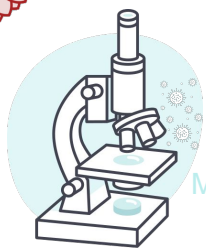


TEAM443
MICROBIOLOGY

Cerebral TB and other chronic cerebral infections

LECTURE 5

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.

Any future corrections will be in the editing file, so please check it frequently

Special thanks to Farah Abukhalaf ♡

Color Index:
Main text
Important
Notes
Boys slides
Girls slides
Extra

Chronic Meningitis

Chronic Meningitis {1}

Definition		Meningeal inflammation that persists for more than 4 weeks.
Causes Chronic Cerebral infection and Meningitis {2}	General causes	- infection - Parameningeal - Neoplastic - Autoimmune - Chemical - Idiopathic
	Microbiological Causes: Bacterial Most important	- Common in Saudi Arabia: 1- Tuberculosis 2 -Brucellosis - Not common in Saudi Arabia : Lyme disease-caused by Borrelia burgdorferi. - Others: ○ Partially treated acute meningitis. ○ Syphilis-caused by Treponema Pallidum. ○ Leptospirosis - caused by Leptospira e.g. L.interrogans L.icterohaemorrhagiae. ○ Nocardiosis-caused by Nocardia species .g N. Asteroids. ○ Actinomycosis caused by actinomyces. ○ Cerebral abscesses can also present as chronic infection
	Fungal	- In Saudi Arabia : ○ Candida species, mainly Candida albicans in immunocompromised patients - Others: ○ Cryptococcus neoformans (Immunosuppressed and HIV patients) ○ Aspergillus species ○ Histoplasma capsulatum
	Parasitic	○ Toxoplasma gondii (most common) . ○ Trypanosomiasis: caused by T.gambiense ○ Rare causes Acanthamoeba spp
	Virus {3}	Some virus can some present as chronic meningitis these include: ○ Mumps ○ Herpes simplex ○ HIV
They should differentiated on the basis of		A) Clinical History b) Occupations {14} C) Clinical symptoms d) Clinical signs in other organism E) Cerebrospinal fluid findings

Epidemiology and Risks Factors

(Clues in the history)

A. Age and Gender (listeria, brucella and SLE)

B. Regional Preponderance

C. Occupation and Recreational Activities

D. Immune status. Sexual Exposure

E. Animals or arthropods ticks contact

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

Clinical Presentation ★

overlong period or can be recurrent

Symptoms	Signs
Chronic headache	+/-Papilloedema
Neck or back pain	positive sign of meningeal irritation Brudzinski or Kerning
Change in personality	Altered mental status, memory loss, etc
Facial weakness	Seventh nerve palsy
Double vision, visual loss	3,4,6th,Nerve palsy
Arm and leg weakness or fever	Ataxia
Clumsiness	Hydrocephalus

Chronic cerebral and meningeal infection can produce:
a) Neurological disability
b) May be 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
Rapid onset of symptoms and signs

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

CNS Tuberculosis

Tuberculosis {4}	
Etiology	Caused by Mycobacterium tuberculosis. (Pure CNS TB not infected)
Epidemiology	○ The most common cause of chronic meningitis ○ It infect one third of human race.
Transmission	Airborne disease, the bacteria is very small and can stay in air for a long time and spread to a long distance.
Clinical presentation {5}	○ The patient usually presents with fever of long duration. ○ Symptoms of cough and coughing of blood (Haemoptysis) when the chest is affected. ○ In 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) It affects the base of the brain in the subarachnoid space where they. cause arachnoid fibrosis which result in increased ICP and hydrocephalus ○ Night sweat,weight loss,chronic fever or chronic cough.
Prevention	Immunization with Bacille Calmette-Guerin (BCG) to newborns.

