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Eosinophilic disorders of the gastrointestinal tract: imaging features

Chandramohan Anuradha, Rohin Mittal, Myla Yacob, M. T. Manipadam, Susy Kurian, Anu Eapen

ABSTRACT

Eosinophilic disorders of the gastrointestinal tract are increasingly rare but remain an important cause of long-standing gastrointestinal symptoms. Diagnosis is usually delayed because the disease mimics other inflammatory disorders and is often not suspected initially. We report a series of four cases to highlight the various imaging appearances of this condition. Two patients presented with upper gastrointestinal involvement, one patient presented with small and large bowel involvement, and one patient presented with diffuse involvement of the entire gastrointestinal tract.

Key words: • *gastrointestinal tract* • *diagnostic imaging* • *eosinophilia*

From the Departments of Radiology (C.A. ✉ *anuradhachandramohan@gmail.com*, A.E.), Surgery (R.M., M.Y.), and Pathology (M.T.M., S.K.), Christian Medical College, Vellore, Tamil Nadu, India.

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Eosinophilic disorders of the gastrointestinal (GI) tract are a group of rare inflammatory conditions characterized by focal or diffuse eosinophilic infiltration of the bowel wall (1). These disorders can involve any segment of the GI tract from the pharynx to the rectum. The location and depth of the involved bowel wall determine the clinical presentation. These disorders should be considered in the differential diagnosis for longstanding non-resolving GI symptoms, such as dysphagia, food impaction, weight loss, diarrhea, and melena (1, 2). Although histopathology is the gold standard for diagnosis, recognition of imaging features of this rare disorder aids in early diagnosis and therapy. Literature on the imaging features of the disease is sparse. We report four cases with varied presentations to highlight the imaging features of this disease.

Case reports

Case 1

A 28-year-old male presented with progressive dysphagia, vomiting, and weight loss for two months. He was receiving treatment for allergic rhinitis. Clinical examination was unremarkable. Initial laboratory tests were unremarkable with no peripheral eosinophilia.

An initial contrast swallow revealed a contained mid-esophageal perforation with a right esophagobronchial fistula. Mucosal irregularity, ulceration and diverticulae of the mid and lower thoracic esophagus, the gastroesophageal junction, and the lesser curve of the stomach were noted. The stomach was non-distensible, and gastric rugae were markedly thickened (Fig. 1a–1c). In addition, computed tomography (CT) of the thorax revealed a short segment of circumferential smooth wall thickening in the upper thoracic esophagus, multiple subcentimeter mediastinal, and lesser omental nodes without central necrosis (Fig. 1d and 1e). Upper GI endoscopy revealed an esophagobronchial fistula at 30 cm with edematous and friable mucosa covered with thick inflammatory exudates along the entire length of esophagus and stomach. Multiple endoscopic biopsies of the esophagus and stomach were non-diagnostic.

The patient underwent laparotomy with a full thickness gastric wall biopsy and a feeding jejunostomy. Gastric biopsy was consistent with eosinophilic gastritis. Oral steroids were administered, and the patient responded well to this treatment. The patient was scheduled for elective surgical repair of the esophagobronchial fistula.

Case 2

A 38-year-old female presented with non-progressive dysphagia that had persisted for one year. The patient had a history of melena and one episode of hematemesis. She had undergone a tracheostomy for

