

Acute esophageal necrosis. An underdiagnosed disease

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ABSTRACT

Acute esophageal necrosis is a rare disorder, and its etiology is unknown, the mechanism of damage being usually multifactorial and secondary to ischemic compromise, acute gastric outlet obstruction, and malnutrition. Endoscopic findings show circumferential black discoloration of the distal esophagus with proximal extension ending sharply at the gastroesophageal junction, which is the most common presentation. Prognosis depends on comorbid illnesses. In this study we analyze all cases reported in a retrospective analysis over a 2-year period to define risk factors, clinical presentation, endoscopic features, histological appearance, treatment and outcome. Our department has recorded 7 cases from 6,003 endoscopies performed in the last 2 years. The finding of a "black esophagus" represented 0.11% of cases.

Key words: Acute esophageal necrosis. Black esophagus. Esophageal ischemia.

RESUMEN

La esofagitis necrotizante aguda (ENA) es una rara entidad cuya etiología es desconocida, siendo el mecanismo patogénico multifactorial, participando fundamentalmente el compromiso isquémico, la malnutrición y la obstrucción del tracto digestivo alto. Los hallazgos endoscópicos muestran una coloración negruzca de la mucosa esofágica con transición brusca a nivel de la unión esofagogástrica. El pronóstico depende de las enfermedades de base. Se revisan los casos de ENA, excluyendo los secundarios a cáusticos, recogidos de forma retrospectiva durante los últimos 2 años. Se analizan los factores de riesgo, la presentación clínica, los hallazgos endoscópicos, la histología, el tratamiento y la evolución. En nuestro departamento, se han diagnosticado 7 casos de ENA en 6.003 gastroscopias realizadas en el periodo de estudio, representando así la ENA el 0,11% de la exploraciones.

Palabras clave: Esofagitis necrotizante aguda. Esófago negro. Isquemia esofágica.

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INTRODUCTION

Acute necrotizing esophagitis (ANE), also designated "black esophagus", is an uncommon condition that was

first described by Goldenberg in 1990 (1) with two case reports; post-mortem cases had been previously reported (2,3).

ANE is more common in males versus females, and its pathogenesis is still unclear, the condition having been associated with hypoperfusion, upper digestive tract obstruction, and malnutrition (1,4-7).

Diagnosis is reached endoscopically with histological support, but a high degree of suspicion is required for older individuals with associated comorbidities and poor general condition.

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Treatment consists of supportive management plus gastric acid inhibition. Mortality is high (up to 50%) (7) albeit related to the patient's underlying condition, and resolution has been reported even in cases with a fatal outcome.

We retrospectively reviewed all ANE cases diagnosed in our department during the last two years, and analyzed risk factors, potential pathogenetic mechanisms, and the relevance of endoscopy for its diagnosis.

MATERIAL AND METHODS

A retrospective study of acute necrotizing esophagitis (ANE) cases diagnosed in our hospital in the last two years – from February 2006 to February 2008 – was undertaken. We reviewed all upper digestive endoscopic procedures performed during that period of time and included in the Endoscopy Unit's database (Olympus Endobase).

Diagnosis with ANE was based on endoscopic images – an esophagus with a distal diffuse, circumferential, blackish lesion at times associated with exudation, that extends proximally and abruptly stops at the esophago-gastric junction – with the support of histology findings.

ANE cases from caustic substance ingestion were excluded from the study.

Demographic characteristics, clinical presentation, esophageal lesion extension, comorbidities, triggering factors, associated endoscopic findings, histological characteristics, and outcome were all analyzed for each ANE case (Table I).

RESULTS

From February 2006 to February 2008 6003 upper digestive endoscopies were performed. A diagnosis with ANE was reached in 7, which represents 0.11%.

Of these 7 diagnosed cases 4 were males and 3 were females.

The youngest age at presentation was 63 years, the oldest was 94 years, and mean age at diagnosis was 79.5 years.

Mean hospital stay was 14.4 days with a range of 4 to 28 days.

