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

ARUP LABORATORIES

Patient: [redacted]
DOB: [redacted] Age: [redacted] Sex: [redacted]
Patient Identifiers: [redacted]
Visit Number (FIN): [redacted]

Client: [redacted]
Physician: [redacted]

ARUP Test Code: 3016534

Collection Date: 11/20/2024
Received in lab: 11/22/2024
Completion Date: 11/22/2024

Immunodermatology Serum Test Report Navigation Guide

The Immunodermatology TESTING REPORT from the University of Utah follows "See Note" and is arranged as outlined below on the following pages:

CLINICAL INFORMATION
This content is provided by the ordering clinician and includes the reason for testing.

Specimen Details
This includes specimen identification with collected and received dates.

DIAGNOSTIC INTERPRETATION
This is a synopsis of key findings from the testing and their diagnostic relevance.

RESULTS
This section reports the discrete finding and value of each test component, along with the reference range.

COMMENTS
Specific

These comments provide an explanation of the test results as they relate to clinical considerations, and include reference to any concurrent and/or previous testing.

General

These comments summarize fundamental information about the test(s) and the component(s) assessed to aid in interpretation of their clinical applicability.

TESTING METHODS
The section lists the procedures performed, the test source(s), and the applicable laboratory developed test disclaimer(s).

TEST RESULTS SUMMARY CHART
A chart tabulating results of tests ordered for the patient by the same client is included if previous and/or concurrent testing has been performed.

ELISA RESULTS GRAPH
A graph of ELISA results also is included if previous and/or concurrent testing has been performed; the graph may be found on a subsequent page.

For testing algorithm and additional information, refer to:
arupconsult.com/content/immunobullous-skin-diseases-screening

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IMMUNODERMATOLOGY LABORATORY REPORT

[redacted]

Submitter

ARUP Sendouts

Paraneoplastic Pemphigus (Paraneoplastic Autoimmune Multiorgan Syndrome) Expanded Antibody Panel by IIF with ELISA (Final result)

TESTING REPORT follows "See Note"
See Note

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

Specimen Details
[redacted] - ; Collected: 11/20/2024; Received: 11/22/2024

DIAGNOSTIC INTERPRETATION

Consistent with paraneoplastic pemphigus/paraneoplastic autoimmune multiorgan syndrome:

- Positive IgG epithelial antibody reactivity with rodent bladder substrates, including rat bladder, by indirect immunofluorescence; and
- Increased IgG envoplakin antibody level by ELISA

(See Results and Comments)

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RESULTS
Indirect Immunofluorescence (IIF)

Paraneoplastic Pemphigus IgG Antibodies

IgG: Positive, cell surface, titer 1:40 (H),
rat bladder substrate
Positive, basement membrane zone, titer 1:10 (H),
rat bladder substrate

Positive, cell surface, titer 1:40 (H),
mouse bladder substrate
Positive, basement membrane zone, titer 1:10 (H),
mouse bladder substrate

Negative, intercalated discs, mouse heart substrate

Negative, portal tracts, 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/intercellular substance,
monkey esophagus substrate
Positive, 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: 1.07 ratio U/mL (H)

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

[redacted]

[redacted]

Specific

IgG antibodies reacting with rodent substrates, including cell surface/intercellular substance and basement membrane zone antibodies with rat and mouse bladder substrates and cell surface/intercellular substance and basement membrane zone antibodies with monkey esophagus substrate, as detected in this indirect immunofluorescence testing, along with an increased level of IgG envoplakin antibodies by ELISA, 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 by indirect immunofluorescence 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 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 correlate with extent of mucocutaneous paraneoplastic pemphigus disease expression.

Clinical correlation is needed. If indicated 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 comprehensive testing that includes the epithelial antibody tests below, order
- Immunobullous Disease Antibody Panel (ARUP test number 3001409);

Alternatively, to assess for specific disease-associated epithelial antibodies or individual antibody targets, order
- 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), and
- Collagen Type VII Antibody, IgG by ELISA (ARUP test number 2010905).

Detection, levels, and patterns of diagnostic antibodies may fluctuate with disease manifestations. Monitoring of 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, including request for additional testing on this serum specimen, 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

[redacted]

[redacted]

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 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) with two limiting dilution, end-point titers (antibody titer X 2)]

Enzyme-Linked Immunosorbent Assay (ELISA)

IgG envoplakin serum antibody level determined by ELISA (Euroimmun US, Inc.). The performance characteristics of this test have been validated by the University of Utah Immunodermatology Laboratory and meet specifications required by the Clinical Laboratory Improvement Amendment of 1988 (CLIA). The test has CE Mark certification as an in vitro diagnostic in the European Union. The testing has not been cleared or approved by the US Food and Drug Administration (FDA). The testing was performed in a CLIA-certified laboratory and is intended for clinical purposes. [One ELISA]

Electronically signed by [redacted] on 11/22/24 at 7:19 PM.

Resulting Laboratory

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