Pathology - Topic 34 - Central Nervous System

Meningitis

- Meningitis is inflammation of the leptomeninges and cerebrospinal fluid spaces.

Routes of Infection and Tissue Response

Definition and Routes of Infection

- Infection can reach these spaces through blood, spread from nearby tissue or enter after trauma or a procedure.

Barrier Injury and Neurological Complications

- Inflammation increases blood–brain barrier permeability and can impair CSF circulation.
- Raised intracranial pressure, vascular injury and neuronal damage account for many complications.

Clinical Context and Presenting Features

- The causative organisms vary with age, immune status, vaccination and exposure.
- Clinical features and laboratory tests must therefore be interpreted together.
    - Fever, headache, neck stiffness and altered consciousness are important features, but their absence does not exclude disease in every age group.

Major Infective Patterns

1. Acute Pyogenic Meningitis

Organisms and Gross Appearance

- Acute bacterial meningitis produces a neutrophil-rich exudate in the subarachnoid space.
- The meninges may be congested, opaque and covered by purulent material.
- Common organisms include pneumococcus and meningococcus in relevant populations.
- Group B streptococcus and Gram-negative organisms are important in neonates, while Listeria is relevant in selected older or immunocompromised patients.
- The list is not exhaustive, and prior antibiotics can alter both culture results and CSF appearance.

Microscopic Response and Clinical Consequences

- Microscopy shows neutrophils around meningeal vessels and within CSF spaces.
- Extension into vessels may cause thrombosis and cerebral infarction.
- Complications include hydrocephalus, ventriculitis, hearing impairment, seizures and neurological deficits.

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- Severe systemic infection may accompany the meningeal disease.

Vascular and Systemic Injury

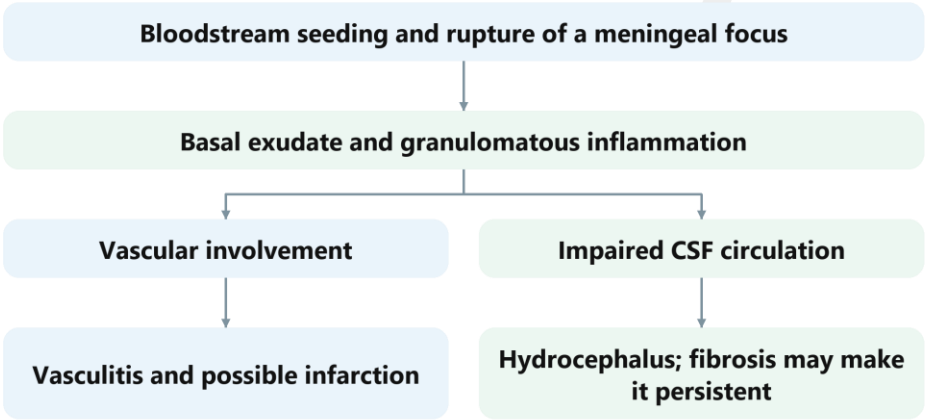
- Endothelial injury, inflammatory mediators and vasculitis impair cerebral perfusion while oedema raises intracranial pressure.
- Meningococcal bloodstream infection may produce purpura, shock and DIC; severe adrenal haemorrhage is classically associated with Waterhouse–Friderichsen syndrome.

2. Viral or Aseptic Meningitis

- Viral meningitis usually produces a mainly lymphocytic response without the thick purulent exudate of typical bacterial disease.
- Enteroviruses are important causes in many settings.
- The term **aseptic meningitis** describes a syndrome with negative routine bacterial cultures and is not identical to proven viral infection.
- Drugs, partially treated infection and other disorders can produce the same syndrome.
  - Early viral disease may initially show neutrophils, so one early cell count can be misleading.
- Many uncomplicated viral cases resolve without major damage, but outcome depends on the organism and whether brain tissue is also involved.

3. Tuberculous Meningitis

Tuberculous meningitis: pathways to major complications



- Tuberculous meningitis commonly follows rupture of a small focus near the meninges after previous bloodstream spread.
- It often produces a thick basal exudate.
- Granulomatous inflammation can involve vessels and cranial nerves.
- Vasculitis may cause infarction, while obstruction of CSF pathways can cause hydrocephalus.
  - The relatively gradual presentation can delay recognition.
  - Immunosuppressed patients may have less typical cellular responses.

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Basal Distribution

- The gelatinous exudate is particularly conspicuous around the basal cisterns, explaining involvement of traversing cranial nerves.
- Organisation and fibrosis can leave persistent communicating hydrocephalus even after the initial inflammatory burden has fallen.

4. Fungal Meningitis

- Fungal meningitis is important in patients with impaired immunity, although some fungi also affect immunocompetent people.
- Cryptococcus is a major cause.
- The inflammatory response may be scant in severe immunosuppression.
- Organisms and extracellular material can obstruct CSF absorption and raise intracranial pressure.
    - Cryptococcal antigen testing is more useful than relying on a negative India ink preparation, which has limited sensitivity.

Safety Before Lumbar Puncture

- If imaging or clinical findings suggest a mass lesion, obstructive hydrocephalus or dangerous pressure gradients, the safety and sequence of lumbar puncture require clinical assessment.
    - This matters because removing CSF in the presence of a major pressure gradient can precipitate herniation.