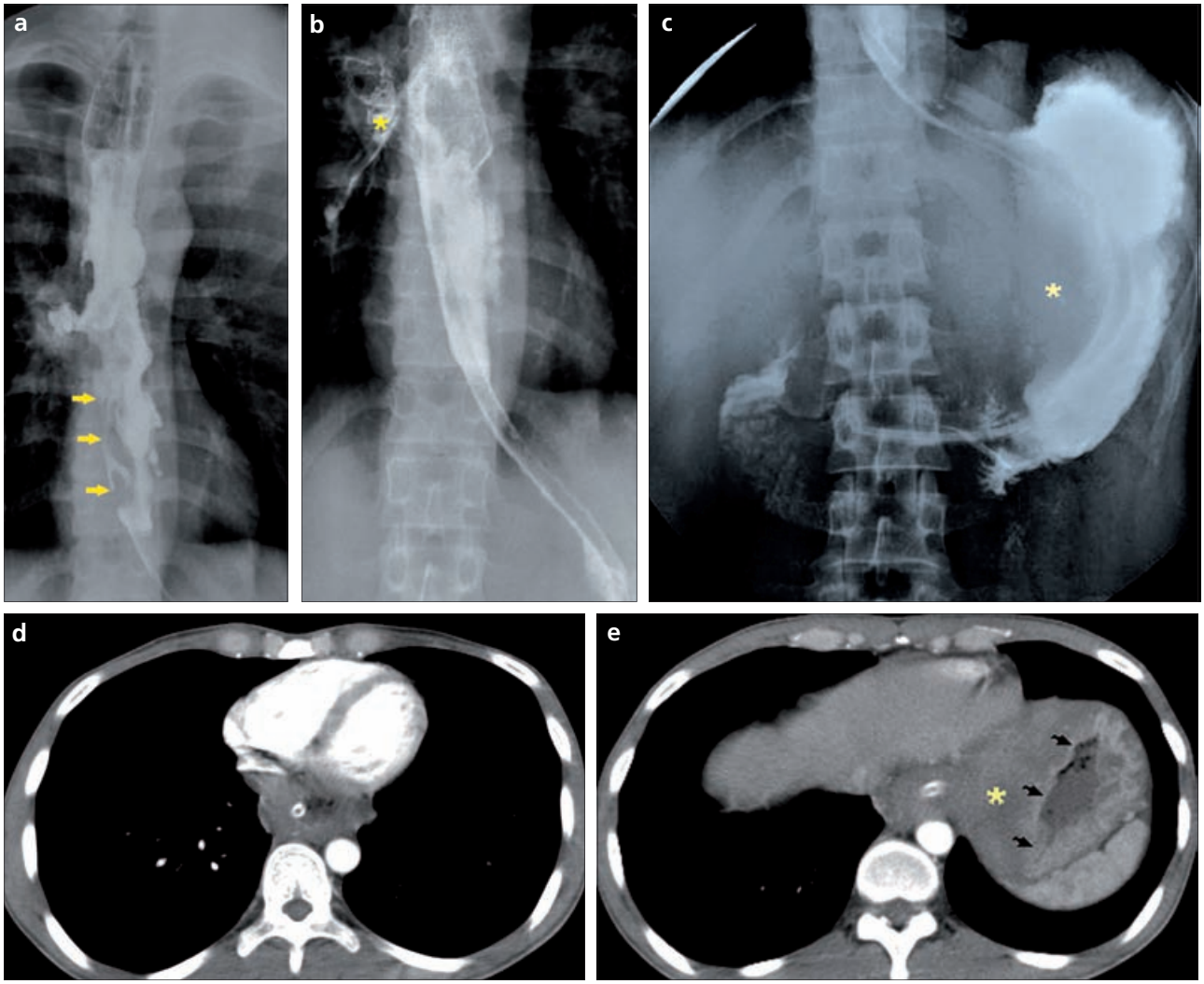

Figure 1. a–e. Contrast swallow **(a–c)** shows mucosal irregularity, ulceration and diverticulae **(a**, *arrows***)** in the mid and lower thoracic esophagus, mid-esophageal perforation and right esophagobronchial fistula **(b**, *asterisk***)**, poor gastric distension with thickened gastric rugae and gastric wall thickening **(c**, *asterisk***)**. Contrast-enhanced CT of the thorax and abdomen reveals diffuse esophageal thickening **(d)** and gastric wall thickening **(e**, *asterisk***)**. Note the preserved mucosal lining **(e**, *arrows***)** of the stomach wall.

idiopathic laryngeal stenosis 12 years ago. The patient was receiving treatment for rheumatoid arthritis and hypothyroidism. Clinical examination of the neck and abdomen was unremarkable except for the tracheostomy. Hematological investigations revealed a peripheral eosinophilia (34%).

An upper GI endoscopy revealed an ulcerated polypoidal growth at the gastroesophageal (GE) junction. CT revealed an asymmetrical homogenous circumferential wall thickening of the oropharynx, the entire esophagus and GE junction with an upper thoracic esophageal diverticula and a large polypoidal mass that projected into the stomach lumen at the fundus (Fig. 2a–2e). Significant mediastinal adenopathy and luminal narrowing at the level of pharynx were present.

