Test Definition: PVLE

Paraneoplastic Vision Loss Eval, S

Overview

Useful For

Evaluating patients with rapidly progressive vision loss where a paraneoplastic cause for vision loss (retinopathy or optic neuritis with other findings [eg, retinitis] is suspected)

Evaluating patients with small cell carcinoma who develop vision loss

Profile Information

Test ID	Reporting Name	Available Separately	Always Performed
PVLEI	Paraneoplas Vision Loss Interp, S	No	Yes
CRMS	CRMP-5-IgG, S	No	Yes
RCVBS	Recoverin Immunoblot, S	Yes	Yes

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
CRMWS	CRMP-5-IgG Western Blot, S	Yes	No

Testing Algorithm

If the indirect immunofluorescence assay (IFA) patterns suggest collapsin response-mediator protein-5 (CRMP-5) antibody, then CRMP-5 IFA titer and CRMP-5 Western blot are performed at an additional charge.

Method Name

PVLEI: Medical Interpretation

CRMS: Indirect Immunofluorescence Assay (IFA)

CRMWS: Western Blot (WB)

RCVBS: Immunoblot (IB)

NY State Available

Yes

Specimen

Specimen Type

Serum

Necessary Information

Provide the following information:

-Relevant clinical information

-Ordering provider name, phone number, mailing address, and e-mail address

Specimen Required

Patient Preparation:

1. For optimal antibody detection, specimen collection is recommended prior to initiation of immunosuppressant medication.

2. This test should not be requested in patients who have recently received radioisotopes, therapeutically or diagnostically, because of potential assay interference. The specific waiting period before specimen collection will depend on the isotope administered, the dose given, and the clearance rate in the individual patient. Specimens will be screened for radioactivity prior to analysis. Radioactive specimens received in the laboratory will be held 1 week and assayed if sufficiently decayed, or canceled if radioactivity remains.

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 4 mL

Forms

If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

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

Clinical and Interpretive

Clinical Information

There are 2 recognized forms of paraneoplastic vision loss: paraneoplastic autoimmune optic neuropathy with retinopathy accompanying collapsin response-mediator protein-5 (CRMP-5)-IgG, and cancer associated retinopathy (CAR) accompanying recoverin antibody. Both occur in the setting of occult small cell carcinoma of the lung or other body region.

Patients with CRMP-5-IgG associated optic neuropathy typically present with painless bilateral visual loss over weeks to months. At onset, there is typically bilateral optic disc edema without evidence of enhancement of the optic nerve on magnetic resonance imaging or elevated opening pressure on lumbar puncture. Visual acuity can range from 20/20 to hand motion. Patients typically have co-existing vitritis or retinitis. In addition, patients can have diplopia, typically from cerebellar involvement. The majority of patients with CRMP-5 associated optic neuropathy will have other neurologic deficits from CRMP-5 autoimmunity, such as asymmetric axonal polyradiculoneuropathy. CAR typically presents with subacute painless progressive bilateral (although asymmetry has been described) progressive vision loss over weeks to months, reflecting both rod and cone retinal dysfunction in most patients. Accordingly, symptoms often include nyctalopia (inability to see in dim light or at night), impaired dark adaptation, photopsia (flashes of light in the field of vision), photosensitivity, dyschromatopsia, and ultimately, severe visual acuity loss.

Patients with CRMP-5-IgG-related ophthalmitis may have improvements with intra-ocular or systemic corticosteroid treatment. Patients with recoverin-related retinopathy are unlikely to have vision improvement with treatment.

Reference Values

COLLAPSIN RESPONSE-MEDIATOR PROTEIN-5 TITER

<1:240

RECOVERIN IMMUNOBLOT

Negative

COLLAPSIN RESPONSE-MEDIATOR PROTEIN-5 WESTERN BLOT

Negative

Titers lower than 1:240 are detectable by recombinant CRMP-5 Western blot analysis. CRMP-5 Western blot analysis will be done on request on stored serum (held 4 weeks). This supplemental testing is recommended in cases of chorea, vision loss, cranial neuropathy, and myelopathy. Call 1-800-533-1710 to request CRMP-5 Western blot. Neuron-restricted patterns of IgG staining that do not fulfill criteria for CRMP-5-IgG may be reported as "unclassified antineuronal IgG." Complex patterns that include non-neuronal elements may be reported as "uninterpretable."

