuberculosis are usually more severe in the vicinity of the circle of Willis, and produce a vasculitis-like syndrome. Cerebral infarctions are most common around the sylvian fissure and in the basal ganglion. Hemorrhagic transformation of infarcted tissue is not unusual [17-19].The most serious consequence of TBM, however, is the development of vasculitis in the vessels of the circle of Willis, the vertebrobasilar system, and the perforating branches of the middle cerebral artery, resulting in infarctions in the distribution of these vessels. Direct contact of the exudate with the brain surface causes a border zone reaction that damages the underlying brain tissue. Rich and Mc Cordock ascribed most of these changes to a hypersensitivity response [20,21].

Clinical features

TB meningitis accounts for 5% of all extra pulmonary TB and is one of the most devastating manifestations of TB infection [22]. It occurs more frequently in children, particularly those <1 year of age [23,24]. Of adults with TB meningitis, 40%–66% have extrameningeal TB at the time of diagnosis [25]. The most common symptoms of TB meningitis include fever, headache, vomiting, and altered level of consciousness. Children are more likely to present with seizures, nausea, and vomiting; headache is less frequent [26]. The basilar meninges and cistern are frequently affected and cause cranial nerve dysfunction, especially of the sixth (abducens) and seventh (facial) cranial nerves [27,28]. Hydrocephalus is common during TB meningitis owing to high protein levels causing obstruction of cerebrospinal fluid (CSF) flow [29]. Intracranial vasculopathy is also frequent in TB meningitis, and stroke can occur as a complication of vasospasm, thrombosis, vasculitis, or hemorrhagic infarction [30]. In HIV-infected patients, TB is more likely to produce meningitis [31].

Diagnosis

Clinical

1. Fever and headache (for more than 14 days)
2. Vomiting
3. Altered sensorium or focal neurological deficit

CSF

1. Pleocytosis (more than 20 cells, more than 60% lymphocytes)

2. Increased proteins (more than 100 mg/dl)

3. Low sugar (less than 60% of corresponding blood sugar)

4. India ink studies and microscopy for malignant cells shouldbe negative

Imaging

1. Exudates in basal cisterns or in sylvian fissure hydrocephalus

2. Infarcts (basal ganglionic)

3. Gyral enhancement

4. Tuberculoma formation

5. Evidence of tuberculosis elsewhere

Treatment

Given the low sensitivity of existing CSF tests for detecting TB and the slow growth of *M. tuberculosis* in culture, anti-tuberculous treatment is often initiated empirically. Treatment is more complex for tuberculoma (tuberculous granuloma),multidrug-resistant TB (MDR TB; resistant to isoniazid [INH] and rifampicin) and extensively drug-resistant TB (resistant to INH, rifampin, fluoroquinolones, capreomycin, kanamycin, and amikacin).The use of corticosteroids is widely accepted as adjuvant therapy for CNS TB, particularly for TB meningitis, as well as for CNS TB-associated IRIS [32] or patients with pulmonary TB and HIV infection who have not recently initiated antiretroviral therapy (ART), emerging evidence supports early initiation of ART to reduce mortality—especially in patients with CD4 cell counts <50 cells/mm^3-despite the increased incidence of IRIS [33]. The WHO recommends initiation of ART after starting TB treatment irrespective of CD4 cell count; however, timing of ART initiation in patients with TB meningitis has not been addressed and may differ.

Tuberculomas are firm, avascular, spherical granulomatous masses, measuring about 2–8 cm in diameter. They are well limited from surrounding brain tissue which is compressed around the lesion and shows oedema and gliosis. The inside of these masses may contain necrotic areas composed of caseous material, occasionally thick and purulent, in which tubercle bacilli can be demonstrated. Intracranial tuberculomas can occur at any age. In developing countries young adults and children are predominantly affected while in developed countries they are more common in older patients.