Mucosal biopsy of the pharynx and GE junction was diagnostic of eosinophilic pharyngitis and esophagitis with 20–100 eosinophil cells/high power field (Fig. 2f). Oral steroids were administered, and a marked improvement was observed. A follow-up CT of the thorax after six months revealed marked improvement (Fig. 2g–2i). The patient was symptom-free with a normal peripheral eosinophil cell count and erythrocyte sedimentation rate at a one-year follow-up.

Case 3

A 35-year-old male presented with colicky abdominal pain, vomiting, and diarrhea of one-month duration. Clinical examination was unremarkable. Hematological investigations revealed peripheral eosinophilia (39%–43%).

CT revealed diffuse wall thickening of the entire GI tract from the esophagus to the rectum with a sparing of small segments of the distal ileum. A "halo sign" due to a layering of the bowel wall and an "araneid-limb-like" sign due to diffuse mucosal fold thickening were present (Fig. 3). The transverse colon and the ascending colon were predominantly involved with marked surrounding fat stranding. There was minimal ascites and no lymphadenopathy. Upper GI endoscopy and colonoscopy revealed no mucosal abnormalities. A full thickness open biopsy of the small bowel was consistent with eosinophilic enteritis. A tapering

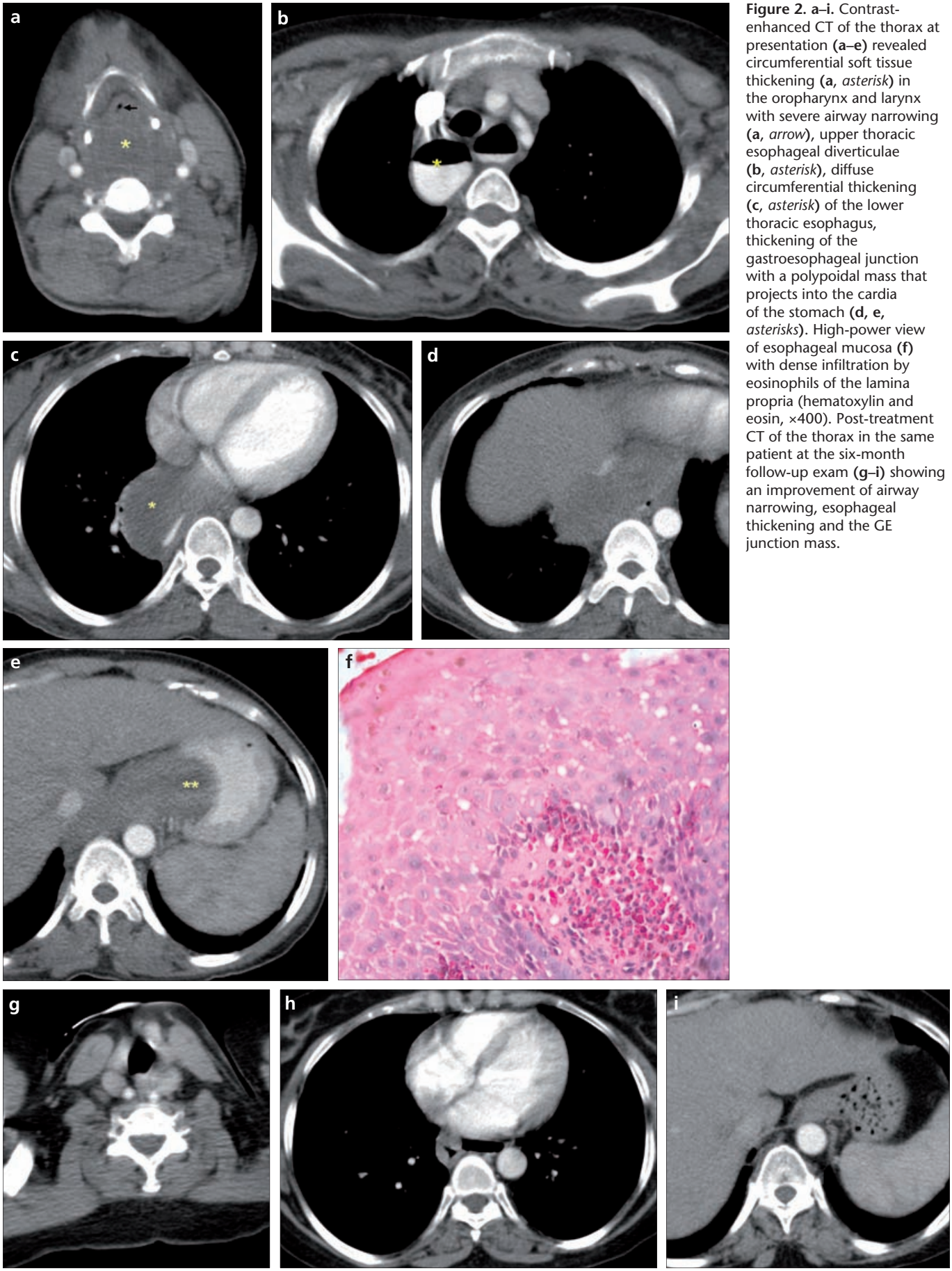

Figure 2. a–i. Contrast-enhanced CT of the thorax at presentation **(a–e)** revealed circumferential soft tissue thickening **(a**, *asterisk***)** in the oropharynx and larynx with severe airway narrowing **(a**, *arrow***)**, upper thoracic esophageal diverticulae **(b**, *asterisk***)**, diffuse circumferential thickening **(c**, *asterisk***)** of the lower thoracic esophagus, thickening of the gastroesophageal junction with a polypoidal mass that projects into the cardia of the stomach **(d, e,** *asterisks***)**. High-power view of esophageal mucosa **(f)** with dense infiltration by eosinophils of the lamina propria (hematoxylin and eosin, ×400). Post-treatment CT of the thorax in the same patient at the six-month follow-up exam **(g–i)** showing an improvement of airway narrowing, esophageal thickening and the GE junction mass.

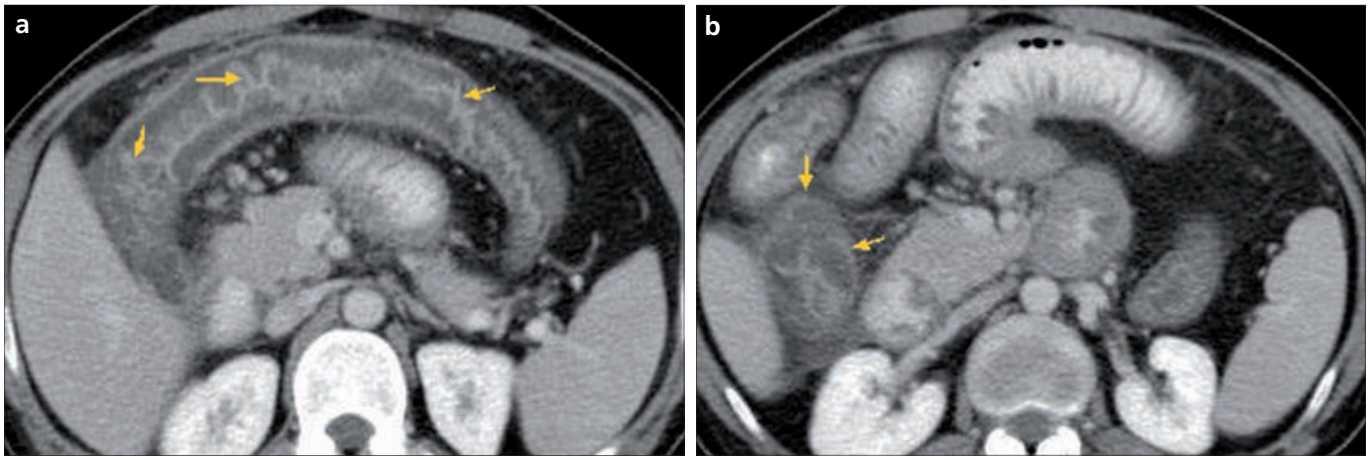

Figure 3. a, b. Contrast-enhanced CT of the abdomen reveals diffuse circumferential mural thickening of the small bowel loops and the colon. Ascending and transverse colon shows an "araneid-limb-like" sign **(a**, *arrows***)** due to mucosal fold thickening and contrast trapped between the thickened folds and a layering of the bowel wall **(b**, target sign, *arrows***)**.

