Idiopathic eosinophilic oesophagitis : atypical presentation of a rare disease

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Abstract

A 72 year-old man presented severe dysphagia and weight loss of recent onset. Repeated oesophageal endoscopy and biopsies with macroforceps were normal. Oesophageal manometry disclosed features compatible with achalasia. Oesophageal EUS endoscopy localized an infiltrating process between muscular layers of the oesophageal wall and CT scan delimited a circular thickening in the inferior part of the oesophagus. Because of severe clinical presentation mimicking a possible oesophageal neoplasm like a lymphoma, partial oesophagectomy was performed and revealed eosinophilic oesophagitis. This unusual presentation emphasizes that idiopathic eosinophilic oesophagitis must be proposed in the differential diagnosis of dysphagia, even in old patient without apparent oesophageal lesion at endoscopy. (Acta gastroenterol. belg., **2004**, 67, **232-235**).

Key words : idiopathic eosinophilic oesophagitis.

Introduction

Eosinophilic infiltration of the oesophagus is a poorly characterized process, which may be observed in patients with gastroesophageal reflux, allergic gastrointestinal disorders, cow's milk-associated oesophagitis and idiopathic eosinophilic oesophagitis (IEO). IEO is a rare disease in which the eosinophilic infiltration can be limited to the oesophageal wall or involve other segments of the digestive tract, like the stomach or the small bowel, and then be a part of idiopathic eosinophilic gastroenteritis syndrome (IEG). Among the few cases of IEO reported to date, usual symptoms include progressive dysphagia and heartburn. Diagnosis is most often observed by histological analysis of oesophageal biopsy samples. The present report describes a case of IEO with atypical clinical and radiological presentations characterized by severe dysphagia and thickened oesophageal wall at CT scan. Histological features are also unusual, with eosinophilic infiltration limited to the muscular layers of the oesophagus. This original presentation explains the delay in diagnosis wich was finally obtained after inferior oesophageal resection by surgery.

Case report

A 72-year-old man presented with complaints of dysphagia and liquid regurgitations. He had had pulmonary tuberculosis two years before the admission for which he received tritherapy antibiotics (isoniazide, pyrazinamide, myambutol) during 9 months. He had no other past history, no known allergy and did not take any medication. The initial OGD was normal within the exception of a functional spasm located at the lower part of the oesophagus. Routine antrofundic biopsies were normal. The patient came back 3 months later because of persistant severe dysphagia, liquid regurgitations causing bronchoaspirations and weight loss of 5 kg. Oesophageal manometry disclosed a severe motility disorder characterized by non peristaltic waves in the whole length of the oesophagus, some spontaneous giant aperistaltic waves (amplitude up to 200 mmHg) in the lower oesophagus, high resting lower oesophageal sphincter (LOS) pressure (40 to 60 mmHg) and partial relaxation of the LOS, features consistent with achalasia. Barium oesophagogram showed slight narrowing and dysmotility in the lower oesophagus. Thoracic CT scan demonstrated circular thickening of the inferior oesophagus, without significant satellite or mediastinal lymph nodes (Fig. 1). At EUS endoscopy, a hypodense infiltrating process was seen at the level of the muscularis propria, which was poorly differentiated from the submucosa and the adjacent tissues. Oesogastroduodenoscopies were repeated in order to take more biopsies with classical forceps and macrobiopsies were performed using a

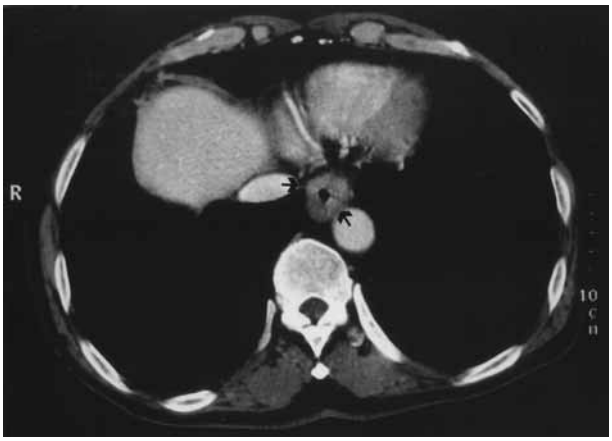

Fig. 1. — Thoracic CT scan disclosed centimetric regular and circular thickening restricted to the third inferior oesophagus without significant satellites adenopathies nor evidence of gastric involvement.