Treatment

Total 9-12 months

- For the first 2 months:
  - Rifampicin
  - Isoniazid (INH)
  - Pyrazinamide
  - Ethambutol
- For the next (4-6), (7-10) months:
  - Rifampicin
  - Isoniazid (INH)

Brucellosis

Brucellosis	
Etiology	The commonest causes in Saudi Arabia is Br. Melitensis
Epidemiology	It is a common disease in Saudi Arabia. (More common in winter and less in summer)
Transmission	It affect people who: - Are in contact with domestic animals. - Consume raw milk and milk products. - And through inhalation.
Clinical presentation	- 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. - Influenza-like symptoms. (Weight loss is another sign).
Can cause	- It can cause chronic cerebral infections & meningitis (can also cause bone and joint infection)
Prevention	- Prevention in animal: Vaccination. (no vaccination for humans) - Eradication: can only be achieved by test-and slaughter combined with effective prevention measures and control of animal movements ❖ Cook the meat, avoid contact with animals when they are giving birth and drink pasteurized milk.

Treatment

Two of the following 3 drugs:

1 **Tetracycline** 2 **Rifampicin** 3 **Co-trimoxazole**

Note :Usually Rifampicin and Cotrimoxazole are preferred as they have good penetration power in the blood brain- barrier

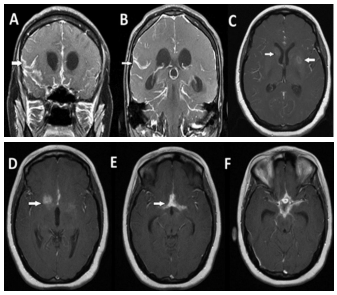
Others Rare causes of chronic meningitis

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, ↑ protein, normal glucose, -serum & CSF-VDRL	IV Penicillin G 10-14 days	Depend on the stage of the disease
Lyme Disease (neuroborreliosis)	Borrelia burgdorferi	Exposure to an ixodes scapularis or tick. Endemic area	Peripheral and cranial neuropathies	lymphocytosis, ↑ protein, normal glucose, -Serology	IV ceftriaxone, Penicillin G or Doxycycline	Resolve slowly over weeks to months
Leptospirosis	Leptospira interrogans	Exposure to Rat urine	Intense throbbing Headache and delirium Anicteric second stage 50%	lymphocytosis, ↑ protein, normal glucose, - Serology, - PCR,	Ceftriaxone, Penicillin G or Doxycycline	Meningoence phalitis /hemiplegia

Diagnosis ★

Diagnosis of chronic cerebral & meningeal infections {6}

- History for brucellosis & TB {7}
- Clinical examination {8}
- Laboratory findings {9}
- Imaging : X-ray, MRI or Ultrasound



Tuberculosis basilar meningitis

CSF Findings in different cases

	Opening pressure (cm H2O)	CSF leukocytes (cells/ µL)	Predominant cell type	CSF protein (g/L)	CSF-to- blood glucose ratio
Normal CSF	≤20	0-5	Lymphocytes	0.15-0.45	0.6
Bacterial meningitis	>20	≥1000	Neutrophils	≥1.0	≤0.5
Viral meningitis	≤20	<1000	Lymphocyte (may be neutrophilic within first 48h)	<1.0 (except HSV and VZV >1.0 g/l)	0.6
Tuberculous meningitis	Normal or elevated	100-500 (5-300 and 500-1000 in 20% of cases)	Lymphocytes (early Lympho, and PMN progress to lymphocytic)	≥1.0 (100-200 mg/dl, 1000-2000 mg/l)	≤0.5 (median 40 mg/dl)
Parasitic eosinophilic meningitis	Normal or elevated	<1000	≥10% eosinophils (or > 10 cell/µL)	<1.0	0.6
Cryptococcal meningitis	>20	<200	Lymphocytes	>0.45	≤0.5

