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PATIENT REPORT

Patient Age/Sex: 51 years Female

Specimen Collected: 21-Jun-22 15:36

Epithelial BMZ Ab, IgG **|Received: 22-Jun-22 09:45** **Report/Verified: 22-Jun-22 12:25**

Procedure	Result	Units	Reference Interval
Epithelial BMZ Ab,IgG	See Note [f1]		

Result Footnote

f1: Epithelial BMZ Ab, IgG
CLINICAL INFORMATION
Skin fragility, tense blisters, vesicles, erosions, and milia. Presumptive diagnosis is epidermolysis bullosa acquisita versus porphyria cutaneous tarda.

Specimen Details
S22-IP0000499 - Serum; Collected: 6/21/2022; Received: 6/22/2022

DIAGNOSTIC INTERPRETATION
Positive IgG, including IgG4, basement membrane zone antibodies demonstrating dermal localization (floor) with split skin substrate by indirect immunofluorescence and concurrent testing demonstrating an increased IgG type VII collagen antibody level by ELISA; 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 1:5,120 (H), monkey esophagus substrate
Positive, dermal pattern (floor), titer 1:2,560 (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 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, mucous membrane pemphigoid)

Dermal (floor) IgG and/or IgG4 BMZ antibodies =

Result Footnote

f1: Epithelial BMZ Ab, IgG
epidermolysis bullosa acquisita or bullous lupus erythematosus or anti-laminin-332 pemphigoid or anti-p200 (laminin gamma-1) pemphigoid or another rare pemphigoid subtype

(H) = high/positive

COMMENTS

Specific

Based on the dermal localization of IgG, including IgG4, basement membrane zone antibodies with human split skin substrate (also known as salt split skin), the 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 at end of report (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.

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 in this and concurrent testing is consistent with epidermolysis bullosa acquisita, the findings may be observed in bullous lupus erythematosus and do not rule out the diagnoses of 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. 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 and with consideration for monitoring antibody profiles by indirect immunofluorescence and antibody levels by ELISAs to 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 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 pattern of antibody localization on split skin substrate distinguishes the diseases. IgG4 subclass

Result Footnote

f1: Epithelial BMZ Ab, IgG
reactivity by indirect immunofluorescence 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 "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. In certain patients with pemphigoid, IgG BP180 and/or IgG BP230 antibody levels by ELISAs may be more sensitive diagnostic markers than indirect immunofluorescence, and, in certain patients with epidermolysis bullosa acquisita, the IgG type VII collagen antibody level by ELISA may be a more sensitive diagnostic marker than indirect immunofluorescence.

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 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, 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 Number	Date of Specimen	IgG and IgG4 BMZ Titers	IgA BMZ Titers	BP 180	BP 230	Col VII
22-0497	06/21/22	IgG ME: NA IgG SS: NA IgG4 ME: NA IgG4 SS: NA	ME: NA SS: NA	NA	NA	88
22-0499	06/21/22	IgG ME: 1:5120 IgG SS: Derm, 1:2560 IgG4 ME:>1:20 IgG4 SS: Derm, >1:20	ME: NA SS: NA	NA	NA	NA

ELISA Reference Ranges:

IgG BP180 and IgG BP230 Antibody Levels

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*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab

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Result Footnote

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f1:     Epithelial BMZ Ab, IgG
                  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:

        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

        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

        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
               lupus 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
               floor) on split skin substrate (IgG -
               pemphigoid and pemphigoid variants; IgA - linear
               IgA disease)

        BP 180 = IgG BP 180 antibody level (U/mL) by ELISA
        BP 230 = IgG BP 230 antibody level (U/mL) by ELISA
        Col VII = IgG Collagen VII antibody level (U/mL) by
                  ELISA

        NA  = Not Assayed
        ____________________________________________________________

        Electronically signed by Kristin M. Leiferman, MD, on 06/22/22 at 12:24 PM.
        Performed At: IMMUNODERMATOLOGY LABORATORY
        417 S. WAKARA WAY, SUITE 2151
        SALT LAKE CITY, UT  84108
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Result Footnote

f1: Epithelial BMZ Ab, IgG
Medical Director: JOHN JOSEPH ZONE, MD
CLIA Number: 46D0681916

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab