Case discussions

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Case 1

• 12 year old teen
• Progressive cough and dysphagia following flu-like symptoms
• Family history of asthma
• Erythema in lower oesophagus
What is Eosinophilic Oesophagitis?

- Gastroenterology, 2007- TIGERS
  - Clinicopathologic condition characterized by oesophageal symptoms and a dense oesophageal eosinophilia both of which persist despite PPI treatment, whereas eosinophilic infiltration is absent in the other parts of GIT

AGA guidelines (2007)

- Clinical symptoms of oesophageal dysfunction
  - Adults – dysphagia, food impaction, retrosternal pain
  - Children – chest pain, upper abdominal pain, vomiting, food refusal, regurgitation, failure to thrive
- Histologic: at least 15 eosinophils/hpf
- Exclusion of GERD
  - No response to therapy with PPIs
  - Normal pH monitoring
- Exclusion of other conditions associated with oesophageal eosinophilia
Clinical features

- Male predominance
- Children and young adults
- Intermittent (solid food) dysphagia and food impaction
- History of atopy or allergic diseases
- Peripheral eosinophilia in 50%
- Food or airborne allergen hypersensitivity

Endoscopy

- White stipple-like exudates, patches or plaques
- Oesophageal furrows, strictures and rings (trachealization)
- Longitudinal shearing, friability
- Normal in 1/3
Pathology

- Eosinophilic infiltration of the epithelium (>15-20)
- Preferential localization in superficial epithelium
- Eosinophilic microabscesses (>4 cells)
- Degranulating eosinophils
- Necrotic keratinocytes on the surface
- Lamina propria fibrosis
- Patchy – multiple biopsies needed
- Long-linear extent of infiltration in the oesophagus
- Increase in intraepithelial mast cell and IgE-bearing cells
- Marked basal cell hyperplasia, papillary elongation, DIS
<table>
<thead>
<tr>
<th>Oesophageal eosinophilia</th>
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<tbody>
<tr>
<td>• Eosinophilic oesophagitis</td>
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<tr>
<td>• GERD</td>
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<tr>
<td>• Crohn’s disease</td>
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<td>• Collagen vascular disease</td>
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<tr>
<td>• Infectious oesophagitis (Herpes and Candida)</td>
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<td>• Drug-induced oesophagitis</td>
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<td>• Eosinophilic gastroenteritis</td>
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<td>• Hypereosinophilic syndromes</td>
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<td>• Allergic vasculitis / PAN</td>
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**vs**

- Clinical features
- Endoscopic findings
- Pathogenesis
- Pathology
Clinical features

- Male predominance
- Children and young adults
- Intermittent (solid food) dysphagia and food impaction
- History of atopy or allergic diseases
- Peripheral eosinophilia in 50%
- Food or airborne allergen hypersensitivity
- Genetic predisposition
- No risk of cancer
- Steroid treatment

- Male predominance
- All ages
- Heartburn, epigastric pain, regurgitation, dyspeptic symptoms
- No allergy
- No known genetic predisposition
- Risk for Barrett's oesophagus & adenocarcinoma
- PPI treatment

Endoscopic features
Pathogenesis

- Diminished oesophageal clearance resulting from defective peristalsis
- Decreased oesophageal sphincter pressure
- Increased gastric acid production
- Delayed gastric emptying or abnormal gastric contractility
- Decreased salivary flow

Oesophageal involvement
Pathology

- Eosinophilic infiltration of the epithelium (>15-20)
- Preferential localization in superficial epithelium
- Eosinophilic microabscesses (>4 cells)
- Degranulating eosinophils
- Necrotic keratinocytes on the surface
- Lamina propria fibrosis
- Increase in intraepithelial mast cell and IgE-bearing cells
- Marked basal cell hyperplasia, papillary elongation, DIS
- Balloon cells
- Vascular lakes
- Dilated intercellular spaces
  - Ladder
  - Bubble
- Epithelial hyperplasia
  - Basal cell hyperplasia
  - Papillary elongation
- Inflammation (eos <7-10/ hpf, pmns, lymphocytes)
- Multinucleated epithelial cells
- Carditis

Case 2

- 4 year-old girl with diarrhoea, steatorrhoea, weight loss
- Symptoms started in infancy
- Unremarkable family history
- Duodenal biopsy performed
• Normal villi
• Normal crypts
• No IEL
• Cytoplasmic vacuolization in enterocytes
Reporting:
Lipid deposition in surface enterocytes
Should be detected for conditions causing such deposition

When in doubt ask for fresh tissue!

- “Lipid hang-up”
  physiologically normal
  vacuolization of the
  enterocyte cytoplasm
  after a fatty meal

- PAS/AB (-)
- Oil Red O (+)
Lipid deposition in enterocytes

- A/hypo-betalipoproteinemia
- Malnutrition
- Familial hypoproteinemia
- Diabetes
- GSE
- Cow’s milk-sensitive enteropathy
- Anderson’s disease (chylomicron retension disease)
- Fasting states / diet
- Juvenile nutritional megaloblastic anemia
- Tropical sprue
- Ingestion of a fatty meal

Case cnt’d

- Serum lipid profile:
  - Cholesterol ↓↓
  - Triglycerides ↓↓
  - LDL ↓ ↓

- No other systemic manifestation
A/hypo-betalipoproteinemia

- Otosomal codominant
- Genetic defect in lipid assembly
- Plasma concentrations of apolipoprotein B, cholesterol, triglycerides, VLDL and LDL are low or absent
- Systemic manifestations – acanthocytosis, steatorrhea, severe hypolipidemia, retinitis pigmentosa, cerebellar ataxia, mental retardation

Abetalipoproteinemia

- Inherited disorder of the genesis and secretion of [beta]-apolipoproteins
- **microsomal triglyceride transfer protein (MTM)** mutation
  - apoB100 & apoB48 absent
  - defective chylomicron assembly
  - Inability to synthesize certain apoproteins

Intestinal manifestations
Normal fat absorption

- Passive diffusion of fatty acids across absorptive cell membrane
- ER - triglyceride resynthesis and chylomicron formation
- Phospholipids, cholesterol, apolipoproteins
- Chylomicrons accumulate in golgi - glycosylation and final assembly
- Chylomicrons ejected by exocytosis & enter lymphatics
In Abeta – dietary fat diffuses normally into enterocytes
Lack of chylomicrons and VLDL in ER and golgi leads to accumulations of lipid in the absorptive cells

Clinical findings
- Infancy or early childhood presentation
- Earliest manifestations are intestinal
- Diarrhea, steatorrhea, failure to thrive
- Accentuates after a fatty meal
Histopathology

- Accumulation of fat vacuoles in enterocytes
- Tall columnar shape
- Marked in villous tips
- Goblet cells normal
- Villous architecture intact
- No inflammation
- Lipid-laden macrophages may be present in LP
- Frozen section + Oil red O
- EM – lysosomes filled with lipid + myelin figures

Peretti N, 2010
Thank you...