Microbiology
437

MED437
KING SAUD UNIVERSITY

CEREBRAL INFECTION

CEREBRAL TB & OTHER CHRONIC CEREBRAL BACTERIAL INFECTION

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Chronic Cerebral and Meningeal Infection

- ★ Can produce:
  - ○ Neurological disability and, may be.
  - ○ Fatal if not treated.
- ★ They usually have:
  - ○ Slow insidious onset.
  - ○ 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.
- ★ Diagnosis:
  - ○ History for Brucellosis and Tuberculosis.
  - ○ Clinical examination.
  - ○ Imaging, X-ray or MRI or ultrasound.
  - ○ Laboratory findings.

★ Symptoms and signs of chronic cerebral and meningitis infection: over long period or can be recurrent

SYMPTOM:	SIGN:
Chronic headache	+/-Papilloedema
Neck or back pain	Brudzinski or Kerning 'positive sign of meningeal irritation
Change in personality	Altered mental status, memory loss, etc
Facial weakness	Seventh nerve palsy
Double vision ,visual loss	3,4,6 th,Nerve palsy
Arm and leg weakness	Ataxia
Clumsiness	Hydrocephalus (bc of increase in ICP)




★ Microbiological Causes Of Chronic Cerebral Infection and Meningitis:

Bacterial Most important	• **Tuberculosis** ← in Saudi Arabia • **Brucellosis** • Partially treated acute meningitis • Syphilis-caused by **Treponema Pallidium** • Liptosporosis- caused by **L.Icter haemorraghia** (south america & india) • Lyme disease-caused by **Borrelia burgdorferi** (north american & europe) not common in Saudi Arabia • Nocardiosis-caused by Nocardia species (immunocompromised patients) e.g **N. Asteroids** • Cerebral abscesses can also same, preferred as chronic infection
Fungal	• **Cryptococcus neoformans** (in HIV patients) • Candida species in Saudi Arabia species mainly **Candida albicans** in immunocompromised patients • **Aspergillus species** • **Histoplasma capsulatum**
Parasitic	• **Toxoplasma gonodii** (most common) acquired from cats • Trypanosoiasis:caused by **T.gambiense** in south american and africa • Rare causes : **Acanthamoeba spp**
Virus	Some virus can some present as chronic meningitis these include: • Mumps • Herpes simplex • HIV




Brucellosis

- ★ Is a common disease in Saudi Arabia.
- ★ It affect people who
  - ○ are in contact with domestic animals.
  - ○ consume raw milk and milk products.
  - ○ And through inhalation
- ★ 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 cause chronic cerebral infection and meningitis
- ★ The commonest causes in Saudi Arabia is **Br.melitensis**

Tuberculosis

- ★ Is caused by **Mycobacterium tuberculosis.**
- ★ Which infect one third of human race.
- ★ 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.

Diagnostic Features of Tuberculous Meningitis		
Clinical	CSF	Imaging
• Fever and headache (for more than 14 days). • Vomiting. • Altered sensorium or focal. • neurological deficit.	• Pleocytosis (more than 20 cells, more than 60% lymphocytes) • Increased protein (more than 100 mg/dl) • Low sugar (less than 60% of corresponding blood sugar) • India ink studies and microscopy for **cryptococcus Neoformans** • Malignant cells should be negative	• Exudates in basal cisterns or in sylvian fissure hydrocephalus • Infarcts (basal ganglionic) • Gyral enhancement • Tuberculoma formation




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

CSF Findings

★ Increased CSF pressure indicating increased intracranial pressure
★ Increased protein level due to presence of inflammatory substance,
dead organism, protein and WBC
★ Reduced glucose level (Normally is 2/3 of serum glucose level)
★ Increased local white cell count but in chronic infection the differential shows lymphocytosis while in acute infections there is increased % of polymorph
★ Gram stain can same time rarely shows causative organism
★ Z-N Stain can show AFB of T.B while modified Z-N can show Nocardia
★ VDRL and other serological causes for syphilis
★ Wet preparation of CSF for fungal and parasite
★ India ink for Cryptococcus neoforman
★ Culture for CSF for Brucella,T.B Mycobacterium tuberculosis, Leplospira other Bacteria

Laboratory Findings

Mainly related to the laboratory examination of cerebrospinal fluid including:

★ Collect of 2-5 ml of CSF and checking for the pressure (other infections 1ml but TB stick with mycolic.acid)
★ Biochemical investigation for:
  ○ Total protein
  ○ Glucose level in comparison to the serum glucose level
★ Microscopy:
  ○ Presence of organism
  ○ Total white cell count
  ○ Differential count mainly for:
    ■ Polymorphic
    ■ Lymphocytes ⟶ Neutrophil

Laboratory Diagnosis

★ Mantoux test, Tuberculin skin test(TST)
★ Chest x-ray for primary focus
★ CSF microscopy for AFB
★ CSF culture a solid medium L.J or fluid medium
★ PCR or other molecular biopsy test for presence of bacterial element
★ Culture of CSF for Brucella
★ Serology for Brucella

Treatment

Tuberculosis

For the first 2 months:
A. Rifampicin
B. Isoniazid (INH)
C. Ethambutol
D. Pyrazinamide

For the next 4-6 months:
A. Rifampicin
B. INH

Brucellosis

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 BBB




Alsomily's Notes:

Gray is less important
But sometimes we have to leave it for the sake of understanding

- Chronic meningitis has in insidious onset why? Because in the first 3 weeks the patient will have mild symptoms like mild fever or headache but later the symptoms will be more severe,while in acute meningitis the patient will come early because he will be sick, its very important to know the clinical presentation
- It has some involvement to the brain tissue it affects blood vessels, may cause infarction and if he present late he might be in coma so you need to know more about TB
- **Symptoms**:chronic headache, neck rigidity, gait problems, personality changes and cranial nerves damage and clumsiness
- TB go mainly to the base of the skull so it might affect CSF circulation and increasing ICP and that will lead to papilloedema so you need to examine the patient.
- these are the clinical presentation and there might be hydrocephalus so don't forget to examine papilloedema and if positive think about TB
- **Etiology:** We are endemic of TB and brucella,partially treated meningitis the other differential diagnosis :

Bacterial:

- Syphilis (VDRL serology)
- Leptospirosis (serology)
- Lyme disease (serology)
- nocardiosis(no serology,culture)
- **Fungal**:cryptococcus in HIV(india ink), histoplasma in united state
- **parasite**:Toxoplasma gondii is common in HIV patients
- **viral:**herpes(PCR)
- I need you to Remember 1 organism from every category(fungi,parasite...)
  In case you will be asked about differential diagnosis
- When we talk about meningitis it's mainly bacterial but when we talk about viral meningitis is mild(self limiting) viral is mainly encephalitis we rarely talk about encephalitis in bacterial but we talk about brain abscess




Alsomily's Notes cont. :

-Diagnosis So if you have a patient you should

1-take history (drug,travel,family,sexual) Then

2-physical exam (like papilloedema) it will tell you if there is hydrocephalus and if you can do lumbar puncture+exam the heart and lung because it might be the source

-Brucella: its common in saudi arabia and common in the exam (:

Most common is brucella melitensis

Affect people who consumes raw milk Can be transmitted by inhalation

-Mycobacterium tuberculosis:

initially they will have primary infection carrying the organism in latent period then it might get reactivation,pulmonary reactivation is the most common but sometimes extrapulmonary

Its usually Slow insidious onset

Early they will have focal and meningeal symptoms and late then paralytic, and that would be after 4 weeks, this is just a revision

Diagnosis:1-history 2-clinical exam 3-laboratory tests 4-imaging

What Laboratory tests you would do ?

specimen : CSF+blood

Blood:culture ,CBC,biochemistry

CSF: WBC(differential count) glucose,protein, culture and stain

If gram stain showed no organism and you saw pus cells

You will think about TB then what will you do ?

1-ziehl-neelsen stain 2-culture on LJ media

If the results were negative you do serology and PCR for the other differential diagnosis

However some people prefer to do these tests at the same time

CSF diagnosis is simple(revision):

stains(gram stain,india ink)culture media(fungus,bacteria) PCR(TB) serology test of CSF

-treatment:rifampicin+isoniazid+ethambutol+pyrazinamide → 2 months

Then rifampin INH → 4-6 months

Brucella: 2 out of 3

Rifampin,cotrimoxazole,tetracycline

TB treatment covers brucella

- If the patients is HIV prolong the treatment

Summary

Chronic cerebral and meningetic infection

Symptom	Sign
Chronic headache - Neck or back pain Change in personality - Facial weakness Double vision - visual loss – clumsiness Arm and leg weakness	+/- Papilloedema - Brud Zinc or Kerning Altered mental status - memory loss Ataxia - Hydrocephalus 3,4,6,7 th Nerve palsy

