Cerebrospinal fluid analysis for Creutzfeldt-Jakob Disease Diagnosis

Cerebrospinal fluid 14-3-3 protein detection remains an important test in the Creutzfeldt-Jakob Disease Diagnosis. Due to a loss in specificity in acute neurological events, the interpretation of positive 14-3-3 results needs to be performed in the clinical context.

a) routine labs: usually normal, although protein may occasionally be elevated

b) abnormal proteins:

● abnormal proteins (designated 130 & 131) have been identified in the CSF of patients with Creutzfeldt-Jakob Disease, [1] but the assay is technically difficult and is therefore not practical for routine clinical use

● proteins 130/131 were identified as the normal neuronal protein 14–3-3, and a relatively simple immunoassay for this was developed for use on as little as 50 mcl of CSF [2]

Detection of the 14–3-3 protein in the CSF has 96% sensitivity and specificity for CJD among patients with dementia. False positives may occur in other conditions involving extensive neuronal destruction including acute stroke, herpes encephalitis, multi-infarct dementia, primary CNS lymphoma, and rarely SDAT (most cases of SDAT test negative). Requires CSF (cannot be done on blood).

CSF was tested for 14-3-3, Tau, NSE, and S100b in 1,859 patients with sporadic, genetic, iatrogenic, and variant CJD, and in 1,117 controls.

Results: The highest sensitivity was achieved for 14-3-3 and Tau in sporadic CJD (85% and 86%), and a combined determination of 14-3-3 and Tau, S100b, or NSE increased the sensitivity to over 93%. Multivariate analysis showed that the sensitivity of all tests was highest in patients with the shortest disease duration, age at onset >40 years, and homozygosity at codon 129 of the prion protein gene. In a group of patients with repeated lumbar punctures, a second test also increased the diagnostic sensitivity.

Conclusions: The detection of elevated levels of brain-derived proteins in the CSF in patients with suspected Creutzfeldt-Jakob disease is a valuable diagnostic test. A second lumbar puncture may be of value in patients with atypical clinical course in whom the first test was negative [3].

1)
Harrington MG, Merril CR, Asher DM, et al. Abnormal Proteins in the Cerebrospinal Fluid of Patients with Creutzfeldt-Jakob Disease. N Engl J Med. 1986; 315:279–283
2)
Hsich G, Kenney K, Gibbs CJ, et al. The 14-3-3 Brain Protein in Cerebrospinal Fluid as a Marker for Transmissible Spongiform Encephaloptahies. N Engl J Med. 1996; 335:924–930
3)
Sanchez-Juan P, Green A, Ladogana A, Cuadrado-Corrales N, Sáanchez-Valle R, Mitrováa E, Stoeck K, Sklaviadis T, Kulczycki J, Hess K, Bodemer M, Slivarichová D, Saiz A, Calero M, Ingrosso L, Knight R, Janssens AC, van Duijn CM, Zerr I. CSF tests in the differential diagnosis of Creutzfeldt-Jakob disease. Neurology. 2006 Aug 22;67(4):637-43. doi: 10.1212/01.wnl.0000230159.67128.00. PMID: 16924018.