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

**PATIENT REPORT**

Patient Age/Sex: 34 years Female

**Specimen Collected: 21-Jun-22 15:37**

| **Eosinophil Granule MBP, Tissue** | **Received: 22-Jun-22 10:03** | | **Report/Verified: 22-Jun-22 10:10** |
|---|---|---|---|
| **Procedure** | **Result** | **Units** | **Reference Interval** |
| EER Eosinophil Granule MBP in Tissues | See Note f1 | | |

| **Eosinophil Granule MBP, Tissue** | **Received: 22-Jun-22 10:18** | | **Report/Verified: 27-Jun-22 15:09** |
|---|---|---|---|
| **Procedure** | **Result** | **Units** | **Reference Interval** |
| SO Source | **Mucosa** #1 f2 | | |
| Eosinophil Granule MBP in Tissues | **See Below** t1 #2 f3 | | |

## Interpretive Text

t1: 21-Jun-22 15:37 (Eosinophil Granule MBP in Tissues)
Eosinophil Granule MBP in Tissues

## Corrected Results

#1: SO Source
Result comment modified on 27-Jun-22 15:09 by SYSTEM
Amended Report: this section has been changed.
Performed At: IMMUNODERMATOLOGY LABORATORY
417 S. WAKARA WAY, SUITE 2151
SALT LAKE CITY, UT 84108
Medical Director: JOHN JOSEPH ZONE, MD
CLIA Number: 46D0681916
Result comment modified on 24-Jun-22 00:30 by SYSTEM
Performed At: IMMUNODERMATOLOGY LABORATORY
417 S. WAKARA WAY, SUITE 2151
SALT LAKE CITY, UT 84108
Medical Director: JOHN JOSEPH ZONE, MD
CLIA Number: 46D0681916
Result comment added on 22-Jun-22 11:35 by Contributor_system, UHRT

#2: Eosinophil Granule MBP in Tissues
Result comment modified on 27-Jun-22 15:09 by SYSTEM
Performed At: IMMUNODERMATOLOGY LABORATORY
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SALT LAKE CITY, UT 84108
Medical Director: JOHN JOSEPH ZONE, MD
CLIA Number: 46D0681916
Corrected from See Note on 24-Jun-22 00:30 by Contributor_system, UHRT
Result comment modified on 24-Jun-22 00:30 by SYSTEM
CLINICAL INFORMATION
Eosinophilic esophagitis, eosinophilic gastrointestinal disease (EGID)

Specimen Details
B22-00862 A - Esophagus, proximal; Collected: 6/21/2022; Received: 6/22/2022
B22-00862 B - Duodenum, bulb; Collected: 6/21/2022; Received: 6/22/2022

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DIAGNOSTIC INTERPRETATION
Positive cellular and extracellular eosinophil granule major basic protein 1 (eMBP1), abnormally increased cells in proximal esophagus (Specimen A) with relatively intense extracellular distribution along one edge, and likely abnormally distributed positive staining in duodenum (Specimen B); the findings in the esophagus (Specimen A) provide support for the diagnosis of eosinophilic esophagitis or other eosinophil-related inflammation, and the findings in duodenum further suggest eosinophilic

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

## Corrected Results

#2: Eosinophil Granule MBP in Tissues
gastrointestinal disease (EGID)

Esophagus, proximal (Specimen A)
Overall grade, 2+
Approximate tissue area with staining, 35 percent

Duodenum, bulb (Specimen B)
Overall grade, 2-3+
Approximate tissue area with staining, 50 percent

(See Results, Comments, and Previous and Current Test Results Summary Chart)

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RESULTS
EOSINOPHIL MAJOR BASIC PROTEIN 1 TESTING

Examination of the tissue sections from proximal esophagus (Specimen A) and duodenal bulb (Specimen B) tested for eosinophil granule major basic protein 1 (eMBP1) reveals:

| | | |
|---|---|---|
| Specimen A | Cellular*: 3+ intensity, 2+ extent (Eosinophil count, 23 per high power field, 400x) | |
| | Extracellular: 2-3+ intensity, 2+ extent with with patchy interstitial granules and patchy confluent tissue | |
| Specimen B | Cellular*: 3+ intensity, 2-3+ extent (Eosinophil count, 36 per high power field, 400x) | |
| | Extracellular: 2-3+ intensity, 2-3+ extent with patchy confluent tissue and patchy granules | |

* Intact cells showing positive eMBP1 staining counted per 400x (40x objective lens and 10x eyepiece lens) high power field (HPF) 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.

