

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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1971	
Gender:	Female	
Patient Identifiers:	01234567890ABCD, 012345	
Visit Number (FIN):	01234567890ABCD	
Collection Date:	00/00/0000 00:00	

Basement Membrane Zone (Epithelial) Antibodies, IgG by IIF

ARUP test code 0092056

EER Epithelial BMZ Ab, IgG See Note Authorized individuals can access the ARUP Enhanced Report using the following link: Epithelial BMZ Ab, IgG See Note CLINICAL INFORMATION Skin fragility, tense blisters, vesicles, erosions, and milia. Presumptive diagnosis is epidermolysis bullosa acquisita versus porphyria cutaneous tarda. Specimen Details - ; Collected: 11/17/2023; Received: 11/17/2023 DIAGNOSTIC INTERPRETATION Positive IgG, including IgG4, basement membrane zone antibodies demonstrating dermal localization (floor) with split skin substrate by indirect immunofluorescence and concurrent ELISA testing demonstrating an increased IgG type VII collagen antibody level, consistent with subepidermal immunobullous disease, including epidermolysis bullosa acquisita or bullous lupus erythematosus (See Results, Comments, separate concurrent Collagen Type VII Antibody, IgG by ELISA testing report with additional findings and comments, and Basement Membrane Zone Antibody Test Results Summary Chart with concurrent findings) RESULTS Indirect Immunofluorescence (IIF) Basement Membrane Zone (BMZ) IgG and IgG4 Antibodies IgG: Positive, titer 1:5120 (H), monkey esophagus substrate Positive, dermal pattern (floor), titer 1:2560 (H), human split skin substrate IgG4: Positive, titer greater than 1:20 (H), monkey esophagus substrate Positive, dermal pattern (floor), titer greater than 1:20 (H), human split skin

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

substrate

Unless otherwise indicated, testing performed at:



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

IGA and IGG basement membrane zone antibodies may be co-expressed in basement membrane zone antibody-associated diseases

(H) = high/positive

COMMENTS

Specific

Based on the dermal localization (floor) of IgG, including IgG4, basement membrane zone antibodies with human split skin substrate (also known as salt split skin), these indirect immunofluorescence findings support the diagnosis of epidermolysis bullosa acquisita. In addition, the IgG type VII collagen antibody level is increased by ELISA in concurrent testing, further supporting the diagnosis of epidermolysis bullosa acquisita (separate report with additional comments). See chart (below) for summary of concurrent basement membrane zone antibody test results.

A subset of patients with bullous systemic lupus erythematosus has the same indirect immunofluorescence reactivity as epidermolysis bullosa acquisita with dermal (floor) IgG basement membrane zone antibody localization on split skin substrate and also may exhibit increased levels of IgG type VII collagen antibodies. Two subsets of pemphigoid, namely, anti-laminin-332 and anti-p200 (laminin gamma-1) pemphigoid, demonstrate IgG basement membrane zone antibody reactivity with the dermal side of the split skin substrate, although these two pemphigoid subsets do not characteristically demonstrate increased levels of IgG type VII collagen antibodies, as observed in this patient. Furthermore, IgG and IgA basement membrane zone antibodies may be co-expressed which may have implications for disease severity and treatment considerations. If indicated to further define the immunopathological profile with respect to basement membrane zone antibodies, 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 for:

 Basement Membrane Zone (Epithelial) Antibodies, IgA by indirect immunofluorescence (ARUP test number 0092057).

Patients with inflammatory bowel disease, including Crohn disease and ulcerative colitis, with and without mucocutaneous manifestations of epidermolysis bullosa acquisita or associated with lupus erythematosus may demonstrate increased levels of IgG type VII collagen antibodies. Therefore, although the overall immunopathological profile is consistent with epidermolysis bullosa acquisita, the findings may be observed in bullous lupus erythematosus and do not rule out the diagnoses of

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ARUP LABORATORIES | 800-522-2787 | aruplab.com 500 Chipeta Way, Salt Lake City, UT 84108-1221 Jonathan R. Genzen, MD, PhD, Laboratory Director Patient: Patient, Example ARUP Accession: 23-321-114328 Patient Identifiers: 01234567890ABCD, 012345 Visit Number (FIN): 01234567890ABCD Page 2 of 5 | Printed: 10/24/2024 7:24:36 AM 4848



anti-laminin-332 pemphigoid or anti-p200 (laminin gamma-1) pemphigoid with increased IgG type VII collagen antibodies associated with another condition.

