CSF Abnormalities in Different Neurological Diseases

Essay

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In Neuropsychiatry

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تغيرات السائل النخاعى فى الأمراض العصبية المختلفة

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Introduction

Cerebrospinal fluid is Clear, colourless liquid that surrounds the brain and spinal cord and fills the spaces in them. It helps support the brain, acts as a lubricant, and maintains pressure in the skull ***(Johnston, 2003).*** It contains 15 to 45 mg/dl protein and 50-80 mg/dl glucose. Normal CSF contains 0-5 mononuclear cells. The CSF pressure, measured at lumbar puncture (LP), is 100-180 mm of H2O with the patient lying on the side ***(Ballabh et al., 2004).***

Cerebrospinal Fluid (CSF) provides a window into the changes that occur in the central nervous system (CNS) in health and disease. Through analysis of the CSF, we discern indirectly the state of health of the CNS, and correctly or incorrectly, draw conclusions regarding mechanisms of CNS injury and repair ***(Rammohan, 2009).***

Intracranial pressure monitoring is crucial to identify the problem and treat it right away. Raised intracranial pressure means that both nervous system (neural) and blood vessel (vascular) tissues are being compressed. If left untreated, it can result in permanent neurologic damage. In some cases, it can be fatal ***(Fletcher and Nathan, 2007).***

The study of markers of neurological diseases is a modern, important, and multidisciplinary field of science. Many recent reports have been focused on the search for changes in the contents of the CSF that are specific for some disease ***(Brylev, 2009).***

The CNS immune response often leads to characteristic interrelated biochemical changes in cerebrospinal fluid. Multiple analytes, i.e. cell count, cell differential, evaluation of barrier function and intrathecal IgG, IgA and IgM synthesis should be included in basic diagnostic workup ***(Regenitra et al., 2008).***

CSF proteins are used to determine the total protein content in the cerebrospinal fluid using the method of electrophoresis. Quantitative measures of CSF protein fractions aid in the diagnosis of inflammatory and demyelinating disease of CNS ***(Dohi et al., 2005).***

Detection of oligoclonal immunoglobulin bands in the CSF is now established as the single most useful laboratory marker in the CSF to aid in the diagnosis of multiple sclerosis ***(Rammohan, 2009)***.

When there are clinical indications for subarachnoid haemorrhage but no abnormalities on the CT-scan, it can be either demonstrated or excluded by means of spectrophotometric analysis of blood pigments in the CSF ***(Verbeek et al., 2005).***

Differential diagnosis of Alzheimer's disease (AD) and dementia with Lewy bodies (DLB) is often crucial. CSF Tau protein and Amyloid-beta (Aβ) peptides have shown diagnostic value for the diagnosis of AD, but discrimination from DLB was poor ***(Bibl et al., 2006).***

In the diagnostic workup of relatively young dementia patients, CSF Neurofilament levels may play a role in the discrimination between frontotemporal lobe degeneration and,

early onset Alzheimer's disease especially in combination with amyloid β42 protein and tau phosphorylated at threonine 181 analyses ***(De jong et al., 2007).***

Idiopathic normal pressure hydrocephalus is an important cause of dementia in the elderly; however, idiopathic NPH is often difficult to differentiate from normal aging and vascular dementias. In patients with idiopathic NPH, the CSF volume was significantly increased in the ventricles and decreased in the superior convexity and medial subarachnoid spaces as compared with patients with other dementias ***(Kitagaki et al., 1998).***

Chemokines are likely to contribute to the pathogenesis of chronic inflammatory demyelinating polyneuropathy (CIDP), as evidenced by data from experimental autoimmune neuritis. The α and β chemokines in the cerebrospinal fluid (CSF) and serum from patients with CIDP were analysed using an enzyme linked immunosorbent assay. CXCL9, CXCL10, and CCL3 were raised in the CSF in CIDP compared with controls and non-demyelinating neuropathies ***(Mahad et al., 2002)***.

Cerebrospinal fluid analysis and electrodiagnostic tests of nerves and muscles are common tests ordered in the diagnosis of Guillain Barre` Syndrome. Typical CSF findings include albumino-cytological dissociation. As opposed to infectious causes, this is an elevated protein level (100–1000 mg/dL), without an accompanying increased cell count pleocytosis. A sustained increased white blood cell count may indicate an alternative diagnosis such as infection ***(Kuwabara, 2004).***

Aim of the Work

The aim of this study is to highlight the role of CSF study in diagnosis and hence treatment of different neurological diseases.