Interpretation

Recoverin IgG:

Seropositivity is consistent with a diagnosis of paraneoplastic retinopathy. Considerations include small cell carcinoma, pulmonary or extrapulmonary.

Collapsin response-mediator protein-5 IgG:

Seropositivity is consistent with a diagnosis of paraneoplastic retinitis or ophthalmitis. Considerations include small cell carcinoma, pulmonary or extrapulmonary.

Cautions

Negative results do not exclude the diagnosis of paraneoplastic eye disease.

Clinical Reference

1. Cross SA, Salomao DR, Parisi JE, et al: Paraneoplastic autoimmune optic neuritis with retinitis defined by CRMP-5-IgG. Ann Neurol. 2003;54:38-50 doi: 10.1002/ana.10587.

2. Lopez A, McKeon A, Lachance D, et al: Recoverin antibody: Ophthalmologic and oncologic significance. Neurology. 2016 April 5;86(16 Supplement)P6.131

Performance

Method Description

Indirect Immunofluorescence Assay:

Before testing, patient's serum is preabsorbed with liver powder to remove nonorgan-specific autoantibodies. After applying to a composite substrate of frozen mouse tissues (brain, kidney, and gut) and washing, fluorescein-conjugated goat-antihuman IgG is applied to detect the distribution and pattern of patient IgG binding.(Pittock SJ, Kryzer TJ, Lennon VA: Paraneoplastic antibodies coexist and predict cancer, not neurological syndrome. Ann Neurol. 2004;56:715-719; 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)

Western Blot:

Neuronal antigens extracted aqueously from adult rat cerebellum, full-length recombinant human collapsin response-mediator protein-5 (CRMP-5), or full-length recombinant human amphiphysin protein is denatured, reduced, and separated by electrophoresis on 10% polyacrylamide gel. IgG is detected autoradiographically by enhanced chemiluminescence.(Yu Z, Kryzer TJ, GriesmannGE, et al: CRMP-5 neuronal autoantibody: marker of lung cancer and thymoma-related autoimmunity. Ann Neurol. 2001;49[2]:145-154; Dubey D, Jitprapaikulsan J, Bi H, et al: Amphiphysin-IgG autoimmune neuropathy: A recognizable clinicopathologic syndrome. Neurology. 2019 Oct 17 pii: 10.1212/WNL.0000000000008472. doi: 10.1212/WNL.0000000000008472)

Immunoblot:

All steps are performed at ambient temperature (18-28 degrees C) utilizing the EUROBlot One instrument. Diluted patient specimen (1:12.5) is added to test strips (strips containing recombinant antigen manufactured and purified using biochemical methods) in individual channels and incubated for 30 minutes. Positive specimens will bind to the purified recombinant antigen and negative specimens will not bind. Strips are washed to remove unbound antibodies and then incubated with anti-human IgG antibodies (alkaline phosphatase-labelled) for 30 minutes. The strips are again washed to remove unbound anti-human IgG antibodies and nitroblue tetrazolium chloride/5-bromo-4-chloro-3-indolylphosphate (NBT/BCIP) substrate is added. Alkaline phosphatase enzyme converts the soluble substrate into a colored insoluble product on the membrane to produces a black band. Strips are digitized via picture capture on the EUROBlot One instrument and evaluated with the EUROLineScan software.(O'Connor K, Waters P, Komorowski L, et al: GABAA receptor autoimmunity: A multicenter experience. Neurol Neuroimmunol Neuroinflamm. 2019 Apr 4;6[3]:e552 doi: 10.1212/NXI.0000000000000552)

PDF Report

No

Specimen Retention Time

28 days

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

86255 x1

84182 x1

84182 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
PVLE	Paraneoplastic Vision Loss Eval, S	In Process

Result ID	Test Result Name	Result LOINC Value
83077	CRMP-5-IgG, S	94815-8
610009	Recoverin Immunoblot, S	83003-4
607411	Paraneoplas Vision Loss Interp, S	In Process