Test Definition: CRMWC

Collapsin Response-Mediator Protein-5-IgG, Western Blot, Spinal Fluid

Overview

Useful For
Evaluation of cases of chorea, vision loss, cranial neuropathy and myelopathy

Method Name
Western Blot

NY State Available
Yes

Specimen

Specimen Type
CSF

Ordering Guidance
It is recommended an evaluation be ordered in conjunction with this testing if not previously performed. Multiple neurological phenotype-specific autoimmune/paraneoplastic evaluations are available. For more information as well as phenotype-specific testing options, see Autoimmune Neurology Test Ordering Guide.

Shipping Instructions
Send specimen refrigerated.

Necessary Information
Provide the following information:
-Relevant clinical information
-Ordering healthcare professional name, phone number, mailing address, and e-mail address

Specimen Required
Container/Tube: Sterile vial
Specimen Volume: 3 mL

Specimen Minimum Volume
2 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

Autoantibodies specific for neurons and muscle are important serological markers of neurological autoimmunity. Most are highly predictive of specific neoplasms that are metastatic when diagnosed, but usually limited in spread to regional lymph nodes and adjacent structures.(1-4)

Collapsin response-mediator protein-5 (CRMP-5) is highly expressed in small-cell lung carcinomas (SCLC), in neurons throughout the adult central and peripheral nervous systems, and in a subset of glial cells.(1) In Western blot analyses, the native antigen is a 62-kDa protein (recombinant human CRMP-5 is 68 kDa).(1) CRMP-5-IgG (also known as "anti-CV-2")(4,5) is a more common autoantibody accompaniment of SCLC than antineuronal nuclear antibodies-1 (ANNA-1; anti-Hu) and sometimes occurs with thymoma.

The neurological presentation of CRMP-5 seropositive patients is usually multifocal, and can affect any level of the neuraxis. Neurological presentations that suggest a CRMP-5-IgG-related syndrome include subacute chorea or cranial neuropathy (particularly loss of vision, taste, or smell), dementia, myelopathy and gastrointestinal dysmotility in a patient with risk factors for lung cancer, or encephalopathy or neuromuscular hyperexcitability in a patient with serological or clinical evidence of myasthenia gravis.(1) Fourteen percent of patients have thromboembolic phenomena. Seropositive patients who have thymoma usually present with other myasthenia gravis neurological manifestations (eg, encephalopathy, disorders of continuous muscle fiber activity).(3)

CRMP-5-IgG is defined in serum or spinal fluid by its characteristic immunofluorescence (IF) staining pattern on a mixed tissue substrate of adult mouse central and peripheral neurons. However, CRMP-5-IgG is not detectable by standard IF screening if the titer is low (serum <1:240; CSF <1:2) or if coexisting autoantibodies, either neuron-specific or nonorgan-specific antinuclear and antimitochondrial antibodies, preclude identification of CRMP-5-IgG with certainty. In these situations, CRMP-5-IgG may be detected by Western blot analysis.

Reference Values

Negative

Interpretation

A positive result confirms that a patient's subacute neurological disorder has an autoimmune basis and is likely to be associated with a small-cell lung carcinoma (SCLC) or thymoma, which may be occult.(1,2) A positive result has a predictive value of 90% for neoplasm (77% SCLC, 6% thymoma).(1) Seropositivity is found in approximately 3% of

patients who have SCLC with limited metastasis without evidence of neurological autoimmunity.(6)

Clinical-serological correlations have not yet been established for children.

Western blot analysis is indicated when interfering nonorgan-specific or coexisting neuron-specific autoantibodies in serum or spinal fluid preclude unambiguous detection of CRMP-5-IgG by indirect immunofluorescence assay, or when the immunofluorescence assay is negative in a patient whose neurological presentation suggests a CRMP-5-IgG-related syndrome.

Cautions

Seronegativity does not exclude the presence of a neoplasm.

Supportive Data

In the Neuroimmunology Laboratory's current clinical service activity, the frequency of collapsin response-mediator protein-5 (CRMP-5)-IgG detection is approximately 2 per 1,000 sera tested, approximating that of the Purkinje cell cytoplasmic autoantibody-type 1 (PCA-1, or "anti-Yo"). A lung carcinoma was found in 77% of 116 patients, mostly limited small cell type; 6% had thymoma and 7% had miscellaneous neoplasms.

Clinical Reference

1. Yu Z, Kryzer TJ, Griesmann GE, et al. CRMP-5 neuronal autoantibody: marker of lung cancer and thymoma-related autoimmunity. Ann Neurol. 2001;49(2):146-154
2. Vernino S, Tuite P, Adler CH, et al. Paraneoplastic chorea associated with CRMP-5 neuronal antibody and lung carcinoma. Ann Neurol. 2002;51(5):625-630
3. Vernino S, Lennon VA. Autoantibody profiles and neurological correlations of thymoma. Clin Cancer Res. 2004;10(21):7270-7275
4. Galanis E, Frytak S, Rowland KM Jr, et al. Neuronal autoantibody titers in the course of small cell lung carcinoma and platinum associated neuropathy. Cancer Immunol Immunother 1999;48(2-3):85-90
5. Klein CJ. Autoimmune-mediated peripheral neuropathies and autoimmune pain. In: Pittock SJ, Vincent A, eds. Handbook of Clinical Neurology; Autoimmune Neurology. Elsevier; 2016 pp 417-446

Performance

Method Description

Western blot is performed on denatured full-length recombinant human collapsin response-mediator protein-5 (CRMP-5), reduced and subjected to electrophoresis on 10% polyacrylamide gel. IgG is detected autoradiographically by enhanced chemiluminescence.(Yu Z, Kryzer TJ, Griesmann GE, et al. CRMP-5 neuronal autoantibody: marker of lung cancer and thymoma-related autoimmunity. Ann Neurol. 2001;49[2]:146-154; Dubey D, Jitprapaikulsan J, Bi H, et al. Amphiphysin-IgG autoimmune neuropathy: A recognizable clinicopathologic syndrome. Neurology. 2019;93[20]:e1873-e1880. doi:10.1212/WNL.0000000000008472)

PDF Report

No

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Day(s) Performed
Monday through Thursday

Report Available
5 to 10 days

Specimen Retention Time
28 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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
84182

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CRMWC	CRMP-5-IgG Western Blot, CSF	53707-6

Result ID	Test Result Name	Result LOINC® Value
21747	CRMP-5-IgG Western Blot, CSF	53707-6