Chapter (1)
CSF Circulation & its Analysis, Normal Findings

Anatomy of CSF

Cerebrospinal fluid (CSF) is a clear bodily fluid that occupies the subarachnoid space and the ventricular system around and inside the brain (the brain "floats" in it). It occupies the space between the arachnoid mater and the pia mater. It constitutes the content of all intra-cerebral ventricles, cisterns, and sulci, as well as the central canal of the spinal cord ***(Zakharov et al., 2003)***.

Seventy percent of CSF is produced by the choroid plexus in the fourth, third, and lateral ventricles, at a rate of 0.2 to 0.4 cm3/min or 300 to 500 cm3/day. 20% of CSF is produced by capillary ultrafiltrate, and 10% is produced by water metabolism. In adults the average CSF volume is 90 to 150 cm3, with 40 cm3 in the lateral ventricles ***(Moza et al., 2005).***

CSF circulation

CSF flows from its production sites in the two lateral ventricles through the foramina of Monro into the third ventricle and then to the fourth ventricle through the aqueduct of Sylvius which then continues and communicates with the cisterna magna through the midline foramen of Magendie and

the two lateral foramina of Luschka. Then it flows dorsally into the subarachnoid space of the cerebellum, caudally into the spinal subarachnoid space, and rostrally into several subarachnoid cisterns of the brain (pontis, interpeduncularis, ambiens, and the suprasellar), from these cisterns the CSF reaches the subarachnoid space of the cerebral hemispheres (figure 1) ***(Han and Backous, 2005).***

It had been thought that CSF returns to the vascular system by entering the dural venous sinuses via the arachnoid granulations or villi. However, some have suggested that CSF flow along the cranial nerves and spinal nerve roots allow it into the lymphatic channels ***(Zakharov et al., 2003)***.

CSF analysis

CSF analysis is a set of laboratory tests that examine a sample of the fluid surrounding the brain and spinal cord,the purpose of its analysis is to diagnose medical disorders that affect the central nervous system(CNS) ***(Griggs et al., 2007).***

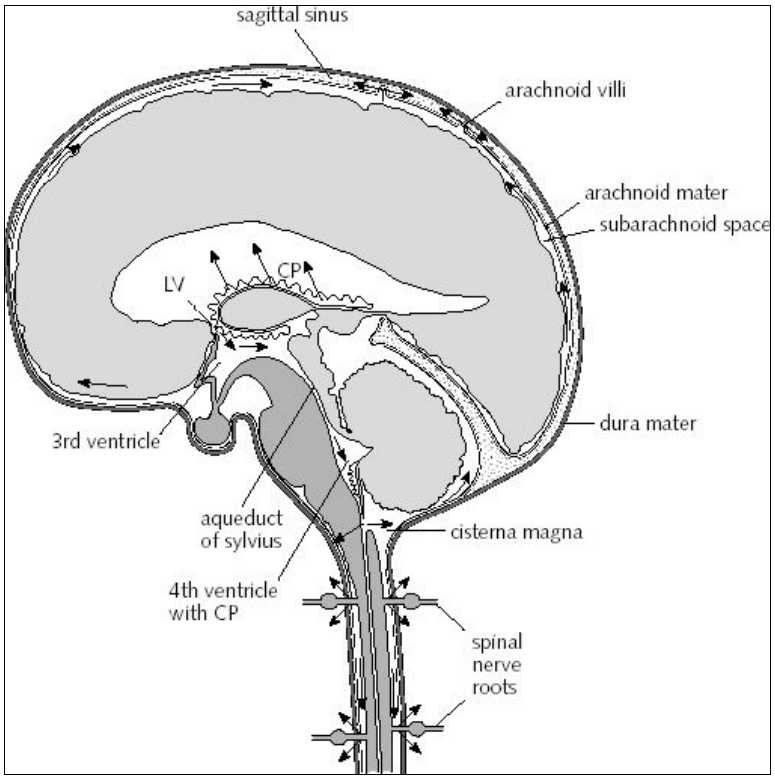

Figure (1): A diagrammatic vertical section through the brain showing the location of the ventricles and the direction of flow of CSF ***(Han and Backous, 2005).***

CSF collection

There are different ways to get a sample of CSF. Lumbar puncture (LP) is the most common method. The test is usually done like this:

- The patient lies on his side, with knees pulled up toward the chest, and chin tucked downward. Sometimes the test is done with the person sitting up, but bent forward.
- After the back is cleaned by agerm cleaning solution, a local numbing medicine (anesthetic) is injected into the lower spine.
- Locate the L3-L4 interspace by palpating the right and left posterior superior iliac crests and moving the fingers

medially toward the spine.Palpate that interspace (L3-L4) as well as one above (L2-L3) and one below (L4-L5) to find the widest space then a spinal needle is inserted (figure 2).

