ALZHEIMER DISEASE

Frontal cortex biopsy samples can predict Alzheimer disease

The presence of both amyloid- β (A β) and hyperphosphorylated tau in frontal cortex biopsy samples is a strong indicator of future Alzheimer disease (AD), according to a new study. “The fact that A β from living brain tissue predicts the development of clinical AD is in line with the amyloid hypothesis, postmortem studies and molecular imaging,” says Ville Leinonen, lead author of the new study. However, “many patients with A β develop a clinical dementia other than AD.”

Brain A β deposition is widely believed to be an early event in AD, and A β plaques, along with intracellular neurofibrillary tangles, which largely comprise hyperphosphorylated tau, are considered to be neuropathological hallmarks of this disorder. Owing to safety issues linked to brain biopsies, few studies have directly verified the existence of plaques and neurofibrillary tangles in living patients. Indeed, a definite diagnosis of AD can only be confirmed at autopsy.

Leinonen and colleagues obtained frontal cortex biopsy samples from 433 patients

with suspected normal pressure hydrocephalous during 24 h intracranial pressure monitoring involving an intraventricular catheter. The researchers conducted immunohistochemistry on the brain tissue, and examined the relationship between A β and hyperphosphorylated tau immunoreactivity in the biopsy samples and the subsequent development of AD in these patients (median follow-up period of 4.4 years).

Among the biopsy samples analyzed, 10% exhibited both A β and tau immunoreactivity, 33% showed only A β pathology, and 57% had neither A β nor tau aggregates. Of the 433 study participants, 94 developed AD and 167 developed non-AD dementia over the follow-up period.

The presence of both A β and tau immunoreactivity in brain biopsy samples was strongly associated with a diagnosis of AD (odds ratio [OR] 68.2, 95% CI 22.1–210). Moreover, the presence of both pathologies conferred high specificity (98%) for this disease, although the

sensitivity of the combined markers for AD was low (36%). A β immunoreactivity alone also showed a notable association with AD (OR 10.8, 95% CI 4.9–23.8) and exhibited high sensitivity (87%) for this disease. This marker had, however, a lower specificity (69%) for AD than did the combination of both pathologies. The absence of both A β and tau immunoreactivity was associated with a low probability of developing AD.

The researchers argue that their results support the concept of preclinical AD, and that brain biopsies may be useful for identification of novel markers of this disease in a research setting. Nevertheless, the investigators stress that in the clinic and in therapeutic trials, noninvasive techniques should still be preferred to brain biopsies for patient diagnosis.

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