WHAT IS AUTOIMMUNE ENCEPHALOPATHY?

Autoimmune encephalopathies extend beyond the recognized clinical and radiological spectrum of “limbic encephalitis.” The diversity of presentations includes a subacute or insidious onset of confusional state, psychosis, delirium, memory loss, hallucinations, movement disorder, sensory or motor complaints, seizures, dyssomnia, ataxia, eye movement problems, nausea, vomiting, inappropriate antidiuresis, coma, dysautonomia or hypoventilation.

Importantly, some cases are paraneoplastic.

CLUES HELPFUL FOR IDENTIFYING PATIENTS WITH AN AUTOIMMUNE ENCEPHALOPATHY:

1. Relatively rapid onset and progression of symptoms or radiological findings suggesting brain inflammation
2. Serum autoantibody or cerebrospinal fluid markers of inflammation (e.g., elevated protein or leukocytosis)
3. Objective evidence of improvement with immunotherapy trial

WHY CONSIDER AN AUTOIMMUNE ETIOLOGY?

TO AVOID MISDIAGNOSIS
Many cases of encephalopathy previously considered toxic, metabolic, or infectious are now recognized to have an autoimmune cause.

BECAUSE EARLY DIAGNOSIS CAN MAKE A MEANINGFUL DIFFERENCE
Early-initiated immunotherapy gives patients the best possible outcome. Informative serological testing may also expedite the search for a limited stage cancer.

WHEN SHOULD I TEST FOR AN AUTOIMMUNE ETIOLOGY?*

CONSIDER AN AUTOIMMUNE ETIOLOGY WITH:

- Abrupt onset and rapid progression
- Fluctuating course
- Psychiatric accompaniments (psychosis, hallucinations)
- Movement disorder (myoclonus, tremor, dyskinesia)
- Headache
- Autoimmune stigmata (e.g., physical signs or personal/family history of diabetes, thyroid disorder, vitiligo, prematurely gray hair, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- History of cancer
- Smoking history (20+ pack years) or other cancer risk factors
- Inflammatory cerebrospinal fluid
- Neuroimages suggesting inflammation (signal abnormality, limbic or extra-temporal)

*We strongly advise obtaining serum and CSF before starting immunotherapy

MAYO MEDICAL LABORATORIES: YOUR PARTNER IN COMMUNITY LABORATORY MEDICINE

With a strong emphasis on patient care and community-based medicine, Mayo Medical Laboratories does more than deliver groundbreaking testing solutions. We connect you with world-renowned neurologists and laboratory experts who help you work with your results every step of the way.

FOR INFORMATION ABOUT DIAGNOSIS AND TREATMENT OF AUTOIMMUNE ENCEPHALOPATHY, CONTACT US AT 855-516-8404
WHICH TESTS SHOULD I ORDER?

- Encephalopathy Autoimmune Evaluation, CSF (Mayo ID: ENCEC)
  TAT: 3 days negative / 5 days positive
- Encephalopathy Autoimmune Evaluation, Serum (Mayo ID: ENCES)
  TAT: 4 days negative / 7 days positive

WHY TEST BOTH CSF AND SERUM?

Some neural autoantibodies are detected more readily in serum (e.g., VGKC-complex IgG), while others can be detected more readily in CSF (e.g., NMDA receptor IgG). Testing both, simultaneously or sequentially, maximizes diagnostic yield.

NEURAL ANTIBODIES EVALUATED

NUCLEAR AND CYTOPLASMIC SPECIFICITIES

<table>
<thead>
<tr>
<th>ANTIBODY</th>
<th>ONCOLOGICAL ASSOCIATION</th>
<th>APPROX. FREQUENCY OF CANCER</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANNA-1</td>
<td>Small-cell lung carcinoma, neuroblastoma, thymoma</td>
<td>90%</td>
</tr>
<tr>
<td>ANNA-2</td>
<td>Small-cell lung carcinoma, breast adenocarcinoma</td>
<td>90%</td>
</tr>
<tr>
<td>ANNA-3</td>
<td>Aerodigestive carcinoma</td>
<td>90%</td>
</tr>
<tr>
<td>AGNA-1 (SOX1)</td>
<td>Small-cell lung carcinoma</td>
<td>90%</td>
</tr>
<tr>
<td>PCA-1</td>
<td>Ovary, other mullerian or breast</td>
<td>90%</td>
</tr>
<tr>
<td>PCA-2</td>
<td>Small-cell lung carcinoma</td>
<td>90%</td>
</tr>
<tr>
<td>PCA-Tr</td>
<td>Hodgkin lymphoma</td>
<td>90%</td>
</tr>
<tr>
<td>CRMP-5</td>
<td>Small-cell lung carcinoma, thymoma, thyroid, or renal carcinoma</td>
<td>90%</td>
</tr>
<tr>
<td>Amphiphysin</td>
<td>Small-cell lung carcinoma, breast adenocarcinoma</td>
<td>90%</td>
</tr>
<tr>
<td>GAD65</td>
<td>Occasionally (e.g., thymoma)</td>
<td>&lt; 10%</td>
</tr>
</tbody>
</table>

PLASMA MEMBRANE SPECIFICITIES

<table>
<thead>
<tr>
<th>ANTIBODY</th>
<th>ONCOLOGICAL ASSOCIATION</th>
<th>APPROX. FREQUENCY OF CANCER</th>
</tr>
</thead>
<tbody>
<tr>
<td>VGKC-complex*</td>
<td>Small-cell lung carcinoma, thymoma, adenocarcinoma of breast, prostate</td>
<td>&lt; 15%</td>
</tr>
<tr>
<td>NMDA receptor</td>
<td>Teratoma (ovarian or extra-ovarian)</td>
<td>50%</td>
</tr>
<tr>
<td>AMPA receptor</td>
<td>Thymoma, lung and breast carcinoma</td>
<td>70%</td>
</tr>
<tr>
<td>GABA-B receptor</td>
<td>Small-cell lung carcinoma, other neuroendocrine neoplasm</td>
<td>70%</td>
</tr>
<tr>
<td>P/Q and N-type calcium channel</td>
<td>Lung, breast or gynecologic carcinoma</td>
<td>15%</td>
</tr>
<tr>
<td>Muscle AChR</td>
<td>Thymoma, lung, breast, gynecologic, or prostate carcinoma</td>
<td>&lt; 15%</td>
</tr>
<tr>
<td>Neuronal ganglionic AChR</td>
<td>Miscellaneous carcinomas, thymoma</td>
<td>&lt; 15%</td>
</tr>
</tbody>
</table>

*VGKC radioimmunoassay sensitively detects antibodies to LGI1, CASPR2, and other VGKC-complex antigens.

Abbreviations: AGNA, antigliarial/neuronal nuclear antibody; ANNA, antineuronal nuclear antibody; PCA, Purkinje cell cytoplasmic antibody; CRMP-5, collapsin response-mediator protein-5; GAD65, glutamic acid decarboxylase-65; VGKC, voltage-gated potassium channel; NMDA, N-methyl D-aspartate; AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; GABA, gamma-aminobutyric acid; AChR, acetylcholine receptor.
CLINICAL REFERENCES FOR AUTOIMMUNE ENCEPHALOPATHY

TAP INTO THE EXPERTISE OF MAYO CLINIC

The Mayo Clinic Neuroimmunology Laboratory was the first to introduce comprehensive serological evaluations to aid the diagnosis of neurological autoimmunity. The laboratory continues to discover and clinically validate novel autoantibody profiles that inform neurological decision-making and guide the search for cancer.

The clinical and research activities of the Mayo Clinic Neuroimmunology Laboratory focus on autoimmunity affecting the brain, optic nerve, retina, spinal cord, autonomic and somatic nerves and muscle. The neuroimmunology laboratory complements Mayo Clinic’s Autoimmune Neurology Clinic.

FOR MORE INFORMATION ABOUT AUTOIMMUNE NEUROLOGY TESTING
MayoMedicalLaboratories.com/neurology