The clinical presentation of CNS tuberculoma is usually more subtle than that of TB meningitis and may include headache, seizures, focal neurologic deficits, and papilledema [34]. Tuberculomas accompany TB meningitis in 10% of patients and are multiple in a third of patients [35]. Lesions may occur in the brain, spinal cord, subarachnoid, subdural, or epidural space; they may be solitary but are most often multiple and accompanied by surrounding edema and ring enhancement [36]. In children, lesions tend to be infratentorial, whereas in adults they are typically supratentorial [37].On CT, tuberculomas are characterised as low- or high-density and rounded or lobulated masses and show intense homogenous or ring enhancement after contrast administration. They have an irregular wall of varying thickness. Moderate to marked perilesionaloedema is frequently present. Tuberculomas may be single or multiple and are more common in frontal and parietal lobes, usually in parasagittal areas. On CT, the 'target sign', a central calcification or nidus surrounded by a ring that enhances after contrast administration, is considered pathognomonic of tuberculoma[38].The MRI features of tuberculoma depend on whether the lesion is non-caseating, caseating with a solid centre, or caseating with a liquid centre. The non-caseating granulomas are hypointense on T1-weighted images and hyperintense on T2-weighted images; after contrast administration the lesion usually shows homogenous enhancement. The second type of tuberculoma ishypointense or isointense on T1-weighted images and also on T2-weighted image. After contrast administration there is ring enhancement. These types of granuloma have variable degree of perilesionaloedema. The MRI features of tuberculoma depend on whether the lesion is non-caseating, caseating with a solid centre, or caseating with a liquid centre. The non-caseating granulomas are hypointense on T1-weighted images and hyperintense on T2-weighted images; after contrast administration the lesion usually shows homogenous enhancement. The second type of tubercular ishypointense or isointense on T1-weighted images and also on T2-weighted image. After contrast administration there is ring enhancement. These types of granuloma have variable degree of perilesionaloedema. Stereotactic diagnostic biopsy can help in establishing an accurate diagnosis [39].

Intracranial tuberculous abscess

Tuberculous brain abscess is a condition distinct from CNS tuberculoma. In developing countries tuberculous abscesses have been reported in 4% to 7.5% of patients with CNS tuberculosis. The histopathological diagnosis of tuberculous brain abscess depends on the following criteria: microscopic evidence of pus in the abscess cavity, microscopic changes in the abscess wall, and isolation of *M tuberculosis* [40]. Abscesses are usually solitary and larger and progress much more rapidly than tuberculomas. CT and MRI pictures of a tuberculous abscess show a granuloma with a liquid centre, however, they are much larger and frequently multiloculated and with marked surrounding oedema. Clinical features include partial seizures, focal neurological deficit, and raised intracranial tension [41]. Surgical exploration and drainage of pus may produce excellent long-term results.

Tuberculous arachnoiditis

Tuberculous arachnoiditis is a relatively common cause of myeloradiculopathy in countries endemic for tuberculosis. The inflammatory exudate surrounds, but does not infiltrate, the spinal cord and nerve roots. Frequently, there is vascular involvement with peri-arteritis and occlusion of small vessels. Neuronal structures are damaged by direct compression as well as by ischaemia. The changes of arachnoiditis may be focal, multifocal, or diffuse. In tuberculous arachnoiditis features of spinal cord or nerve root involvement may predominate but most often there is a mixed picture. Frequently, there is clinical evidence of multifocal radiculo myelopathy, but even when meningeal involvement is widespread, symptoms may arise from a single level. The hallmark of diagnosis is the characteristic myelographic picture, showing poor flow of contrast material with multiple irregular filling defects, cyst formation, and sometimes spinal block. Rarely, myelography may be normal. The CSF changes are those of chronic meningitis, frequently CSF sugar concentration is normal. Occasionally lumbar tap may be dry. These patients need adequate anti-tuberculous treatment for at least one year. The role of corticosteroids is uncertain, but there are several reports of apparently marked improvement following corticosteroid administration. If the

patient does not respond to medical treatment, surgery may be required [42,43].

Spinal tuberculous meningitis

A predominantly spinal form of tuberculous meningitis may result from rupture of Rich's focus into the spinal arachnoid space rather than the basal meninges. The acute form presents with fever, headache, and radiating root pains, accompanied by myelopathy. The chronic form usually localized to a few segments, presents with progressive spinal cord compression and may suggest a spinal cord tumour. The characteristic MRI features include CSF loculation and obliteration of the spinal subarachnoid space with loss of outline of spinal cord in the cervico-thoracic region and matting of nerve roots in the lumbar region. Spinal forms of tuberculous meningitis may be associated with syrinx formation [42].

Pott's spine and Pott's paraplegia

It is estimated that involvement of the spine occurs in less than 1% of patients with tuberculosis. It is a leading cause of paraplegia in developing nations. Infection in the vertebral bodies usually starts in cancellous bone adjacent to an intervertebral disc or anteriorly under the periosteum of the vertebral body; the neural arch is rarely affected. Vertebral destruction leads to collapse of the body of the vertebra along with anterior wedging. Spinal cord compression in Pott's spine is mainly caused by pressure from a paraspinal abscess which is retropharyngeal in the cervical region, and spindle shaped in thoracic and thoracolumbar regions. Neurological deficits may also result from dural invasion by granulation tissue and compression from the debris of sequestrated bone, a destroyed intervertebral disc, or a dislocated vertebra. Rarely, vascular insufficiency in the territory of the anterior spinal artery has also been suggested. Neurological involvement can occur at any stage of Pott's spine and even years later, when there has been apparent healing, because of stretching of the cord in the deformed spinal canal. The thoracic spine is involved in about 65% of cases, and the lumbar, cervical and thoracolumbar spine in about 20%, 10% and 5%, respectively. The atlanto-axial region may also be involved in less than 1% of cases. Males are affected more often than females in most series, and the disease generally affects young person's [44-46].

Tuberculous encephalopathy

Tuberculous encephalopathy, a syndrome exclusively present in infants and children, has been described by Udani and Dastur [47] in Indian children with pulmonary tuberculosis. The characteristic features of this entity are the development of a diffuse cerebral disorder in the form of convulsions, stupor and coma without signs of meningeal irritation or focal neurological deficit. CSF is largely normal or may show a slight increase in proteins and cells. Pathologically, there is diffuse oedema of cerebral white matter with loss of neurons in grey matter. A picture resembling haemorrhagic leukoencephalopathy or a post-infectious demyelinating encephalomyelitis may be observed [47].

Non-osseous spinal cord tuberculosis

Non-osseous spinal cord tuberculosis can occur in the form of tuberculomas. Dastur [48]reviewed 74 cases of tuberculous paraplegia without evidence of Pott's disease and observed that extradural tuberculomas occured in 64% while arachnoid lesions without dural involvement, and subdural/extramedullary lesions occured in 8% of patients in each group. Intramedullary tuberculomas are extremely rarely reported, reports from developing countries have also been sporadic. The clinical features are indistinguishable from those of any extramedullary or intramedullary tumour, although acute worsening may occur. Intramedullary lesions are frequently located in the thoracic region. More than one site in the spinal cord may also be affected. One case with conusmedullaris syndrome has been described. Non-osseous spinal cord tuberculomas may increase in size while the patient is on anti-tuberculous therapy. MRI is the investigation of choice for these lesions [49].

CNS tuberculosis in HIV infected persons

Mycobacterium tuberculosis and atypical tubercle bacilli *Mycobacterium aviumintracellulare* infection have been described as uncommon CNS manifestations of AIDS. The clinical spectrum of CNS tuberculosis with HIV infection includes meningitis, cerebral abscesses and tuberculomas. CNS involvement occurs in 10–20% patients with AIDS-related tuberculosis, and in these patients mortality is high. HIV-infected intravenous drug abusers are, in particular, at high risk of developing focal CNS tuberculosis. Clinical features, including imaging characteristics, are similar to those seen in patients without HIV infection. In patients with *M aviumintracellulare* infection, single or multiple mass lesions appear to be more than twice as common as meningitis. Every effort should be made to establish the correct diagnosis as most types of CNS tuberculosis in HIV-infected patients are responsive to treatment.

Treatment of CNS tuberculosis

In contrast to the rapid advances in the management of pulmonary tuberculosis, there have been only a few clinical studies in patients with CNS tuberculosis, including tuberculous meningitis. There is currently no general consensus about the form of chemotherapy or optimal duration of treatment.

