Normal pressure hydrocephalus (NPH)

What is normal pressure hydrocephalus (NPH)?

Normal pressure hydrocephalus (NPH) describes the condition of ventricular dilatation in the absence of raised CSF pressure on a lumbar puncture (also known as a spinal or CSF tap), characterised by a **triad of gait abnormality, urinary (usually) incontinence and dementia**. The importance of this diagnosis lies in the fact that it is a potentially reversible cause of dementia, accounting for up to 6% of dementias [1] .

It was first described by Hakim and Adams in 1965. The three patients identified in the original series had dilation of the cerebral ventricles without an increase in CSF pressure on lumbar puncture.

The pathogenesis of idiopathic normal pressure hydrocephalus (iNPH) is still unclear but the current expert opinion is that ventriculomegaly resulting from cerebrospinal fluid (CSF) dynamics may initiate a vicious cycle of injuries in iNPH [2] . Pathophysiological factors including hypoperfusion, glymphatic impairment, disturbance of metabolism, astrogliosis, neuroinflammation, and blood-brain barrier disruption contribute to the formation of white and grey matter lesions, and later cause the typical symptoms.

Aetiology [3]

There are two forms of normal pressure hydrocephalus:

1. Idiopathic (primary) NPH - there is no identifiable cause (in approximately 50% of cases).

2. Symptomatic (secondary) NPH - this may be secondary to:

    - Subarachnoid haemorrhage.
    - Meningitis.
    - Head injury.
    - Central nervous system (CNS) tumour.

Common features of iNPH and secondary normal pressure hydrocephalus are that both are communicating types of hydrocephalus and both carry a similar prognosis. The significant difference between them is that secondary NPH affects persons of all ages, while iNPH is mainly a disease of the elderly.

All these conditions can cause hydrocephalus but the pathological process which leads to NPH is not clear. These patients must be differentiated from patients whose ventricular enlargement is a result of shrinkage of surrounding tissue, as in Alzheimer's disease, for example.

Epidemiology

In a population-based study from western Sweden, the prevalence of iNPH was estimated at 0.2% (200 out of 100,000 individuals) in the age group of 70-79 years, and 5.9% (5,900 out of 100,000 individuals) for age 80 years and older [4] . In the same geographic area, the incidence of patients with iNPH who were treated with a CSF shunt was about only two to three operations per 100,000, which implies that iNPH may be underdiagnosed.

The average age of onset is approximately 70 years, and men and women are affected in equal numbers [3] . Idiopathic NPH is thought to account for roughly 6% of all cases of dementia.

Normal pressure hydrocephalus (NPH) symptoms [5]

The (gradually progressive) classic Hakim-Adams triad of NPH symptoms is:

- **Gait disturbance** - this is usually the first symptom and is due to distortion of the corona radiata by the dilated ventricles. This area contains the sacral motor fibres that innervate the legs. Movements are slow, broad-based and shuffling. The clinical impression is thus one of Parkinson's disease, except that rigidity and tremor are less marked and there is no response to carbidopa/levodopa. Freezing episodes can also occur. True ataxia and weakness are absent and the gait disturbance is referred to as gait apraxia.
- **Sphincter disturbance** - this is also due to involvement of the sacral nerve supply. Urinary incontinence is predominant although bowel incontinence can also occur.
- **Dementia** - this is due to distortion of the periventricular limbic system. The prominent features are memory loss, inattention, inertia and bradyphrenia (slowness of thought). Their disorientation is more in time rather in space. Often it is difficult for patients to set out the history of their case.The dementia progresses less rapidly than that seen with Alzheimer's disease.

One of the frequent complaints in patients suffering from NPH is dizziness, which they describe as a sense of instability in movement - eg, in sharp bends of the trunk. The following set of symptoms related to lower extremities occurs in more severe cases: spasticity, sudden 'freezing' and hyperreflexia.

Signs

- Pyramidal tract signs may be present.
- Reflexes may be brisk.
- Papilloedema is absent (but there has been found to be an association with glaucoma, so glaucomatous optic disc changes may be noticed) [6] .

