Test Definition: AGNTC

Anti-Glial/Neuronal Nuclear Antibody-Type 1 (AGNA-1) Titer, Spinal Fluid (Non-Orderable)

Overview

Useful For

Only orderable as a reflex. For more information see:
DMC2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

Reporting an end titer result from cerebrospinal fluid (CSF) specimens

Serological evaluation using CSF specimens from patients who present with a subacute neurological disorder of undetermined etiology, especially those with risk factors for primary lung carcinoma

Directing a focused search for cancer

Investigating neurological symptoms that appear during, or after, cancer therapy and are not explainable by metastasis

Differentiating autoimmune neuropathies from neurotoxic effects of chemotherapy

Monitoring the immune response of seropositive patients during cancer therapy

Detecting early evidence of cancer recurrence in previously seropositive patients

Testing Algorithm

If the indirect immunofluorescence pattern suggests anti-glial/neuronal nuclear antibody-type 1 (AGNA-1), then this test will be performed at an additional charge.

Method Name

Only orderable as a reflex. For more information see:
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-ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
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Indirect Immunofluorescence Assay (IFA)

NY State Available

Yes

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Specimen

Specimen Type
CSF

Ordering Guidance
Serum is preferred; see AGN1S / Anti-Glial/Neuronal Nuclear Antibody-Type 1, Serum.

Spinal fluid is particularly useful if interfering antibodies are present.

Specimen Required
Only orderable as a reflex. For more information see:
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-ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

Container/Tube: Sterile vial
Specimen Volume: 2 mL

Specimen Minimum Volume
1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Refrigerated (preferred)	28 days	
	Ambient	72 hours	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Anti-glial/neuronal nuclear autoantibody-type 1 (AGNA-1) is recognized clinically as a marker of a patient's immune response to a lung cancer that is usually limited in metastasis but manifests as an autoimmune neurological disorder.

AGNA-1 is an IgG marker of an immune response to cancer (usually a small-cell lung carcinoma: SCLC) in patients presenting with a subacute, generally multifocal, paraneoplastic neurological disorder.(1-3) It binds to the nucleus, but not cytoplasm, of SCLC cell lines and, in the adult central nervous system, to nuclei in subsets of astrocytes and neurons, as well as ependyma. Its previous name was antineuronal nuclear antibody (ANNA)-4.(2) The most common neurological presentations of patients who are positive for AGNA-1 are Lambert-Eaton myasthenic syndrome, sensorimotor or autonomic neuropathy, limbic encephalopathy, and ataxias.

To date, all 45 seropositive patients identified in the Mayo Clinic Neuroimmunology Laboratory have been smokers. SCLC was confirmed in more than 80% of cases. In 59% of patients, one or more identifiable coexisting paraneoplastic autoantibodies support the prediction of SCLC: P/Q-type Ca(++) channel antibody (41%) greater than collapsin response-mediator protein-5 (CRMP-5)-IgG equal to ANNA-1 greater than other antibodies.

Reference Values

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-DMC2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MDC2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
-MAC1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

<1:2
Neuron-restricted patterns of IgG staining that do not fulfill criteria for anti-glial/neuronal nuclear antibody-type 1 may be reported as "unclassified anti-neuronal IgG." Complex patterns that include nonneuronal elements may be reported as "uninterpretable."

Interpretation

A positive result confirms that the patient's subacute neurological disorder has an autoimmune basis and predicts with greater than 80% certainty that the patient has a lung carcinoma (usually small-cell lung carcinoma: SCLC), either new or recurrent, and confined to the chest. Fifteen percent of seropositive patients who are eventually proven to have SCLC additionally have an unrelated, often more obvious, cancer, either coexisting or by past history.

Anti-glial/neuronal nuclear autoantibody-type 1 (AGNA-1) has not been encountered in healthy subjects (n=170). Its onconeural antigen is the nuclear transcription factor Sox1.(2) IgG of this specifically has been reported detectable in 30% to 40% of patients with SCLC who lack neurological complications.(4)

Cautions

Anti-glial/neuronal nuclear autoantibody-type 1 (AGNA-1) is difficult to detect by immunofluorescence when it coexists with other neuronal nuclear autoantibodies, such as antineuronal nuclear antibody (ANNA)-1 or ANNA-2, unless the titer of AGNA-1 exceeds that of the coexisting autoantibodies. It has not been detected by Western blot.(1)

Clinical Reference

1. Graus F, Vincent A, Pozo-Rosich P, et al: Anti-glial nuclear antibody: marker of lung cancer-related paraneoplastic

neurological syndromes. J Neuroimmunol. 2005 Aug;165(1-2):166-171
2. Lachance D, Kryzer TJ, Pittock SJ, et al: Anti-neuronal nuclear antibody type 4 (ANNA-4), a novel paraneoplastic marker of small-cell lung carcinoma (SCLC). Neurology. 2006;66 (Suppl 2):A340
3. Sabater L, Saiz A, Titulaer MG, et al: Sox1 antibodies are markers of paraneoplastic Lambert-Eaton myasthenic syndrome. Neurology. 2008 Mar 18;70(12):924-928
4. Gure AO, Stockert E, Scanlan MJ, et al: Serological identification of embryonic neural proteins as highly immunogenic tumor antigens in small cell lung cancer. Proc Natl Acad Sci USA. 2000 Apr 11;97(8):4198-4203
5. McKeon A, Pittock SJ: Paraneoplastic encephalomyelopathies: pathology and mechanisms. Acta Neuropathol. 2011 Oct;122(4):381-400
6. Horta ES, Lennon VA, Lachance DH, et al: Neural autoantibody clusters aid diagnosis of cancer. Clin Cancer Res. 2014 Jul 15;20(14):3862-3869
7. Pittock SJ, Kryzer TJ, Lennon VA: Paraneoplastic antibodies coexist and predict cancer, not neurological syndrome. Ann Neurol. 2004 Nov;56(5):715-719

Performance

Method Description
The patient's specimen is tested by a standardized immunofluorescence assay that uses a composite frozen section of mouse cerebellum, kidney, and gut tissues. After incubation with the specimen and washing, fluorescein-conjugated goat-antihuman IgG is applied. Neuron-specific autoantibodies are identified by their characteristic fluorescence staining patterns. Specimens that are scored positive for any neuronal nuclear or cytoplasmic autoantibody are titrated. Interference by coexisting non-neuron-specific autoantibodies can usually be eliminated by serologic absorption.(Honorat JA, Komorowski L, Josephs KA, et al. IgLON5 antibody: Neurological accompaniments and outcomes in 20 patients. Neurol Neuroimmunol Neuroinflamm. 2017;4[5]:e385. Published 2017 Jul 18. doi:10.1212/NXI.0000000000000385)

PDF Report
No

Day(s) Performed
Monday through Sunday

Report Available
6 to 8 days

Specimen Retention Time
2 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

86256

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AGNTC	AGNA-1 Titer, CSF	94355-5

Result ID	Test Result Name	Result LOINC® Value
43443	AGNA-1 Titer, CSF	94355-5