CEREBRAL TB AND OTHER CHRONIC CEREBRAL BACTERIAL INFECTION

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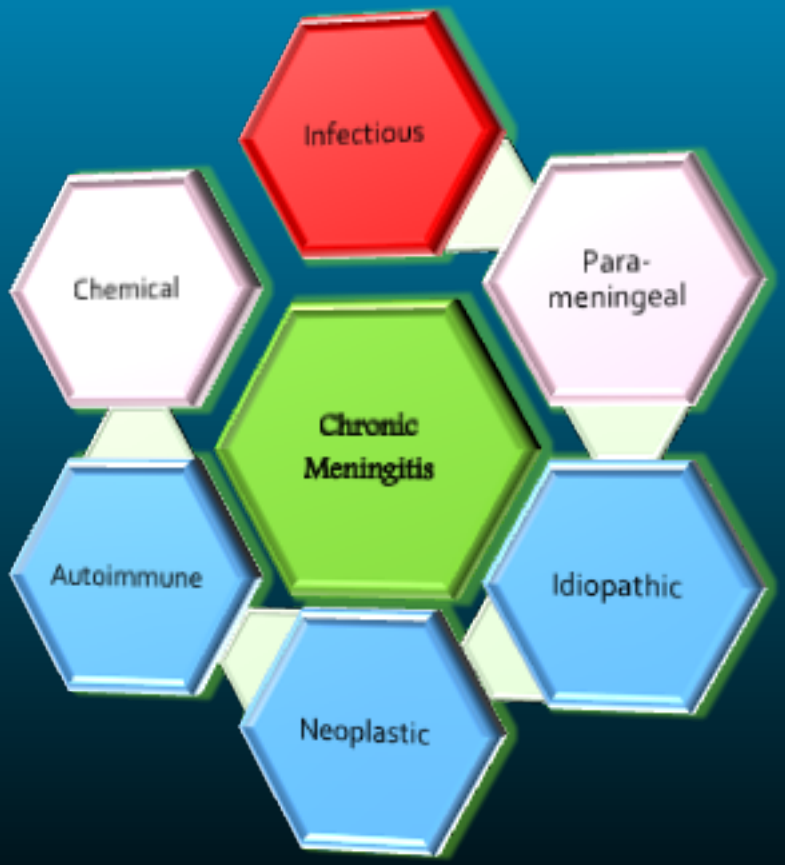
Objectives

- Identify the epidemiology and risk factors for chronic meningitis
- Define chronic meningitis and the various causes of chronic meningitis
- Determine microbiological etiology of chronic meningitis
- Differentiate the clinical presentation of chronic meningitis from other clinical syndromes
- Interpret the laboratory investigations used for the diagnosis of chronic meningitis
- Explain the management approach for a patients suspected to have chronic meningitis
- Define the prevention measures of these infection in the community

Definition and Causes of chronic meningitis:



Infectious causes

- Defined as meningeal inflammation that persists for more than 4 weeks

1. Bacterial including TB
2. Viral
3. Fungal
4. Parasitic

Epidemiology and risk factors (clues in the history)

- Should be differentiated from recurrent aseptic meningitis
- Chronic meningitis affects about 10% of patients diagnosed with meningitis

a) Age and Gender (listeria, brucella and SLE)
b) Regional Preponderance
c) Occupation and Recreational Activities
d) Immune status
e) Sexual Exposure
f) Animals or ticks contact

Symptoms and signs of chronic cerebral and meningetic infection: overlong period or can be recurrent

Symptoms

- Chronic headache
- Neck or back pain
- Change in personality
- Double vision ,visual loss
- Facial weakness
- Arm and leg weakness
- clumsiness

Signs

- Altered mental status, memory loss, etc
- +/-Papilloedema
- BrudZinki or Kerning 'positive sign of meningeal irritation
- Seventh nerve palsy
- 3,4,6 th,Nerve palsy
- Ataxia
- Hydrocephalus

