ARUP LABORATORIES
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Jonathan R. Genzen, MD, PhD, Chief Medical Officer

Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	2/21/1974
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Paraneoplastic Pemphigus (Paraneoplastic Autoimmune Multiorgan Syndrome) Expanded Antibody Panel by IIF With ELISA

ARUP test code 3016534

EER Paraneoplastic Pemphigus Expanded Ab

See Note

Authorized individuals can access the ARUP Enhanced Report using the following link:

[redacted]

Paraneoplastic Pemphigus Expanded Ab

See Note

CLINICAL INFORMATION
No clinical information provided.

Specimen Details
[redacted] - ; Collected: 11/12/2024; Received: 11/14/2024

DIAGNOSTIC INTERPRETATION

Negative/normal findings without evidence of paraneoplastic pemphigus/paraneoplastic autoimmune multiorgan syndrome antibodies:

- Negative IgG antibody reactivity with rodent substrates, including rat bladder, by indirect immunofluorescence; and
- Normal IgG envoplakin antibody level by ELISA

(See Results and Comments including further testing recommendations)

RESULTS
Indirect Immunofluorescence (IIF)

Paraneoplastic Pemphigus IgG Antibodies	
IgG:	Negative, cell surface, rat bladder substrate
	Negative, basement membrane zone, rat bladder substrate
	Negative, cell surface, mouse bladder substrate
	Negative, basement membrane zone, mouse bladder substrate
	Negative, intercalated discs, mouse heart substrate
	Negative, portal tracts, mouse liver substrate

H=High, L=Low, *=Abnormal, C=Critical

Reference Range:
Negative - Titer less than 1:5
Borderline - Titer 1:5
Positive (H) - Titer greater than 1:5

Negative, cell surface/intercellular substance, monkey esophagus substrate
Negative, basement membrane zone, monkey esophagus substrate

Reference Range:
Negative - Titer less than 1:10
Borderline - Titer 1:10
Positive (H) - Titer greater than 1:10

(H) = high/positive

Enzyme-Linked Immunosorbent Assay (ELISA)

Envoplakin IgG Antibodies

IgG envoplakin antibody level: 0.25 ratio U/mL

Reference Range:
Normal (negative) = Less than 1.00 ratio U/mL
Increased (H) (positive) = 1.00 ratio U/mL and greater

(H) = high/positive
U = antibody level in ELISA units

COMMENTS

Specific

The negative IgG paraneoplastic pemphigus antibodies with rat bladder, mouse bladder, mouse heart, and mouse liver substrates by indirect immunofluorescence and the normal IgG envoplakin antibody level by ELISA do not provide support for, but do not rule out, the diagnosis of paraneoplastic pemphigus (PNP)/paraneoplastic autoimmune multiorgan syndrome (PAMS), or other malignancy-associated disorder. Clinical correlation is needed, including with direct immunofluorescence test findings on a biopsy specimen, histopathological examination of formalin-fixed tissue, and other serum epithelial antibodies.

Notably, various serum epithelial antibodies may develop in paraneoplastic pemphigus and other paraneoplastic presentations by various tests with differing sensitivities. ELISA may be more sensitive than indirect immunofluorescence testing for detecting antibodies, especially low levels. To further evaluate the immunopathological profile, additional testing may be performed on this serum specimen by contacting ARUP Client Services at 1-800-242-2787, option 2, with add-on test request(s) for:
Broad epithelial antibody assessment in the initial diagnosis or monitoring of disease progression/changes with
- Immunobullous Disease Antibody Panel (ARUP test number 3001409), or

Specific disease-associated epithelial antibodies,
- Pemphigus Antibody Panel, IgG (ARUP test number 0090650),
- Pemphigus Antibodies, IgA by IIF (ARUP test number 0092106), and/or
- Basement Membrane Zone Antibody Panel (ARUP test number 3001410), alternatively,

Specific antibodies that may develop to other epithelial antigens in patients with PNP/PAMS and other immunobullous diseases,
- Desmoglein 1 and Desmoglein 3 (Pemphigus) Antibodies, IgG by ELISA (ARUP test number 0090649),
- Bullous Pemphigoid (BP180 and BP230) Antibodies, IgG

by ELISA (ARUP test number 0092566), and/or
- Collagen Type VII Antibody, IgG by ELISA (ARUP test number 2010905).

Detection, levels, and patterns of diagnostic antibodies may fluctuate with disease manifestations. Monitoring serum antibody profiles by indirect immunofluorescence testing and antibody levels by ELISAs may aid in assessing disease expression and activity, particularly with persistent, progressive, or changing disease, and in response to therapy.

If it would be helpful to discuss the patient case with this report, contact ARUP Client Services at 1-800-242-2787, option 2, and ask to speak with the Immunodermatology Laboratory at the University of Utah regarding patient results.