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COMMENTS
Specific
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The results from this testing for eosinophil granule major basic protein 1 (eMBP1) show abnormal increased infiltration of eosinophils and extracellular eMBP1 deposition in the proximal esophagus tissues (Specimen A), implicating involvement of eosinophils in the pathogenic activity. The extracellular deposition is out-of-proportion to the infiltrating eosinophils in amount and distribution in patchy areas. The positive findings in the proximal esophagus tissues support the diagnosis of eosinophilic esophagitis or other eosinophil-related inflammation. The cell numbers in these tissues are sufficient to constitute a criterion for the diagnosis of eosinophilic esophagitis; extracellular eMBP1 deposition is not established as a diagnostic feature but often is observed in the disorder.

The results from this testing for eMBP1 in the duodenal bulb tissues (Specimen B) are positive but

## Corrected Results

#2: Eosinophil Granule MBP in Tissues

indeterminate for being abnormal and the degree of positivity relative to normal. As judged by the staining, eosinophil activity, as a contributor to the pathophysiology, does not appear to be prominently increased, although the distribution of extracellular eMBP1, including the confluent tissue eMBP1 deposition, likely is abnormal, reflecting local ongoing or recent previous eosinophil activity. The cell numbers should be compared to known normal numbers in this tissue area; of note, the numbers may not account for cells that have infiltrated and degranulated, and, therefore, may be spuriously low. Moreover, the findings should be considered in view of the size and fragmentation of the tissues. Small tissue specimens are more prone to crush artifact in procurement and freeze artifact in processing. Other considerations are that the findings in the tissues could be a remnant of a previous state with greater eosinophil involvement and do not exclude the possibility of more prominent involvement elsewhere. Patients with eosinophilic esophagitis often show prominent eMBP1 immunostaining in small bowel tissues, but this is not a defined diagnostic criterion for eosinophilic esophagitis.

See chart (below) for summary of previous and current eosinophil granule protein testing results. Note that the findings may not be directly comparable because of variability in the location from which the tissue biopsies have been obtained and the architecture of the specimens, as well as the often patchy nature of eosinophil inflammation in the gastrointestinal tract.

Correlation of the findings with clinical presentation is needed, including with respect to 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.

High resolution, color digital images of representative direct immunofluorescence findings are available for this testing (see images 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

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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) immunostaining normally is positive in specimens from the duodenum but normally is negative in esophagus. In normal gastrointestinal tract tissues from small bowel, eosinophils showing positive eMBP1 staining tend to be clustered near the muscularis mucosa with positive extracellular granules dispersed around and among the positive cellular staining.

Eosinophil granule proteins, including eMBP1, have various and numerous toxic effects on tissues and organs. 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 may 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). Extracellular eosinophil granule proteins may persist in tissues for a long time after deposition and may not reflect current activity. Moreover, some positive staining likely is the result of crush artifact in the specimen procurement and freeze artifact in processing, especially extracellular granules in areas where eosinophils normally are present and/or infiltrate. Crush artifact may be prominent in small specimens. Also, 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.

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TESTING METHODS

The specimens from esophagus, proximal (Specimen A) and duodenum, bulb (Specimen B) received in Michel

## Corrected Results

#2: Eosinophil Granule MBP in Tissues
transport medium, after washing and cryoembedding, are sectioned. Sections from each specimen 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. The 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 serial sections 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 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 Kristin M. Leiferman, MD, on 06/22/22 at 11:32 AM.
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Medical Director: JOHN JOSEPH ZONE, MD
CLIA Number: 46D0681916
Result comment added on 22-Jun-22 11:35 by Contributor_system, UHRT

## Result Footnote

f1: EER Eosinophil Granule MBP in Tissues
Authorized individuals can access the ARUP
Enhanced Report using the following link:

f2: SO Source
Amended Report: this section has been changed.
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f3: Eosinophil Granule MBP in Tissues
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SALT LAKE CITY, UT 84108
Medical Director: JOHN JOSEPH ZONE, MD
CLIA Number: 46D0681916