Microbiological Causes Of Chronic Cerebral Infection And Meningitis

A. Bacterial, Most important

a) Tuberculosis } in Saudi Arabia
b) Brucellosis
c) Partially treated acute meningitis
d) Syphilis-caused by *Treponema Pallidium*
e) Liptosporosis- caused by Leptospira. *Icter haemorraghia*
f) Lyme disease-caused by *Borrelia burgdorferi* not common in Saudi Arabia
g) Nocardiosis-caused by *Nocardia* species e. g. *N. Asteroids*
h) *Actinomycosis caused by Actinomyces*
i) Cerebral abscesses can also same presented as chronic infection

The most important causes of chronic bacterial cerebral and meningitic infection in Saudi Arabia are:

1. Tuberculosis
2. Brucellosis

They should differentiated on the basis of:

a) Clinical History

b) Occupations

c) Clinical symptoms

d) Clinical signs in other organism

e) Cerebrospinal fluid findings

B. Fungal Causes

- Cryptococcus neoformans
- Candida species in Saudi Arabia species mainly Candida albicans in immunocompromised patients
- Aspergillus species
- Histoplasma capsulatum

C. Parasitic

- Toxoplasma gonodii(most common)
- Trypanosoiasis: caused by T. gambiense/T.Cruzi
- Rare causes Acanthamoeba spp

D. Virus

- Mumps
- Herpes simplex
- VZV
- HIV

Brucellosis

- Is common disease in Saudi Arabia
- It affect people who are in contact with domestic animals or those who consume raw milk and milk products
- It usually presents with Pyrexia(fever) of unknown organism of intermittent nature
- The fever is accompanied by night sweating, in between the attacks of fever the patient is not very ill.
- Same reasons it can caused chronic cerebral infection and meningitis
- The commonest causes in Saudi Arabia is *Br. Melitensis*
- *Prevention in animal : Vaccination*
- *Eradication :Eradication can only be achieved by test-and slaughter combined with effective prevention measures and control of animal movements.*

Tuberculosis

- Is caused by *Mycobacterium tuberculosis*
- Which infect one third of human race
- It the most common cause of chronic meningitis
- The patient usually presents with fever of long duration
- Symptoms of cough and coughing of blood (Haemoptoysis) when the chest is affected
- It some cases present as meningitis and cerebral infection presenting chronic neurological symptoms and signs
  - Headache, vomiting, meningeal signs, focal deficits, vision loss, cranial nerve palsies, and raised ICP

Chronic cerebral and meningeal infection can produce:-

a) Neurological disability and, may be

b) Fatal if not treated

They usually have:-

a) Slow insidious onset

b) with progression of signs and symptoms over a period of weeks

They differ from those of acute infection which have

a) Rapid on set of symptoms and signs

They are usually diagnosed ,if the neurological syndrome exists for > 4 weeks

Complications

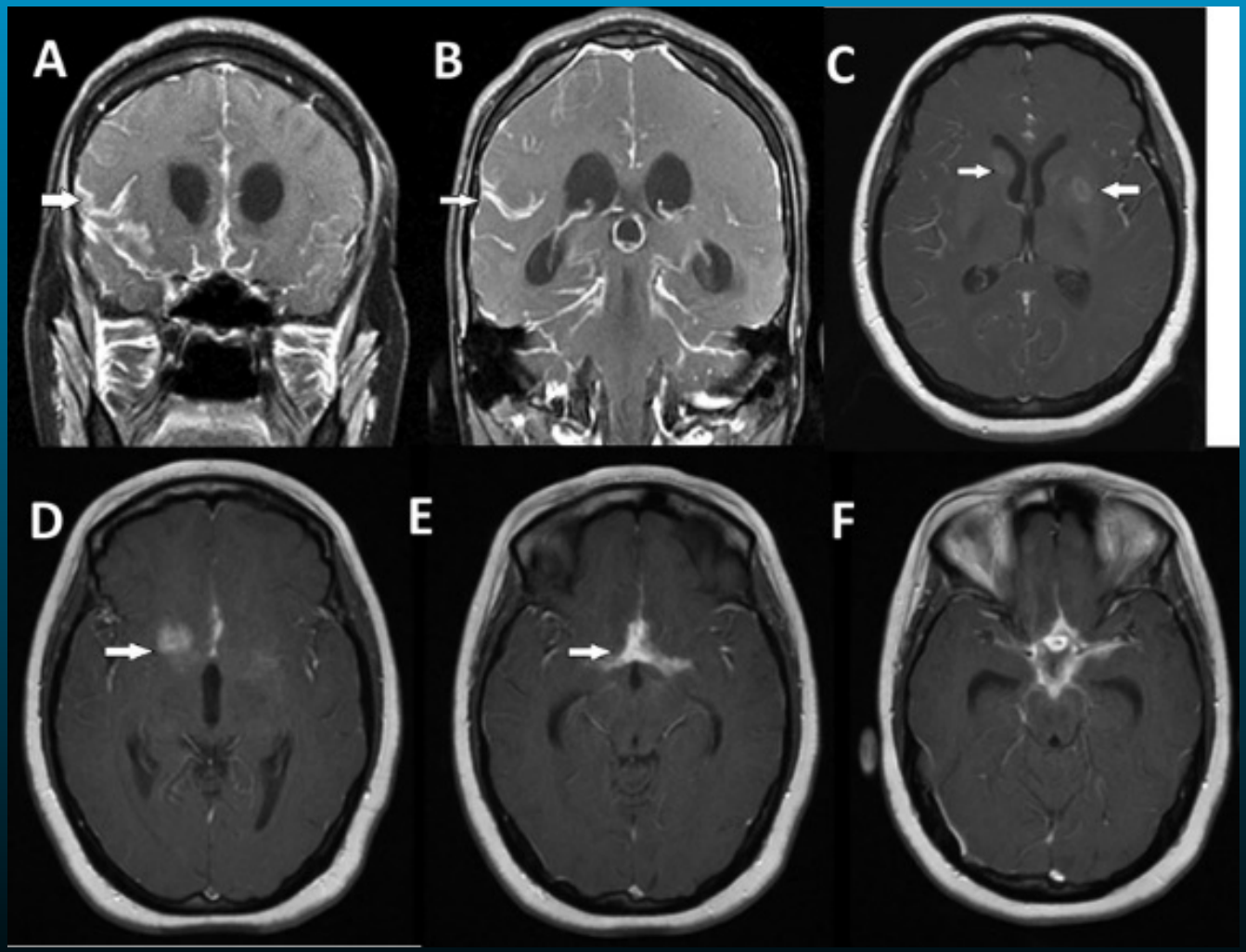
- Hydrocephalus due to obstruction of the foramina of Luschka and Magendie or the aqueduct of Sylvius
- Vasculitis, sometimes causing arterial or venous occlusion and stroke
- Cranial nerve deficits, particularly of the 2nd, 7th, and 8th cranial nerves

Diagnosis of chronic cerebral and meningeal infections

a) History as mentioned for Brucellosis and Tuberculosis if
b) Clinical examination
c) Imaging by x~ ray or MRI or ultrasound
d) Laboratory findings

	Bacterial meningitis	Tuberculous Meningitis	Viral meningitis	Fungal meningitis
Cell count 0-5	>1000-20000 cell/mcL predominantly neutrophil;	100-2000 cell/mcL predominantly lymphocytes	< 2000 cell/mcL predominantly lymphocytes	100-500 cell/mcL predominantly lymphocytes
Glucose 45-100	<40 mg/dl (<40% of serum Glucose)	<40 mg/dl	30-70 mg/dl	30-70 mg/dl
Protein 15-50	>250 mg/dl	100-500 mg/dl	30-150 mg/dl	40-150 mg/dl

Tuberculosis basilar meningitis



Laboratory Findings

This is mainly related to the laboratory examination of cerebrospinal fluid including:~

a) Collect of 2~5 ml of CSF and checking for the pressure

b) Biochemical investigation for :

1. Total protein
2. Glucose level in comparison to the serum glucose level

a) Microscopy:

1. Presence of organism
2. Total white cell count
3. Differential count mainly for:~
    a) Lymphocytes→ Neutrophil
    b) Polymorphic

