ARUP LABORATORIES
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Jonathan R. Genzen, MD, PhD, Chief Medical Officer

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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1989
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Eosinophil Granule Major Basic Protein, Tissue Biopsy

ARUP test code 2010921

EER Eosinophil Granule MBP in Tissues

See Note

Authorized individuals can access the ARUP Enhanced Report using the following link:

[redacted]

Specimen Medium and Quantity

Tissue

Performed At: IMMUNODERMATOLOGY LABORATORY
417 S. WAKARA WAY, SUITE 2151
SALT LAKE CITY, UT 84108
Medical Director: KRISTIN M. LEIFERMAN, MD
CLIA Number: 46D0681916

Eosinophil Granule MBP in Tissues

See Note

CLINICAL INFORMATION
Odynophagia, evaluate for eosinophilic esophagitis/eosinophil-related inflammation

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

DIAGNOSTIC INTERPRETATION

Abnormal with relatively minimal positive cellular and extracellular eosinophil granule major basic protein 1 (eMBP1), insufficient for eosinophilic esophagitis

Overall grade, 0.5+
Approximate tissue area with staining, 3 percent

(See Results, Comments, and representative image in the Enhanced Electronic Report/EELR and/or available upon request)

RESULTS
Examination of the tissue sections from proximal esophagus tested for eosinophil granule major basic protein 1 (eMBP1) reveals:

Cellular*: 2-3+ intensity, 0.5+ extent
(Eosinophil count, 2 per high power

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

field, 400x, 1 HPF counted)

Extracellular: 2-3+ intensity, 0.5-1+ extent with focal clusters of granules and focal confluent tissue

* Intact cells showing positive eMBP1 staining counted per 400x (40x objective lens and 10x eyepiece lens) high power field (HPF), 0.25 mm2, in areas of sections with maximal cells. Some cells may not be counted as intact cells that are obfuscated by extracellular eMBP1 deposition, and some degranulated cells that appear mainly intact may be included.

COMMENTS
Specific

The positive findings for eosinophil granule major basic protein 1 (eMBP1) in proximal esophagus tissues are abnormal but demonstrate minimal intact cellular infiltration and limited extracellular deposition. As judged by the staining in these tissue sections, eosinophil activity, as a contributor to the pathophysiology, is not prominent. These positive findings are insufficient to support a diagnosis of eosinophilic esophagitis. Of note, the tissue is small, and the findings could be a remnant of a previous state with greater eosinophil involvement and do not exclude the possibility of more prominent eosinophil involvement elsewhere in the esophagus or gastrointestinal tract.

Eosinophil-related inflammation is found in numerous disorders and commonly is observed in antibody-associated mucocutaneous diseases, such as pemphigoid and pemphigus and their variants, which may involve the esophagus, although neutrophil involvement is typically greater than eosinophil involvement in linear IgA disease. Eosinophils characteristically are not found in lichenoid reactions, except lichenoid drug reactions. Direct immunofluorescence can be helpful in identifying diagnostic markers in epithelial antibody-associated diseases and lichenoid reactions and can be performed on this specimen by contacting ARUP Client Services, 1-800-242-2787, option 2, with add-on test request for:
- Direct Immunofluorescence, Tissue Biopsy (Cutaneous, Mucosal, Epithelial) (ARUP test number 0092572).

Serum testing also may be helpful to assess for epithelial antibody-associated diseases and can be accomplished by submitting a serum specimen through ARUP Laboratories for:
- Immunobullous Disease Antibody Panel (ARUP test number 3001409).

Correlation of the findings with clinical presentation is needed, including with respect to medication use and treatment status. Correlation with histopathological examination of formalin-fixed tissue may be helpful, although extracellular granule protein deposition and degranulated cells may not be recognized in formalin-fixed tissues.

Digital scanned images of the eMBP1 immunostaining and negative control are available for this testing (see representative eMBP1 image in the Enhanced Electronic Report/EELR). If you would like a hard copy or an electronic file of the images and/or 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

Eosinophil infiltration and/or degranulation normally are present in thymus, lymph node, gastrointestinal tract from stomach through large intestine, and bone marrow; therefore, cellular and extracellular eosinophil granule major basic

protein 1 (eMBP1) localization normally is negative or minimal in esophagus tissue. Some eosinophils may be observed in tissues from incidental intravascular presence, more common in patients with peripheral blood eosinophilia and more common in highly vascularized tissues and in areas of hemorrhage.