Mean follow-up was 23.85 days, with a maximum of 630 days and a minimum of 4 days.

The presentation symptom shared by all patients was upper gastrointestinal bleeding (UGIB) as overt hematemesis, ground-coffee vomits or rapid transit rectorrhagia. Four additionally had epigastralgia.

Table I. Demographic, clinical, and endoscopic characteristics in our series

	<i>Sex/age (years)</i>	<i>Underlying disease</i>	<i>Clinical picture</i>	<i>Total proteins (g/dl)</i>	<i>Extension</i>	<i>Other endoscopic lesions</i>	<i>Outcome</i>
Case 1	M/82	Heart disease Valvulopathy Chronic AF Dicumarin therapy	Hematemesis Epigastralgia	6,5	Entire esophagus	None	<i>Good</i> Asymptomatic on discharge
Case 2	F/87	DM, HBP Chronic AF Dicumarin therapy	Hematemesis Rectorrhagia	6,5	Middle & lower thirds	None	<i>Good</i> Asymptomatic on discharge
Case 3	F/71	Heart disease Diabetic ketoacidosis	Coffee-ground vomiting Epigastralgia	5,8	Entire esophagus	None	<i>Dies</i> after 20 days from multiple organ failure
Case 4	M/77	Renal failure	Coffee-ground vomiting Epigastralgia	5,9	Middle & lower thirds	Duodenal bulb ulcer	<i>Good</i> Asymptomatic on discharge
Case 5	M/83	Renal failure	Hematemesis	6,6	Entire esophagus	None	<i>Good</i> Asymptomatic on discharge
Case 6	M/63	COPD GEN	Coffee-ground vomiting Dyspepsia	6,1	Middle & lower thirds	Duodenal bulb ulcer x 2	<i>Good</i> Asymptomatic on discharge
Case 7	F/94	Hiatal hernia Reflux esophagitis, grade IV Renal failure	Coffee-ground vomiting	5,9	Entire esophagus	None	<i>Dies</i> after 28 days from sepsis and multiple organ failure

Most common underlying conditions included (in this order): heart disease, cardiovascular risk factors (diabetes mellitus, dyslipemia, and high blood pressure), renal failure, hiatal hernia with severe peptic esophagitis, prostate cancer, and chronic obstructive pulmonary disease.

Laboratory tests revealed total protein levels equal or inferior to 6.6 g/dl in all patients, with hypoalbuminemia (< 2 g/dl) in two; no other nutritional parameters were available.

Endoscopy (Figs. 1-4) revealed a friable, blackish (in a consistent or patchy manner) esophageal mucosa with ulcers and exudate, and at times active diffuse bleeding. In 3 of 7 cases the lesion endoscopically extended to the entire esophageal mucosa; in other 3 cases to the distal thirds, and in one case to the distal esophageal third, with

the esophago-gastric junction being spared in all cases.

Biopsies were obtained from the esophageal mucosa in 5 of 7 cases. Pathology revealed a squamous mucosa with erosion or ulceration, extensive necrosis, and underlying vascular thrombosis, and viral cytopathic evidence as well as fungal infection were ruled out. Bacterial overinfection was seen in one sample.

ANE-associated pathological endoscopic findings were assessed; only in 2 patients was an unrelated condition found, in both cases a bulb ulcer covered in fibrin with hematin remnants (Forrest IIc); one bulbar ulcer was dual (in both the anterior and posterior aspects). A second endoscopic procedure was performed in 5 patients after 7-15 days, which showed ANE undergoing resolution in all patients.