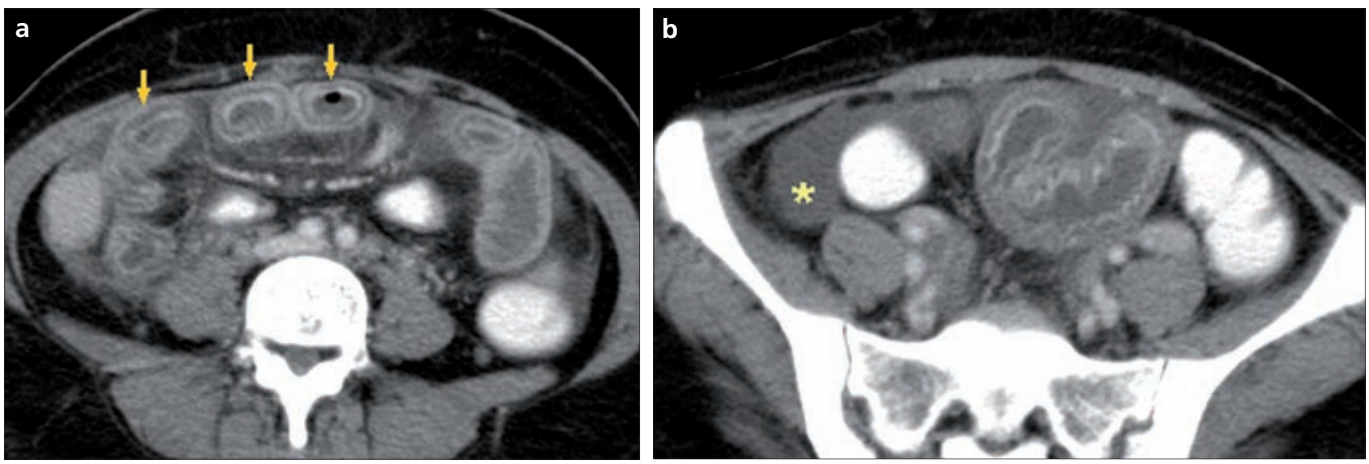

Figure 4. a, b. Contrast-enhanced CT of the abdomen showing a diffuse thickening of ileal loops with a positive halo sign **(a**, *arrows***)** and moderate ascites **(b**, *asterisk***)**.

dose of steroids was administered with a dramatic improvement of symptoms. A complete resolution of symptoms and peripheral eosinophilia were observed at a one-year follow-up exam.

Case 4

A 33-year-old female presented with abdominal pain, vomiting and loose stools that had persisted for six months. The patient also had bilateral symmetric polyarthralgia for six years. Clinical examination and basic hematological reports were normal.

Upper and lower GI endoscopies were unremarkable. CT of the abdomen revealed a diffuse thickening of the terminal ileum and the appendix with a positive "halo sign" and moderate ascites (Fig. 4). Ascitic fluid was not analyzed. No significant lymphadenopathy was observed. The patient underwent a limited right hemicolectomy and transverse colostomy with a provisional diagnosis of inflammatory bowel disease. Final histopathology revealed eosinophilic enteritis predominantly in the muscular and serosal layers and mild eosinophilia in the regional nodes.

High-dose corticosteroids were administered, and the patient developed uncontrolled blood sugar that was stabilized with oral hypoglycemic agents and insulin. Six weeks after the index operation, dense adhesions were observed during surgery to reverse the stoma that necessitated small bowel resection and ileocolonic anastomosis. The patient developed an anastomotic leak that required relaparotomy, the dismantling of ileocolonic anastomosis and end ileostomy, which prolonged hospitalization. The patient was discharged on a tapering dose of corticosteroids and she gradually improved. She was scheduled for elective ileostomy closure at a later date.

Discussion

Kaijser first described eosinophilic disorders of the GI tract in 1937. These disorders are classified as primary when no apparent inciting cause can be demonstrated and secondary when the disorder appears in response to various infections, allergies or connective tissue disorders (1), as observed in three of our patients. In 50% to 70% of these patients, a personal or a family history of food allergies or atopic disorder can be elicited (3).

