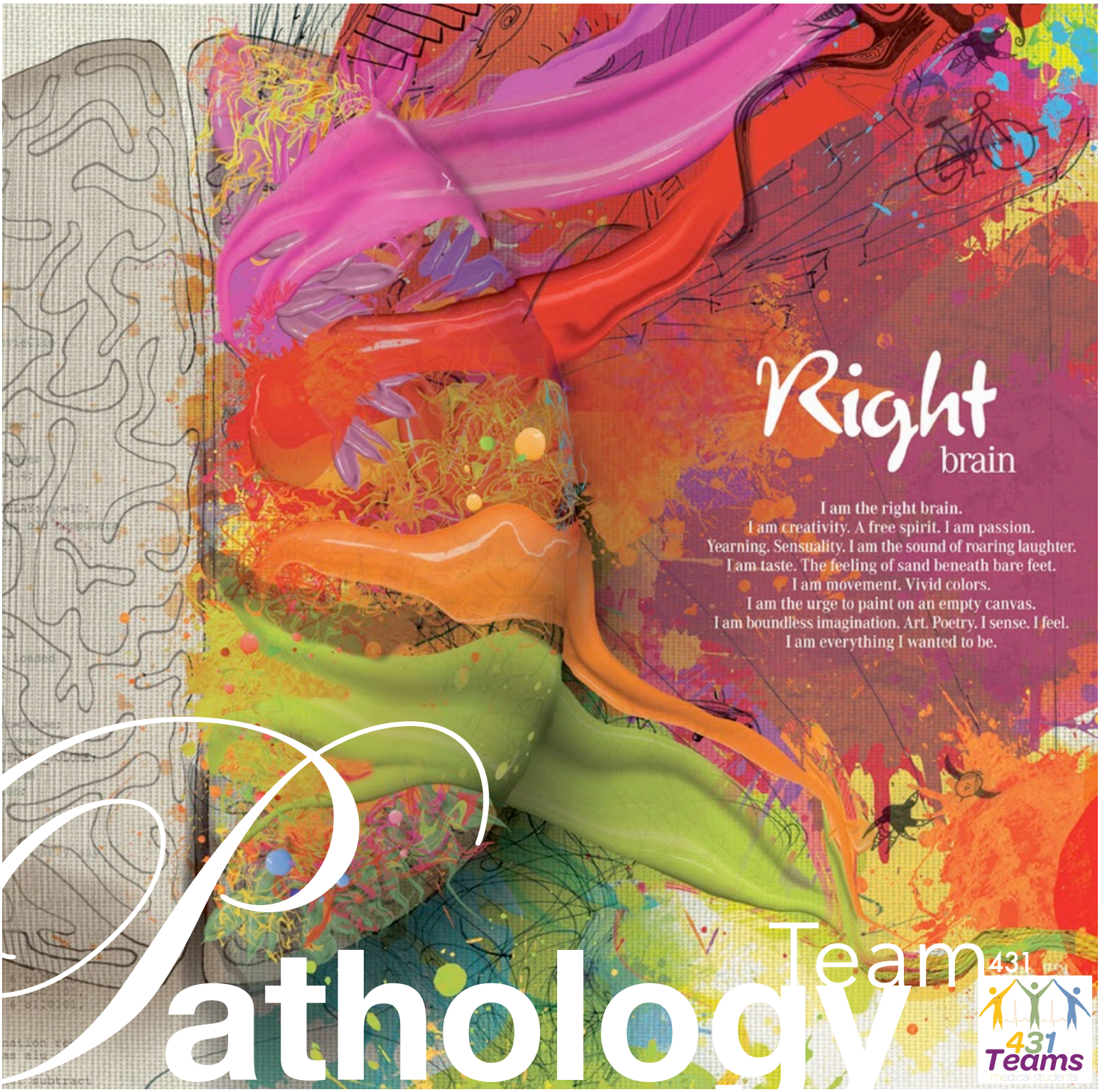


Pathology Team 431

431 Teams medical students

9 /9

CNS Block

Done by:

Saleh AlHejjei &

Alaa AlAqeel

Checked by:

Abdulrahman Alghadeeb

CNS Infections:

- ***Portals of entry of infection into the CNS:***

1. **Hematogenous spread:**

   - The Most Common example: Infective Endocarditis.

2. **Direct implantation:**

(Traumatic or in congenital CNS malformation) (Or surgery).

3. **Local extension:**

(Occurs secondary to an established infection in a nearby organ (air sinus mostly, an infected tooth or middle ear) (especially in children).

