International Journal of Pharmaceutical Science Invention
ISSN (Online): 2319 – 6718, ISSN (Print): 2319 – 670X
www.ijpsi.org || Volume 4 Issue 1|| January 2015 || PP.06-12

Diagnostic Approaches to Chronic Fungal and Tuberculous Meningitis

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ABSTRACT: *Bacterial meningitis is common in Brazil and in endemic region of Sub-SaharanAfrica. Chronicmeningitis (CM) is defined as meningitis lasting for four weeks or more and have signs of chronic inflammation in the cerebrospinal fluid.CM is a diagnostic dilemma, with limited literature on the subject.CM is common in immunocompromised, immunocompetent and in patients infected with immunodeficiency virus (AIDS).Less common Mollaret's meningitis and Bachet'sdisease, a chronic multisystem disorder. Common pathogens isolated include enteroviruses,Mycobacterium tuberculosis,Cryptococcus neoformans, Treponema pallidum,Coccidioides immitis,rare pathogens include Angiostrongylus cantonennesis, Naegleriafowleri. Treatment of choice in tuberculous meningitiswith four-drug regimen,and amphotericin B with flucocytosine or fluconazole for 4 to 6 weeks for cryptococcal meningitis. Prompt diagnosis and antibiotic therapy with long-term follow up have a better outcome.*

KEYWORDS: *Chronic meningitis,Cryptococcal meningitis,Tuberculous meningitis,Diagnosis,*

I. INTRODUCTION

Meningitis is a notifiable disease in many countries, the exact incidence rate is unknown [1].As of 2010 it is estimated that meningitis resulted in 420,000 deaths excluding cryptococcal meningitis [2,3].Bacterial meningitis occurs in 3 people per 100,000 annually in Western countries. In Brazil, the rate of bacterial meningitis is higher, at 45.8 per 100,000 annually[4].Sub-Saharan Africa has been plagued by large epidemics of meningococcal meningitis for over century, leading it being labelled the "meningitis belt" [5].Meningococcal disease occurs in epidemics in areas where many people live together for first time, such as army barracks during mobilization, college campuses and the annual Hajj pilgrimage(visit to Holy Land in Saudi Arabia)[6,7].There are local differences in the local distribution of causes for bacterial meningitis.For instance, while *N.meningitidis* group B and C cause most disease episodes in Europe, group A is found in Asia and continues to dominate in Africa, with 80 to 85 % of documented meningococcal meningitis cases [8].Chronic meningitis(CM) is defined as patients with chronic central nervous system infection for at least four weeks and have signs of chronic inflammation in the cerebrospinal fluid[9]CM is common in immunocompromised, immunocompetent and in patients infected with immunodeficiency virus (AIDS).CM is characterized by a progressive,sub- acute onset of lepomeningeal disease and persisting cerebrospinal(CSF) abnormalities such as elevated protein level and pleocytosis for at least one month[10].Frequently isolated pathogens in chronic meningitis include viruses(enteroviruses,herpesvirus,type 2,varicella zoster virus,Mollaret's meningitis a chronic recurrent form of herpes meningitis),bacterial(*Mycobacterium tuberculosis,N.meningitidis*,group B streptococci**,** *Treponema pallidum Borrelia burgdoerferi*(lymediseases), fungal (*Cryptococcus neofomans, Coccidioides immitis, Histoplasma capsulatum, Blastomycesdermatitidis, Candidaalbican)and parasitic (Angiostrongylus cantonnensis* and *Naegleria fowleri*).Noninfectious include Becher's disease, a chronic multisystem disorder [11].Differential diagnosis include tests for inflammatory markers(e.g.C-reactive protein)FBC,CSF examination, computedtomography(CT),or magnetic resonance imaging(MRI)[12].Empiric treatment with broad –spectrum antibiotics and mechanical ventilation as required. The paper reviews the current literature, etiologies, clinical presentation and therapy of chronic meningitis.

II. HISTORICAL PERSPECTIVE

Some authorities suggest that Hippocrates may have realized the existence of meningitis, and it seems that meningsm was known to pre-Renaissance physicians such as Avicenna(Ibnu-senna)[4,13].The description of tuberculous meningitis, then called "dropsy in the brain", is often attributed to Edinburgh physician Sir Robert Whytt in a postmothous report that appeared in 1768,although the link with tuberculosis and its pathogen was not made until next century[13].It appears that epidemic meningitis is a relatively recent phenomenon[14].The first recorded major outbreak occurred in Geneva in 1805[14].Several other epidemics in Europe and the United States were described shortly afterward, and first report of an epidemic in Africa appeared in 1840.Africal epidemics became much more common in the 20thcentury,strating with a major

epidemic sweeping Nigeria and Ghana in 1905-1908[14]. The first report of bacterial infection underlying meningitis was by the Austrian bacteriologist Anton Weichselbaum,who in 1887 described the meningococcus[15].Mortality from meningitis was very high(over 90%) in early reports. In 1906,antiserum was produced in the horses, this was developed further by the American scientist Simon Flexner and markedly decreased mortality from meningococcal disease[16].In 1944,pencillin was reported to be effective in meningitis[17].The introduction in the late 20th century of Haemophilus vaccines let to a marked fall in cases associated with this pathogen[18],and in 2002 evidence emerged that treatment with steroids could improve the prognosis of bacterial meningitis[16].

III. ETIOLOGIC AGENTS

Fungal agents of meningitis. **Cryptococcalmeningitis**. *Cryptococcus neoformans* and *Cryptococcus gattii* are the most common causes of fungal meningitis [19].The majority of patients are immunosuppressed, but the previously healthy patients with cryptococcosis has fewer organisms in CSF and present more of a diagnostic dilemma. In the latter group, symptoms can be indolent, with headaches present for weeks or months [19].Dementia may attract attention only after automobile accident or inattention to business or personal matters create a crisis. Skinlesions precede meningeal symptoms in about 10% of patients and are useful for diagnosis. MRI is most often normal unless hydroenchalitis has supervened.CSF cultures of AIDS patients with cryptococcal meningitis became positive in few days, but CSF cultures from indolently ill patients may require 2- weeks incubation and culture of more than 1 ml.of CSF.CSF antigen being more often positive than serum antigen, with the CSF antigen being negative only in most indolent patients, those being the patients with profound hypoglycorrhachia,high protein level and high cell count[19].

HistoplasmaMeningitis. Chronic meningitis can be the presenting sign of *Histoplasma* meningitis in previously healthy patients or may be part of more systemic illness, particularly in the immunocompromised patients. Patients at risk of dissemination to brain and other organs include patients with AIDS, solid organ transplant recipients, or those taking adrenal corticosteroids or tumor necrosis factor-α(TNFα) inhibitors[20].Signs of dissemination outside the neuraxis, if present, are extremely variable, including Addison's disease, chronic granulomatous hepatitis,endocarditis, orpancytopenia. Patients do not give a historysuggesting acute pulmonary histoplasmosis before the diagnosis of meningitis. Accompanying pulmonary symptoms are minimal or absent. MRI may show an intracerebral granuloma in some patients. *Histoplasma* antigen or antibody may be detected in the CSF.CSF cultures are usually negative, though a high -volume of culture is occasionally successful. Serum or urine test is negative unless dissemination is suggested by nonneural findings [19].

Candida Meningitis. *Candida* is commonly found in multiple small brain abscesses in patients dying of disseminated candidiasis, but presentation as chronic meningitis is rare. Most such patients are very low birth weight newborns or post neurosurgery or immunosuppressed patients [21].Newborns with *Candida* meningitis have typically had long stays in the neonatal intensive care unit and required prolonged use of intravascular catheters. Others are infants with severe congenital abnormalities of the intestine or urinary tract required complicated surgical repair. *Candida* enters the bloodstream through intravascular catheters from complications of intestinal surgery or from an obstructed urinary tract. Difficulty assessing the neurologic status of these newborns and the absence of fever cause delay in diagnosis. Hydrocephalus may already be present when the diagnosis of Candida meningitis is made.CSF is markedly abnormal, but culture has such few organisms that contamination of the CSF culture may be suspected [22].CSF shunts infected with Candida may present as partial or complete blockage of the shunt, usually in children with multiple shunt revisions or skin ulcers over the shunt valve or tubing. Patients with hematologic malignancies may develop meningitis as a part of disseminated candidiasis. Meningitis may only be recognized after antifungal therapy and return od marrow function has allowed control of the other manifestations of disseminations of disseminated candidiasis [22].

CoccidioidalMeningitis.Principal areas of exposure for coccidioidal meningitis are central and southern Arizona and Central Valley of California, though the endemic area is much broader. Spotty endemic areas exist in contiguous parts of the Southwest. Winds can carry the spores' long distances outside the endemic area. Extremely briefexposure of visitors from outside the endemic area is sufficient to cause infection.The initial illness may be diagnosed as a community acquired pneumonia and seem to improve temporarily with antibiotics.0r the initial respiratory phase may not even prompt medical attention. Previously healthy people with meningitis may present with indolent onset of headache, present for weeks or months at time of diagnosis. The pulmonaryportal, prominent earlier, at the time symptoms of meningitis appear may be only visible as hilar adenopathy or a small pulmonary infiltrate.The patient may recall the pneumonia as a period of fever and cough occurring 2 to 4 weeks following exposure [23].Immunosuppressed patients, including those with AIDS are more likely to present with systemic illness, including fever, headache, profound malaise, and lesions in bone or

skin. The chest x-rays of immunosuppressed patients may show single or diffuse infiltrates.Low grade eosinophilia in the blood and more commonly the CSF is a valuable sign; through Wright-Giemsa staining of CSF may be needed to detect eosinophilia. The single best test is not culture or smear of CSF,which are uncommonly positive, but positive complement fixation test done in a reliable reference laboratory [24].The complement fixation test on CSF is specific and sensitive.CSF antibody detected by an immunodiffusion test with a band of identity is useful screen because it is sensitive, but it is less specific than the complement fixation test.None of the commercially available enzyme-linked immunosorbent assays (ELISAs) have sufficient sensitivity or sensitivity to be useful and may be misleading.Serum complement fixation tests are usually positive but remain positive after remote infection, a so- called serologic scar[23].

BlastomycosisMeningitis. Patients with blastomycosis present with one or more brain abscesses in the central nervous system. When a brain abscess ruptures into the ventricular system, a rapidly progressive purulent meningitis results with a strong tendency to obstruct the aqueduct of sylvius, accelerating the progression to coma.Skin, bone, or lung lesions of blastomycosis are present in most patients and permit diagnosis [19].

SporotrichosisMeningitis. The published cases of sporotrichosis meningitis due to *Sporotrichum schenckii* have presented formidable diagnostic difficulties because the organism has proven very difficult to recover in CSF cultures. A few cases have had disseminated skin lesions that provided a site for biopsy diagnosis. Infection has occurred in previously healthy and in immunosuppressed patients [25]

PhaeohyphomycosisMeningitis.Dark-walled molds have a predisposition for spread to the brain, causing a brain abscess,phaeohyphomycosis meningitis or both,CSF cultures are sterile and brain biopsy is required for diagnosis Most patients are previously healthy and have no visible pulmonary portal or other disease outside the central nervous system. Because these molds can be air contaminants in a culture, the rare positive CSF culture may bedisregarded as a contaminants [26,27]

Miscellaneous fungal Meningitis.Several less significant fungal agents has been involved in CNS infection. *Scedosporium prolificans*, and *scedosporium apiospermum* infections have a predisposition for hematogenous spread to CNS,usually presenting a brain abscess but occasionally as chronic meningitis. Immunosuppression is present in majority of patients, though intravenous drug users may also develop the infection. Patients with aspergillosis and mucromycosis in the CNS and commonly present with angioinvasion with hemorrhagic infection, not chronic meningitis [19].

