

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

Physician: Doctor, Example

Patient: Patient, Example

DOB: 6/17/1957
Gender: Female
Patient Identifiers: 01234567890ABCD, 012345
Visit Number (FIN): 01234567890ABCD
Collection Date: 00/00/0000 00:00

Basement Membrane Zone Antibody Panel

ARUP test code 3001410

Basement Membrane Zone Ab Panel

See Note

IMMUNODERMATOLOGY REPORT

Specimen(s):
1. Serum specimen

Clinical/Diagnostic Information:
No clinical information provided.

DIAGNOSTIC INTERPRETATION

Slightly increased IgG type VII collagen antibody level by ELISA, indeterminate for epidermolysis bullosa acquisita or bullous lupus erythematosus, also possible association with inflammatory bowel disease; negative IgG, including IgG4, and IgA basement membrane zone antibodies by indirect immunofluorescence, and normal IgG BP 180 and IgG BP 230 antibody levels by ELISAs

(See Results and Comments)

RESULTS

Indirect Immunofluorescence

Basement Membrane Zone (BMZ) IgG, IgG4, and IgA Antibodies

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

IgG4: Negative, monkey esophagus substrate
Negative, human split skin substrate

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

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

Pattern on Human BMZ Split Skin:
IgG epidermal or epidermal-dermal combined BMZ antibody pattern = pemphigoid

IgG dermal BMZ antibody pattern = epidermolysis bullosa acquisita

IgA epidermal, epidermal-dermal combined, or,

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

dermal BMZ antibody pattern = linear IgA bullous dermatosis

(H = high/positive)

Enzyme Linked Immunosorbent Assay (ELISA)

Bullous Pemphigoid (BP) 180 and 230 IgG Antibodies

IgG BP 180 antibodies: 3 units

Reference Range:

Positive (H) = Greater than or equal to 9 units

Negative = Less than 9 units

IgG BP 230 antibodies: 2 units

Reference Range:

Positive (H) = Greater than or equal to 9 units

Negative = Less than 9 units

Collagen VII IgG Antibodies

IgG Collagen VII antibodies: 7 units (Slightly increased)

Reference Range:

Positive (H) = Greater than or equal to 9 units

Slightly increased, positive (H) = 7-8 units

Normal/negative = 0-6 units

(H = high/increased; units = units/mL serum)

COMMENTS

Specific

The IgG type VII collagen antibody level by ELISA is slightly increased, providing support for the diagnosis of epidermolysis bullosa acquisita, but the indirect immunofluorescence is negative for IgG, including IgG4, and IgA basement membrane zone antibodies, which typically are positive in a dermal pattern on split skin substrate in epidermolysis bullosa acquisita. The ELISA testing was repeated with similar findings in each assay. The indirect immunofluorescence, therefore, does not provide additional support for the diagnosis of epidermolysis bullosa acquisita or other disorders with associated basement membrane zone antibodies, including bullous pemphigoid or linear IgA bullous dermatosis.

The IgG type VII collagen antibody level by ELISA may be more sensitive for diagnosing epidermolysis bullosa acquisita than indirect immunofluorescence, and this finding may reflect evolving or treated disease. IgG type VII collagen antibodies have been reported in mucous membrane pemphigoid; in this pemphigoid subtype, a large proportion of patients, otherwise, do not have detectable circulating basement membrane zone antibodies. Moreover, patients with bullous lupus erythematosus also may develop antibodies to type VII collagen. Therefore, these results do not rule out the diagnosis of mucous membrane pemphigoid or bullous lupus erythematosus in which antibodies to type VII collagen may develop. The IgG type VII collagen antibody level is relatively slightly increased and could be nonspecific.

Atypical antibody profiles may be found in: atypical immunobullous disease presentations; autoimmune diseases in patients who are autoantibody producers; drug reactions; nonspecific expression of antibodies; as well as associated with paraneoplastic conditions/malignancy including paraneoplastic pemphigus and other conditions. Detection and levels of diagnostic antibodies may fluctuate with disease expression. Clinical correlation is needed, including correlation with direct immunofluorescence on a biopsy specimen and treatment

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status, with consideration for monitoring antibody profiles and levels to aid in assessing disease expression and activity.

If it would be helpful to discuss this patient's 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

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. Approximately 20 percent of patients with mucous membrane pemphigoid, including cicatricial/mucous membrane pemphigoid, demonstrate antibodies to basement membrane zone components. The pattern of staining on split skin specifies disease. IgG4 subclass reactivity may be more sensitive than IgG in some patients with immunobullous diseases.

Major molecular structures in the basement membrane zone to which IgG pemphigoid antibodies bind have been identified and termed "BP 180" for a 180 kDa bullous pemphigoid antigen and "BP 230" for a 230 kDa bullous pemphigoid antigen. BP 180 is a transmembrane component of the basement membrane zone with collagen-like domains and is a principal antigenic target in mucous membrane pemphigoid. BP 230 is located in the hemidesmosomal plaque of basal cells in the epidermis. Serum levels of IgG BP 180 and IgG BP 230 antibodies are in the negative range in normal individuals, and serum levels of IgG BP 180 may correlate with disease activity in pemphigoid, diminishing with treatment response. Patients with pemphigoid may show reactivity to multiple basement membrane zone components in addition to or other than the BP 180 and BP 230 epitopes expressed in these ELISAs.

Collagen VII 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 collagen VII. Patients with inflammatory bowel disease, including Crohn's disease and ulcerative colitis, with and without mucocutaneous manifestations of epidermolysis bullosa acquisita and patients with bullous lupus erythematosus also may develop antibodies to collagen VII. The major epitopes for epidermolysis bullosa acquisita 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 collagen VII. This ELISA contains combined purified recombinant antigens from both NC1 and NC2 for detection of IgG antibodies in serum. The reference range for this assay indicates a threshold level at 6 units/mL, and levels above this threshold may correlate with disease activity. The IgG type VII collagen antibody level by ELISA is a sensitive diagnostic marker together with dermal pattern IgG basement membrane zone antibody reactivity on split skin substrate by indirect immunofluorescence in patients with epidermolysis bullosa acquisita and in a subset of patients with bullous lupus erythematosus, although patients with these disorders may demonstrate antibodies to basement membrane zone antigens in addition to or other than the collagen VII epitopes expressed in this ELISA.

TESTING METHODS

Indirect Immunofluorescence

Basement Membrane Zone (BMZ) IgG, IgG4, and IgA Antibodies

The patient's serum is progressively diluted beginning at 1:5 in three two-fold screening dilutions, layered on sections of monkey esophagus substrate and human basement membrane zone split skin substrate, and stained with fluorescein-conjugated

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anti-IgA and anti-IgG using Analyte Specific Reagents (ASRs). 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. Fluorescein-conjugated anti-IgG4 also is tested to increase test sensitivity (maximum serum dilution of 1:20). These tests were developed and their performance characteristics determined by the Immunodermatology Laboratory at the University of Utah. They have not been cleared or approved by the U.S. Food and Drug Administration. ASRs are used in many laboratory tests necessary for standard medical care and generally do not require FDA approval. These tests should not be regarded as investigational or for research only. [Immunofluorescence studies, three antibodies on two substrates]

Enzyme Linked Immunosorbent Assay (ELISA)

IgG BP 180 and IgG BP 230 serum antibody levels determined by U.S. Food and Drug Administration-approved ELISAs (Mesacup, MBL BION).
 [Two ELISAs]

Collagen VII IgG serum antibody level determined by ELISA (Mesacup, MBL International). This test 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 U.S. Food and Drug Administration. [One ELISA]

Kristin M Leiferman, MD
 Immunodermatologist
 Electronically signed 5/10/2019 6:01:04PM
 Performed at: ARUP - University Hospital Laboratory 50 N. Medical Drive Salt Lake City UT 84132

EER Basement Membrane Zone Ab Panel

See Note

Performed at: ARUP - University Hospital Laboratory 50 N. Medical Drive Salt Lake City UT 84132

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Basement Membrane Zone Ab Panel	19-122-401312	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
EER Basement Membrane Zone Ab Panel	19-122-401312	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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