Treatment Regimens

The Centres for Disease Control recommend [50] that treatment is started with isoniazid (10–20 mg/kg/day up to 300 mg), rifampicin (10–20 mg/kg/day, up to 600 mg/day) and pyrazinamide (15–30 mg/kg/day, up to 2 g a day). Patients should be monitored for hepatotoxicity from rifampicin which is seen in up to 20% of patients. Ethambutol or streptomycin may be added if the response is not satisfactory. The duration of therapy should be at least 6 months and in some instances up to 12 months treatment is required. The World Health Organization (WHO) [51] put CNS tuberculosis under TB treatment Category , and recommends initial phase therapy (for 2 months) with streptomycin, isoniazid, rifamipicin and pyrazinamide, followed by a 7-month continuation phase with isoniazid and rifampicin. However, a number of other studies report varying experiences with short-course (6 months) treatment. A similar drug regimen has been recommended for all forms of CNS tuberculosis. The optimal regimens for the treatment of CNS tuberculosis due to atypical mycobacteria in persons with HIV infection have not been finally established, although a four-drug regimen is needed to treat *M aviumintracellulare* infection. Current recommendations include using azithromycin (500–100 mg/day) and clarithromycin (500 to 1000 mg/day) in combination with ethambutol (15 mg/kg/day) or clofazimine (100 mg/day). Alternative regimens include the use of ciprofloxacin and rifampicin. A significant increase in the frequency of

adverse reactions to anti-tuberculous therapy has been observed in patients with HIV infection [52-53].

Role of Corticosteroids

The response to steroids may be dramatic with rapid clearing of sensorium, regression of abnormalities of CSF, defervescence and relief of headache [54].Earlier It was believed that corticosteroids had no place in the management of tuberculous meningitis because the drug did not alter the clinical outcome, however, more recent studies have shown that corticosteroids improved both survival rate and neurological outcome in patients with tuberculous meningitis [55-56]. Schoeman et al. [55] confirmed the useful role of corticosteroids in young children. They observed that, in addition to survival, corticosteroids significantly improved intellectual outcome and enhanced resolution of the basal exudates and intracranial tuberculoma were shown by serial CT scanning. Prednisolone treatment (60 mg/day in adults and 1–3 mg/kg/day in children) is suggested in patients with tuberculous meningitis [57]. The dosage may reduced by 50% in the second and third week and then be tapered gradually over the next 4 weeks. There is no need for intrathecal corticosteroids. The main argument against using corticosteroids is that they decrease meningeal inflammation and, in turn, can affect CSF penetration of anti-tuberculous drugs.