General

Paraneoplastic pemphigus (PNP), also known as paraneoplastic autoimmune multiorgan syndrome (PAMS), may affect all ages and develops as a severe mucocutaneous blistering and erosive disease in association with malignancies, most often hematologic (lymphoma, leukemia) and sarcoma. It also may develop in association with benign neoplasia, especially Castleman disease, which is the most frequent association in children and adolescents. Antibodies targeting the various types of epithelia can lead to involvement of various organs and tissues, for example, eyes, lungs, gastrointestinal tract, kidney, and thyroid and is the basis of the name, paraneoplastic autoimmune multiorgan syndrome.

Positive indirect immunofluorescence testing results indicate the presence of serum antibodies to multiple epithelia (simple, columnar, transitional) with several possible epithelial targets, predominantly to plakins (envoplakin, periplakin, desmoplakin I, desmoplakin II, epiplakin, plectin, BP230), also cadherins (desmoglein 1, desmoglein 3; desmocollin 1, desmocollin 2, desmocollin 3), alpha-2-macroglobulin-like-1 (A2ML1), laminin-332, and/or BP180 and support a diagnosis of paraneoplastic pemphigus (paraneoplastic autoimmune multiorgan syndrome). Increased IgG envoplakin antibodies develop in many patients with PNP/PAMS and rarely in patients with other immunobullous diseases. The tested ELISA identifies IgG antibodies to the N-terminal recombinant fragment of envoplakin. Specificity of the test has been reported to be high at 96-99 percent and sensitivity of the test more variably reported at 55-86 percent. Envoplakin and periplakin are principal antigenic targets in the disease, and, based on the high sensitivity, an increased IgG envoplakin antibody level is a diagnostic marker for paraneoplastic pemphigus (paraneoplastic autoimmune multiorgan syndrome). IgG envoplakin antibody levels correlate with extent of mucocutaneous paraneoplastic pemphigus disease expression. After successful tumor therapy, envoplakin antibody levels decrease significantly.

For positive antibody panel testing results without known malignancy, perform aggressive evaluation for neoplasia/malignancy and, if not found, monitor for developing malignancy. For negative results, correlate with histopathological examination of formalin-fixed tissue in addition to direct immunofluorescence findings on a perilesional mucocutaneous biopsy specimen and epithelial antibodies in serum characteristic of other immunobullous diseases; negative paraneoplastic pemphigus antibody findings by indirect immunofluorescence and ELISA testing do not rule out paraneoplastic/malignancy-associated disease. Other known paraneoplastic epithelial autoantibody associations include nonclassical, intercellular IgG/IgA dermatosis and anti-laminin 332 pemphigoid.

TESTING METHODS
Indirect Immunofluorescence (IIF)

IgG Paraneoplastic Pemphigus/Paraneoplastic Autoimmune Multiorgan Syndrome Antibodies

The patient serum is progressively diluted in calcium-containing buffer beginning at 1:5 in three two-fold screening dilutions, layered on rodent substrates, including rat bladder, mouse bladder, mouse heart, and mouse liver, and also on monkey esophagus substrate, and reacted with fluorescein isothiocyanate (FITC)-conjugated antibody to IgG. When positive on rodent substrate(s), the serum is further diluted in two-fold reductions to the limiting dilution of antibody detection or to a maximum dilution of 1:40,960. The limiting-dilution, end-point titer is reported for each rodent substrate. This indirect immunofluorescence testing was developed and its performance characteristics determined by the Immunodermatology Laboratory at the University of Utah. It has not been cleared or approved by the FDA (US Food and Drug Administration). FDA clearance or approval currently is not required for this testing performed in a CLIA-certified laboratory (Clinical Laboratory Improvement Amendments) and intended for clinical use. [Indirect immunofluorescence, one antibody on five substrates (IIF X 5)]

Enzyme-Linked Immunosorbent Assay (ELISA)

IgG envoplakin serum antibody level determined by ELISA (Euroimmun US, Inc.). The performance characteristics of this test have been determined and validated by the Immunodermatology Laboratory at the University of Utah. The U.S. Food and Drug Administration (FDA) has not approved or cleared this test; however, FDA clearance or approval currently may not be required for this testing performed in a CLIA-certified laboratory (Clinical Laboratory Improvement Amendments) and intended for clinical purposes. [One ELISA]

Electronically signed by [redacted] on 11/18/24 at 4:16 PM.
Performed At: IMMUNODERMATOLOGY LABORATORY
417 S. WAKARA WAY, SUITE 2151
SALT LAKE CITY, UT 84108
Medical Director: KRISTIN M. LEIFERMAN, MD
CLIA Number: 46D0681916

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
EER Paraneoplastic Pemphigus Expanded Ab	24-317-110060	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Paraneoplastic Pemphigus Expanded Ab	24-317-110060	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical