Eosinophil Granule Major Basic Protein, Tissue Biopsy

ARUP LABORATORIES

Patient: [redacted] DOB: [redacted] Age: [redacted] Sex: [redacted] **Patient Identifiers:** [redacted] **Visit Number (FIN):** [redacted]	Client: ARUP Example Report Only 500 Chipeta Way Salt Lake City, UT 84108 Physician: [redacted]	ARUP Test Code: 2010921 Collection Date: 02/02/2024 Received in lab: 02/02/2024 Completion Date: 02/12/2024

Immunodermatology Eosinophil Granule Major Basic Protein 1 Tissue Test Report Navigation Guide

The Immunodermatology TESTING REPORT from the University of Utah follows "See Note" and is arranged as outlined below on the following pages:

CLINICAL INFORMATION
This content is provided by the ordering clinician and includes the indications for testing.

Specimen Details
This includes specimen identification, clinician-provided body location, procurement information and date, and laboratory received date.

DIAGNOSTIC INTERPRETATION
This is a synopsis of key test findings and their diagnostic relevance.

RESULTS
This section reports discrete findings including presence of intact eosinophils and maximal counts per high power field, description of the extracellular eosinophil granule protein deposition pattern graded on a visual analog scale, and percentage estimate of positive tissue staining.

COMMENTS
Specific

These comments provide an explanation of the test results as they relate to clinical considerations and may include recommendations to correlate with other testing. If prior eosinophil granule protein testing has been performed, this section includes a summary chart of previous and current findings from testing ordered by the same clinician client.

General

These comments present information about the test(s) and the component(s) assessed to aid interpretation of clinical applicability.

TESTING METHODS
The section summarizes the procedures performed, the interpretation schema, and the applicable laboratory-developed test disclaimer.

RESULT IMAGES (included and available when applicable)
Images of representative positive, unusual, and/or special interest findings* are displayed in this section, which may be found on the next page. High resolution, color digital files of the images may be requested by contacting 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.

* Note that immunofluorescence-stained tissue slides are not kept longer than two weeks after testing because of degradation in findings; therefore, additional images cannot be acquired after that time without retesting.

Biopsy site and adequate tissue are critical for accurate diagnostic findings. For additional information, refer to:
arupconsult.com/content/eosinophil-associated-diseases

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IMMUNODERMATOLOGY LABORATORY REPORT

[redacted]

Submitter

ARUP Sendouts

Eosinophil Granule Major Basic Protein, Tissue Biopsy (Final result)

Specimen Source
Tissue

TESTING REPORT follows "See Note"
See Note

CLINICAL INFORMATION
Eosinophilic esophagitis, eosinophilic gastrointestinal disease (EGID)

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

DIAGNOSTIC INTERPRETATION

Positive cellular and extracellular eosinophil granule major basic protein 1 (eMBP1), abnormally increased in proximal esophagus (Specimen A) and likely abnormal distribution in duodenal bulb (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 gastrointestinal disease (EGID)

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

Duodenum, bulb (Specimen B)

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Overall grade, 2-3+
Approximate tissue area with staining, 55 percent

(See Results, Comments, Previous and Current Test Results Summary Chart, and representative current images in the Enhanced Electronic Report/EELR and/or available upon request)

RESULTS
Examination of the proximal esophagus (Specimen A) and duodenal bulb (Specimen B) tissue sections 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 patchy 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), 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 results from this testing for eosinophil granule major basic protein 1 (eMBP1) show abnormal increased infiltration of eosinophils and extracellular eMBP1 deposition in the tissues from proximal esophagus (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 proximal esophagus tissue 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 duodenal bulb (Specimen B) are positive but indeterminate for the degree of positivity relative to normal. In normal gastrointestinal tract tissues from duodenum, eosinophils showing positive eMBP1 staining tend to be clustered near the muscularis mucosa

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with positive extracellular granules dispersed around and among the positive cellular staining and minimal or no extension into villi. Therefore, the distribution of cellular and extracellular eMBP1 throughout the tissue and into villi likely is abnormal. Furthermore, extracellular eMBP1 is out-of-proportion to cellular infiltration, including the confluent tissue eMBP1 deposition. 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 may be spuriously low. Overall, the findings suggest support for eosinophilic gastrointestinal disease (EGID) or other eosinophil-related inflammation. Patients with eosinophilic esophagitis often show prominent eMBP1 immunostaining in small bowel tissues, but this is not a defined diagnostic feature with eosinophilic esophagitis.

Other considerations are that these findings could be a remnant of a previous state with greater eosinophil involvement and do not exclude the possibility of more prominent involvement elsewhere. 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.

Digital images of the eMBP1 immunostaining and negative controls are available for this testing (see representative eMBP1 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.

TEST RESULTS SUMMARY CHART

Eosinophil Granule Protein Localization

Specimens		eMBP1, eosinophil major basic protein 1, staining grade and cell count*					
		Small Bowel Duodenum		Stomach		Esophagus	
Specimen Number	Date of Specimen	Grade	Cell Count	Grade	Cell Count	Grade	Cell Count
22-1112	05/04/22	2+	40	2+	20	1+	15
24-0281	02/02/42	2-3+	36	NB		2+	23

Chart Key:

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NB = Not Biopsied

* The tissue sections tested for eMBP1 by indirect immunofluorescence are graded on a visual analog scale with reference images. Intact cells showing positive eMBP1 staining are counted per 400x (40x objective lens and 10x eyepiece lens) high power field (HPF), 0.25 mm2, in areas of maximal cells.