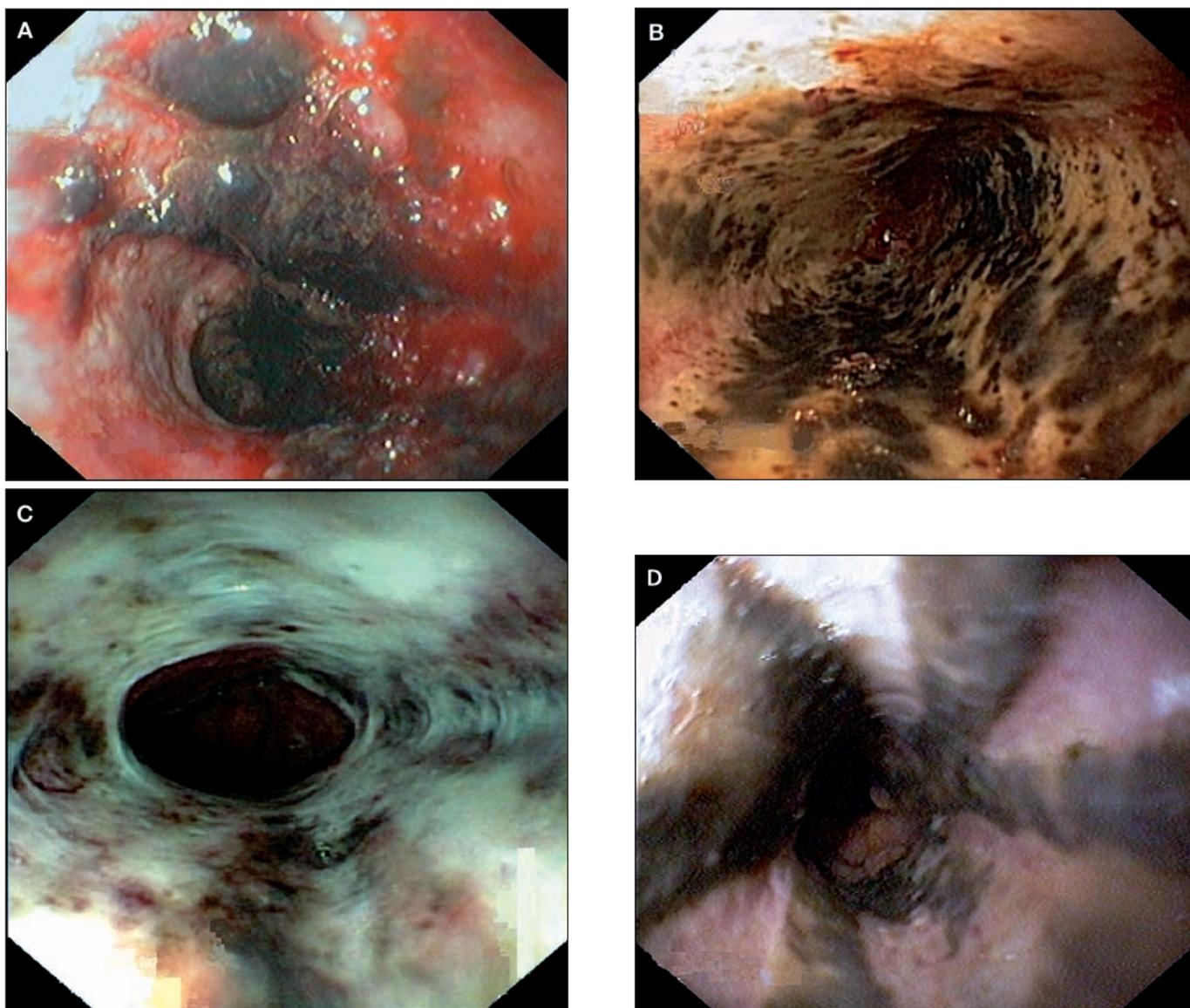


Fig. 1. Endoscopic images of acute necrotizing esophagitis: a blackish mucosa, friable in the distal third, with proximal extension.

Patient management focused on comorbidity control and nutritional status improvement, together with high-dose proton pump inhibitors (PPIs). Furthermore, therapy with oral anticoagulants was eventually discontinued in patients thus treated. One patient received wide-spectrum antibiotic therapy for sepsis with multiple organ failure.

Five patients were discharged with no symptoms, hemodynamic stability, and good oral tolerance; the remaining two died from causes other than ANE.

