Client: Example Client ABC123
123 Test Drive

UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB

Sex:

Patient Identifiers: 01234567890ABCD, 012345

Visit Number (FIN): 01234567890ABCD

Collection Date: 01/01/2017 12:34

Basement Membrane Zone and Cell Surface (Epithelial) Antibodies, IgG and IgA by IIF

ARUP test code 0090299

Epithelial Skin Antibodies

See Note

CLINICAL INFORMATION
Blisters, erosions, fine scaly patches on skin. Presumptive diagnosis is immunobullous disease, possible pemphigus or pemphigoid.

Specimen Details
S22-IP0000501 - Serum; Collected: ; Received:

DIAGNOSTIC INTERPRETATION

Consistent with IgG-variant pemphigus without evidence for pemphigoid

(See Results and Comments including further testing recommendations)

RESULTS
Indirect Immunofluorescence (IIF)

Cell Surface (CS)/Intercellular Substance (ICS) IgG and IgA Antibodies

IgG: Positive, titer 1:640 (H), monkey esophagus substrate
Positive, titer 1:160 (H), intact human skin substrate

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

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

(H) = high/positive

Basement Membrane Zone (BMZ) IgG and IgA Antibodies

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

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

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

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 = 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)

(H) = high/positive

COMMENTS

Specific

The indirect immunofluorescence findings, demonstrating positive IgG cell surface (CS), also known as intercellular substance (ICS), antibodies on both monkey esophagus substrate and intact human skin substrate, support the diagnosis of pemphigus vulgaris or pemphigus foliaceus or another IgG-variant pemphigus. Pemphigus foliaceus and pemphigus vulgaris can be distinguished by the predominance of IgG desmoglein 1 or IgG desmoglein 3 antibodies, respectively, determined by enzyme-linked immunosorbent assay (ELISA). ELISA testing for IgG desmoglein 1 and IgG desmoglein 3 antibodies is highly sensitive, with greater than 90 percent of pemphigus patients showing increased levels of one or both antibodies. Correlation with ELISA testing for IgG desmoglein 1 and IgG desmoglein 3 antibody levels is recommended. The additional testing can be accomplished on this serum specimen by contacting ARUP Client Services, 1-800-242-2787, option 2, with add-on test request for:
- Desmoglein 1 and Desmoglein 3 (Pemphigus) Antibodies, IgG by ELISAs (ARUP test number 0090649).

IgG CS/ICS antibody titers by indirect immunofluorescence and IgG desmoglein antibody levels by ELISA correlate with disease activity in pemphigus foliaceus and pemphigus vulgaris. Of note, cell surface reactivity by indirect immunofluorescence may be observed transiently and/or nonspecifically in normal individuals, and in patients with infections, drug reactions, and other mucocutaneous disorders.

The negative indirect immunofluorescence findings for IgG and IgA basement membrane zone antibodies do not provide support for, but do not rule out, the diagnoses of concurrent pemphigoid, epidermolysis bullosa acquisita, and linear IgA disease or a mixed epithelial antibody profile. The results do not rule out mucous membrane/cicatricial pemphigoid because most patients with this pemphigoid variant do not have positive/increased basement membrane zone antibodies detected.

IgG BP180 and/or IgG BP230 antibody levels, determined by ELISAs, may be more sensitive diagnostic markers than indirect immunofluorescence in pemphigoid, and the IgG type VII collagen antibody level, determined by ELISA, may be a more sensitive diagnostic marker than indirect immunofluorescence in

epidermolysis bullosa acquisita. If clinically indicated to further evaluate for concurrent pemphigoid and/or epidermolysis bullosa acquisita and/or mixed epithelial antibody expression, additional testing can be accomplished on this serum specimen by contacting ARUP Client Services, 1-800-242-2787, option 2, with add-on test request(s) for:
- Bullous Pemphigoid (BP180 and BP230) Antibodies, IgG by ELISAs (ARUP test number 0092566) and/or
- Collagen Type VII Antibody, IgG by ELISA (ARUP test number 2010905).

Clinical correlation is needed, including with direct immunofluorescence findings on a biopsy specimen and treatment status, with consideration for additional recommended ELISA testing, particularly for IgG desmoglein 1 and IgG desmoglein 3 antibodies, and for monitoring antibody profiles by indirect immunofluorescence and antibody levels by ELISAs in assessing disease expression and activity, including response to therapy.

General

Greater than 80 percent of patients with pemphigus have positive epithelial cell surface (CS), also known as intercellular substance (ICS), antibodies in their sera identified by indirect immunofluorescence. IgG CS/ICS antibodies characteristically are positive by indirect immunofluorescence in IgG pemphigus variants, including pemphigus foliaceus and pemphigus vulgaris. IgA CS/ICS antibodies, are positive by indirect immunofluorescence in patients with IgA pemphigus and in some pemphigus variants along with positive IgG CS/ICS antibodies. Serum antibody titers correlate with disease activity, and CS/ICS antibodies may be in low titer or negative in patients whose disease activity is minimal and/or under therapeutic control. Cell surface antibodies are implicated in the pathophysiology of pemphigus. However, cell surface reactivity may be observed transiently and/or nonspecifically in normal individuals and in patients with infections, drug reactions, and other mucocutaneous disorders, including other immunobullous diseases, generally in low titer.

Approximately 80 percent of patients with bullous pemphigoid and epidermolysis bullosa acquisita have positive IgG 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 (also known as salt split skin) distinguish the diseases.

Positive serum IgA epithelial basement membrane zone antibodies are highly specific diagnostic markers for linear IgA disease and are present in up to 80 percent of patients with linear IgA bullous dermatosis. Titers of positive IgA basement membrane zone antibodies may be useful markers in following disease expression and activity. IgA basement membrane zone antibodies 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 and characteristically in linear IgA/IgG bullous dermatosis. When co-expressed, the presence of two antibody classes with reactivity toward basement membrane zone may have implications for disease severity and treatment considerations. Based on the presence of IgA epithelial antibodies, dapsone therapy may be indicated if glucose-6-phosphate dehydrogenase, G6PD, enzymatic activity in blood is normal.

Mixed antibody profiles may be found in: concurrent disease presentations with co-dominant autoantibody expression; incidental overlapping antibodies with dominant features of one immunobullous disease; autoimmune diseases in patients who are multiple autoantibody producers; drug reactions; nonspecific expression of one or more of the antibodies; and associated with paraneoplastic conditions/malignancy.

TESTING METHODS
Indirect Immunofluorescence (IIF)

IgG and IgA Epithelial Basement Membrane Zone (BMZ) and Cell Surface (Intercellular Substance or ICS) Antibodies

Patient serum is progressively diluted beginning at 1:5 in four two-fold screening dilutions, layered on sections of human skin split at the basement membrane zone, intact human skin 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, two antibodies on three substrates (IIF X 6) with two limiting dilution, end-point titers (antibody titer X 2)]

Electronically signed by , MD, on at .
Performed At:

Medical Director: , MD
CLIA Number:

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Epithelial Skin Antibodies	22-172-118725			

END OF CHART

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