Esophagitis dissecans superficialis : a case series of 7 patients and review of the literature

Elias Fiani[1], François Guisset[1], Quitterie Fontanges[2], Jacques Deviere[1], Arnaud Lemmers[1]

(1) Gastroenterology, Hepatopancreatology and Digestive Oncology Department. Erasme Hospital. ULB (Université Libre de Bruxelles) Brussels, Belgium ; (2) Pathology Department, Erasme Hospital, ULB (Université Libre de Bruxelles) Brussels, Belgium.

Abstract

Introduction : **Esophagitis dissecans superficialis (EDS) is a rare desquamative disorder of the eso-phagus, characterized by sloughing of the superficial mucosa. It is a benign entity of uncertain etiology. Most cases of EDS are idiopathic but can be caused by medications, hot beverages, chemical irritants, celiac disease and many skin conditions.**

Aim : **Knowing that few case series have described this entity, we decided to review all the cases diagnosed in our center to characterize them.**

Methods : **The pathological institutional database of Erasme University Hospital (Brussels, Belgium) was searched for the diagnosis of EDS. We reviewed retrospectively the clinical and endoscopic findings as well as histological features of all cases of EDS (Table 1). During this period of time, 21497 upper gastrointestinal endoscopies have been performed in our institution.**

Results : **From January 2010 to September 2016, we identified 7 cases of EDS diagnosed in our institution in this time period. During the same period, 21497 upper gastrointestinal endoscopies were performed (incidence 0.03%). Endoscopic findings evoked in 2 patients a suspicion of an esophageal tumor; the first one was described as a raised detached lesion of the distal third of the esophagus with suspicion of squamous cell carcinoma (Fig. 1) and the second as a suspected tumor of the proximal third of the esophagus (Fig. 2). For other patients, EDS was misdiagnosed as unspecific esophagitis in 2, reflux or mycotic esophagitis in 2. Only one patient was suspected to have sloughing esophagitis. Histologic features present in all of those cases were characterized by the presence of a sloughing and necrosis of the superficial layer of the esophageal squamous epithelium with negative anti HSV and anti CMV antibodies, negative periodic acid Schiff stain for fungal infections as well as absence of signs of dysplasia or signs of malignancy. In 2 patients, there was a presence of multiple bacterial colonies on the superficial epithelium. Acute inflammation was reported in 4 of the patients with the presence of eosinophils in the superficial epithelium described in 2 of these patients and of polymorphonuclear leukocytes in 2 other patients (Fig. 3).An endoscopic follow up 2 months after PPI treatment performed in 3 patients, 2 of them had an atypical endoscopic presentation with suspicion of a tumor on endoscopic examination showed a complete resolution of the esophageal lesions was observed in these patients.**

Conclusion : **EDS is a rare benign entity that endoscopists must be aware of in order not to mistake it for other entities such as esophagitis or squamous cell carcinoma. The diagnosis is based on biopsies. The prognosis is good after stopping the causative agent.**
(Acta gastroenterol. belg., **2017**, 80, **371-375**).

Introduction

Esophagitis dissecans superficialis (EDS) is a rare desquamative disorder of the esophagus, characterized by sloughing of the superficial mucosa (1). It is a benign entity of uncertain etiology. Most cases of EDS are idiopathic but can be caused by medications, hot beverages, chemical irritants, celiac disease and many skin conditions. Literature concerning this entity is weak because it is mainly based on case reports and few case series.

In order to further describe this rare benign entity, we report 7 cases of EDS diagnosed in our institution from 2010 to 2016 and review the literature. We will describe their clinical presentations, endoscopic and histological findings.

Methods

The pathological institutional database of Erasme University Hospital (Brussels, Belgium) was searched for the diagnosis of EDS from January 2010 to September 2016. We reviewed retrospectively the clinical and endoscopic findings as well as histological features of all cases of EDS. During this period of time, 21497 upper gastrointestinal endoscopies have been performed in our institution.

