Basement Membrane Zone Antibody Panel

ARUP LABORATORIES

Patient: [redacted]
DOB: [redacted] Age: [redacted] Sex: [redacted]
Patient Identifiers: [redacted]

Visit Number (FIN): [redacted]

Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108

Physician: [redacted]

ARUP Test Code: 3001410

Collection Date: 02/02/2024
Received in lab: 02/02/2024
Completion Date: 02/07/2024

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

Basement Membrane Zone Antibody Panel (Final result)

TESTING REPORT follows "See Note"
See Note

CLINICAL INFORMATION
Urticarial plaques with blistering on skin, few milia, and mucosal involvement with recent antibiotic therapy. Presumptive diagnosis is pemphigoid, epidermolysis bullosa acquisita, linear IgA disease.

Specimen Details
[redacted] - ; Collected: 2/2/2024; Received: 2/6/2024

DIAGNOSTIC INTERPRETATION

Consistent with pemphigoid:

Positive IgG basement membrane zone antibodies, epidermal (roof) localization with split skin substrate (salt split skin), and negative IgA basement membrane zone antibodies by indirect immunofluorescence, and

Increased IgG BP230 antibody level with normal IgG BP180 and IgG type VII collagen antibody levels by ELISAs

(See Results and Comments)

RESULTS

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Page: 1 of 6

[redacted]

PCP: Unspecified

Indirect Immunofluorescence (IIF)

Basement Membrane Zone (BMZ) IgG and IgA Antibodies

IgG: Positive, titer 1:2560 (H),
monkey esophagus substrate
Positive, epidermal pattern (roof), titer 1:1280 (H),
human split skin substrate

IgA: Negative, monkey esophagus substrate
Negative, human split skin substrate

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

Localization Pattern on Human BMZ Split Skin:
Epidermal (roof) or combined epidermal-dermal
(roof and floor) IgG and/or IgG4 BMZ antibodies
= pemphigoid (including pemphigoid gestationis,
bullous pemphigoid, some types of mucous
membrane pemphigoid)

Dermal (floor) IgG and/or IgG4 BMZ antibodies =
epidermolysis bullosa acquisita or bullous lupus
erythematosus or anti-laminin-332 pemphigoid or
anti-p200 (laminin gamma-1) pemphigoid or another
rare pemphigoid subtype

Epidermal (roof), combined epidermal-dermal (roof
and floor), or dermal (floor) IgA BMZ antibodies
= linear IgA disease (including linear IgA bullous
dermatosis and chronic bullous disease of
childhood)

IgA and IgG basement membrane zone
antibodies may be co-expressed in basement
membrane zone antibody-associated diseases

(H) = high/positive

Enzyme-Linked Immunosorbent Assay (ELISA)

Bullous Pemphigoid (BP)180 and BP230 IgG Antibodies

IgG BP180 antibody level: 3 U/mL

Reference Range:
Normal (negative) = Less than 9 U/mL
Increased (H) (positive) = 9 U/mL and greater

Chart continues on following page(s)

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PCP: Unspecified

IgG BP230 antibody level: 28 U/mL (H)

Reference Range:
Normal (negative) = Less than 9 U/mL
Increased (H) (positive) = 9 U/mL and greater

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

Type VII Collagen IgG Antibodies

IgG type VII collagen antibody level: 1 U/mL

Reference Range:
Normal (negative) = Less than 7 U/mL
Slightly increased (H) (positive) = 7-8 U/mL
Increased (H) (positive) = 9 U/mL and greater

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

COMMENTS

Specific

The positive IgG basement membrane zone antibodies with monkey esophagus substrate and epidermal localization (roof) with human split skin substrate, also known as salt split skin, by indirect immunofluorescence and the increased IgG BP230 antibody level by ELISA support the diagnosis of pemphigoid. The IgG type VII collagen antibody level is normal by ELISA, and, together with the absence of dermal (floor) IgG basement membrane zone antibody reactivity on split skin substrate by indirect immunofluorescence, is against the diagnosis of epidermolysis bullosa acquisita. The absence of IgA basement membrane zone antibody reactivity is against the diagnosis of linear IgA disease or linear IgA/IgG bullous dermatosis.

Detection, levels, and patterns of diagnostic antibodies may fluctuate with disease manifestations, and IgG BP180 antibody levels correlate with disease activity in some patients with pemphigoid. Clinical correlation is needed, including with direct immunofluorescence findings on a biopsy specimen and treatment status. Monitoring antibody profiles by indirect immunofluorescence and antibody levels by ELISAs may be useful in assessing disease activity and expression, including response to therapy.

General

Approximately 80 percent of patients with bullous pemphigoid,

epidermolysis bullosa acquisita, and linear IgA bullous dermatosis have positive antibodies to basement membrane zone components in their sera detected by indirect immunofluorescence. Approximately 50 percent of patients with mucous membrane/cicatricial pemphigoid demonstrate antibodies to basement membrane zone components detected by indirect immunofluorescence. The immunoglobulin class of basement membrane zone antibodies and pattern of antibody localization on split skin substrate distinguish the diseases. Positive serum IgA epithelial basement membrane zone antibodies are highly specific diagnostic markers for linear IgA disease. IgA basement membrane zone antibodies by indirect immunofluorescence may be found in variant presentations of mucous membrane pemphigoid and epidermolysis bullosa acquisita. IgA basement membrane zone antibodies may be co-expressed with IgG basement membrane zone antibodies in some patients with pemphigoid including mucous membrane/cicatricial pemphigoid.

Major molecular structures in the basement membrane zone to which IgG pemphigoid antibodies bind have been identified and termed "BP180" for a 180 kDa bullous pemphigoid antigen (also known as bullous pemphigoid antigen 2, BPAG2, or type XVII collagen, COL17) and "BP230" for a 230 kDa bullous pemphigoid antigen (also known as bullous pemphigoid antigen 1, BPAG1). BP180 is a transmembrane component of the basement membrane zone with collagen-like domains; the non-collagenous 16A (NC16A) antigenic domain of BP180 has been identified as a main antigenic target. BP230 is located in the hemidesmosomal plaque of basal cells in the epidermis. Serum levels of IgG BP180 and IgG BP230 antibodies are determined by enzyme-linked immunosorbent assays (ELISA), and serum levels of IgG BP180 antibodies may correlate with disease activity in pemphigoid, diminishing with treatment response. Up to 7 percent of individuals who do not have pemphigoid, including patients with other immunobullous diseases, have increased levels of IgG BP180 and/or BP230 antibodies by ELISAs. Patients with pemphigoid may show reactivity to multiple basement membrane zone components in addition to or other than the BP180 and BP230 epitopes displayed in the tested ELISAs.

Type VII collagen is a component of anchoring fibrils within epithelial basement membrane zone (skin and mucous membranes), and patients with epidermolysis bullosa acquisita characteristically develop IgG antibodies to type VII collagen. Together with dermal (floor) IgG basement membrane zone antibody localization on split skin substrate by indirect immunofluorescence, an increased serum IgG type VII collagen antibody level by ELISA provides support for the diagnosis of epidermolysis bullosa acquisita and also for a subset of bullous lupus erythematosus. Patients with inflammatory bowel disease, including Crohn disease and ulcerative colitis, with and without mucocutaneous manifestations of epidermolysis bullosa acquisita, may demonstrate increased levels of antibodies to type VII collagen. The major epitopes for antibody reactivity reside in the non-collagenous amino-terminal domain, NC1, with minor epitopes in the non-collagenous carboxy-terminal domain, NC2, of the three identical alpha chains that comprise type VII collagen. The tested ELISA contains combined purified recombinant antigens from both NC1 and NC2 for detection of IgG antibodies. Serum

[redacted]
PCP: Unspecified

antibody levels above the reference range threshold of 6 U/mL may correlate with disease activity. Patients with epidermolysis bullosa acquisita or bullous lupus erythematosus may develop antibodies to basement membrane zone antigens in addition to or other than the type VII collagen epitopes displayed in this ELISA, and patients with other epithelial antibody-associated disorders may develop overlapping basement membrane zone antibody expression with an increased level of IgG type VII collagen antibodies.

Tests that detect antibodies with specificity for other basement membrane zone antigens, including laminin-332, p200 (laminin gamma-1), and alpha6beta4 integrin, may be more sensitive than indirect immunofluorescence but are not currently available, except laminin-332 IgG antibodies in select laboratories. Mucous membrane involvement is predominant in anti-laminin-332 pemphigoid. Recognition of the association of this pemphigoid variant with underlying or developing malignancy (typically solid tumor) in up to one third of cases is critical so appropriate clinical evaluation is conducted. Patients with anti-p200 (laminin gamma-1) pemphigoid tend to be younger than those with bullous pemphigoid and have lesions that clinically resemble both bullous pemphigoid and the inflammatory epidermolysis bullosa acquisita variant that may include mucosal involvement. For those patients with antibodies to alpha6beta4 integrin, alpha6 epitopes primarily are targeted in oral pemphigoid, and beta4 epitopes primarily are targeted in ocular pemphigoid.

TESTING METHODS
Indirect Immunofluorescence (IIF)

IgG and IgA Epithelial Basement Membrane Zone (BMZ) Antibodies

Patient serum is progressively diluted beginning at 1:5 in three two-fold screening dilutions, layered on sections of human skin split at the basement membrane zone and monkey esophagus substrates, and reacted with fluorescein isothiocyanate (FITC)-conjugated antibodies to IgG and IgA. When positive, 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 substrate, and the pattern of staining on split skin substrate also is reported. 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 assays, two antibodies on two substrates (IIF X 4) with two limiting dilution, end-point titers (antibody titer X 2)]

Enzyme-Linked Immunosorbent Assays (ELISA)

[redacted]
PCP: Unspecified

IgG BP180 and IgG BP230 serum antibody levels determined by U.S. Food and Drug Administration (FDA)-approved ELISAs (Mesacup, MBL BION). [Two ELISAs]

IgG type VII collagen serum antibody level determined by ELISA (Mesacup, MBL International). The performance characteristics of this ELISA testing were determined by the Immunodermatology Laboratory at the University of Utah. The testing 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. [One ELISA]

Electronically signed by [redacted] on 02/07/24 at 11:45 AM.

Resulting Laboratory

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