Clinical features depend on the segment of bowel and the layers of bowel wall that are involved. Talley et al. (2) and Klein et al. (4) have classified eosinophilic GI disorders as mucosal, muscular or serosal disease according to the predominant layer of the bowel

wall that is involved. Mucosal disease is the most common (25%–100%) and presents with nausea, vomiting, abdominal pain, diarrhea, weight loss and GI bleeding. Muscular disease is the next most common (13%–70%) and presents with symptoms of obstruction or its related complications. Serosal disease is less common (12%–40%) and is characterized by intense peripheral eosinophilia and eosinophilic ascites (1). Serosal disease promptly responds to steroid therapy (1–3, 5). Rare associations with pleural effusion, pericardial effusion, urinary bladder and gall bladder thickening, pancreatitis and focal lesions in the spleen and liver have been described (1, 5).

Although any segment of the GI tract can be affected by eosinophilic GI disorder, the stomach is most commonly involved (43%) followed by a combined involvement of the stomach, duodenum and proximal small bowel and esophageal involvement. Large bowel involvement is less common, and eosinophilic pharyngitis is extremely rare (1, 2, 6). Peripheral eosinophilia has been reported in up to 80% of cases with a higher absolute eosinophil count in serosal disease (1, 2, 5, 6). Peripheral eosinophilia was observed in two of our patients; one patient had mucosal disease, and the other patient had serosal disease.

Eosinophilic esophagitis is more common in children than adults. Adults with eosinophilic esophagitis are usually 30 to 50 years old, and the disease has a mild male predominance (1). Imaging features of eosinophilic esophagitis depend on the degree of inflammation and the layer of esophageal wall that is involved. In a study of idiopathic eosinophilic esophagitis in adults, Zimmerman et al. (7) demonstrated that 71% of patients with eosinophilic esophagitis had esophageal strictures, and 50% of these patients had a "ringed esophagus". A ringed esophagus is multiple, fixed tracheal rings that appear as closely packed indentations on the esophageal lumen. Although this sign is observed in only 50% of patients, it is highly suggestive of the diagnosis of eosinophilic esophagitis when present. The differential diagnosis for ringed esophagus includes peptic strictures, which are fixed transverse fold indentions in the lumen that appear as a step ladder but not continuous rings; feline esophagus, which may be mistaken for ringed esophagus but is a transient phenomenon; and congenital esophageal stenosis (8, 9).

Smooth segmental strictures are observed in 70% of patients predominantly in the mid and distal portions of the esophagus. Esophageal stricture with irregular ulcerated lumen is not commonly observed (10%); granular mucosa, which is suggestive of esophagitis, is observed in approximately 30% of patients (8, 10). Other signs, such as "small caliber esophagus", have been described in which the esophagus appears essentially normal on barium esophagogram except for small lumen size, but this reduction in size does not qualify as a stricture (11). Hiatal hernia and reflux esophagitis are commonly associated with eosinophilic esophagitis in 77% and 69% of patients, respectively (8). Diffuse esophageal wall thickening is observed on CT (9, 10).

Our first patient had unusual imaging findings, such as severe diffuse mucosal irregularity and ulcerations, spontaneous esophageal perforation and esophagobronchial fistula. To our knowledge, an esophagobronchial fistula secondary to eosinophilic esophagitis has not been reported previously in the literature. Spontaneous esophageal rupture has been described previously, but it is extremely rare, especially in adults (12). Most perforations in eosinophilic esophagitis are iatrogenic and occurred after endoscopy and esophageal stricture dilatation (13). Our patient also had severe mucosal irregularity and ulcerations. This degree of mucosal abnormality has not been described in previous reports.

The involvement of the pharynx and larynx in eosinophilic esophagitis is extremely rare in adults (14). Airway involvement is reported more commonly in children with eosinophilic esophagitis, and 15% of children with eosinophilic esophagitis have airway and extra-intestinal symptoms (15). Pharyngeal and laryngeal stenosis was observed in one of our patients.

Conditions such as esophageal tuberculosis, lymphoma, malignancy and Crohn's disease share similar imaging findings. Although tuberculosis is a very common infection in our country, esophageal tuberculosis is uncommon. However, esophageal tuberculosis is more common in the setting of HIV (16). Most incidences of the esophageal tuberculosis are secondary and are associated with mediastinal lymphadenopathy, which is necrotic with peripheral rim enhancement and abnormal lung densities. Primary esophageal tuberculosis is extremely rare. Moreover, esophagobronchial fistula in tuberculosis occurs where large mediastinal necrotic nodes indent and erode into the esophagus and bronchus (16, 17).