References

1. Phypers M, Harris T, Power C (2006) CNS tuberculosis: a longitudinal analysis of epidemiological and clinical features. Int J Tuberc Lung Dis 10: 99-103.
2. Snider DE Jr, Roper WL (1992) The new tuberculosis. N Engl J Med 326: 703-705.
3. Harries AD (1990) Tuberculosis and human immunodeficiency virus infection in developing countries. Lancet 335: 387-390.
4. Raviglione MC, Snider DE Jr, Kochi A (1995) Global epidemiology of tuberculosis. Morbidity and mortality of a worldwide epidemic. JAMA 273: 220-226.
5. Wood M, Anderson M (1998) Chronic meningitis. Neurological infections; major problems in Neurology, vol 16. (WB Saunders, Philadelphia), 169–248
6. Farer LS, Lowell AM, Meador MP (1979) Extrapulmonary tuberculosis in the United States. Am J Epidemiol 109: 205-217.
7. Berenguer J, Moreno S, Laguna F, Vicente T, Adrados M, et al. (1992) Tuberculous meningitis in patients infected with the human immunodeficiency virus. N Engl J Med 326: 668-672.
8. Dubé MP, Holtom PD, Larsen RA (1992) Tuberculous meningitis in patients with and without human immunodeficiency virus infection. Am J Med 93: 520-524.
9. Rana FS, Hawken MP, Mwachari C, Bhatt SM, Abdullah F, et al. (2000) Autopsy study of HIV-1-positive and HIV-1-negative adult medical patients in Nairobi, Kenya. J Acquir Immune DeficSyndr 24: 23-29.
10. Yaramiş A, Gurkan F, Elevli M, Söker M, Haspolat K, et al. (1998) Central nervous system tuberculosis in children: a review of 214 cases. Pediatrics 102: E49.
11. Klein NC, Damsker B, Hirschman SZ (1985) Mycobacterial meningitis. Retrospective analysis from 1970 to 1983. Am J Med 79: 29-34.
12. Ogawa SK, Smith MA, Brennessel DJ, Lowy FD (1987) Tuberculous meningitis in an urban medical center. Medicine (Baltimore) 66: 317-326.
13. Verdon R, Chevret S, Laissy JP, Wolff M (1996) Tuberculous meningitis in adults: review of 48 cases. Clin Infect Dis 22: 982-988.
14. Bidstrup C, Andersen PH, Skinhøj P, Andersen AB (2002) Tuberculous meningitis in a country with a low incidence of tuberculosis: still a serious disease and a diagnostic challenge. Scand J Infect Dis 34: 811-814.
15. Kingkaew N, Sangtong B, Amnuaiphon W, Jongpaibulpatana J, Mankatittham W, et al. (2009) HIV-associated extrapulmonary tuberculosis in Thailand: epidemiology and risk factors for death. Int J Infect Dis 13: 722-729.
16. Molavi A, LeFrock JL (1985) Tuberculous meningitis. Med Clin North Am 69: 315-331.
17. Newton RW (1994) Tuberculous meningitis. Arch Dis Child 70: 364-366.
18. Dastur DK, Manghani DK, Udani PM (1995) Pathology and pathogenetic mechanisms in neurotuberculosis. Radiol Clin North Am 33: 733-752.
19. Leonard JM, Des Prez RM (1990) Tuberculous meningitis. Infect Dis Clin North Am 4: 769-787.
20. Donald PR, Schaaf HS, Schoeman JF (2005) Tuberculous meningitis and miliary tuberculosis: the Rich focus revisited. J Infect 50: 193-195.
21. Rich AR, McCordock HA (1933) The pathogenesis of tuberculous meningitis. Bull. Johns Hopkins Hosp. 52:5-37.
22. Daikos GL, Cleary T, Rodriguez A, Fischl MA (2003) Multidrug-resistant tuberculous meningitis in patients with AIDS. Int J Tuberc Lung Dis 7: 394-398.
23. Comstock GW, Livesay VT, Woolpert SF (1974) The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol 99: 131-138.
24. Garg RK (2010) Tuberculous meningitis. Acta Neurol Scand 122: 75-90.
25. Verdon R, Chevret S, Laissy JP, Wolff M (1996) Tuberculous meningitis in adults: review of 48 cases. Clin Infect Dis 22: 982-988.
26. Rock RB, Olin M, Baker CA, Molitor TW, Peterson PK (2008) Central nervous system tuberculosis: pathogenesis and clinical aspects. Clin Microbiol Rev 21: 243-26.
27. Garg RK (2010) Tuberculous meningitis. ActaNeurolScand 122: 75-90.
28. LINCOLN EM, SORDILLO VR, DAVIES PA (1960) Tuberculous meningitis in children. A review of 167 untreated and 74 treated patients with special reference to early diagnosis. J Pediatr 57: 807-823.
29. Christensen AS, Andersen AB, Thomsen VO, Andersen PH, Johansen IS (2011) Tuberculous meningitis in Denmark: a review of 50 cases. BMC Infect Dis 11: 47.
30. Leonard JM, Des Prez RM (1990) Tuberculous meningitis. Infect Dis Clin North Am 4: 769-787.
31. Sanchez-Portocarrero J, Perez-Cecilia E, Jimenez-Escrig A, et al; (1996) Tuberculous meningitis: clinical characteristics and comparison with cryptococcal meningitis in patients with human immunodeficiency virus infection. Arch Neurol 53: 671-676.
32. Thwaites G, Chau TT, Mai NT, Drobniewski F, McAdam K, et al. (2000) Tuberculous meningitis. J Neurol Neurosurg Psychiatry 68: 289-299.
33. Lawn SD, Török ME, Wood R (2011) Optimum time to start antiretroviral therapy during HIV-associated opportunistic infections. CurrOpin Infect Dis 24: 34-42.
34. Garcia-Monco JC (1999) Central nervous system tuberculosis. Neurol Clin 17: 737-759.
35. Arseni C (1958) Two hundred and one cases of intracranial tuberculoma treated surgically. J Neurol Neurosurg Psychiatry 21: 308-311.
36. Bernaerts A, Vanhoenacker FM, Parizel PM, Van Goethem JW, Van Altena R, et al. (2003) Tuberculosis of the central nervous system: overview of neuroradiological findings. Eur Radiol 13: 1876-1890.
37. Dastur DK, Lalitha VS, Prabhakar V (1968) Pathological analysis of intracranial space-occupying lesions in 1000 cases including children. 1. Age, sex and pattern; and the tuberculomas. J Neurol Sci 6: 575-592.
38. van Dyk A (1988) CT of intracranial tuberculomas with specific reference to the "target sign". Neuroradiology 30: 329-336.
39. Rajshekhar V, Chandy MJ (1997) Tuberculomas presenting as isolated intrinsic brain stem masses. Br J Neurosurg 11: 127-133.
40. Dastur DK, Manghani DK, Udani PM (1995) Pathology and pathogenetic mechanisms in neurotuberculosis. Radiol Clin North Am 33: 733-752.

41. Farrar DJ, Flanigan TP, Gordon NM, Gold RL, Rich JD (1997) Tuberculous brain abscess in a patient with HIV infection: case report and review. Am J Med 102: 297-301.
42. Wadia NH (1973) Radiculomyelopathy associated with spinal meningitis (arachnoiditis) with special reference to spinal tuberculous variety. Spillane JD, ed, Tropical neurology. (Oxford University Press, London), pp 63–72.
43. Wadia NH, Dastur DK (1969) Spinal meningitides with radiculo-myelopathy. 1. Clinical and radiological features. J Neurol Sci 8: 239-260.
44. Rezai AR, Lee M, Cooper PR, Errico TJ, Koslow M (1995) Modern management of spinal tuberculosis. Neurosurgery 36: 87-97.
45. Nussbaum ES, Rockswold GL, Bergman TA, Erickson DL, Seljeskog EL (1995) Spinal tuberculosis: a diagnostic and management challenge. J Neurosurg 83: 243-247.
46. Vidyasagar C, Murthy HK (1994) Management of tuberculosis of the spine with neurological complications. Ann R CollSurgEngl 76: 80-84.
47. Udani PM, Dastur DK (1970) Tuberculous encephalopathy with and without meningitis. Clinical features and pathological correlations. J NeurolSci 10: 541-561.
48. Dastur HM (1983) Diagnosis and neurosurgical treatment of tuberculous disease of the CNS. Neurosurg Rev 6: 111-117.
49. Mantzoros CS, Brown PD, Dembry L (1993) Extraosseous epidural tuberculoma: case report and review. Clin Infect Dis 17: 1032-1036.
50. Snider DE Jr, Rieder HL, Combs D, Bloch AB, Hayden CH, et al. (1988) Tuberculosis in children. Pediatr Infect Dis J 7: 271-278.
51. Harries A, Maher (1997) TB: a clinical manual for South East Asia. (World Health Organisation, Geneva).
52. Kemper CA, Meng TC, Nussbaum J, Chiu J, Feigal DF, et al. (1992) Treatment of Mycobacterium avium complex bacteremia in AIDS with a four-drug oral regimen. Rifampin, ethambutol, clofazimine, and ciprofloxacin. The California Collaborative Treatment Group. Ann Intern Med 116: 466-472.
53. Small PM, Schecter GF, Goodman PC, Sande MA, Chaisson RE, et al. (1991) Treatment of tuberculosis in patients with advanced human immunodeficiency virus infection. N Engl J Med 324: 289-294.
54. Berger JR (1994) Tuberculous meningitis. Curr Opin Neurol 7: 191-200.
55. Schoeman JF, Vanzyl LF, Laubscher JA, Donald PR (1997) Effect of cortico- steroids on intracranial pressure, computed tomographic findings, and clinical outcome in young children with tuberculous meningitis. Pediatrics 99:226–231.
56. Kumarvelu S, Prasad K, Khosla A, Behari M, Ahuja GK (1994) Randomized controlled trial of dexamethasone in tuberculous meningitis. Tuber Lung Dis 75: 203-207.
57. Holdiness MR (1990) Management of tuberculosis meningitis. Drugs 39: 224-233.