Interpreting Cerebrospinal Fluid

Core Measurements and Glucose Interpretation

- CSF assessment includes opening pressure, appearance, cell count and differential, protein, glucose and microbiological tests.
- Glucose is compared with a paired blood sample.
    - A ratio is often more informative than an isolated CSF glucose concentration because blood glucose affects the expected value.
- The normal CSF-to-blood glucose ratio is commonly about 0.5–0.8; a ratio of 0.4 or lower is abnormally low and supports bacterial, tuberculous or fungal causes in the appropriate setting.
- Reduced CSF glucose reflects disturbed transport and metabolic consumption during inflammation, whereas increased protein reflects barrier dysfunction and altered CSF circulation.

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Typical CSF Patterns and Their Limits

Typical pattern	Cells	Glucose and protein
Pyogenic bacterial	Neutrophils usually predominate.	Glucose is often low; protein is raised.
Viral	Lymphocytes usually predominate after the early phase.	Glucose is usually preserved; protein is mildly or moderately raised.
Tuberculous	Lymphocytes usually predominate.	Glucose is often low; protein can be markedly raised.
Fungal	Lymphocytes may predominate; cells can be few with immunosuppression.	Glucose may be low; protein is often raised.

- These are typical patterns rather than absolute rules.
- Early infection, partial treatment, severe immunosuppression and mixed disease can produce atypical results.
- A traumatic tap can add peripheral blood cells and protein; arithmetic correction does not replace interpretation of the clinical and microbiological findings.

Applying the CSF Pattern

- For example, 1,800 white cells/µL with 90% neutrophils, protein 180 mg/dL and CSF glucose 25 mg/dL with paired blood glucose 100 mg/dL gives a glucose ratio of 0.25.
- This combination strongly favours acute bacterial meningitis, but microbiological testing is needed to identify the organism and assess alternatives.

Etiological Tests and Viable-organism Recovery

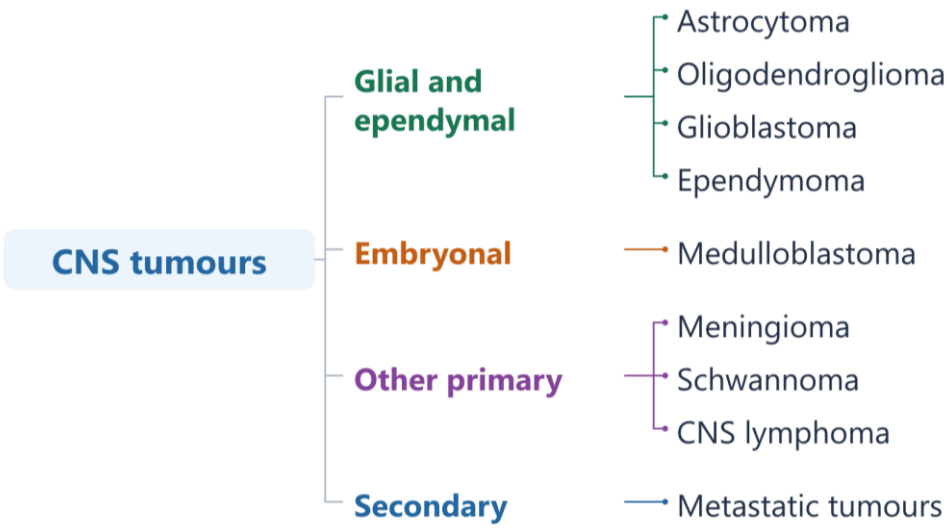
- Gram stain and culture can support bacterial diagnosis.
- Molecular assays, mycobacterial tests and fungal antigen tests are selected according to the suspected cause.
  - A negative smear does not exclude tuberculosis or fungal disease.
  - Culture and molecular tests have different sensitivities and turnaround times.
- Blood cultures can identify the organism when CSF sampling is delayed or CSF culture is negative.
  - A positive molecular result may persist despite reduced organism viability, whereas culture provides viable organisms for susceptibility assessment.

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Central Nervous System Tumours

- CNS tumours are classified using location, microscopic appearance and molecular features.

Classification and General Effects



Integrated Classification and Grade

- An integrated diagnosis can be more precise than morphology alone.
- Histological grade describes biological behaviour, but location also strongly affects outcome. A slowly growing tumour can still be dangerous if it obstructs CSF flow or compresses vital structures.

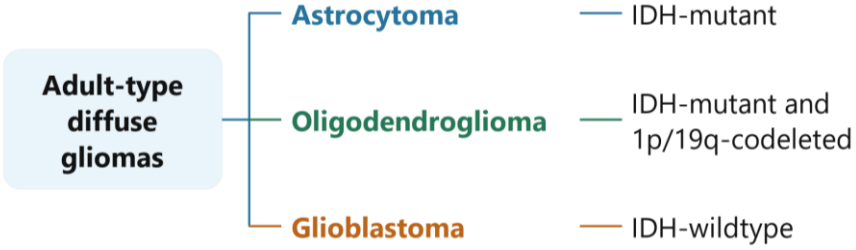
Mass Effect and Clinical Presentation

- The rigid skull limits expansion, so oedema and mass effect may produce more damage than tumour size alone suggests.
- Presentations include seizures, focal deficits, cognitive change, headache and features of raised intracranial pressure.
- Spinal lesions may cause pain, weakness or sensory and sphincter disturbance.

Routes of Spread and Metastatic Lesions

- Most primary CNS tumours spread locally or through CSF rather than widely outside the nervous system.
- Metastatic tumours from other organs are also important intracranial lesions.

Diffuse Gliomas



Molecular features define the principal adult-type diffuse glioma groups

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