CSF and Laboratory findings ★

Diagnosis	CSF and Laboratory Findings
Tuberculosis & Brucellosis	Collect of 2-5 ml of CSF and check for the pressure → ↑ CSF pressure indicating increased intracranial pressure common with TB.
	- Biochemical investigation for: ○ Total protein→ ↑ protein level due to presence of inflammatory substance, dead organism, protein and WBC. ○ Glucose level in comparison to the serum glucose level → ↓ glucose level (Normally is 2/3 of serum glucose level).
	- Microscopy: ○ Presence of organism. ○ Total white cell count →↑ local white cell count but in chronic infection the differential shows lymphocytosis while in acute infections there is ↑of polymorph. ○ Differential count mainly for: Lymphocytes —> neutrophils Polymorphic ○ Gram stain can same time rarely shows causative organism. ○ CSF microscopy for AFB ○ Z-N Stain can show AFB of T.B
	- Culture for CSF: ○ For Brucella (keep it for a long time), TB, Mycobacterium tuberculosis, Leptospira other Bacteria. ○ Media :CSF culture a solid medium L.J or fluid medium.
	- PCR Or other molecular biopsy test for presence of bacterial element {10} - {13} - Serology: For Brucella.(CSF & serum).
	- Other: ○ Mantoux test, Tuberculin skin test (TST). ○ Chest x-ray for primary focus. ○ Combination of these finding with clinical history and examination finding
Other organisms	○ India ink for Cryptococcus neoforman {11} ○ Modified Z-N stain can show Nocardia. ○ VDRL and other serological causes for syphilis. ○ Wet preparation of CSF for fungal and parasite.

Acute Meningitis & Chronic Meningitis

Description	Acute bacterial meningitis	Chronic meningitis
Etiology	Variable, *neisseria meningitidis* 13-56% and *streptococcus pneumonia* 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-etiology dependent 19.7-25% overall	Variable-etiology dependent 29% overall
Cerebrospinal fluid analysis	10% -lymphocytic 90%-neutrophilic Gram stain (+) 57-90%	>90% lymphocytic <10% neutrophilic Gram stain (+) <10%
Hyponatraemia	<10%	>90%
Elevated WCC,CPR AND ESR	Elevated	Normal or mildly elevated
Abnormal CT	2.7-13%	60%

Summary

Chronic Cerebral infection and Meningitis

Definition of chronic meningitis	Meningeal inflammation that persists for more than 4 weeks.

Causes

Bacterial	Fungal	Parasitic	Virus

Clinical Presentation of chronic cerebral & meningitic infection

Symptoms	Signs
- Chronic headache. - Neck or back pain Change in personality. - Facial weakness. - Double vision, visual loss. - Arm and leg weakness. - Clumsiness.	- +/-Papilloedema. - Brudzinski or Kerning 'positive sign of meningeal irritation. - Altered mental status, memory loss, etc. - Seventh nerve palsy. - 3,4,6th,Nerve palsy. - Ataxia. - Hydrocephalus.
Risk factors	**CSF and Laboratory Findings**
- Age and Gender (listeria, brucella and SLE) - Regional preponderance. - Occupation and Recreational activities. - Immune status. - Sexual exposure - Animals or ticks contact.	↑CSF pressure => ↑ICP Biochemical: ↑protein ↓glucose Microscopy: ↑ WBC (lymphocyte) Presence of organism. Gram stain can same time rarely shows causative organism. Culture PCR SPECIAL: - India ink for Cryptococcus neoforman. - Modified Z-N stain can show Nocardia. - VDRL and other serological causes for syphilis. - Wet preparation of CSF for fungal and parasite.

Dr Notes

(1) Types of meningitis:

- Chronic → caused by many organisms ,ex: parasite, fungi,virus
- Acute→ mainly by bacteria
- the difference between chronic and acute in their symptoms:

A- Chronic: first the patient will suffer from headache followed by vomiting , weight loss that could potentially lead to weakness in his hand
(in other words the onset start gradually)

B- Acute: the symptoms are very severe and might lead to death.

(2) The most common two causes of meningitis in KSA: 1-Brucella 2-TB
there are other disease that could lead to meningitis :

-Lung disease
- syphilis
-Hiking (means when a person face animals while hiking)
-Fungal infection

(3) Viruses might cause meningitis but with very mild symptoms and it won't lead to death

(4) Also a person who deals with or works in a job related to" المجاري " is at risk of being infected with organism called'' leptospira '' , present in Rat urine.

(5) TB will affect the base of the skull and block the CSF which would eventually lead to hydrocephalus which in turn cause edema and compress the cranial nerves

(6) Q:What is your approach to a patient come to ER with fever headache……., (symptoms of meningitis) , how will you deal with him?

- History
- physical examination
- Investigation

Dr Notes

(here in this page we will continue talking of the previous note NO.4)

(7) In history we will look at many things:

- symptoms history→ ex: headache, weight loss,vomiting, nausea , symptoms related to cranial nerves and cerebrum , consciousness.
- social history
- family history→ if they have been affected in TB before , or are they suffering from some symptoms as the patient does(similar episodes)
- surgery history
- drug history
- post-medical history→ chronic disease ex: DM, hypertension , HIV
- travel history→ Ask the patient about the recent country they have been to, because the organism that cause the disease may differ from place to place ex: India and Bangladesh (foodborne) , Southeast Asia (mosquito) , exposure areas or crowded area (sexual contact which related to HIV and syphilis)
- Note: we have to ask the patient about the fever if it comes continuously or in an interrupted way (pattern of fever) , because the pattern of fever in brucella is in interrupted way , so by knowing the pattern we will be able to differentiate the main cause of the fever.

(8) - physical examination: check eye, neck (Neck stiffness), neurological examination
- investigation: - Blood test (count WBC, hemoglobin,ECR,platelets)
  - biochemistry(liver functional test,glucose,electrolytes
  - microbiology lab (LP, Blood)
  - Radiology(X-ray , MRI, CT scan)

(9) We will discuss in detail about microbiology lab (LP)
So with CSF we will look at two things:
1- concentration of protein ,glucose, cell count
2- gram stain,bacterial culture , TB culture , molecular(TB) ,serology(for brucella,syphilis , lung disease)

(10) if the TB didn't grow in culture we will do PCR.
(11) fungi has different stains , ex: indian ink (we will study it later)
(12) virus have direct florence , PCR, culture (we will study it later)
(13) most of the times we like to do molecular test , why? because it's highly sensitive

Dr Notes

Q: how does a job related to chronic meningitis?
maybe while dealing with patient doctors will catch the infection , or while dealing with animals(brucella),

Q:What is your approach to a patient come to ER with fever headache……., (symptoms of meningitis) , how will you deal with him?

- History
- physical examination
- Investigation

{15} Most of TB infections occur in the lung followed by reactivation action which in turn leads to hematogenous spread to meninges and cause meningitis

General note :

- It's not allowed to begin investigations by taking CSF , because it's too dangerous
- Blood culture in bottle → will lead to rapid growth of brucella (good thing)
- Brucella grows in liquid and in solid , if i doesn't grow, we do serology instead

MCQs

Q1 - A 44 year-old male suffering from AIDS dies after an attack of meningoencephalitis. An autopsy shows soap-bubble lesions that are visible with India-ink preparation. Which organism is most likely responsible for the patient's condition?			
A- M.tuberculosis	B- Neisseria	C- Strep.pneumonia	D- Cryptococcus
Q2 - Which of the following is the classical CSF finding seen in Tuberculous Meningitis?			
A-↑protein ↓glucose ↑lymphocytes	B-↑protein ↑glucose ↑neutrophils	C-↑protein ↑glucose ↑lymphocytes	D-↓protein ↑glucose ↑lymphocytes
Q3 - Which of the following antibiotic combination is used in TB for the last 7-10 months?			
A- iNH- Ethambutol	B- Rifampicin-INH	C-INH-Pyrazinamide	D- Ethambutol-Rifampicin
Q4 -A farmer came to the hospital complaining of fever, headache and night sweating. Which one of the following is the most likely causative organism?			
A-Br.melitensis	B-Mycobacterium tuberculosis.	C-Toxoplasma gonodii	D-Borrelia burgdorferi
Q5 - which of the following drugs are preferred in treatment of brucellosis?			
A-Rifampicin + Pyrazinamide	B-Rifampicin + Ethambutol	C-Rifampicin + co trimoxazole	D-Rifampicin + Isoniazid
Q6 - Which of the following is one of the main ways Brucellosis is contracted?			
A- bites from ticks	B- contact with farm animal	C- infected medical equipments	D- infected person
Q7 -Which of the following is a diagnostic method that detect Br.melitensis:			
A-Z-N stain	B-serology	C-Mantoux test	D-India Ink

1) D 2) A 3) B 4)A 5)C 6) B 7B

TEAM 443
MICROBIOLOGY

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