IV. BACTERIAL MENINGITIS.

Tuberculous meningitis is probably the most common cause of chronic meningitis, and because diagnosis can be difficult, *Mycobacterium tuberculosis* is the agent that may be treated empirically when all other diagnostic measures fail. Children with hematogenously disseminated tuberculosis are prone to a more rapid course than is typical for adults, with as little as 2 to 4 weeks of symptoms before diagnosis. Fever, miliary lesions in the lung, andretina, marrowsuppression, and hepatosplenomegaly may herald the systemic disease, whereas headache followed by confusion and coma portend a poor prognosis from CNS disease[19].Disease in previously healthy adults tends to be more indolent with fewer signs of disseminated tuberculosis other than fever, weight loss, night sweats, and malaise. Chest x-rays is normal in only about half of patients. Diagnosis is suspected from country of origin or household exposure to tuberculosis, both occurring years before symptoms are evident. Tuberculin skin test and interferon-ɣ(IFN-ɣ) test may be negative, and neither support or exclude the diagnosis. MRI may be normal or show small lesions in the cortical sulci or may show hydrocephalus. Hypoglycorrachia is usual, as are pleocytosis of up to a few hundred cells and an elevated protein level. Adenosine deaminase may be elevated in the CSF but is not more helpful than low CSF glucose. Smear rarely demonstrate acid- fast bacilli. Culture in automated broth culture techniques is positive in half the cases but requires about 2 weeks of incubation, often two slow to assist early therapeutic diagnosis [19].The old literature spoke of taking the clot that forms in CSF from tuberculosis patient as it stands the so-called pellicle and using those clumped strands of cells and clot from several milliliters of CSF for smear and culture. Although no modern laboratory would consider using such a time-consuming technique, the popularity of the technique speaks to small inoculum of organisms in the CSF and need for culturing more than minimal volumes of CSF.The Gen-Probe MTB Direct test is not approved for use on CSF, but the problem is lack of sensitivity not false-positive results, making this test important for early diagnosis. Although many referral laboratories are offering PCR diagnosis, the lack of standardization makes interpretation difficult [19].

SyphliticMeningitis. *Treponema pallidum* is the agent of syphilitic meningitis.CNS manifestations of syphilis are not as easily divided into categories as might be desired. Secondary syphilis causes aseptic meningitis, but

illness resolves either spontaneously or with therapy so that chronicity at this stage of infection is uncommon.Meningovascular syphilis is a later complication that occurs 2 to 10 years after infection as an ischemic stroke in a young person. Presenting symptoms of parenchymal disease are gumma formation or general paresis,15 to 20 years after infection, or tabes dorsalis even later. General paresis has prominent encephalopathy signs and may have ocular signs as well [19].Tabes dorsalis has prominent spinal cord signs and symptoms with radicular pain ("Lightning pains")that sets it symptoms apart from usual patient with chronic meningitis in whom spinal cord symptoms are uncommon.Patients with neurosyphlis, although uncommon present simply with chronic meningitis with a CSF pleocytosis and elevated protein level but normal glucose level. Some of these patients will have a waxing and waning course, perhaps beginning when they had secondary syphilis .A significant minority have a negative nontreponemaltests, such as VDRL or RPR on serum and CSF. These can be falsely positive in the presence of an otherwise unexplained abnormal CSF ,a history of multiple sexual partners or sexually transmitted diseases, and clinical signs compatible with chronic meningitis, a serum treponemal test should be performed[19].There is no no "gold standard test".The FTA-abs (flurorescent treponemal antibody-absorbed),TPPA(*Treponema pallidum* particle agglutination),MHA-TP(microaggultination antibody-*Treponema pallidum*),TPHa(*Treponema pallidum* hemaggultination),and EIA(enzyme immunoassay) are all useful test varying in specificity and sensitivity.Westren blot test are now rarely performed.Referral laboratories prefer automated EIA tests, which use one or more cloned antigens or protein from *Treponema pallidum* subsp. pallidum. Sensitivity and specificity vary so widely that clinical decision is difficult to make without knowing performance characteristics of the test.In the presence of negative RPR or VDR, a positive EIA-IgG should be confirmed with another treponemal test[28].