DISCUSSION

The estimated incidence of ANE in necropsy studies is 10.3% (8), which is in contrast to the frequency described in endoscopy studies (lower than 0.3%). The study by Moretó et al. (9), performed for 16 years, identified 10 cases in 80,000 upper endoscopies. Augusto et al., in their retrospective series for 5 years, diagnosed ANE in 0.28% of studies (10). The one prospective study, by Soussan et al for 1 year, the prevalence of ANE was 0.2% (7).

Incidence is likely much higher, either from underdiagnosis or erroneous endoscopic labeling of findings as reflux esophagitis. During 24 months our series identified 7 cases; however, if we analyze each of the two years separately according to a greater awareness for this condition in the last 12 months, prevalence was 0.07% for the first year and 0.15% for the second one.

UGIB is the usual presentation form, and may be associated with symptoms such as epigastralgia, anemic syndrome, vomiting, and dysphagia. Ischemia has been suggested for the etiopathogenesis of ANE, supported by the commonly involved distal third of the esophagus, an area with poorer vascularization, and histological findings, highly similar to those of ischemic colitis (11,12).

In our series UGIB from duodenal ulcer was the only associated endoscopic finding in 2 patients, which may have temporarily contributed to reduced blood flow as previously described (1,9,13). Along this same line it has also been suggested that exposure to gastric acid may directly harm the mucosa, a process aggravated by the failing mucosal defense mechanisms in the presence of blood hypoperfusion (13).

Another key co-factor in ANE development is nutritional status, since malnutrition may compromise mucosal defense and healing. Thus, the study by Moreto et al. and the series by Soussan et al. found malnutrition with reduced proteins in 40 and 75%, respectively, in patients with this condition (7,9). Our series found hypoproteinaemia in 87.5%.

Predisposing conditions leading to the development of ANE and quoted in the literature are many, including: viral infection (cytomegalovirus and herpesvirus) (14,15), hypersensitivity to some wide-spectrum antibiotics (16),

gastric outlet obstruction (17), aortic rupture or dissection (5), hyperglycemia (6), neoplasms (6,7), Stevens-Johnson syndrome (18), hypothermia (19), shock (4), severe vomiting after alcohol ingestion (20), liver disease (21), anti-phospholipid syndrome and other coagulopathies (22), and diabetic ketoacidosis (23).

Diagnosis is through endoscopy, which reveals a blackish, friable, bleeding esophageal mucosa in the distal third of the esophagus that extends proximally, with a normal esophago-gastric junction. Biopsies should be obtained for histology and a differential diagnosis with: melanosis as seen in chronic esophagitis (24,25), pseudomelanosis resulting from lysosomal degradation (26), acanthosis nigricans (commonly associated with abdominal tumors) (27), primary or metastatic melanoma (28), carbon ingestion (29), and other caustic and corrosive agents that may induce esophageal necrosis.

Regarding histological findings, severe mucosal and submucosal necrosis may be seen with inflammation and partial destruction of adjacent muscle fibers, and on occasion thrombosis and capillary destruction (9).

Between 30% and 60% of patients die from their underlying disease rather than ANE (6,7). In our series mortality reached a lower percentage (28.6%). The most common ANE-related complication is the development of esophageal stenosis (15%), which usually requires dilation. Similarly, mediastinal abscesses secondary to trans-wall compromise have been exceptionally reported (6,7,9).

The management of this condition starts with adequate hydration and bowel rest in the first few days, associated with the specific management of underlying disease and adequate nutritional support. A regimen is scheduled with a proton pump inhibitor in high doses to prevent the esophageal mucosa from being damaged by acid. Early during oral tolerance the use of sucralfate allegedly as esophageal mucosal protector has been suggested (30). Antibiotics are used according to each individual patient and their septic status. An NGT is recommended for gastric outlet obstruction or refractory vomiting.

Finally, we may say that suspicion is a key factor in the diagnosis of ANE, particularly in older patients with associated morbidity and evidence of upper digestive bleeding.

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