Lymphoma of the esophagus is an uncommon condition, but primary esophageal lymphoma without extra-esophageal manifestation has been reported in fewer than 10 cases in the literature (18). Imaging features include mucosal thickening, submucosal nodules, ulcers and erosions, the relative preservation of the lumen despite a large mass, achalasia-cardia-like appearance, spontaneous perforation and esophagobronchial fistula. Inflammatory bowel diseases, such as Crohn's disease, have multifocal areas of involvement.

Imaging features of eosinophilic gastroenteritis include bowel wall thickening, layering of the bowel wall, diffuse mucosal fold thickening and luminal narrowing with or without intestinal obstruction. Signs such as the "halo sign" and the "araneid limb-like" sign have been described previously (19) and were observed in our cases. The halo sign is observed due to submucosal edema, which causes a layering of the bowel wall. When diffuse mucosal thickening is present, contrast within the mucosal sinuses in the longitudinal section of the bowel on CT produces an "araneid-limb-like" sign. Both of these signs are only observed in inflammatory pathologies, which aids in the differentiation of eosinophilic gastroenteritis from neoplastic conditions, such as lymphoma and carcinoma.

In tuberculosis, bowel obstruction is due to ulcerohypertrophic disease and fibrotic strictures of the bowel, which predominantly occur in the duodenum and the ileum. The ileocecal junction is involved in 80%–90% of gastrointestinal tuberculosis. Peritoneal and omental thickening are commonly associated (20). However, eosinophilic gastroenteritis is a predominantly muscular disease that shows features of obstruction, and unlike tuberculosis, it is not associated with ascites, peritoneal

and omental thickening. In lymphoma, there is a homogenous circumferential thickening of the bowel wall with no bowel wall layering or features of bowel obstruction, which may be associated with an "aneurysmal dilatation" of bowel. These features should aid in the differentiation of these two conditions.

Eosinophil-rich ascites have a well described association with serosal predominant disease (19). Serosal disease is non-obstructive in nature (19). Two of our patients with serosal predominant disease showed some ascites. However, ascitic fluid was not analyzed due to the small amounts of ascites. Eosinophilic mesenteric lymphadenopathy is associated with serosal disease. However, the imaging features of these nodes are limited to a few case reports in which nodes with central necrosis have been described (19). Mesenteric nodes with peripheral enhancement and central necrosis are classically observed in tuberculosis, and 80% of disseminated tuberculosis and 52% of non-disseminated tuberculosis are associated with abdominal lymphadenopathy (21). Although abdominal lymphadenopathy is observed in lymphoma, these nodes are homogenous in nature and become necrotic only after treatment (20). None of our patients showed significant lymphadenopathy.

Therefore, protean clinical and imaging appearances of eosinophilic GI disorders closely mimic other diseases, such as tuberculosis, Crohn's disease, lymphoma and malignancy. The diagnosis of eosinophilic GI disorders is not often considered at initial presentation. The diagnosis is confirmed by a histopathological examination of the tissue that is obtained by endoscopy or open biopsy. Multiple biopsies are often required to prove the diagnosis because eosinophilic infiltration is patchy (2). Therefore, the final diagnosis and treatment are delayed (1). This delay was observed in our first patient in whom multiple endoscopic biopsies did not reveal the diagnosis despite the gross radiological abnormalities, and full thickness open biopsy was required. Approximately 90% of patients with eosinophilic GI disorders respond well to treatment with systemic steroids. Patients may have a relapsing and remitting disease course, but many patients have long periods of remission. Patients with eosinophilic esophagitis have chronic disease due to strictures (1, 2, 5). All four patients in our series responded well to corticosteroid treatment. One patient with serosal disease had multiple surgeries and a morbid postoperative period.

In conclusion, radiology plays an important role in the management of patients with eosinophilic disorders of the GI tract by the accurate identification of the site of the abnormality, which allows for the targeting of biopsies to the correct site. In the appropriate clinical setting, imaging features aid in the diagnosis of suspect eosinophilic gastrointestinal disorders. Imaging also helps in the identification of complications and in the follow-up examination of these patients.

Conflicts of interest disclosure

The authors declared no conflicts of interest.

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