Test Definition: AN1TS

Antineuronal Nuclear Antibody-Type 1 (ANNA-1) Titer, Serum

Overview

Useful For

Diagnosis of paraneoplastic autoimmune neuropathies, encephalomyeloradiculopathies, related neurologic disorders, and intestinal pseudo-obstruction/dysmotility associated with small-cell lung carcinoma

Reporting an end titer result from serum specimens

This test alone **should not be used as** a general screening test for carcinoma of the lung.

Testing Algorithm

If the indirect immunofluorescence pattern suggests antineuronal nuclear antibody type 1 (ANNA-1), then this test will be performed at an additional charge.

Method Name

Only orderable as a reflex. For more information see:
-AIAES / Axonal Neuropathy, Autoimmune/Paraneoplastic Evaluation, Serum
-DMS2 / Dementia, Autoimmune/Paraneoplastic Evaluation, Serum
-DYS2 / Dysautonomia, Autoimmune/Paraneoplastic Evaluation, Serum
-ENS2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Serum
-EPS2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Serum
-GID2 / Gastrointestinal Dysmotility, Autoimmune/Paraneoplastic Evaluation, Serum
-MAS1 / Myelopathy, Autoimmune/Paraneoplastic Evaluation, Serum
-MDS2 / Movement Disorder, Autoimmune/Paraneoplastic Evaluation, Serum
-PAVAL / Paraneoplastic, Autoantibody Evaluation, Serum
-PCDES / Pediatric Autoimmune Encephalopathy/CNS Disorder Evaluation, Serum

Indirect Immunofluorescence Assay (IFA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

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Specimen Minimum Volume
0.6 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information
A spectrum of paraneoplastic neurologic disorders (often multifocal) is found with antineuronal nuclear antibody type 1 (ANNA-1), also known as anti-Hu. Most frequent are neuropathies: mixed sensorimotor, pure sensory, predominantly autonomic, and least commonly, predominantly motor. Other manifestations include limbic encephalitis, subacute cerebellar degeneration, myelopathy, or radiculopathy.

Small-cell lung carcinoma (SCLC) is almost always present, although difficult to find. Extrapulmonary primary small-cell carcinoma thymoma or neuroblastoma is rarely encountered as the pertinent neoplasm. Whole body positron emission tomography (PET) scanning is justifiable in seropositive patients when no cancer is found.

ANNA-1 antibody is an extremely valuable marker of paraneoplastic intestinal dysmotilities associated with SCLC, ranging from gastroparesis to pseudo-obstruction. In this context it may be accompanied by muscle or ganglionic acetylcholine receptor (AChR) antibody, voltage-gated potassium channel antibody, striational antibody, glutamic acid decarboxylase 65 (GAD65) antibody, or thyroid or gastric parietal cell antibodies.

ANNA-1 antibody is uncommon in patients with SCLC without a neuropathy, including patients with Lambert-Eaton myasthenic syndrome or pure cerebellar ataxia.

ANNA-1 has been encountered in children with intestinal dysmotility, cerebellar ataxia, brain stem encephalitis, and myeloneuropathy with and without evident cancer (neuroblastoma).

Reference Values

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-PCDES / Pediatric Autoimmune Encephalopathy/CNS Disorder Evaluation, Serum

<1:240
Neuron-restricted patterns of IgG staining that do not fulfill criteria for antineuronal nuclear antibody type 1 may be reported as "unclassified anti-neuronal IgG." Complex patterns that include nonneuronal elements may be reported as "uninterpretable."

Interpretation

This autoantibody is rarely found in adult patients without asbestos exposure, or a long history of tobacco use or passive exposure. Sixty-six percent of seropositive patients are female; small-cell lung carcinoma (SCLC) has been confirmed in 83% of those with adequate follow-up. In 15% with confirmed SCLC, an unrelated and more obvious primary malignancy coexists with SCLC.

Antineuronal nuclear antibody type 1 is found before SCLC is diagnosed in 55% of cases.

Positron emission tomography (PET) scanning, magnetic resonance imaging of the chest, and transesophageal ultrasound sometimes reveal malignant adenopathy when computerized tomography is negative. An extrapulmonary primary small cell carcinoma should be considered, especially in nonsmoking patients (eg, skin, larynx, tongue, breast, cervix, ovary, prostate, endocrine, or pancreas).

Autopsy sometimes reveals SCLC in patients who lack evidence of tumor in life.

Cautions

A cancer other than small-cell lung carcinoma (SCLC) may be found first but will coexist with SCLC in 15% of cases.

Antineuronal nuclear antibody type 1 (ANNA-1) is only 1 of 7 neuronal (or glial) nuclear or cytoplasmic autoantibodies that are currently recognized as a serological marker of neurologic autoimmunity associated with SCLC. The others are

ANNA-2, ANNA-3, amphiphysin, Purkinje cell cytoplasmic autoantibody type 2, collapsin response-mediator protein-5 (CRMP-5-IgG), and antiglial neuronal nuclear antibody (AGNA-1).

Clinical Reference

1. Lucchinetti CF, Kimmel DW, Lennon VA. Paraneoplastic and oncologic profile of patients seropositive for type 1 antineuronal nuclear autoantibodies. Neurology. 1998;50(3):652-657
2. Vernino S, Eggenberger ER, Rogers LR, Lennon VA. Paraneoplastic neurological autoimmunity associated with ANNA-1 autoantibody and thymoma. Neurology. 2002;59(6):929-932
3. Pranzatelli MR, McGee NR. Neuroimmunology of OMS and ANNA-1/anti-Hu paraneoplastic syndromes in a child with neuroblastoma. Neurol Neuroimmunol Neuroinflamm. 2017;5(2):e433. doi:10.1212/NXI.0000000000000433
4. Horta ES, Lennon VA, Lachance DH, et al. Neural autoantibody clusters aid diagnosis of cancer. Clin Cancer Res. 2014;20(14):3862-3869

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

Fees & Codes

Test Definition: AN1TS

Antineuronal Nuclear Antibody-Type 1 (ANNA-1) Titer, Serum

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
AN1TS	ANNA-1 Titer, S	94342-3

Result ID	Test Result Name	Result LOINC® Value
43431	ANNA-1 Titer, S	94342-3