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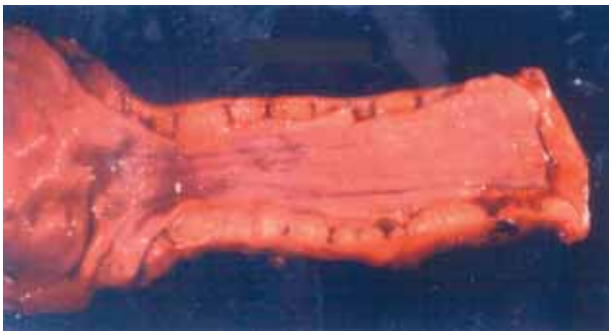

Fig. 2. — Macroscopic examination of oesogastrectomy piece. The resected oesophagus measured 15 × 3.5 centimeters and exhibited diffuse circular thickening up to 1.2 centimeters in his lower part. The stomach segment measured 11 centimeters and was macroscopically normal.

5 mm biopsy forceps passed through a 6 mm therapeutic channel (Olympus XT 30). Histopathology showed slight oedema with rare eosinophils and neutrophils in the submucosal layer. Serological markers and thoraco-abdominal scanner were not suggestive for a primitive tumor. Initial laboratory findings were normal (including eosinophil count : 3% eosinophils for 6700 WBC) except a slight polyclonal hypergammaglobulinemia at 1.6 g/dl (normal values ranging from 0.4 to 1.2 g/dl). Three months later, antinuclear factor (1/80 titer with spotty pattern) and eosinophilia rising to 1700/mm^3 in absolute value appeared. Ig E level was within normal range at 82 U/ml (normal < 150 U/ml). Search for parasites was negative in stool at 4 repeated times and parasitic serologies for strongyloidiasis, ascaridiasis, toxicariasis, trichinosis, and filiariosis were negative. Sclerodermia was excluded by capillaroscopy, hand radiography and pulmonary CT-scan.

The infiltrating aspect of the process which remained of undetermined nature despite macrobiopsies and extensive check-up, the persistent dysphagia despite several therapeutic trials (nifedipine 30 mg/d, cisapride 80 mg/d and omeprazole 40 mg /d) and the progressive weight loss justified the decision for surgery. Lower half oesophagectomy combined to polar superior gastrectomy with intrathoracic anastomosis was performed. Macroscopic examination of the resected oesophagus exhibited circular thickening in its 15 inferior centimetres (Fig. 2). Microscopic analysis revealed discrete oedema and few eosinophils in the submucosa contrasting with a dense eosinophilic infiltration of the muscularis, dissociating muscular fibers and progressing up to the adventice (Fig. 3). Eosinophils were also detected surrounding damaged axons of the neural digestive plexus (Fig. 4). Superior oesophageal margins contained few scattered eosinophils in the submucosa whereas inferior margins within the stomach were normal. As no etiology could be identified to explain this eosinophilic infiltration, the proposed diagnosis was IEO.

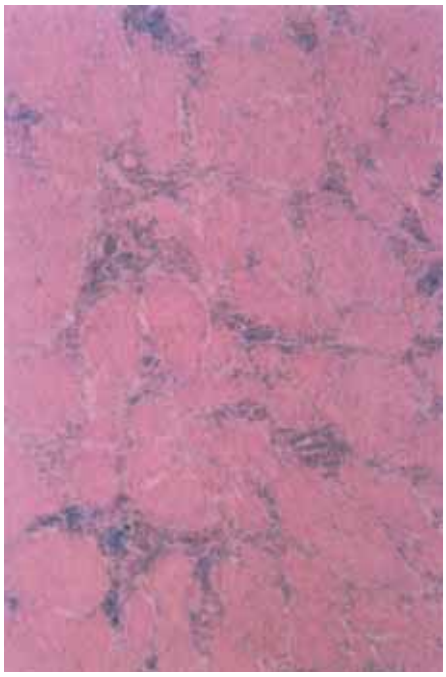

Fig. 3. — Microscopic examination of the resected oesophagus disclosed severe eosinophilic infiltration strictly located in the muscular layers and dissociating muscular fibers.

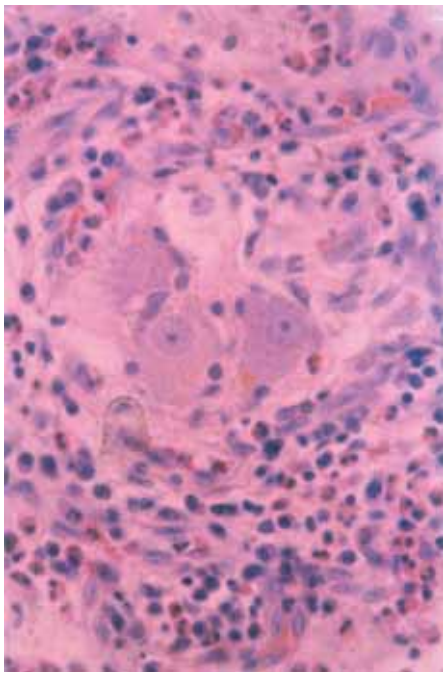

Fig. 4. — Microscopic examination detected eosinophils around suffering axons of the digestive neural plexus with baloonized cytoplasm.