As in acute pyogenic infections, in chronic cerebral and meningeal infections the following CSF finding will be as follows

a) Increased CSF pressure indicating increased intra cranial pressure common with TB
b) Increased protein level due to presence of inflammatory substance, dead organism, protein and WBC
c) Reduced glucose level (Normally is 2/3 of serum glucose level)
d) Increased local white cell count but in chronic infection the differential shows *lymphocytosis*
e) Gram stain can same time rarely shows causative organism
f) Z-N Stain can show AFB of T.B
g) Modified Z-N can show *Nocardia*

Diagnosis continued

g) VDRL and other serological causes for syphilis
h) Wet preparation of CSF for fungal and parasite
i) India ink for Cryptococcus neoforman
j) Culture for CSF for *Brucella*, T.B *Mycobacterium tuberculosis*, *Leplospira* other Bacteria

Diagnosis of cerebral and meningitis Tuberculosis and Brucellosis

a) Mantoux test, Tuberculin skin test(TST)

b) Chest x-ray for primary focus

c) CSF microscopy for AFB < 30%

d) CSF culture an solid medium L.J and fluid medium 70%

e) PCR or other molecular biopsy test for presence of bacterial element 50-70%

f) Culture of CSF for Brucella

g) Serology for Brucella

Combination of these finding with clinical history and examination finding

Treatment for cerebral and meningeal Tuberculosis and Brucellosis

Tuberculosis

4 Drugs are used there are:~ total 9~12 months

1~ Rifampicin

2~ Isonized(INH) most important

3~ Ethambutol

4~Pyrazinamide

} for 2 month

Then,

- Rifampicin
- INH

} for 7~10 month

Dexamethasone added in case of increased intracranial pressure

Brucellosis Treatment

Two of the following 3 drugs

a) Tetracycline

b) Rifampicin

c) Cotrimoxazole

Usually Rifampicin and Cotrimoxazole are preferred as they have good penetration power in the blood brain~ barner

Others rare causes of chronic meningitis

Disease	Etiology	RF	Presentation	Diagnosis	Treatment	Prognosis
Syphilis (Neurosyphilis)	Treponema pallidum	Only from Human Secondary Syphilis HIV/AIDS	headache and confusion cranial nerves VII and VIII	lymphocytosis, increased protein levels, normal glucose levels -serum &CSF- VDRL	IV Penicillin G 10-14 days	Depend on the stage of the disease
Lyme Disease (Neuroborreliosis)	Borrelia burgdorferi	Exposure to an ixodid scapularis tick. Endemic area	Peripheral and cranial neuropathies	lymphocytosis, increased protein levels, normal glucose levels -Serology	IV ceftriaxone , penicillin G or Doxycycline	resolve slowly over weeks to months
Leptospirosis	Leptospira interrogans	Exposure to Rat urine	Intense throbbing Headach and delirium Anicteric second stage 50%	lymphocytosis, increased protein levels, normal glucose levels - Serology - PCR	ceftriaxone , penicillin G or Doxycycline	Meningoencephalitis /hemiplegia

Description	Acute bacterial meningitis	Chronic meningitis
Aetiology	Variable Neisseria meningitides 13–56% Streptococcus pneumoniae 24–37%	Variable TB- 40–60% Malignancy 8–13% Cryptococcus 7–11% Unknown 30–33%
Clinical features	Boos C, Daneshvar C, Hinton A, Dawes M. An unusual case of chronic meningitis. BMC Fam Pract. 2004;5:21.	
~ Classic triad of fever, headache and neck stiffness	85%	10%
~ Fever	78–91%	44%
~ Headache	32–68%	79%
~ Neck Stiffness	58–82%	75%
~ Altered Mental state	52–82%	41%
~ Focal neurology	23%	32%
~ Papilloedema	<1–4%	30%
~ Cranial Nerve Palsies	4%	24%
Mortality	Variable – aetiology dependent 19.7–25% overall	Variable – aetiology dependent 29%- overall
Elevated WCC, CRP and ESR	Elevated	Normal or only mildly elevated
Hyponatraemia	<10%	>90%
Cerebrospinal fluid analysis	10% – lymphocytic 90% – neutrophilic Gram stain positive 57–90%	>90% lymphocytic <10% neutrophilic Gram stain positive <10%
Abnormal CT	2.7 – 13%	60%