Neural autoantibody testing for autoimmune encephalitis

Serum and available cerebrospinal fluid (CSF) specimens were tested using a standardized indirect immunofluorescence assay utilizing a composite of mouse tissues (brain, kidney and gut) for IgGs binding selectively to neuronal and glial nuclei (antineuronal nuclear antibody type 1 [ANNA-1 or anti-Hu], type 2 [ANNA-2 or anti-Ri], and type 3 [ANNA-3], antiglial and/or neuronal nuclear antibody type 1 [AGNA-1], and kelch-like protein 11 [KLHL11]), neuronal cytoplasmic elements (PCA [types 1 and 2, also known as Yo and microtubule associated protein 1B respectively], collapsin-response mediator protein 5 [CRMP-5], and amphiphysin), neural filaments (glial fibrillary acidic protein, and neuronal intermediate filaments) or receptors (n-methyl-D-aspartate [NMDA], α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid [AMPA], ɣ amino butyric acid-B [GABA-B], delta-notch epidermal-like growth factor–related receptor [DNER, also known as PCA-Tr] and metabotropic glutamate receptor 1 [mGluR1]) and dipeptidyl peptidase like 6 (DPPX). The reference values for all antibodies were less than 1:240 in serum and less than 1:2 in CSF. Serum samples were tested by radioimmunoprecipitation assays for antibodies reactive with P/Q type calcium channels and glutamic acid decarboxylase 65-kDa isoform (GAD65). Reference values for all antibodies were ≤0.02 nmol/L. Cell-based assays (Euroimmun, AG, Lubeck, Germany) were also used to screen for autoantibodies reactive with NMDA-R, AMPA-R, GABA-B-R, DPPX, and mGluR1, leucine-rich glioma inactivated 1 (LGI1) and contactin-associated protein-like 2 (CASPR2).

Diagnostic criteria for possible autoimmune encephalitis

Diagnosis can be made when all three of the following criteria have been met:

1. Subacute onset (rapid progression of less than 3 months) of working memory deficits (short-term memory loss), altered mental status, or psychiatric symptoms
2. At least one of the following:
    - New focal CNS findings
    - Seizures not explained by a previously known seizure disorder
    - CSF pleocytosis (white blood cell count of more than five cells per mm^3)
    - MRI features suggestive of encephalitis
3. Reasonable exclusion of alternative causes

Diagnostic criteria for definite autoimmune limbic encephalitis

Diagnosis can be made when all four of the following criteria have been met:

1. Subacute onset (rapid progression of less than 3 months) of working memory deficits, seizures, or psychiatric symptoms suggesting involvement of the limbic system
2. Bilateral brain abnormalities on T2-weighted fluid-attenuated inversion recovery MRI highly restricted to the medial temporal lobes
3. At least one of the following:
    - CSF pleocytosis (white blood cell count of more than five cells per mm^3)
    - EEG with epileptic or slow-wave activity involving the temporal lobes

4. Reasonable exclusion of alternative causes

Criteria for autoantibody-negative but probable autoimmune encephalitis

Diagnosis can be made when all four of the following criteria have been met:

1. Rapid progression (less than 3 months) of working memory deficits (short-term memory loss), altered mental status, or psychiatric symptoms
2. Exclusion of well-defined syndromes of autoimmune encephalitis (e.g, typical limbic encephalitis, Bickerstaff's brainstem encephalitis, acute disseminated encephalomyelitis)
3. Absence of well characterized autoantibodies in serum and CSF, and at least two of the following criteria:
    - MRI abnormalities suggestive of autoimmune encephalitis
    - CSF pleocytosis, CSF-specific oligoclonal bands or elevated CSF IgG index, or both
    - Brain biopsy showing inflammatory infiltrates and excluding other disorders (eg, tumour)
4. Reasonable exclusion of alternative causes