The Diminishing Role of Biochemistry in Subarachnoid Haemorrhage Diagnosis

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Abstract:

The incidence of subarachnoid haemorrhage (SAH) is 24.6 per 100,000 population. Case fatalities are about 44% in Europe. SAH is misdiagnosed in 12.50% of cases. Non-contrast CT scanning is positive in 96% of patients with SAH who present within 12 hours of the bleed. There is a rapid clearance of subarachnoid blood over time and after one week, the diagnostic sensitivity of CT scanning may be only about 50%. CSF xanthochromia should be sought in patients with suspected SAH and negative CT scans. Red blood cells in the CSF lyse and oxyhaemoglobin, methaemoglobin and bilirubin are produced. False positives for xanthochromia may occur in the spectrophotometric analysis of CSF due to a traumatic spinal tap, hyperbilirubinaemia >325 mol/l, hyperproteinaemia >150 mg/dl and rifampicin. National guidelines on detection of xanthochromia in CSF in suspected SAH have been published in the US and in the UK. Best laboratory practice dictates a minimum of 25 specimens annually.

Non-contrast enhanced CT is the initial investigation of choice with a normal cranial CT scan, a lumbar puncture for blood and xanthochromia is required but not before 12 hours from the signature event. This usually occurs in about 5% of patients. CT angiography (CTA) after an intravenous injection of contrast, magnetic resonance angiography (MRA) and direct intra-arterial catheterisation angiography is the hierarchy for identification, quantification or rule out of an intracranial aneurysm. Sensitivities and specificities depend on the anatomical size of the aneurysms. CTA has reported sensitivities of 0.77 to 0.97 and specificities from 0.87 to 1.00. With aneurysms smaller than 3 mm, CTAs sensitivities range from 0.40 to 0.91. MRA shows sensitivities 0.69 to 0.99 and specificity of 1.00. For small aneurysms under 3 mm, the sensitivity may be as low as 0.38. High quality angiography is usually diagnostic but is invasive with potential for femoral artery injury and renal toxicity. False positive non-contrast CT may occur in cases where a large volume of contrast is used in cardiac angiography and in rare cases of meningitis.

The place of CSF spectrophotometry in the investigation of acute headache in which SAH is a differential appears to be (a) When the initial cranial non-contrast CT is negative (b) When there is a suspicion of a false negative or equivocal initial CT scan. (c) When there is a delay in diagnosis for up to three weeks and the CT is negative but clinical suspicion remains. (d) When the CT and CTA are negative and suspicion remains.

The use of a modified serum bilirubin assay to measure CSF bilirubin as a screening test to select samples for spectrophotometry has been mooted but the effects could be to force CSF spectrophotometry into a few centres which might slow the referral of patients from peripheral hospitals to specialist neurosurgical centres. CSF bilirubin at a cut-off of 359 nmol/l has a reported sensitivity of 100%, a specificity of 92.2% and a predictive value of 100%. Thus it identifies those samples which need to be scanned and eliminates the need in most others. CSF ferritin at a level of 6.4 µg/L could be used adjunctively for its negative predictive value only. However, there is another view. Patients with raised CSF bilirubin should be sent to specialist centres for CT or MRA rather than suffer delay because CSF samples are sent for spectrophotometric scanning at reference or specialist laboratories. In Ireland, Beaumont and Cork University hospitals provide CSF scanning spectrophotometry. Both have specialist centres. In appropriate circumstances, both the patient and sample should be sent to the specialist centres.

At Beaumont hospital, CSF spectrophotometric scans are done in patients with equivocal (25%) or negative non-contrast CT scans and headache 75%, fit or stroke symptom 25%. A family history of SAH lowers the threshold for investigation in headache.

WP Tormey, D McBrierty, P O'Shea
Beaumont Hospital, Beaumont, Dublin 9
Email: billtormey@gmail.com

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Comments: