MAYO CLINIC LABORATORIES

Test Definition: AN2TC

Antineuronal Nuclear Antibody Type 2 (ANNA-2) Titer, Spinal Fluid

Overview

Useful For

Investigating middle-aged or older patients who present with unexplainable signs of midbrain/cerebellar/brain stem disorder and/or myelopathy, especially women with a previous history of breast cancer, and both sexes if there is a history of tobacco abuse or passive exposure

Reporting an end titer result from cerebrospinal fluid specimens

Testing Algorithm

If the indirect immunofluorescence pattern suggests antineuronal nuclear antibody type 2 (ANNA-2), then this test will be performed at an additional charge.

Method Name

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

Indirect Immunofluorescence Assay (IFA)

NY State Available

Yes

Specimen

Specimen Type

CSF

Ordering Guidance

For investigating a smoker presenting with 1 or more elements of encephalomyeloradiculoneuropathy, order PAVAL / Paraneoplastic Autoantibody Evaluation, Serum.

Serum is preferred. Spinal fluid testing is particularly useful when interfering antibodies are present in the serum.

Specimen Required

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

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	Ambient	72 hours	
	Refrigerated (preferred)	28 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information
Antineuronal nuclear autoantibody type 2 (ANNA-2), also known as anti-Ri, is an IgG serologic marker of paraneoplastic neurologic autoimmunity and reflects an immune response to neuronal antigens expressed in certain breast, lung, or gynecologic cancers. These carcinomas are often occult, with the patients presenting with unexplained signs of neurologic dysfunction. ANNA-2 is far less common than ANNA-1. It is one of the rarest paraneoplastic antibodies encountered in the Mayo Clinic Neuroimmunology Laboratory.

Patients who are seropositive for ANNA-2 usually present to a neurologist with signs of midbrain, brain stem, cerebellar, or spinal cord dysfunction. Some have sensorimotor neuropathy. Ocular opsoclonus-myoclonus, laryngospasm, or jaw-opening dystonia may be prominent. Peripheral neuropathic signs and symptoms may occur. These often reflect coexisting autoimmunity to other onconeural proteins (eg, ANNA-1, collapsin response-mediator protein-5 [CRMP-5], calcium channels); coexisting paraneoplastic autoantibodies are found in 73% of cases.

ANNA-2 positive patients are female in 64% of cases. Most have a primary carcinoma of breast or lung; gynecologic cancer is less frequent.

Treatment of the cancer can lead to progressive reduction in ANNA-2 titer and stabilization or striking improvement of the neurologic disorder.

ANNA-2 is not detected in serum or spinal fluid of healthy individuals. It is found in fewer than 2% of patients who have small-cell lung carcinoma without evidence of neurologic dysfunction.

ANNA-2 is identified by an indirect immunofluorescence assay. It characteristically stains neurons in the central nervous system and spares neurons in the peripheral nervous system. ANNA-2 is also identifiable by neuronal Western blot characteristics.

Reference Values

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

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

Interpretation

Detection of antineuronal nuclear autoantibodies type 2 (ANNA-2) in serum or spinal fluid of patients with a clinically unexplainable neurologic disorder:
-Identifies the neurologic problem as autoimmune and almost certainly paraneoplastic
-Prompts a search for underlying malignancy (breast, lung, or gynecologic)
-Leads to early treatment of cancer and consideration of immunosuppressant therapy

Cautions

Seronegativity for antineuronal nuclear antibody type 2 (ANNA-2) does not exclude malignancy.

Clinical Reference

1. Kiers L, Altermatt HJ, Lennon VA: Paraneoplastic anti-neuronal nuclear IgG autoantibodies (type 1) localize antigen in small cell lung carcinoma. Mayo Clin Proc. 1991 Dec;66(12):1209-1216
2. Lennon VA: Paraneoplastic autoantibodies: the case for a descriptive generic nomenclature. Neurology. 1994 Dec;44(12):2236-2240
3. Lennon VA, Kryzer TJ, Griesmann GE, et al: Calcium-channel antibodies in the Lambert-Eaton syndrome and other paraneoplastic syndromes. N Engl J Med. 1995 Jun 1;332(22):1467-1474
4. Chan KH, Vernino S, Lennon VA: ANNA-3 anti-neuronal nuclear antibody: marker of lung cancer-related autoimmunity. Ann Neurol. 2001 Sep;50(3):301-311
5. Pittock SJ, Lucchinetti CF, Lennon VA: Anti-neuronal nuclear autoantibody-type 2: paraneoplastic accompaniments. Ann Neurol. 2003 May;53(5):580-587
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

Performance

Method Description

The patient's sample is tested by a standardized immunofluorescence assay that uses a composite frozen section of mouse cerebellum, kidney, and gut tissues. After incubation with sample and washing, fluorescein-conjugated goat-antihuman IgG is applied. Neuron-specific autoantibodies are identified by their characteristic fluorescence staining patterns. Samples that are scored positive for any neuronal nuclear or cytoplasmic autoantibody are titrated to an endpoint. 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 Jul 18;4(5):e385. doi: 10.1212/NXI.0000000000000385)

If antineuronal nuclear autoantibody type 1 (ANNA-1), antinuclear antibody, or antimitochondrial antibody titers equal or exceed ANNA-2, Western blot analysis is required to establish ANNA-2 specificity with certainty.

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

5 to 8 days

Specimen Retention Time

28 days

Performing Laboratory Location

Rochester

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.

Test Definition: AN2TC

Antineuronal Nuclear Antibody Type 2 (ANNA-2) Titer, Spinal Fluid

CPT Code Information

86256

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AN2TC	ANNA-2 Titer, CSF	94357-1

Result ID	Test Result Name	Result LOINC® Value
43441	ANNA-2 Titer, CSF	94357-1