Disorders with dermal IgG basement membrane zone antibodies on split skin substrate by indirect immunofluorescence cannot be further distinguished with currently available diagnostic laboratory techniques, except laminin-332 IgG antibodies in select laboratories. It is important to note that up to one third of patients with anti-laminin-332 pemphigoid have associated malignancy. Therefore, clinical correlation is needed with clinical evaluation as indicated. Monitoring serum antibody profiles by indirect immunofluorescence and antibody levels by ELISAs may aid in assessing disease expression and activity, including 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

Approximately 80 percent of patients with bullous pemphigoid and epidermolysis bullosa acquisita have positive IgG antibodies to basement membrane zone components in their sera; the pattern of antibody localization on split skin substrate, also known as salt split skin, distinguishes the diseases. Approximately 50 percent of patients with mucous membrane/cicatricial pemphigoid demonstrate antibodies to basement membrane zone components. IgG4 subclass reactivity by indirect immunofluorescence may be more sensitive than IgG in some patients with immunobullous disease. 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, epidermolysis bullosa acquisita, lupus erythematosus, and linear IgA/IgG bullous dermatosis.

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 and "BP230" for a 230 kDa bullous pemphigoid antigen. Type VII collagen is a component of anchoring fibrils within epithelial basement membrane zone (skin and mucous membranes) and is an antigenic target of IgG autoantibodies in patients with epidermolysis bullosa acquisita and in a subset of patients with bullous lupus erythematosus. Antibodies to these molecular structures are determined by enzyme-linked immunosorbent assay (ELISA). ELISA may be more sensitive testing than indirect immunofluorescence in assessing antibody reactivity to certain epitopes of the target components rather than the basement membrane zone in tissue.

TESTING METHODS Indirect Immunofluorescence (IIF)

IgG and IgG4 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. 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. FITC-conjugated anti-IgG4 is tested to increase test sensitivity (maximum serum dilution of 1:20). This

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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)]

TEST RESULTS SUMMARY CHART						
Basement Membrane Zone Antibodies						
Serum Date of IgG and IgG4 IgA BP BP Col Number Specimen BMZ Titers BMZ Titers 180 230 VII						
23-8601 11/03/23 IGG ME: 1:5120 ME: NA NA NA NA IGG SS: Derm, SS: NA 1:2560 IGG4 ME:>1:20 IGG4 SS: Derm, >1:20						
23-8602 11/03/23 IGG ME: NA ME: NA NA NA 88 IGG SS: NA SS: NA IGG4 ME: NA IGG4 SS: NA						
ELISA Reference Ranges:						
IgG BP180 and IgG BP230 Antibody Levels Normal (negative) = Less than 9 U/mL Increased (H) (positive) = 9 U/mL and greater						
IgG Type VII Collagen Antibody Level Normal (negative) = Less than 7 U/mL Slightly increased (H) (positive) = 7-8 U/mL Increased (H) (positive) = 9 U/mL and greater						
Chart Key:						
<pre>IgG BMZ = IgG basement membrane zone (BMZ) antibodies by indirect immunofluorescence IgG4 BMZ = IgG4 basement membrane zone (BMZ) antibodies by indirect immunofluorescence IgA BMZ = IgA basement membrane zone (BMZ) antibodies by indirect immunofluorescence</pre>						
 ME = Antibody absence (negative) or antibody presence (positive endpoint titer) on monkey esophagus (ME) substrate SS = Antibody absence (negative) or antibody presence (positive pattern and endpoint titer) on split skin (SS) substrate 						
<pre>Epi = epidermal localization (roof) on split skin substrate (IgG - pemphigoid including bullous pemphigoid, some mucous membrane pemphigoid, and other pemphigoid variants; IgA - linear IgA disease including linear IgA bullous dermatosis and chronic bullous disease of childhood) Derm = dermal localization (floor) on split skin substrate (IgG - epidermolysis bullosa acquisita, bullous</pre>						
Iupus erythematosus, anti-laminin-332 pemphigoid, anti-p200 (laminin gamma-1) pemphigoid, other rare pemphigoid subtypes; IgA - linear IgA disease including linear IgA epidermolysis bullosa acquisita) Comb = combined epidermal-dermal localization (roof and						

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floor) on split skin substrate (IgG -pemphigoid and pemphigoid variants; IgA - linear IgA disease) BP180 = IgG BP180 antibody level (U/mL) by ELISA BP230 = IgG BP230 antibody level (U/mL) by ELISA Col VII = IgG Collagen VII antibody level (U/mL) by ELISA NA = Not Assayed Electronically signed by 4:17 PM. on 11/17/23 at

4117 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 Epithelial BMZ Ab, IgG	23-321-114328	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00	
Epithelial BMZ Ab, IgG	23-321-114328	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00	

END OF CHART

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