Norcardiosis and Actinomycoses.Nocardiosis has a strong tendency for hematogenous spread from lungs to brain. An acute or sub-acute meningitis can result from rupture of an abscess into CSF, Actinomycosis can cross the dura from a contiguous infection in the paranasal sinus or middle ear and can cause an indolent meningitis. The organism are rarely isolated from the CSF .Infection is predominantly parameningeal[19].

Lyme Borreliosis.Central nervous system disease can occur weeks to months after infection with *Borelliaburgdoferi*.Cranial nerve palsies are common, unlike syphilitic meningitis. Cognitive decline and ataxia may occur because of encephalitis .Seizures, ataxia, painful radiculopathy, or rarely meningitis may also occur.CSF shows a modest pleocytosis, slight elevation of protein levels, and normal glucose level. HA and Westren blot for IgG antibody in CSF are helpful but probable insensitive.PCR detection in CSF is under evaluation but appears promising [19].

Brucellosis. Now rare in the United States, brucellosisremains a common disease in many countries. Ingestion of unpasteurized dairy products from other countries, such as soft cheese is a common source of infection in the United States. Illness is usually acute but may be relapsing or occasionally chronic. A few patients with chronic meningitis have been reported, but positive CSF cultures have been unusual. Serum Brucella agglutinins and an exposure history are helpful to screen patients .Serologies for brucellosis other than agglutinin are not recommended [19].

Parasitic agents of Maningitis. Unlike *Naegleria* (*Naegleriafowleri*, meningitis contracted from freshwater sources[30])which causes acute meningitis cerebral manifestation of *Acanthamoeba* infections evolve over few weeks, with decreased mental status,seizures, fever, headache, meningitis, visua ldisturbance, and ataxia, with hemiparesis as a later manifestation.Most reported patients have suppressed immune function such as patients with AIDS or stem cell transplant recipients.Other have been chronically ill and debilitated [19].*Angiostrongylus cantonensis* is a common cause of meningitis in the United States have been in the travelers recently returned from the pacific,Hawaii, or the Caribbean, who acquired infection from eating uncooked produce. Patients present with an acute eosinophilic meningitis ,though symptoms can linger for several weeks[30].Other parasites implicated are *Gnathostoma spinigerum, Schistosoma*, as well as the conditions cysticcercosis ,toxocariasis, baylisascariasis, paragonimiasis, and a number of rare infections and noninfectious conditions[31].

V. CLINICAL MANIFESTATION AND DIAGNOSIS

Patients with chronic meningitis have the indolent onset symptoms compatible with chronic central nervous system infection for at least four weeks and have signs of chronic inflammation in the cerebrospinal fluid[9].This entity must be distinguished in the history from recurrent aseptic meningitis or persistent sequelae of encephalitis. A careful history from patient or family member may be needed to date the onset of symptoms and distinguish chronic from recurrent meningitis. What may have seemed like a sudden onset may on further questioning, have been the culmination of a longer process, Symptoms of chronic meningitis can wax and wane over weeks and months. An abnormal CSF may not have been repeated to see if improved symptoms were