Clinical findings

During this 6 years period, we have identified 7 patients diagnosed with EDS (incidence 0.03% of gastroscopies) (Table 1). The median age of presentation was 73, with a female predominance (85%). Associated symptoms were variable from weight loss and nausea to epigastric pain, dysphagia and atypical chest pain. The most common co-morbidity found was treated hypertension in 3 patients, hypothyroidism in 2 patients and depression in 2 patients. Other comorbidities were hypercholesterolemia, obstructive sleep apnea, coronary artery disease, chronic obstructive pulmonary disease and autoimmune pancreatitis. There were no skin diseases in any of these patients. Two patients had previous gastric surgery, the first was a gastric bypass and the second was

Correspondence to : Elias Antoine Fiani, Route de Lennik 804, 1070 Brussels
Tel.: 0032488893576
E-mail : elias.fiani@hotmail.com

Submission date : 16/12/2016
Acceptance date : 25/04/2017

Table 1. — **Summary of the clinical, endoscopic and histological features of the patients diagnosed with EDS**

Patients	Age	Gender	Symptoms	Comorbidities	Medication	Endoscopic findings	Histology	Clinical follow up	Endoscopic controle
1	76	Female	weight loss and nausea	COPD Esophagitis grade D CABG HTN Depression	ASA,simvastatin,phenothiazines mirtazapine,lormatazepam, aldactone, nebivolol	Fibrotic and sclerotic aspect of the distal 1/3 of the esophagus	Sloughing of the superficial layer of the esophageal epithelium, with presence of eosiophils on the surface	Yes at 2 months	No
2	70	Female	epigastric pain	gastric bypass	omeprazole	White pseudomembranes of the mid and distal third of the esohagus suspecting candida esophagitis	Sloughing of the superficial layer of the esophageal epithelium, with PMN on the surface separating it from the basal layer.	No	No
3	71	Female	epigastric pain	Arthrodesis L5-S1	Pantoprazole	Surelevated lesion of the distal third of the esophagus suspecting a squamous cell carcinoma	Sloughing of the superficial layer of theesophageal epithelium, with presence of eosiophils on the surface	Yes at 2 months	Yes
4	47	Female	Dysphagia	gastrectomy with oesojejunal anastomosis, Hypothyroidism Autoimmune pancreatitis	elthyroxin, resolor, pregabalin,duloxetine	A sloughed esophageal mucosa in all the esophagus	Sloughing of the superficial layer of the esophageal epithelium, with presence of few bacterial colonies on the surface	No	No
5	77	Female	epigastric pain	HTN Hypercholesterolemia Hepatits C Obstructive sleep apnea	Omeprazole	Sloughing of the esophageal mucosa in the distal 2/3 of the esophagus suspecting an EDS.	Sloughing of the superficial layer of the esophageal epithelium separated from a normal basal layer	Yes at 2 months	Yes
6	86	Male	Atypical chest pain	HTN Hyperuricemia	thiazide,irbesatan,tamsulosine, amlodipine, allopurinol	Grade A Reflux oesphagitis	Sloughing of the superficial layer of the esophageal epithelium separated from a normal basal layer	No	No
7	83	Female	Dysphagia	HTN Hypothyroidism, Alzheimer disease, Depression DVT Hysterectomy Septic athritis	Donepezil,ASA,escitalopram,amlodpine,simvastatin,pantprazole,Trazodonhydrochloride,levothyroxine, clindamycin	Suspicion of an esophageal tumor from 16 to 24 cm of the dental arch, circumferential from 18 to 20 cm	Sloughing of the superficial layer of the esophageal epithelium, with PMN on the surface separating it from a normal basal layer.	Yes at 2 months	Yes

COPD : Chronic obstructive pulmonary disease ; CABG : Coronary artery bypass graft ; HTN : Hypertension ; DVT : Deep vein thrombosis ; ASA : Acetylsalicylic acid ; PMN :polymorphonuclears ; EDS: Esophagitis dissecans superficialis.

a total gastrectomy with eso-jejunal anastomosis. Antihypertensive drugs like amlodipine, irbesartan, thiazide and nebivolol were used in 3 patients, 3 patients were on proton pump inhibitors like omeprazole and pantoprazole, 3 patients were on psychoactive medications like mirtazapine, duloxetine, phenothiazine, 2 patients were on simvastatin for hypercholesterolemia, 2 patients were on levothyroxin supplementation for hypothyroidism, only 1 patient was newly started on antibiotics like clindamycin for septic arthritis.

Endoscopic findings

Only 1 patient had a sloughing white mucosa of the inferior and mid third of the esophagus with suspicion of sloughing esophagitis. In 2 patients, an esophageal tumor was suspected; the first one was described as a raised detached lesion of the distal third of the esophagus with suspicion of squamous cell carcinoma (Fig. 1) and the second as a suspected tumor of the proximal third of the esophagus at 16 to 24 cm from the dental arch (Fig. 2). In 1 patient there was a suspicion of grade A esophagitis (Los Angeles classification) and an unspecific esophagitis was described in 2 patients with the presence of a sloughing esophagus in one of these patients. Candida esophagitis was suspected and was described with the presence of white exudates and pseudomembranes in the distal and mid third of the esophagus one of the patients. Sequelae of a previous esophagitis with the presence of a sclerotic fibrotic mucosa of the distal third of the esophagus were described in the latter. (see Table 1)

Histologic features

A sloughing and necrosis of the superficial layer of the esophageal squamous epithelium with negative anti HSV and anti CMV antibodies, negative periodic acid Schiff stain for fungal infections as well as absence of signs of dysplasia or signs of malignancy were described in all these patients (Fig. 3). In 1 patient, there was a presence of multiple bacterial colonies on the superficial epithelium. The presence of eosinophils in the superficial epithelium was described in 2 patients. Polymorphonuclear leukocytes were found in 2 of these patients.

Treatment and follow-up

Clinical follow up after 2 months was done in 4 of these patients after PPI treatment. The patient with clindamycin induced EDS was treated with pantoprazol 40 mg once daily after stopping clindamycin with complete resolution of the dysphagia. The second patient with suspected raised lesion of the distal third of the esophagus was also treated by pantoprazol once daily with complete resolution of the epigastric pain. The third patient who had a suspicion of esophagitis dissecans on endoscopy was put on pantoprazol twice daily with

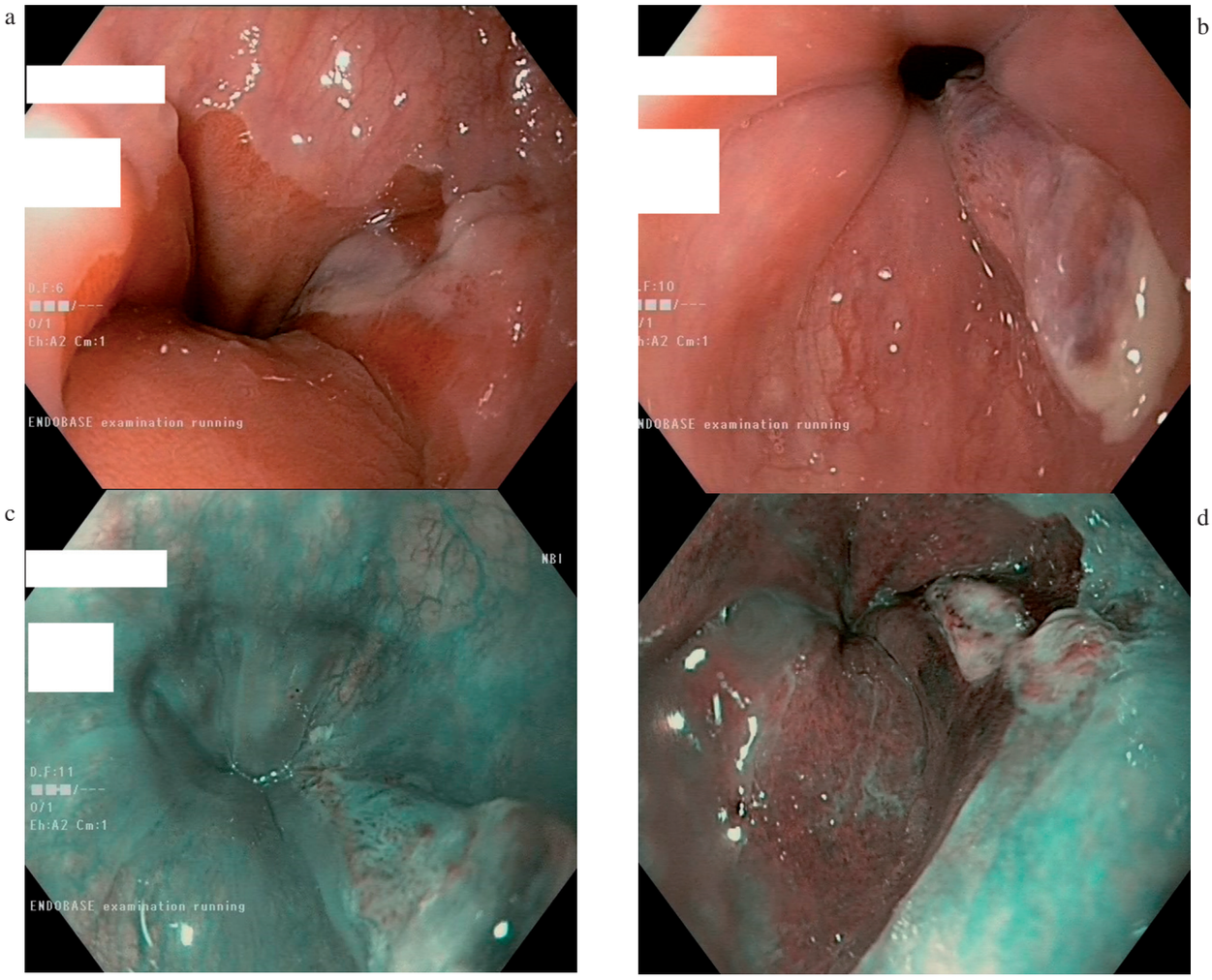

Figure 1. — a, b : Raised detached lesion of the distal esophagus in patient 3 presenting with epigastric pain ; c, d : Same lesion seen on narrow band imaging (NBI)

complete resolution of his symptoms after 2 months and the fourth patient who presented with weight loss and nausea regained a normal appetite 2 months after treatment with omeprazol 20 mg twice daily.

An endoscopic follow-up at 2 months of was performed in the 2 patients who had an atypical endoscopic presentation with suspicion of a tumor on endoscopic examination and in the patient with suspected esophagitis dissecans on upper GI endoscopy. A complete healing of the esophageal lesions was observed in these 3 patients (Fig. 4). No endoscopic follow-up was done on all the other patients knowing the benign prognosis of this rare clinical entity described in the literature.

Discussion

Esophagitis dissecans (EDS) is a rare benign anatomo-clinical entity, that usually affects adults after the age of 50 (2) with a slight female predominance similar to our case series. The clinical presentation ranges from dysphagia and odynophagia to epigastric pain and nausea. Many patients are asymptomatic and undergo the endoscopy for unrelated reasons (1). Although it has been reported in association with certain diseases and medication, most cases remain idiopathic. Hot beverages, medications (bisphosphonates (3,10), non-steroidal anti-inflammatory drugs, antibiotics (4), psychoactive medications like SSRIs or SNRIs and methotrexate (5), chemical irritants (6), celiac disease, chronic renal failure (8) , heavy smoking, esophageal iatrogenic injury (sclerotherapy band ligation, dilation and mediastinal radiation) and skin conditions (prurigo nodularis and bullous dermatoses (7,8) have all been implicated. Only one patient in our series had an identified suspected causative factor, namely clindamycin, knowing the sudden onset of symptoms upon initiating clindamycin for septic arthritis. This patient didn't have any other risk factors predisposing to EDS and developed symptoms of dysphagia during the antibiotherapy with clindamycin. It is the second case of suspected clindamycin-induced EDS described in the literature (4).

Pathogenesis remains unknown. It is speculated that it might represent a reaction of esophageal squamous mucosa to various types of insult (physical, chemical,

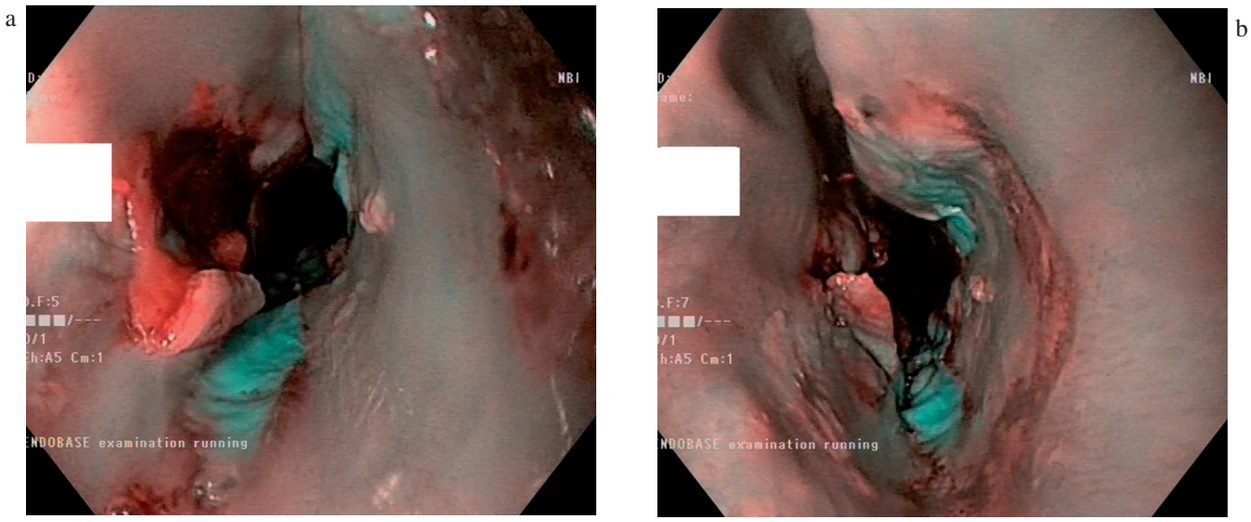

Figure 2. — a, b : Upper GI endoscopy on narrow band imaging (NBI) showing a suspicious circumferential bulging lesion in the upper third of the esophagus in 7 patient with suspicion of clindamycin induced EDS.

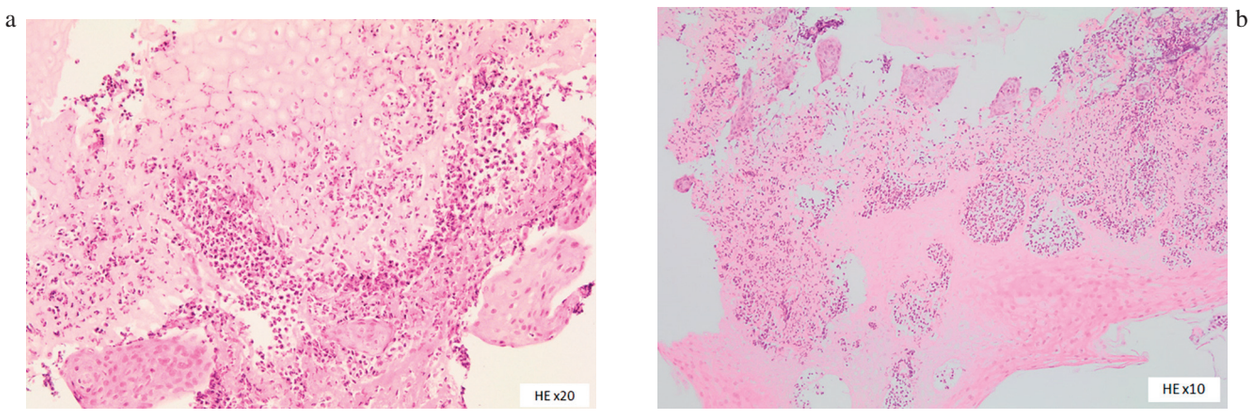

Figure 3. — a, b : In patient 7 with suspicion of clindamycin-induced EDS, pathological analysis of esophageal biopsies disclosed a highly altered esophageal mucosa characterized by parakeratosis and a necrotic, eosinophilic, pale aspect of the superficial layer of the squamous epithelium. The necrotic superficial layer was partially stripped from the hyperplastic basophilic basal layer, giving the lesion a two-toned appearance. A band of neutrophilic infiltrate was separating the detached superficial layer from the hyperplastic basal layer

Figure 4. — Endoscopic control in patient 7 at 8 weeks showing complete healing of the tumor like lesion previously described in the case of suspected clindamycin-induced EDS.

thermal and immunological) or a topical allergic response (9).

The endoscopic features of EDS ranged from single or multiple, white patches of peeling mucosa, extending from the mid to the distal esophagus to diffuse sloughing of the entire esophageal mucosa (1). Only one patient in our series was suspected to have EDS with the typical appearance of a sloughed white mucosa of the distal and mid esophagus on. In all the others, EDS was not suspected and was mistaken with candida esophagitis in one of these patients or Grade A reflux esophagitis in another as well as described as an unspecific esophagitis in 2 others. The confusion may be due to gastroenterologists not being very familiar with this rare benign entity. One of the most interesting points in this case series is that 2 out of 7 patients (28%) were suspected to have an esophageal tumor on endoscopy but histology was in favor of EDS. This illustrates the misdiagnostic rate of this poorly known rare entity, a situation that might be associated to unnecessary medical examinations for the patient. No previous case reports or case series reported such an endoscopic presentation.

The histologic findings in EDS is a sloughing of the superficial squamous epithelium with occasional

bullous separation of the layers, parakeratosis and varying degrees of acute or chronic inflammation, fungal elements may be associated (1). The pathological analysis disclosed typical signs of EDS in all cases of our series. This underlines the importance of biopsies in this setting to distinguish EDS from alternative diagnosis such as squamous cell carcinoma or candidiasis.

There is no a specific treatment for EDS. A combination of acid suppression with PPI and the discontinuation of the offending drugs have been reported to result in the healing of this entity (10, 11). A clinical follow up after 2 months documented a disappearance of the gastro-esophageal symptoms in 4 of these patients. Endoscopic follow up was done in 3 of our 7 patients showed a complete healing of the esophageal mucosa, 2 of them had and atypical endoscopic presentation with suspicion of a tumor like lesion of the esophagus and the third one with typical endoscopic presentation of EDS.

Conclusion

EDS is a rare benign entity that gastroenterologists must be aware of in order not to mistake it for other entities such as esophagitis or squamous cell carcinoma. The diagnosis is easily confirmed by specific pathologic signs on biopsies. The prognosis is good (11) after stopping the causative agent and with PPI treatment.

References

1. CARMACK S.W., VEMULAPALLI R., SPECHLER S.J. *et al*. Esophagitis dissecans superficialis ("sloughing esophagitis") : a clinicopathologic study of 12 cases. *Am. J. Surg. Pathol.*, 2009, **33** : 1789-1794.
2. MATHIEU B., LE GALL P., MOURANI A., MARQUAND A., SCHAEFER J.P. Spontaneous intramural dissection of the esophagus. Gastroenterol. Clin. Biol., 2000, 24 : 1117-21.
3. R CAMERON. Esophagitis dissecans superficialis and alendronate. *Gastrointest. Endosc*., 1997, Dec, **46** (6) : 562-3.
4. DA SILVA J.R., PINHO R., PONTE A., SILVA M., FURTADO A., CARVALHO J. Esophagitis Dissecans Superficialis Associated with Severe Clindamycin Toxicity. *J. Gastrointestin. Liver Dis*., 2014, **23** (4) : 363.
5. ABBASS KHURRAM *et al*. Esophagitis dissecans superficialis due to methotrexate toxicity. *Endoscopy*, 2014, **46** : E99-E100.
6. LONGMAN R.S., REMOTTI H., GREEN H. Esophagitis dissecans superficialis. *Gastrointest. Endosc*. 2011, **74** : 403-4.
7. SHAH R., THOGULUVA V., BANSAL N., MANOCHA D. Esophageal dissecans : a rare life-threatening presentation of recurrent pemphigus vulgaris. *Am. J. Emerg. Med*., 2015, **33**(12) : 1845
8. TIJJANI B.M., MASOODI I., HASSAN S.N. Esophagitis dissecans presenting with massive haematemesis in a patient with bullous pemphigoid. *Niger. J. Med*., 2013, **22** (4) : 354-6.
9. PONSOT P., MOLAS G., SCOAZEC J.Y., RUSZNIEWSKI P., HÉNIN D., BERNADES P. Chronic esophagitis dissecans : an unrecognized clinicopathologic entity. *Gastrointest. Endosc*., 1997, **45** (1) : 38-45.
10. HOKAMA A., IHAMA Y., NAKAMOTO M., KINJO N., KINJO F., FUJITA J. Esophagitis dissecans superficialis associated with bisphosphonates. *Endoscopy,*. 2007, **39**, Suppl 1.
11. HART P.A., ROMANO R.C., MOREIRA R.K., RAVI K., SWEETSER S. Esophagitis Dissecans Superficialis : Clinical, Endoscopic, and Histologic Features. *Dig. Dis. Sci*., 2015, **60** (7) : 2049-57.