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Necrotizing esophagitis (black esophagus): Presentation of cases and literature review

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Abstract

Acute necrotizing esophagitis (black esophagus) is a rare pathology that is characterized by partial or total loss of the epithelium, ulceration up to the circumferential slough of all layers of the mucosa and submucosa, frequent involvement of deep muscle layers, and frequent perforations. Its blackish appearance in endoscopic examinations has given it the name of black esophagus. Five illustrative cases, all concordant with descriptions the medical literature, are presented in this study together with a review of the literature, case descriptions and risk and prognosis factors.

Key words

Necrotizing esophagitis, black esophagus, acute esophageal necrosis, case description, review, risk factors.

INTRODUCTION

Acute esophageal necrosis (AEN) is a rare pathology that presents in the mucosa with severity varying from partial loss of the epithelium with ulceration to the necrosis of all mucosal layers, compromise of deep muscular layers and perforation. It present as focal or extensive necrosis. Due to its blackish color under endoscopic examination, it is best known as *black esophagus*. There is little literature on the subject, its pathophysiology is unknown, and it can be easily confused with caustic burns because of its appearance. The first two cases were described by Brennan and by Lee et al.. in a patient with extensive esophageal necrosis and in a patient with severe hypothermia and spontaneous aortic rupture with extensive esophageal infarction. (1, 2)

Given AEN's dramatic nature from an endoscopic point of view and its clinical picture and possible outcomes, we decided to conduct a review of the available medical literature.

SUBJECTS AND METHODS

We describe five cases of patients with endoscopic diagnoses of acute esophageal necrosis who were treated in medical centers in Bogotá. Their clinical evolutions were compared with findings provided by the literature.

The review was carried out through searches in PubMed, Scielo, Google, Ovid, Hinari, Springer, Ebsco and Sinab (National University), using the terms " Black esophagus", "black esophagus", "black oesophagus", "necrotizing" AND "oesophagitis", "necrotizing" AND "esophagitis", and "necrotizing esophagitis". The search was repeated in the bibliographies of all the articles found. All articles were accepted if they were in English, French, Spanish or Portuguese, or if at least the abstract was in one of these languages. We found a systematic review of the literature by Day and Sayegh, 2010 which included all the cases described until 2008. (3) We proceeded to describe cases reported from then until August 2017. Then we consolidated them into a table by authors in the same format used by

Day and Sayegh to make them comparable and to adequately describe the totality of the cases.

DESCRIPTIONS OF CASES

Case 1 (JL)

The patient was a 79-year-old woman who came to the emergency room because of melena and altered consciousness. Her medical history included resected meningioma, secondary seizure syndrome, uncontrolled arterial hypertension, and chronic obstructive pulmonary disease. Upon examination she was found to have leukocytosis with neutrophilia (89%); creatinine of 1.84 mg/dL, hypochloremia (92 mEq/L) and hyponatremia (129 mEq/L). Endoscopy showed esophageal epithelial necrosis in the lower two thirds and diffuse bleeding (Figures 1, 2, 3 and 4) without changes in the caliber of the esophagus. Her evolution and outcome are unknown.

Case 2 (MDA)

The patient was a 79-year-old who was seen for a follow-up examination due to a history of digestive hemorrhaging. She was treated in the emergency room due to endoscopic findings of proximal candidiasis and circumferential ulceration with a red, brown and black appearance suggesting hematin, areas of necrosis, friability, easy bleeding upon contact with the endoscope in the middle and distal third with severely edematous and rigid mucosa, without stenosis (no photographic document). The alterations disappear at the Z line which was raised to 32 cm. The widened esophageal hiatus had a giant hiatal hernia. She was diagnosed with severe esophagitis suggestive of a caustic injury. Biopsies performed on the distal esophagus showed acute esophagitis with extensive mucosal and submucosal necrosis, reactive epithelial damage, but with a viable muscular layer. The patient and family members said that there was no possibility of ingestion of caustics. The patient had had iron deficiency anemia four years before and had undergone previous endoscopies due to digestive hemorrhaging. She had had a 9 cm hiatal hernia one year earlier and Cameron erosions four years earlier. An endoscopic follow-up one month later showed a giant 9 cm hiatal and chronic erosive gastritis in the antrum with chronic mild non-atrophic gastritis in the antral biopsies.

Case 3 (HS)

The patient was a 76-year-old man who had been referred for consultation due to three days of severe pain in the right hypochondrium with malaise, asthenia and adynamia. The examination was painful, and the patient had tachycardia, tachypnea, jaundice, and labored breathing with rales on the right side. He had no fever but tested positive for Murphy's sign. The patient had a history of type 2 diabetes mellitus and arterial hypertension and had had right basal pneumonia, septicemia, thrombocytopenia, benign prostatic hypertrophy, exacerbated chronic renal failure, cholelithiasis with dilation of the bile duct and choledocholithiasis. An incidental finding during endoscopic ultrasonography was black mucosa throughout the entirety of the esophagus. It was covered with mucous exudate, without erosions, ulcers or narrowing, but the mucosa below the Z-line had

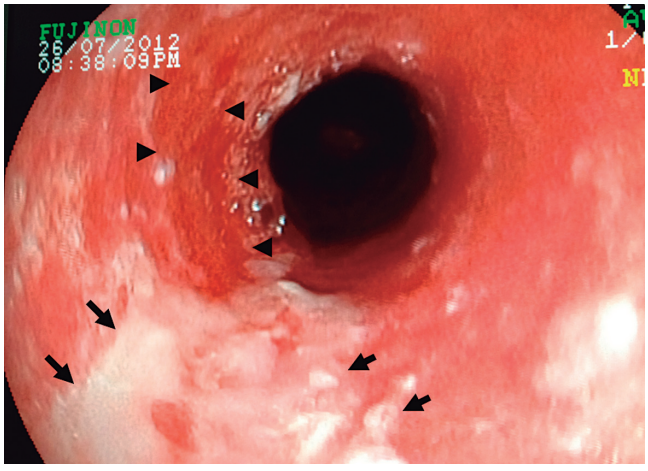

Figure 1. Fragments of necrotized mucosa in the proximal middle third of the esophagus (arrows) and bleeding in mucosal layer (arrowheads) (Case 1).

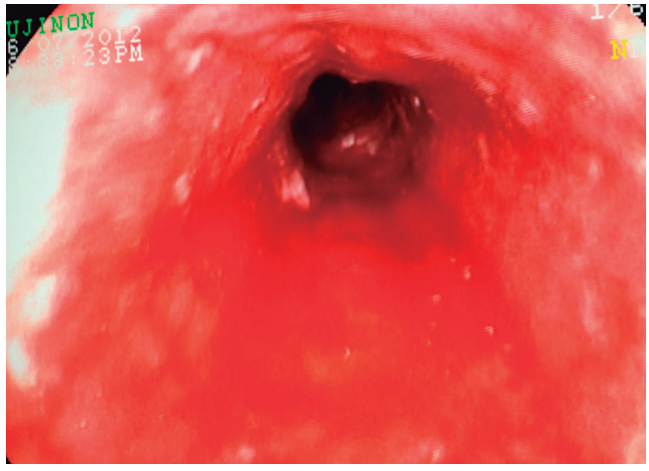

Figure 2. Diffuse necrotized remnants of the mucosa in the middle third of the esophagus with bleeding in mucosal layer (Case 1).

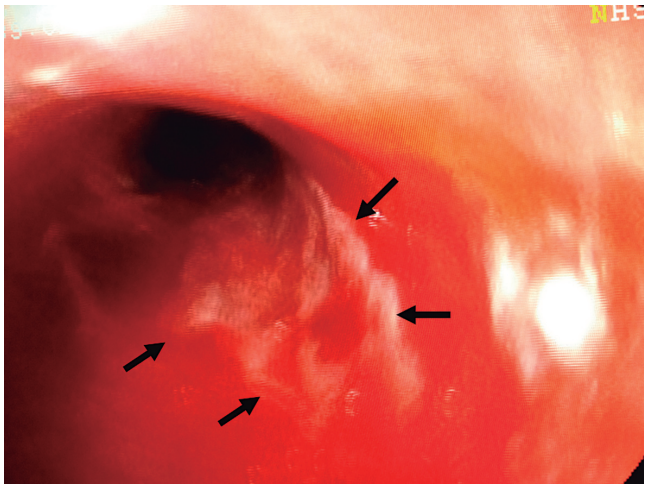

Figure 3. Fragments of necrotized esophageal mucosa in the middle third (arrows) and bleeding in mucosal layer (case 1).