After surgery, the patient experienced a rapid and complete resolution of dysphagia and gained 8 kg after 10 months of follow-up. Blood tests showed that eosinophil count returned to normal range (WBC 9500/mm^3 ; 4,3% eosinophils).

Discussion

IEO represents a variant of an uncommon disease, IEG, characterized by eosinophilic infiltration of the gut wall. Any segment of the digestive tract can be involved but gastric antrum and small bowel are more frequently affected. Oesophageal involvement occurs rarely ; its incidence is difficult to estimate and some authors reported oesophageal involvement in less than 1.5% cases of IEG (1). Since initial description by Dobbins and al. in 1977 (2), approximately 80 articles have been published about IEO in the literature. Typically, IEO occurs in adolescents or young adults with a clear male (three fourths) preponderance. Recent publications suggest that adults can be affected as well, but more data are needed to assess the prevalence of IEO in the adult population (3). One case concerning an elder patient has been published to date (4). Patients present dysphagia as predominant symptom, intermittent but sometimes continuously or progressively worsening, usually without significant weight loss. Endoscopy can be normal or may exhibit particular features like segmental strictures (most commonly proximal) (5), smooth diffuse narrowing or "small-caliber oesophagus" (6), multiples oesophageal rings (7), vertical lines or papular whitish exudate (8). Some endoscopic presentations may be subtle ; minor findings such as unusual "long rents" can be revealed only after oesophageal dilation (9). Oesophageal manometry shows variable motility disorders in up to 40%, like nutcracker oesophagus, diffuse oesophageal spasms, features consistent with achalasia i.e poor relaxation of the lower oesophageal sphincter and simultaneous aperistaltic waves across the body of the oesophagus, or nonspecific alterations (5,10,11). Our patient presented several atypical features of the disease : advanced age, rapid symptomatic evolution upon 6 months, severe weight loss, absence of allergic history and a late onset of blood eosinophilia, which certainly appealed to other diagnoses, neoplasm at first. These clinical features of severe pseudoachalasia prompted us to purpose surgery.

The cause of IEO is unknown and its pathogenesis poorly understood. Allergic conditions are retrieved in 60 to 85% of the patients. Hypersensitivity response could be a causal factor inducing mucosal mast cell degranulation, then allowing attraction and activation of eosinophils. Oesophageal eosinophilic infiltration could be secondary to a reaction to food allergens (12,13), or to a hypersensitivity reaction to aeroallergens in the lung, as recently shown in an animal model (14). Recent works concerning characterization of the oesophageal inflammatory infiltrate shows that IEO involves a selected inflammatory TH2 profile immune response (15) ; these immunopathological features are reversible by topically applied steroids (16).

Histologically, IEO is defined by large numbers of mucosal eosinophils (greater than 15-20 per high power-field). Differential diagnosis must be done with reflux oesophagitis which represents the first cause of intraepithelial eosinophilia, but which is generally predominant in the distal part of the oesophagus. In IEG, full thickness wall infiltration is characteristic even if the infiltrate tends to be more abundant in submucosa and muscularis (17). However, deep involvement requires large biopsy specimens to be demonstrated, either with macrobiopsy-forceps for the submucosa or surgical sampling for muscularis and/or serosa invasion. In IEO, prevalence of deep involvement is unknown since it has been clearly established up to now in only 2 cases who required surgery : a case of oesophageal rupture (18) and, like our patient, a case of severe pseudoachalasia (19). Diffuse oesophageal wall involvement was present in the first case but not in the last one, where, like in our patient, routine mucosal biopsies revealed only chronic inflammation whereas eosinophils were clearly predominant in the muscular layers on surgically resected tissue.

Dysphagia can be explained by oesophageal dysmotility, itself secondary to wall edema and damage to the ganglion cells of the myenteric plexus of Auerbach. Eosinophils mediate tissue damage through the release of lipid mediators such as platelet activating factor and leukotriene C_4, highly reactive brominating species and preformed toxic granule proteins : major basic protein (MBP), eosinophil-derived neurotoxin (EDN), eosinophil cationic protein (ECP) and eosinophil peroxidase (20). Interestingly, on a retrospective surgical series of 9 patients suffering for achalasia, immunostaining of ECP revealed eosinophil infiltration and activation within the muscular layers of the oesophagus and suggesting a participation of eosinophils in the pathogenesis of this disease (21). In the same line, the role of eosinophils was recently put forward in a murine model of oral antigen-induced eosinophil-associated gastrointestinal disease (13) where, like in our patient (Fig. 4), eosinophils were found surrounding damaged axons, indicating a mediator role leading to dysmotility.

We described an atypical anatomoclinical picture of IEO characterized by severe pseudoachalasia in an old man with no past history of allergy. Routine and macroforceps oesophageal biopsies could not establish the diagnosis, eosinophilic infiltration was mainly located in the muscular layers of the oesophagus, as finally revealed on surgically resected tissue.

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