4. Through the peripheral *nervous system into the CNS:*

(Certain viruses, such as rabies and herpes zoster)

- Direct invasion, and Direct implantation are not the same mechanism of spread. As Direct invasion, is a rupture of a tumor vessel that then releases a tumor cell which reaches, and penetrates a remote vessel to grow in the surrounding tissue. Whilst Direct implantation, is a rupture of a primary tumor, releasing malignant tumor cells to float in the fluid and begin to grow on any tissue reached by the fluid.
- Lymphatic cannot cause Meningitis, because, there are no lymph nodes in the brain.

- The **rabies virus** is a neurotropic virus that causes fatal disease in human and animals. Rabies transmission can occur through the saliva of animals.
- Herpes zoster: is a viral disease characterized by a painful skin rash in a limited area on one side of the body, often in a stripe.

1. *Meningitis*:

It is an inflammatory process of the leptomeninges and CSF within the subarachnoid space.

Leptomeninges: refer to the pia mater and arachnoid mater, two of the membranes that surround the brain and the spinal cord.

 Meningoencephalitis?

An inflammation of the meninges and of the brain.

- Pyogenic meningitis = (bacterial meningitis):

- It is a medical emergency

The causative microorganisms are:

• **Neonates**: *Escherichia coli* and group B streptococci.

• **Infants:** *Streptococcus pneumonia.*

• **Adolescents and young adults:** ,*Neisseria meningitidis* (Meningococcal meningitis) and *Haemophilus influenzae (becoming less due to immunization).*

• **Elderly:** listeria monocytogenes and *Streptococcus pneumonia.*

CSF Findings in spinal tap (lumber puncture):

• Cloudy or frankly purulent CSF

• As many as 90,000 neutrophils /mm

• raised protein level

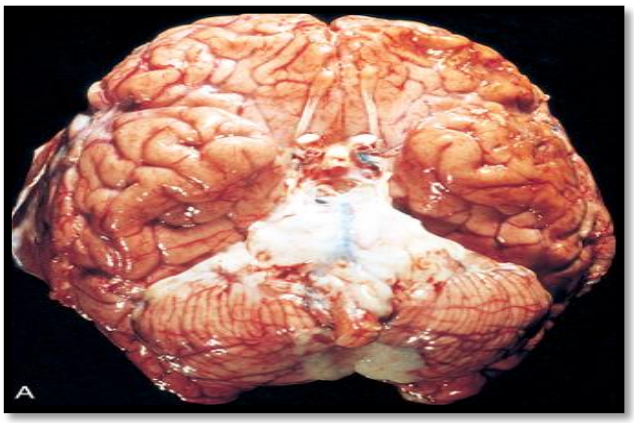
• Markedly reduced glucose content

• Bacteria may be seen on a Gram stained smear or can be cultured, sometimes a few hours before the neutrophils appear.

- The raised protein level is due to: increase the presence of the replicating bacteria, which have a high composition of protein and increase the number of cells that fight infection and inflammation, which are also composed of protein .
- Glucose is consumed by both the Bacteria & WBCs for energy. So, more fall in CSF glucose in the Bacterial Meningitis.

Acute meningitis:

- **Invading the subarachnoid layer.**



Clinical Features:

• Systemic non-specific signs of infection

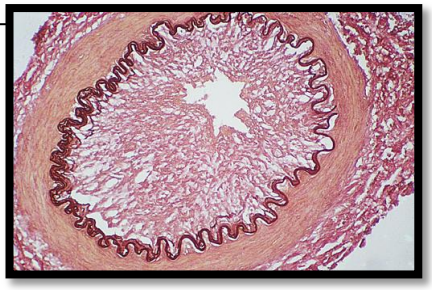
• Meningeal irritation signs and neurologic impairment:
– Headache, photophobia, irritability (especially in kids, this can show as them not wanting to eat, talk, or sleep), clouding of consciousness and neck stiffness (especially for kids).
• Untreated, pyogenic meningitis can be fatal.

• Effective antimicrobial agents markedly reduce mortality associated with meningitis

Complications:

• **Phlebitis** (Inflammation of the walls of a vein) may →

Cause venous occlusion→ hemorrhagic infarction of the underlying brain.



Thrombus occluding an artery

• **Leptomeningeal fibrosis** → hydrocephalus (the pus in the subarachnoid space can result in obstruction which leads to hydrocephalus).

• **Septicemia** → hemorrhagic infarction of the

adrenal glands and cutaneous petechiae (known as Waterhouse-

Friderichsen syndrome (usually with Neisseria), particularly common with meningococcal and pneumococcal meningitis.

• **Focal cerebritis** (encephalitis) & seizures

• **Cerebral abscess**

• **Cognitive deficit**

• **Deafness**

- (the pus and abscess can end up by causing hemorrhage or thrombosis in the brain vessels causing ischemia).

2.Brain abscess:

Most common organisms: Streptococci and staphylococci in non-immunosuppressed populations.

- ***Predisposing conditions:***

• Acute bacterial (infective) endocarditis (usually give multiple microabscesses)

• Cyanotic congenital heart disease in which there is a right-to-left shunt (paradoxiacal) e.g: atrial septic defect.

• Loss of pulmonary filtration of organisms (e.g, bronchiectasis).

Location: most common on cerebral hemispheres

- ***Morphologically:***

• Liquefactive necrosis

• The surrounding brain is edematous , congested & contains reactive astrocytes (gliosis) & perivascular inflammatory cells.

Clinical presentation:

progressive focal neurologic deficits in addition to the general signs of raised intracranial pressure such as: behavior changes, decreased consciousness, headache, lethargy, weakness, numbness, eye movement problems, and double vision, Seizures, Vomiting.

- **Liquefactive necrosis is a type of necrosis which results in a transformation of the tissue into a liquid viscous mass.**
- **happens when inflammatory cells and the enzymes of leukocytes digest ("liquefy") the tissue.**
- **hypoxic death of cells within the central nervous system also results in liquefactive necrosis**

CSF findings:

• Contain only scanty (little) cells.(Why you do not see much of inflammatory cells in the meningies? Because it is localised and not in the ventricles, so in the CSF you see only a few inflammatory cells.

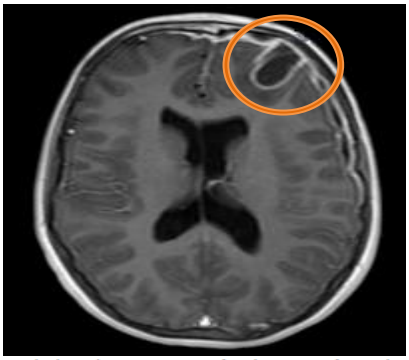
• **Protein:** ↑ (duo to immune system reaction, where most of these are immunoglobins)

• **Glucose:** Normal level.

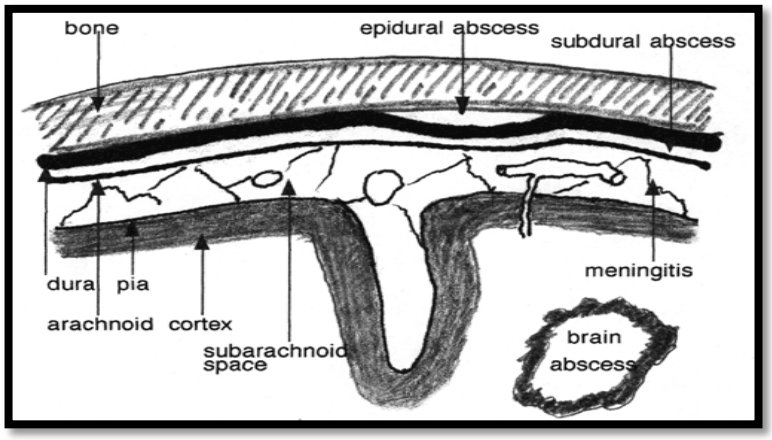
Complications of Brain abscess:

• (Increase in intracranial pressure leading) to herniation

• Rupture of abscess into subarachnoid space or ventricle.
(Sinuses -> pus collection -> Brain abscess -> subarachnoid space-> Meningitis).



Subdural empyema (enhancing) and brain abscess in a patient with sinusitis.



3. Epidural and Subdural Infections:

The epidural and subdural spaces: can be involved with bacterial or fungal infections, usually as a consequence of direct local spread.

• **Epidural abscess**, commonly associated with osteomyelitis (Inflammation of bone or bone marrow), arises from an adjacent focus of infection, such as sinusitis or a surgical procedure.

• When the process occurs in the spinal epidural space, it may cause spinal cord compression and constitute a neurosurgical emergency

Empyema

• Infections of the skull or air sinuses may also spread to the subdural space, producing subdural empyema. The underlying arachnoid and subarachnoid spaces are usually unaffected,

but a large subdural empyema may produce a mass effect • In addition, thrombophlebitis(thrombus in veins)may develop in the bridging veins that cross the subdural space, resulting in venous occlusion and infarction of the brain

Empyema ……. Subdural..(is like saying embedded so it is deeper so it is subdural)

- ***Symptoms include***: those referable to the source of the infection. Most patients are febrile (fever), with headache and neck stiffness, and if untreated may develop focal neurologic signs, lethargy, and coma.
- ***Treatment***: (surgical drainage is the best treatment of any drainage)

  → resolution (termination) of the empyema occurs from the dural side; if resolution is complete, a thickened dura may be the only residual finding. With prompt treatment, complete recovery is usual.

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5. Tuberculosis:

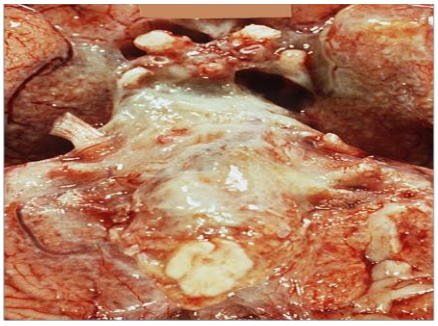
- ***Location:*** the subarachnoid space contains a fibrinous exudate, most often at the **base** of the brain.
- ***Tuberculoma:*** (a ball-like mass***)*** is well-circumscribed intraparenchymal mass:

– Rupture of tuberculoma into subarachnoid space results in tuberculus meningitis

– A tuberculoma may be up to several centimeters in diameter, causing significant mass effect.

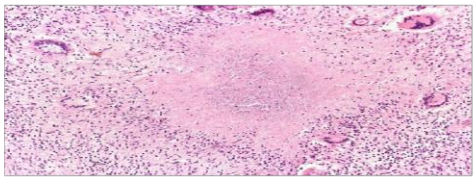
– Almost Always occurs after hematogenous dissemination of organism from

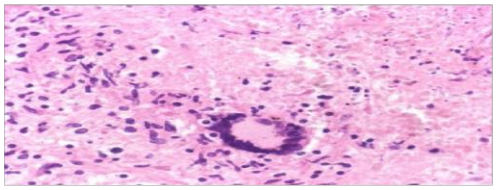
primary pulmonary infection (important).



TB meningtis

Exudate at the base of the brain





Microscopically:

There is usually a central core of caseous necrosis (is a form of cell death in which the tissue maintains a cheese-like appearance) surrounded by a typical tuberculous granulomatous reaction.

- **Langhans giant cells (TB).**
- **Necrotic cells.**

CSF findings:

• There is only a moderate increase in cellularity of the CSF (pleocytosis) (in french the collection of the stars : an abnormal increase in cells (as lymphocytes) in the cerebrospinal fluid different kinds of group of cells) made up of mononuclear cells (lymphocytes) , or a mixture of polymorphonuclear (neutrophils in acute cases) and mononuclear cells

• **The protein:** level is elevated, often markedly

• **The glucose:** typically is moderately reduced or normal (because of low bacteria).

Remember that: Always remember that TB is a chronic infection

Aseptic Meningitis (Viral Meningitis):

Aseptic meningitis is a misnomer

Clinically:

• it is a term for an illness comprising meningeal irritation, fever, and alterations of consciousness of relatively acute onset without recognizable organisms

• The clinical course is less fulminant (sever and sudden) than in pyogenic meningitis, is usually self-limiting, and most often is treated symptomatically

Pathogens:

in approximately 70% of cases, a pathogen can eventually be identified, and most commonly is an enterovirus.

CSF findings:

• **Cells:** an increased number of lymphocytes (pleiocytosis).

• **Protein:** the elevation is only moderate.

• **Glucose**: is nearly always normal.

Macroscopically:

there are no distinctive characteristics except for brain swelling, seen in only some instances.

Microscopically:

There is either no recognizable abnormality or a mild to moderate infiltration of the leptomeninges with lymphocytes.

- Viruses can not be cultured, so, not easily recognized.
- Pus is not significant .

Homework

- **Create a table of CSF findings in Meningitis, aseptic meningitis, TB meningitis, Brain abscess and multiple sclerosis.**

	meningitis	Aseptic meningitis	TB meningitis	Brain abscess	Multiple sclerosis
cells	neutophils	Lymphocytes	Lymphocytes more than neutrophils	Scanty cells (no bacteria in the CSF)	Pylocytosis: Increase number of cell especially WBCs
protein	Markedly elevated	Normal or slight elevation	Markedly elevated	elevated	Elevated especially γ-globulin (oligocolonal band)
glucose	Markedly reduced	normal	Normal or slightly reduced	normal	

MCQs

- **Tuberculoma is almost always occurs after :**

A. Trauma.
B. Cancer
C. Liver infection
D. Primary pulmonary infection.

- **A man came to the ER complaining of headache, fever , the doctor found in his CSF sample: increased number of lymphocytes and mild change in glucose and protein levels. The most common organism causing this condition is:**

A. E.coli.
B. Streptococcus pneumonia.
C. Enterovirus.

- **The Pyogenic Meningitis's most common causative organism for Neonates?**

A. Klepsiella
B. E.coli.
C. Streptococcus pneumoniae
D. Neisseria

- **Hematogenous spread of CNS infections is most commonly by?**
  - Infective Endocarditis.