accompanied by improved CSF abnormalities. Early symptoms of chronic meningitis include headache, nausea, and decreased memory and comprehension. When hydrocephalus complicates indolent meningitis, dementia can be prominent finding, better related by family members than the patient. Later symptoms of chronic meningitis include decreased vision, double vision or other cranial nerve palsies, unsteady gait, emesis, and confusion [32,25].Patients with chronic meningitis may have a normal physical examination. Including absence of fever. Neurologic examination is most frequent abnormality, with decreased recent and remote memory, confusion, and apathy, papilledema, and cranial nerve palsies, particularly sixth nerve palsy. As cerebral edema causes brain stem compression, upper motor neuron signs, increased deep tendon reflexes, ankle clonus, a positive Babinski sign and finally Chekyne-Stokes respiration may be noted. Other than cranial nerve palsies, neurologic signs are decidedly symmetrical. Resting tremor, rigidity, and decreased mental acuity occasionally suggest Parkinson's disease [19].Skin lesions may be important source of biopsy material in sarcoidosis, cryptococcosis, cocidioidomycosis, blastomycosis ,or sporotrichisis, Vitiligo and poliosis may suggest Vogt-Koyanagi-Harada syndrome.Lymphadenopathy may point toward sarcoidosis, lymphoma, or hematogenously disseminated tuberculosis or histoplasmosis.A dilated fundoscopic examination may reveal retinal lesions of Bechet'ssyndrome. Vogt-Koyanagi Haradasyndrome ,sarcoidosis, tuberculosis ,coccidioidomycosis, or cryptpcoccosis .Arygyll Robertson pupil sign is highly suggestive of neurosyphlis[19].

For accurate diagnosis past history can be helpful, in that coccidioidomycosis is rare in patients who have never been in the southwestern United States or northern Mexico. The endemic area for histoplasmosis is broad in the United States it is uncommon in the Pacific Northwest and Rock Mountain states. Immigrants from countries where tuberculosis is prevalent are at increased risk of reactivation, as are patients who have lived in a household where someone had tuberculosis [19]. Neurocysticercosis occurs in residents of endemic countries, rarely in travelers. Lymeborreliosis in northeastern United States. A history of typical lesion of erythema migrants may suggest the diagnosis of Lyme disease. Travelers outside the United States may have been exposed to Angiostrongylus or brucellosis [19].Occupation is rarely helpful diagnostically. Age is important, in that cryptococcosis is uncommon in the first decade of life. A history of multiple sexual partners, men having sex with men, injection drug use or previous sexually transmitted disease should suggest the possibility of neurosyphilis or HIV-associated infections. Underlying disease is important in that AIDS and corticosteroids therapy are majorpredisposing factors to cryptococcal and *Acanthameoba*meningitis [19].

Diagnosis. A contrast-enhanced MRI is the preferred test for imaging the brain and may show intracranial mass lesions, hydrocephalus or parameningeal foci such as mold infection; and actinomycosis of the paranasal sinuses or middle ear [19].Blood tests are performed for markers of inflammation (e.g.C-reactive protein, complete blood count),as well as blood cultures[33].The most important to in identifying or ruling out meningitis is analysis of cerebrospinal fluid(CSF) through lumbar puncture(LP,spinal tap[34].However lumbar puncture is contraindicated if there is a mass in the brain(tumor or abscess) or intracranial pressure(ICP) is elevated, as it may lead to brain herniation. If someone is at risk for either a mass or raised ICP(recent head injury, a known immune system problem, localizing neurological signs, or evidence of a raised ICP),a CT or MRI scan is recommended prior to lumbar puncture[33].The CSF sample is examined for presence and types of white blood cells, red blood cells, protein content and glucose level [33].CSF findings in different forms of meningitis is important. The concentration of glucose level is high in bacterial meningitis but low in tuberculous, fungal and in malignant meningitis, and normal in acute viral meningitis. Protein level high in acute, tuberculous, fungal and malignant meningitis respectively, but normal level in acute viral meningitis.The cells count(PMNs) > $300/mm^3$ in acute bacterial meningitis, but mononuclear < 300^3 in acute viral meningitis,mononuclear,PMNs,< 300^3 in tuberculous meningitis,< 300^3 in fungal meningitis and usually mononuclear in malignant meningitis[35].

A latex agglutination test useful in meningitis caused by *Streptococcus pneumonia*, *Neisseriameningitidis*, *Haemophilus influenza*,*Escherichia coli* and group B streptococci.Similarly limulus lysate test may be positive in meningitis caused by Gram-negative bacteria, but it is of limited use unless other tests have been unhelpful[33].Serum serology can be helpful for cocidioidomycosis,brucellosis(agglutinin only),Lyme disease, and syphilis. In patients with clinical syndrome compatible with neurosyphilis but negative VDRL or RPR, atreponemal test should be requested. Positive treponemal tests preferably should be confirmed by different treponemal test, because false-positive reaction occur.Serum cryptococcal and *Histoplasma* antigen test can be done, though urine *Histoplasma* antigen is preferred over serum[19] Gram staining of the sample(CSF) may demonstrate bacteria in bacterial meningitis, but absence of bacteria does not exclude bacterial meningitis as they are only seen in 60% of cases; this figure is reduced by further 20% if antibiotics were administered before sample taken[33].If tuberculous meningitis is suspected the sample is processed for Ziehl-Neelsenstain, which has a low sensitivity, and tuberculosis culture, which takes long time to process; Polymerase chain reaction(PCR) is being used increasingly. PCR is used to amplify small traces of bacterial DNA in order to

detect the presence of bacterial or viral DNA in CSF; it is a highly sensitive and specific test[1].Diagnosis of cryptococcal meningitis can be made at low cost by an India ink stain of CSF; however testing for cryptococcal antigen in blood or serum is more sensitive, particularly in people with AIDS[31].

VI. THERAPY AND PREVENTION

Therapy of suspected tuberculous meningitis.Patients with high fever and rapid decline in consciousness may be candidates for empirical therapy for tuberculous meningitis with a four-drug regimen (Isoniazid, Rifampin,Pyrazinamide, and Ethambutol(with assessment of visual acuity and color discrimination should be performed).Immigrants from countries with a high incidence of tuberculosis and patients with a history of tuberculosis in the household member are at especially high risk. Before therapy, several milliliters of CSF should be cultured for mycobacteria and sediment examined for fluorochrome stain for acid fast bacilli. If there are lung lesions, sputum to be smeared and cultured for acid fast bacteria as well as Acid –fast stains should be done and nuclear acid amplification test (NAAT) of CSF requested. Administration of corticosteroids can cloud the clinical response by decreasing fever and improving CSF abnormalities [36,19].Despite the controversy, most authorities advocate the use of corticosteroids in selected cases[37].

Fungal meningitis such as cryptococcal meningitis is treated with long courses of high dose antifungals, such as amphotericin B and flucytosine[38].Raised intracranial pressure is common in fungal meningitis, and frequent(ideally daily) lumbar punctures to relieve the pressure are recommended[38].

Prevention .Prevention against meningitis include (a) bacterial and viral meningitis are contagious like common cold or flu, both can be transmitted through droplets of respiratory secretions during close contact, such as kissing, sneezing or coughing on someone, but cannot be spread by only breathing air where a person with meningitis has been [39].Viral meningitis is spread by enteroviruses, and is most commonly spread through fecal contamination. The risk of infection can be decreased by changing the behavior that led to transmission [38].(b)vaccination against *Haemophilus influenza , meningococcus, Streptococcus pneumonia* and childhood BCG vaccination(Bacillus Calmette-Guerin) significantly reduce the rate of tuberculous meningitis[40,41,36].

VI. CONCLUSION

Chronic meningitis is a diagnostic challenge to clinicians. Early diagnosis by lumbar puncture;MRI imaging and prompt antibiotic therapy have a better outcome,

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