- Once the needle is properly positioned, CSF pressure is measured and a sample is collected.
- The needle is removed, the area is cleaned, and a bandage is placed over the needle site. The person is often asked to lie down for a short time after the test. Occasionally, special x-rays are used to help guide the needle into the proper position. This is called fluoroscopy.

(Farley and McLafferty, 2008)

Alternative methods of CSF collection are rarely used, but may be necessary if the person has a back deformity or an infection as follows:

1. Cisternal puncture using a needle placed below the occipital bone.It can be dangerous because it is so close to the brain stem. It is done with fluoroscopy.
2. Ventricular puncture (rare), but may be recommended in people with possible brain herniation. It is usually done in the operating room. A hole is drilled in the skull, and a needle is inserted directly into one of brain's ventricles.
3. CSF may also be collected from a tube that's already placed in the fluid (shunt or a ventricular drain). These sorts of tubes are usually placed in the intensive care unit.

(Nathan, 2003)

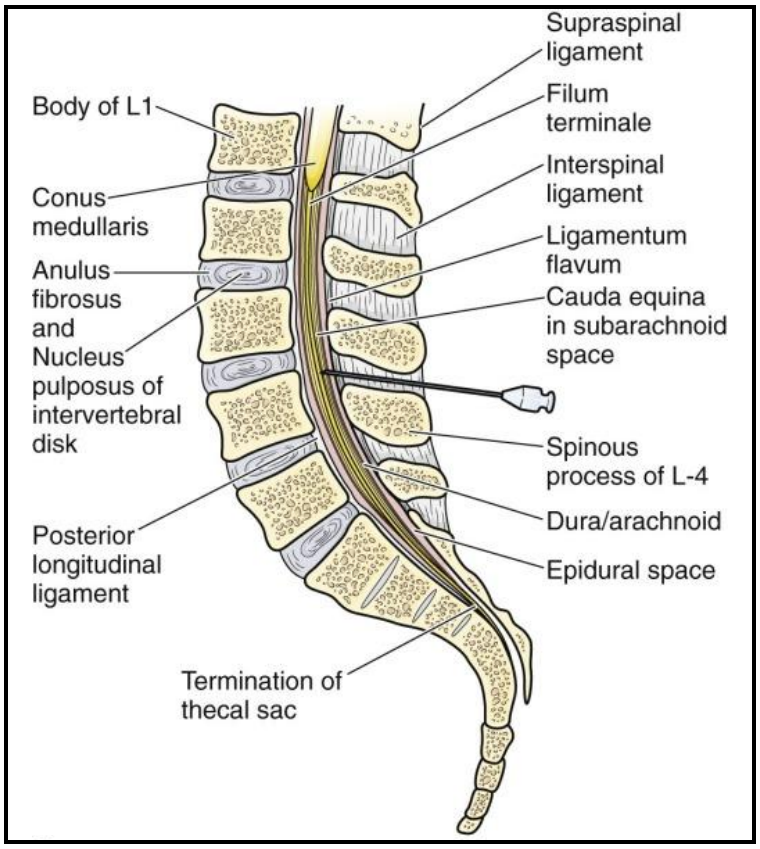

Figure (2): Midsagittal section through the lumbar spinal column with a spinal puncture needle in place between the spinous processes of L3 and L4. Note the slightly ascending direction of the needle. The needle has pierced three ligaments and the dura/arachnoid and is in the subarachnoid space ***(Farley and McLafferty, 2008).***

Risks

- Bleeding.
- Brain herniation or injury from the increased pressure.
- Damage to the brain tissue with continued neurologic effects.
- Inability to find the ventricle and accurately place catheter.
- Infection.
- Risks of general anesthesia ***(Fletcher and Nathan, 2007).***

Indications of CSF analysis

-High specificity:

- Bacterial, tuberculous, and fungal meningitis

-High sensitivity, moderate specificity:

- Viral meningitis
- Subarachnoid hemorrhage
- Multiple sclerosis
- Central nervous system syphilis
- Infectious polyneuritis
- Paraspinal abscess

-Moderate sensitivity, high specificity:

- Meningeal malignancy

-Moderate sensitivity, moderate specificity:

- Intracranial hemorrhage
- Viral encephalitis
- Subdural hematoma ***(Karcher and McPherson, 2011).***

N.B

Sensitivity is the proportion of true positives that are correctly identified by the test while specificity is the proportion of true negatives that are correctly identified by the test ***(Altman and Bland, 1994).***

Contraindications to CSF analysis

Absolute contraindications to lumbar puncture are as follows:

1. Unequal pressures between the supratentorial and infratentorial compartments, usually inferred by characteristic findings on the brain CT scan:
   -Midline shift
   -Loss of suprachiasmatic and basilar cisterns
   -Posterior fossa mass
   -Loss of the superior cerebellar cistern
   -Loss of the quadrigeminal plate cistern
2. Infected skin over the needle entry site

Relative contraindications to lumbar puncture are as follows:

1. Increased intracranial pressure (ICP)
2. Coagulopathy
3. Brain abscess (***Farley and McLafferty, 2008).***

CSF normal findings

-Gross appearance: CSF is clear and colorless.

-CSF opening pressure: 10 -100 mm H_2O (in young children), 60–200mm H_2O (in adults) and up to 250 mm H_2O in obese patients.

-Specific gravity: 1.006–1.009.

-Glucose: 40–80 mg/dL.

CSF glucose is about two thirds of the serum glucose measured during the preceding two to four hours in a normal adult ***(Seehusen et al., 2003)***.

-Total protein: 15–45 mg/dL.

-Lactate dehydrogenase (LD): 1/10 of serum level.

-Lactate: less than 35 mg/dL.

-Leukocytes (white blood cells): 0–5/microL (adults and children); up to 30/microL (newborns).

Differential: 60–80% lymphocytes; up to 30% monocytes and macrophages; other cells 2% or less. Monocytes and macrophages are somewhat higher in neonates.

-Gram stain: negative.

-Culture: sterile.

-Syphilis serology: negative.

-Red blood cell count: normally, there are no red blood cells in the CSF unless the needle passes through a blood vessel on route to the CSF ***(Griggs et al., 2007).***

Chapter (2)
Disorders of CSF Pressure

Opening pressures above 250 mm H2O are diagnostic of intracranial hypertension. Intracranial hypotension is defined as an opening pressure of less than 60 mm H2O ***(Seehusen et al., 2003).***CSF pressure should be measured with the patient in the lateral recumbent position with a manometer attached to narrow-bore spinal needle (to minimize the leakage of CSF in LP) ***(Beri et al., 2010).***

The ICP wave has a pulsatile quality at two different frequencies; one synchronous with the arterial pulse while the other is slower, in time with breathing. The shape of the CSF pressure wave is similar to that of systemic blood pressure and it has three fairly consistent components, the 'percussion wave' (P1), 'tidal wave' (P2) and 'dicrotic wave' (P3) (fig 3) ***(Czosnyka et al., 1996).*** These waveforms provide valuable information regarding compliance of the CSF system, its absorption capacity; it can predict impending neurologic decompensation and herniation ***(Wartenberg et al., 2007).***

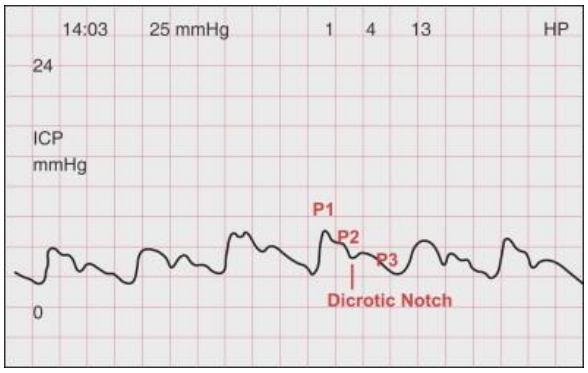

Figure (3): Example of intracranial pressure waveforms. P1, percussion wave with a sharp and constant amplitude; P2, tidal wave (ends at the dicrotic notch); P3, dicrotic wave ***(Czosnyka et al., 1996).***