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 specimens from esophagus and normally is positive in specimens from small bowel. In addition to eosinophils clustering near the muscularis mucosa with positive extracellular granules dispersed around and among the positive cellular staining in normal small bowel, 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. In tissues with positive findings normally, the degree of positivity relative to normal can be difficult to assess.

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

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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
EOSINOPHIL GRANULE MAJOR BASIC PROTEIN 1 TESTING

The proximal esophagus (Specimen A) and duodenal bulb (Specimen B) tissue specimens received in Michel 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, 400 X, 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).

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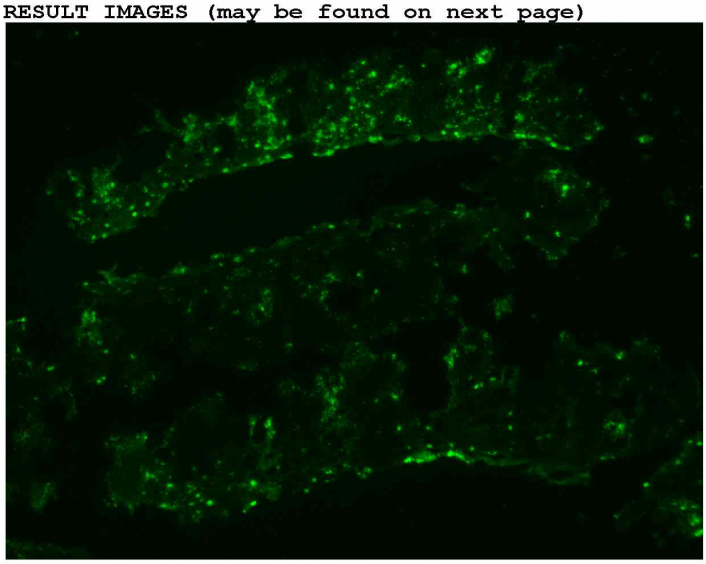
RESULT IMAGES (may be found on next page)

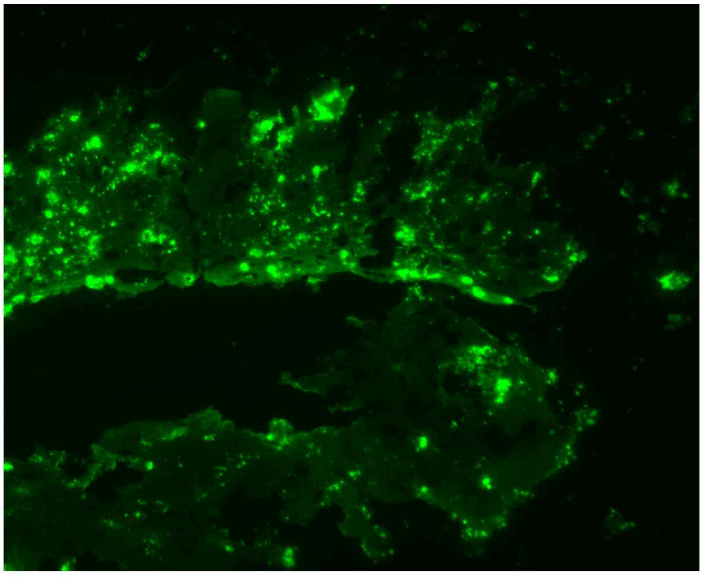


Proximal esophagus

Specimen A

eMBP1

50x



Proximal esophagus

Specimen A

eMBP1

100x

[redacted]

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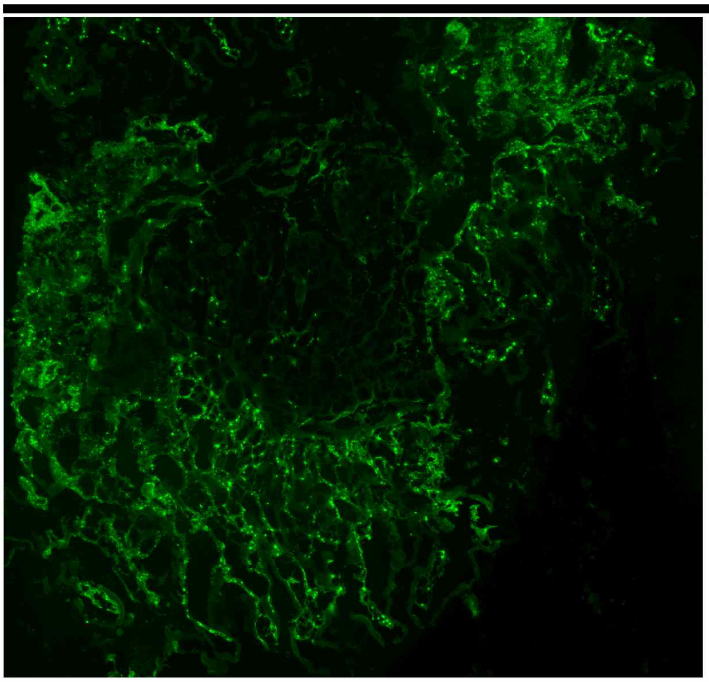

Duodenal bulb

Specimen B

eMBP1

100x
5x5 scan

Resulting Laboratory

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