Eosinophil activity may be recognized by cell infiltration and/or extracellular granule protein deposition in numerous inflammatory reactions including in eosinophilic gastrointestinal diseases (EGID). Eosinophilic esophagitis may be part of the EGID spectrum with involvement of eosinophil inflammatory activity in other parts of the gastrointestinal tract. Eosinophil counts of 15 cells or greater per high power field constitute a criterion for the diagnosis of eosinophilic esophagitis in formalin-fixed tissues; extracellular eMBP1 deposition is not established as a diagnostic feature but often is observed in the disorder.

Eosinophil-related inflammation, found in various pathologic conditions, demonstrates common tissue-destructive, tissue-altering effects, particularly revealed by extracellular deposition of eosinophil granule proteins. Eosinophils have demonstrated profibrotic, prothrombotic, and proinflammatory activities. Positive findings in normally negative tissue areas and findings with proportionately greater positive extracellular eMBP1, out-of-proportion to cellular eMBP1 localization, likely are associated with eosinophil involvement in the pathophysiology. Findings that demonstrate positive cellular eMBP1 with relatively minimal/proportionate extracellular eMBP1 deposition are indeterminate for the relative contribution of eosinophil involvement to the pathophysiology. Confluent tissue distribution of extracellular eosinophil granule proteins likely is abnormal, reflecting local ongoing or recent previous eosinophil activity with tissue deposition.

Eosinophil granule proteins, including eMBP1, have various and numerous toxic effects on tissues and organs. Eosinophil granule proteins may persist in tissues for a long time after deposition and may not reflect current activity; the duration of biological activity of extracellular granule proteins is not known but metabolic activity of extracellular granules has been observed. In determining whether eosinophils and eosinophil granule proteins may be playing a pathogenic role, consideration must be given to the treatment status of the patient (glucocorticoid and other therapies can rapidly reduce eosinophils in tissues as well as blood) and whether the specimens are representative of involved tissues; active eosinophil inflammation of gastrointestinal tissues may be patchy. Moreover, findings should be considered in view of the size and fragmentation of the tissues. Small tissue specimens are more prone to procurement and processing artifact, and some positive staining can be an artifact, especially extracellular granules in areas where eosinophils infiltrate and/or normally are found.

TESTING METHODS

The tissue from proximal esophagus, received in Michel transport medium, after washing and cryoembedding, is sectioned. Sections are reacted with antibody to eosinophil granule major basic protein 1 (eMBP1) by indirect immunofluorescence, utilizing a fluorescein isothiocyanate (FITC)-conjugated secondary antibody for detection, and subsequently examined by fluorescence microscopy to identify intact eosinophils and extracellular eosinophil granule protein deposition. The antibody-stained sections are graded on a visual analog scale with reference images. In addition to the overall grade recorded for cellular and extracellular staining in each specimen, a maximal eosinophil count per high power field, 400x, is performed, and an estimate of the percentage of tissue with positive eMBP1 staining is rendered. A technically adequate hematoxylin and eosin (H and E)-stained section of the tissue is comparatively

examined for morphological features and orientation. The antibody-stained sections also are compared to a serial section stained with normal rabbit IgG (as a negative control). A skin biopsy specimen with multiple infiltrating eosinophils and extracellular eMBP1 deposition serves to establish that the expected specific staining is detected in the assay (as a positive control). This indirect immunofluorescence testing was developed, and its performance characteristics were 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 clinical use of this testing performed in a CLIA-certified laboratory (Clinical Laboratory Improvement Amendments). The results are not intended to be used as the sole means for clinical diagnosis or patient management decisions.

Electronically signed by [redacted] on 02/10/24 at 7:58 PM.
Performed At: IMMUNODERMATOLOGY LABORATORY
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SALT LAKE CITY, UT 84108
Medical Director: KRISTIN M. LEIFERMAN, MD
CLIA Number: 46D0681916

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
EER Eosinophil Granule MBP in Tissues	24-033-118689	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Specimen Medium and Quantity	24-033-118689	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Eosinophil Granule MBP in Tissues	24-033-118689	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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