Investigations

- **Neuroimaging**. MRI or CT scanning may show ventricular enlargement out of proportion to sulcal atrophy and periventricular lucency. Isotope cisternography may also be useful to demonstrate CSF dynamics, particularly when attempting to predict which patients will benefit from surgery[7] .
- **Large-volume lumbar puncture (spinal or CSF tap test)**[8] . CSF pressure will be normal, or mildly elevated[9] . The value of this test is limited in diagnosing NPH but may be useful in narrowing the differential diagnosis.
- **Intraventricular pressure monitoring**.
- **Lumbar infusion test (intrathecal infusion test)**[8] . The CSF absorptive capacity is tested with a fluid challenge. An abnormal, sustained rise in CSF suggests NPH.

Although the invasive tests carry theoretical risks (infection, post-procedure headache, bleeding, localised pain and nerve root damage), evidence suggests that these are actually very safe procedures[8] . In these patients, it is also useful to check the serum sodium, as hyponatraemia has been reported[10] .

Diagnosis[11]

In order to meet the requirements for possible iNPH a person must have:

- More than one symptom in the clinical triad: gait disturbance, cognitive impairment, and urinary incontinence, and these symptoms cannot be completely explained by other neurological or non-neurological disease and other diseases possibly causing ventricular dilation are not obvious.
- A CSF pressure of 200 mm H_2O or less and normal CSF content.

- One of the following two investigational features:
    - Neuroimaging features of narrowing of the sulci and subarachnoid space over the high-convexity/midline surface (DESH) with gait disturbance: small stride, shuffle, instability during walking, and increase in instability on turning.
    - Improvement of symptoms after CSF tap test and/or drainage test[8] . This category is synonymous with 'shunt responder'.

Differential diagnosis[9]

- Alzheimer's disease.
- Aphasia.
- Apraxia and related syndromes.
- Confusional states and acute memory disorders.
- Cortical basal ganglionic degeneration.
- Dementia with Lewy bodies.
- Dementia in motor neurone disease.
- EEG in dementia and encephalopathy.
- Frontal lobe syndromes.
- Frontotemporal dementia (Pick's disease).
- Hydrocephalus.
- Marchiafava-Bignami syndrome (gait disturbance and dementia, usually in people with alcohol dependence, thought to be due to bilateral reduction cerebral blood flow).
- Multi-infarct dementia.
- Multiple system atrophy.
- Paraneoplastic encephalomyelitis.
- Parkinson's disease.
- Parkinson-plus syndromes.

- Uraemic encephalopathy .
- Wilson's disease.

Normal pressure hydrocephalus (NPH) treatment

The identification and treatment of normal pressure hydrocephalus (NPH) is worthwhile, providing patients are carefully selected, as it remains one of the truly reversible causes of dementia.

Medical

Medical treatment of NPH includes carbonic anhydrase inhibitors (acetazolamide) and repeated lumbar puncture. These methods are rarely successful long-term. Carbonic anhydrase inhibitors and serial lumbar punctures are not advisable as alternative treatments, except for a limited time in medically inoperable patients [9] .

Surgical

The mainstay of treatment is surgical insertion of a CSF shunt [8] [11] . This could be to the peritoneum, the right atrium or, more recently, via external lumbar drainage. Selection of patients for surgery is important, as exposing patients to shunt-related complications such as mechanical failure or infection is unwarranted, unless a good clinical outcome is expected. Various parameters are used to predict which patients will benefit from surgery but there is insufficient evidence for their efficacy.

Insertion of a ventriculoperitoneal shunt is the first-line procedure, with ventriculo-atrial shunting being used as an alternative.

Complications of shunt surgery

These are found in up to 10% and include [11] :

- Shunt occlusion
- Catheter breakage
- CSF hypotensive headaches
- Cerebral infarct
- Haemorrhage

- Infection
- Seizures
- Death

Prognosis

Properly selected patients have an 80% to 90% chance of responding to shunt surgery, and all symptoms can improve following shunt surgery [4] . Early treatment within three months of diagnosis is associated with better outcomes [12] .

The combined rate of permanent neurological deficit or death has been reported as 6%, with the need for additional surgery occurring in 22% [1] [13] .

Further reading

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