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Early Juvenile Neuronal Ceroid-lipofuscinosis or Variant Jansky–Bielschowsky Disease: Diagnostic Criteria and Nomenclature

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In 1978 Lake and Cavanagh published a series of five patients under the title 'Early juvenile Batten disease – A recognizable subgroup distinct from other forms of Batten disease'. The age at onset of the disease was 5–6 years, the course was rapid in all cases, and four out of the five patients already showed ataxia at the onset of the disease. All patients showed positive intermittent spikes during photic stimulation (PIPS), highly enlarged visual evoked potential (VEP) and also highly enlarged cortical somatosensory evoked potential (SEP), i.e. neurophysiological findings characteristic of Jansky–Bielschowsky disease (JBD) (Harden and Pampiglione 1982). The electroretinogram was abolished and electron microscopy (EM) showed fingerprint bodies.

Later Santavuori et al (1982, 1991) described 22 patients with onset between 4.5 and 7 years and showing both clinical and neurophysiological features suggesting LINCL or JBD. Our team suggested that the spectrum of JBD is wider than has previously been thought and preferred to call the disorder variant JBD (Santavuori et al 1991).

The early psychomotor development was normal in all our variant JBD patients. Only a few of the children showed slightly retarded speech development, as has also been found in the classical type of JBD. Motor clumsiness, slight problems in standing on one foot (but not real ataxia) and slight mental retardation in addition to slight visual failure (not in all cases) were obvious at the first examination. Ataxia, myoclonia and epilepsy developed 2–5 years after the onset of the disease. Between the ages of 9 and 10.5 years ataxia became marked and walking difficult or impossible. The children were mostly still able to see at a relatively long distance when playing. Athetosis was already present at this age, or developed later. Speech was severely dysarthric. Thus at this stage the clinical picture differed significantly from that seen in JNCL, including JNCL children with rapid progression.

The diagnostic neurophysiological triad (giant VEP and SEP and PIPS in the EEG) (Santavuori et al 1991) usually became evident between 7.5 and 10.5 years of age, sometimes even earlier (Santavuori et al 1982). In one case PIPS were seen in

one single EEG at the age of 10.5 years. Very careful follow-up studies and evoked potential studies are necessary in order not to miss the diagnosis.

At an early stage, especially if ophthalmological findings (slight visual failure, macular degeneration, abnormal ERG) were absent, only MRI and SPECT were able to reveal the character of the progressive brain disorder (Santavuori et al 1991). In our most recent case MRI showed hyperintense zones in the white matter around the lateral ventricles at the age of 6.6 years. The thalami and posterior putamina were hypointense. Slight supra- and moderate infratentorial atrophy was seen. The same MR pattern was seen in four older patients, though with more pronounced findings (Autti et al 1992). It seems likely that in variant JBD patients MRI findings become evident at an early stage of the disease.

The combination of intensity changes in MRI and lack of attenuation changes in CT differentiates variant JBD from sphingolipidoses and other progressive encephalopathies including JNCL (Autti et al 1992; Autti et al unpublished).

Our youngest patient, aged 6.6 years, showed early onset of cerebellar involvement in ^{99m}Tc-HMPAO SPECT (Santavuori et al 1991). An additional four patients, aged between 7 and 9 years, showed moderate or severe cerebellar hypoperfusion (Autti et al 1992). The SPECT findings in variant JBD differ significantly from those seen in JNCL (Heiskala et al, submitted).

Vacuolated lymphocytes have never been found, either in the Finnish patients or in those described in the literature. Electron microscopy of biopsy specimens of various organs and lymphocytes showed inclusions with fingerprint and curvilinear patterns (Santavuori et al 1982, 1991).

Preliminary DNA-linkage data have excluded variant JBD at the JNCL locus (Järvelä, personal communication).

It is obvious that our patients and those of Lake and Cavanagh differ from classical LINCL and JNCL. The same applies to the patients described by Tackman et al (1979) and Kimura and Goebel (1987), although the clinical onset in the latter cases was earlier. The age at onset falls within the range of JNCL, but the clinical manifestations, the course and the neurophysiological findings are very close to LINCL or classical JBD. We agree with Zeman et al (1970) that the clinical manifestations and the course of the disease are important for the classification, while age at diagnosis and the histopathological or electron-microscopic details are of less importance. We emphasize the role of the neurophysiological and imaging findings as complementary, as they closely reflect the neuropathological changes in the central nervous system. We have therefore chosen to classify these patients as variant Jansky–Bielschowsky rather than early juvenile NCL.

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