	Bacterial	Fungal	Parasitic	Virus
Pathogens :	• **<u>Tuberculosis</u>** • **<u>Brucellosis</u>** • Syphilis by **Treponema Pallidium** • Liptosporosis by **L.Icter haemorraghia.** • Nocardiosis by **Nocardia speciese: N.Asteroid.** (more in low immunity patient) • Cerebral abscesses.	• **Cryptococcus neoformans (WITH HIV).** • **Candida albicans** (mainly immunocompromised patients) • **<u>Aspergillus species</u>** • **Histoplasma capsulatum**	• **Toxoplasma gondii** • **T.gambiense** (Trypanosoiasis)	• **Mumps** • **Herpes simplex (HSV2)** • **HIV**
The most important:	Tuberculosis		Brucellosis	
Caused by	**Mycobacterium tuberculosis**		**Br.melitensis**	
Affect:	1/3 of human		affect people who are in contact with domestic animals or consume raw milk	
Symptoms:	fever of long duration - cough - Haemoptoysis		Pyrexia - night sweating	
Extra:	It can be intracranial or spinal			
	Intracranial tuberculosis: Parenchymal CNS involvement can occur in the form of tuberculoma. Tuberculous vasculopathy.	**Spinal tuberculosis:** Pott's spine & Pott's paraplegia		
Diagnosis:	<u>Clinical:</u> fever and headache (↑ 14 days) - vomiting <u>CSF:</u>pleocytosis (lymphocytes) - increased proteins - low sugar <u>Imaging:</u> exudates in basal cisterns or in sylvian fissure hydrocephalus - tuberculoma formation			
Treatment	**Start with 4 drugs (for 2 months):** Rifampicin + Isonized (INH) + Ethambutol + Pyrazinamide Then: Rifampicin + Isonized (INH) **(for 4-6 months)** (in HIV ⟶ up to 1 year)		**Two of the following 3 drugs:** a- Tetracycline b- Rifampicin ← Preferred as they have good penetration power in the BBB c- Cotrimoxazole ←	
CSF finding:	Increased CSF pressure means increased ICP ❖ <u>Biochemical investigation shows:</u> 1) Total protein: Increased 2) Glucose level: Reduced ❖ <u>Microscopical investigation shows:</u> 1) Total WBC count: Increased (in chronic infection ⟶lymphocytosis - in acute infections ⟶polymorph) 2)<u>Presence of organism</u> 1) Gram stain 2) Z-N Stain can show AFB of T.B while modified Z-N can show Nocardia 3) Culture for CSF for Brucella,T.B Mycobacterium tuberculosis 4)If suspect it Syphilis: VDRL and serology test. 5)If fungal & parasite: wet preparation of CSF. 6)India ink for cryptococcus neoforman. 7)Culture of CSF for TB & Brucella (if it does not appear in Gram & Z-N stains) 8)PCR			




MCQs:

A 28 years old man was admitted to the hospital. He suffered from headache and neck pain, his temperature was high the last 20 days. Recently he started to cough blood.
1- what is the most likely causative agent?
A-Br.melitensis
B-Candida albicans
C-Mycobacterium tuberculosis
D-Nocardia speciese

2-What do we expect to see in the CSF?
A- Pleocytosis(especially macrophages).
B-Decreased proteins level.
C- High glucose level.
D- Pleocytosis (especially lymphocytes)

3- A patient was diagnosed with meningeal infection, after microbiological examination, they found Cryptococcus neoforman. What is the most likely test that they used?
A- Blood agar.
B- Culture.
C- VDRL.
D- India ink

4- Increased WBC especially lymphocytes (lymphocytosis) and polymorph occurs in?
A- Only Acute infection.
B-Chronic infection, Acute infection.
C- Only chronic infection
D-Acute infection, Chronic infection

5-CNS tuberculosis can affect the spinal cord and cause?
A-Tuberculoma.
B-Tuberculous abscess.
C- Pott's.
D-Tuberculous vasculopathy.

6- which of the following can cause chronic cerebral infection or meningitis?
A-Proteus species
B-Polioviruses.
C- Syphilis.
D-S.aureus.

1-C 4-B
2-D 5-C
3-D 6-C

SAQ:

- A 39 years old farmer complained of weakness in his arms and legs, headache. he also presented with high temperature 40 c, and night sweating. His wife said he started to forget things. On microbiological examination, WBC shows lymphocytosis. Biochemical investigation shows increased total protein.

1- what is the most likely diagnosis? What is the causative agent?

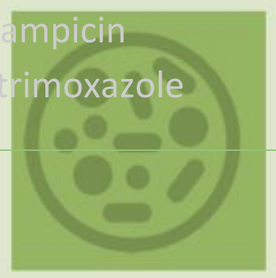
Brucellosis / Br.melitensis

2- what more test that you could do to confirm your diagnosis?

Culture for CSF for Brucella / Glucose level

3- what is your treatment plan?

Two of the following 3 drugs:
a- Tetracycline
b- Rifampicin
c- Cotrimoxazole

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