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	12/31/2004
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Paraneoplastic Pemphigus (Paraneoplastic Autoimmune Multiorgan Syndrome) Screening Antibodies by IIF

ARUP test code 0092107

EER Paraneoplastic Pemphigus Ab Screen

See Note

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

[redacted]

Paraneoplastic Pemphigus Ab Screen

See Note

CLINICAL INFORMATION
Mucosal involvement with extensive erosions and targetoid, urticarial, and scaly skin lesions. Presumptive diagnosis is drug reaction versus pemphigus, including paraneoplastic pemphigus.

Specimen Details
[redacted] - ; Collected: 1/26/2024; Received: 1/29/2024

DIAGNOSTIC INTERPRETATION

Positive antibody reactivity with rodent substrates, including rat and mouse bladders, by indirect immunofluorescence; consistent with paraneoplastic pemphigus/paraneoplastic autoimmune multiorgan syndrome

(See Results and Comments including further testing recommendation and considerations)

RESULTS
Indirect Immunofluorescence (IIF)

Paraneoplastic Pemphigus IgG Antibodies	
IgG:	Positive, cell surface, titer 1:10,240 (H), rat bladder substrate
	Positive, basement membrane zone, titer 1:640 (H), rat bladder substrate
	Positive, cell surface, titer 1:2,560 (H), mouse bladder substrate
	Positive, basement membrane zone, titer 1:1,280 (H), mouse bladder substrate
	Positive, intercalated discs, titer 1:40 (H), mouse heart substrate

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

Positive, portal tracts, titer 1:160 (H),
mouse liver substrate

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

Positive, cell surface, (H)
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

COMMENTS

Specific

IgG epithelial cell surface/intercellular substance and basement membrane zone antibodies reacting with rodent substrates, including rat and mouse bladders, and IgG epithelial cell surface/intercellular substance antibodies with monkey esophagus substrate, as detected in this indirect immunofluorescence testing, support the diagnosis of paraneoplastic pemphigus (PNP), also known as Paraneoplastic Autoimmune Multiorgan Syndrome (PAMS). Antibody reactivity with intercalated discs in rodent heart and/or portal tracts in rodent liver is supportive when antibody reactivity with rodent bladder, either or both rat and mouse, substrate is present.

Various serum epithelial antibodies may be found in patients with PNP/PAMS and other paraneoplastic presentations by various tests with differing sensitivities. Among the several possible epithelial targets, IgG envoplakin antibodies develop in many patients with PNP/PAMS and rarely in patients with other immunobullous diseases. Moreover, when increased, IgG envoplakin antibody levels may correlate with extent of mucocutaneous paraneoplastic pemphigus disease expression.

Clinical correlation is needed, including with direct immunofluorescence findings on a biopsy specimen and histopathological examination of formalin-fixed tissue. Further testing for IgG envoplakin antibodies by ELISA is recommended with consideration for assessment of other serum epithelial antibodies.

Additional testing may be performed on this specimen by contacting ARUP Client Services at 1-800-242-2787, option 2, with add-on test request(s) for:
- IgG Envoplakin Antibody, IgG by ELISA (ARUP test number 3016533);

For comprehensive testing that includes the epithelial antibody tests below, order with
- Immunobullous Disease Antibody Panel (ARUP test number 3001409);

Alternatively, to assess for specific disease-associated epithelial antibodies or individual antibody targets, order with
- 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);

Or
- 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), with or without
- 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) develops as a severe mucocutaneous blistering and erosive disease in association with malignancies, most often hematologic (lymphoma, leukemia) and sarcoma, and affects all ages. It also may develop in association with benign neoplasia, especially Castleman disease, which is the most frequent association in children and adolescents. Antibodies targeting 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 Paraneoplastic Pemphigus (Paraneoplastic Pemphigus Autoimmune Multiorgan Syndrome) Screening Antibodies by indirect immunofluorescence testing 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). Envoplakin and periplakin are principal antigenic targets in the disease, and, based on high specificity, an increased envoplakin antibody level by ELISA is a diagnostic marker for PNP/PAMS. Of note, ELISA may be more sensitive than indirect immunofluorescence testing for detecting antibodies, especially low levels, but indirect immunofluorescence testing with rodent substrates demonstrates antibodies to a broader range of epithelial targets than epitopes displayed in ELISA. For positive antibody screen testing results, with or without an increased IgG envoplakin antibody level by ELISA, and no known malignancy, perform aggressive evaluation and monitoring for malignancy.

Negative Paraneoplastic Pemphigus (Paraneoplastic Pemphigus Autoimmune Multiorgan Syndrome) Screening Antibodies by indirect immunofluorescence 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. For negative PNP/PAMS indirect immunofluorescence screen testing results, correlate with findings by histopathological examination of formalin-fixed tissue in addition to direct immunofluorescence testing on a biopsy specimen, serum IgG envoplakin antibody level by ELISA, and serum epithelial antibodies characteristic of other

immunobullous diseases with further clinical evaluation as indicated.

TESTING METHODS
Indirect Immunofluorescence (IIF)

IgG Paraneoplastic Pemphigus 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)]

Electronically signed by [redacted] on 02/07/24 at 1:00 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 Ab Screen	24-026-122384	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Paraneoplastic Pemphigus Ab Screen	24-026-122384	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