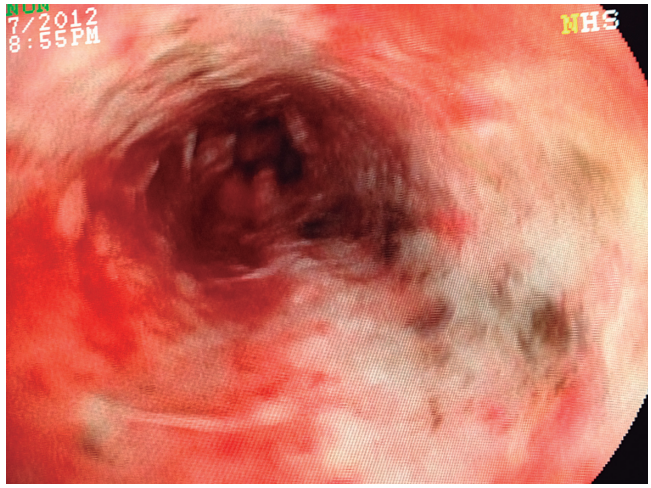

Figure 4. Diffuse necrotized detritus of the esophageal mucosa with extensive ulceration, foci of necrosis in the distal third and areas of bleeding in mucosal layer (case 1).

the usual appearance. Videoendoscopy demonstrated esophageal ulceration from 21 cm of the dental arch which became circumferential at 23 cm. It was covered by black and gray fibrin from 27 cm to the gastroesophageal junction (Figures 5, 6 and 7) but the cardiac mucosa was unaffected (Figure 8). Endoscopic retrograde cholangiopancreatography (ERCP) demonstrated a dilated extrahepatic bile duct with filling defect in the middle and distal third. A small sphincterotomy was performed to address thrombocytopenia (31,000 platelets/mm^3) (Figure 9), and small stones were removed with a balloon,. A 7 Fr x 7 cm plastic stent was placed. Bile drainage was clear but with microcalcifications. The patient's development was satisfactory, and he was discharged after resolution of pain and jaundice. At 10 weeks he was asymptomatic and chose not to continue follow-up procedures.

Case 4 (JMR)

The patient was an 81-year-old man who had been diagnosed with mesenteric thrombosis and gastrointestinal bleeding. Digestive endoscopy showed that the entire esophageal mucosa had areas of necrosis, hemorrhaging, and ulcerated lesions covered by fibrin. However, there were no signs of active bleeding or perforations. The irregular Z line was located at 38 cm from the dental arch. The diagnosis

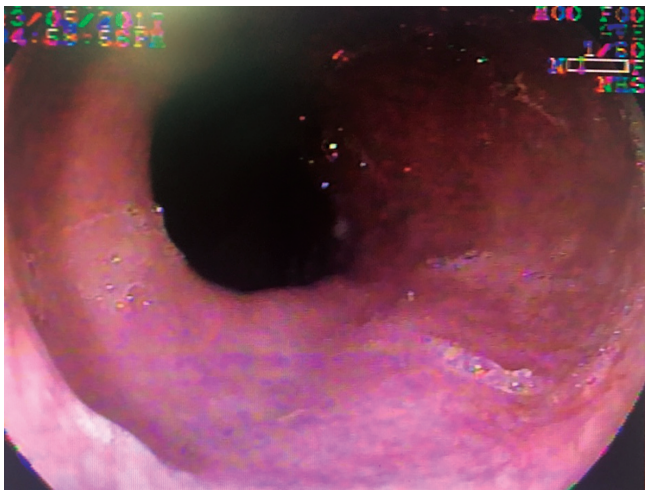

Figure 5. Normal cervical esophagus (case 3).

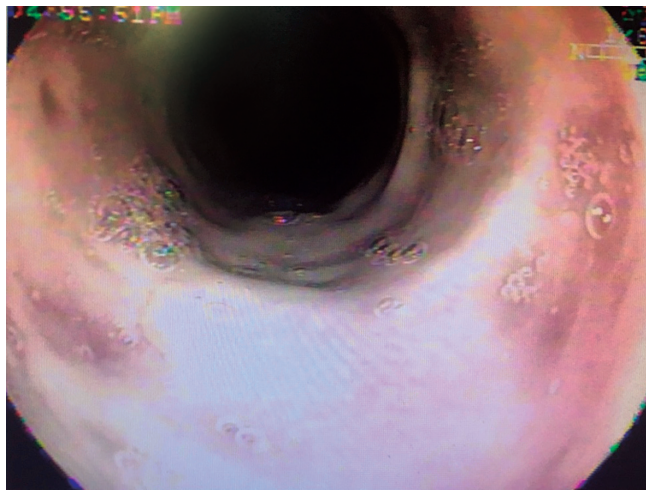

Figure 6. Circumferential proximal esophageal ulceration covered by fibrin (case 3).

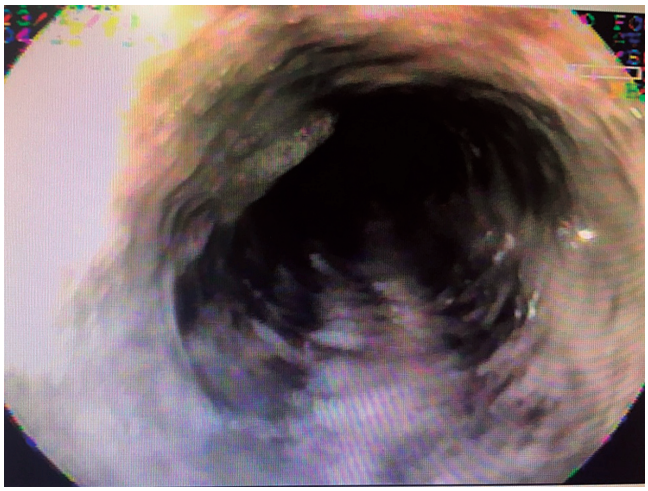

Figure 7. Black and grayish distal esophagus (case 3).

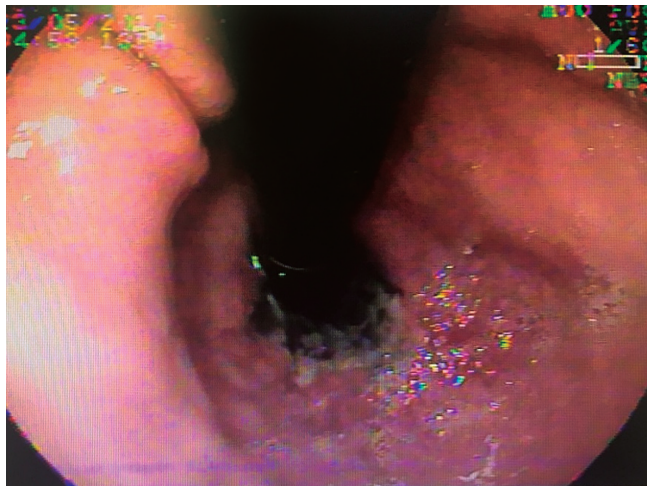

Figure 8. Gastroesophageal junction in retrovision with cardiac mucosa unaffected (case 3).

was pancreatic necrosis and chronic pangastritis. There are no photographic records or later records of this patient.

Case 5 (MECL)

The patient was a 73-year-old woman who had been diagnosed with digestive hemorrhaging. Digestive endoscopy showed a large hematoma in the posterior wall of the esophagus, with mucosal dissection and spontaneous bleeding. There was mucosa in the middle third with areas of necrosis and mucosal fragments, but the distal third was normal. There are no photographic records or later records of this patient.

DISCUSSION

Epidemiology

Acute esophageal necrosis (AEN), or black esophagus, is a rare condition that was initially described in autopsies of isolated cases. (1, 2) Then a series of autopsies found a frequency of 0% to 0.02%, (4, 5) and more recently a series of 310 autopsies found 32 cases of esophageal necrosis for an incidence of 10.3%. (6) According to the authors of one study, the subsequent appearance of endoscopy has led to findings of frequencies that range from 01% to 0.28% of endoscopies. (7) Grudell reported an incidence of 0.008% (Six cases out of 78,847 endoscopies), (8) Ramos described an incidence of 0.28% in a series of 3,976 consecutive endoscopies, (9) Gómez reported an incidence of 0.11% in a series of 6,011 consecutive endoscopies, (10) and Yasuda reported an incidence of 6% for endoscopies performed due to acute digestive hemorrhaging over a period of three years. (11) Our cases do not allow establishment of relative frequency, given that they are isolated cases in third-level institutions, although no episodes were found in a set of 12,638 endoscopies performed at a second-level diagnostic center. (12) This reflects the severity of the entity which, according to the literature, has associated comorbidities in 83% of all cases. (3, 7). There is a predominance of male patients and elderly patients, particularly in the seventh and eighth decades. (3, 7) The average age of our patients was 78 years. There were three women (60%) for 70 years and male dominance (3: 1) in the total series (Table 1).

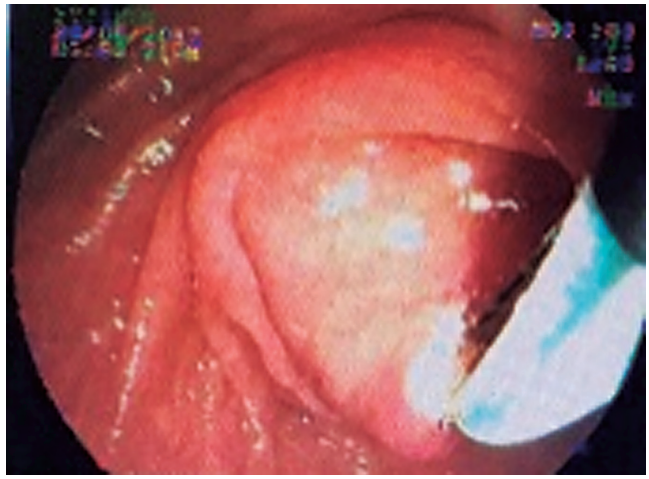

Figure 9. Small sphincterotomy for drainage and stone extraction (case 3).

Table 1. Summary of the most frequent findings in patients with necrotizing esophagitis (black esophagus) described in the literature*

Age-sex **	Symptoms	Endoscopic findings	Length of necrosis	Histological findings	Outcome	Base diseases
†n = 261	n = 148	n = 241	n = 106	n = 39	n = 261	n = 157 Serious disorders: 78%
70 years 172/M 61/F 26/?	Digestive hemorrhages: 66% Pain: 20% Hematemesis: 20% Melena: 16% Vomiting: 11% Melanemesis: 10% Dysphagia: 9% Shock: 7% Anemia: 4% Sudden death: 3% Unconsciousness: 3%	Black esophagus: 91% Necrosis: 10% Esophageal ulcer: 2.5% Duodenal ulcer: 4% Active bleeding: 1.7% Perforation: 1.3% Gastric ulcer: 1% Esophageal stenosis: 1%	1/3: 22.9 % 2/3: 40 % 3/3: 33 % 1/2: 3.8 %	Autopsy: 8 Necrosis: 97% Inflammation: 45% Ischemia Esophagus: 24% Stomach: 5% Duodenum: 5% Esophagus ulcer: 16% Thrombosis: 16% Hemorrhages: 8%	Cured: 38% Improvement: 5% Death: 32% Stenoses: 10% Residual: 6% Stents: 1% Multi-organ failure: 3% Esophagectomy: 1.5% Pneumothorax and pneumomediastinum: 1% Esophageal fistula: 0.3% Esophagus-gastrostomy: 0.3% Duodenal perforation: 0.3% Mesenteric ischemia: 0.3% Gastric volvulus: 0.3%	n = 104 Hemorrhaging and shock: 36% Hypertension: 27% Heart disease: 24% Hepatic insufficiency: 24% Diabetic ketoacidosis: 20% Renal insufficiency: 18% Septicemia: 14% Alcoholism: 14% †† NSAID: 10% Hiatal hernia: 6% Atrial fibrillation: 6% Neoplasia: 4% ECV sequelae: 4% Amputation: 4%

* Consolidated clinical findings and outcomes in all cases described in the literature (3, 8-11, 13-81).
** Sex: M: male, F: female.
† n: number of patients whose description is available for the corresponding item
†† NSAIDs: non-steroid anti-inflammatory drugs.

Clinical presentation

The previous literature described 261 cases of AEN. Together with the five cases described here, there are now 266 published cases. The vast majority of studies are descriptions of isolated cases, but there are some large series including one with 29 cases, (13) and one with 16 cases. (11) Only three extensive reviews of the literature were found. In 2006, Grudell et al. collected the first 52 cases of AEN reported between 1963 and 2003. (8) In the second, published in 2007, Gurvitts et al. collected 88 additional cases. (81) In the third study, Day and Sayegh collected the remaining cases until 2008. (3) Tables 1 and 2 show the data and findings of all the cases described in the literature. (3, 8-11, 13-81)

As can be seen, our patients were older adults who were hospitalized and whose main indication was upper gastrointestinal bleeding (4/5). Active bleeding was confirmed in three cases, as were the total cases (Table 1). Other less frequent findings included dysphagia, shock, anemia, unconsciousness and sudden death. In our series, one patient was diagnosed incidental during study of complicated bile duct pathology.

Diagnosis of AEN is essentially endoscopic although it is occasionally made during emergency surgery or autopsies (Table 1). (1, 2, 4) The lesion lesions of four of the five cases were circumferential, and four cases had zones of necrosis. Necrosis was diffuse in cases 3 and 4, located in the distal two thirds of the esophagus in cases 1 and 2, and in the middle third of the esophagus in case 5. Seventy-three percent of the cases had two thirds of more the esophagus compromised (Table 1). The appearance of AEN is similar to caustic esophagitis which was suspected in one of our cases. It was clinically ruled out by the patient and family members who also demonstrated that he had already presented two episodes of bleeding as a result of a giant hiatal hernia and Cameron's ulcerations.

Endoscopic findings are diverse, so diagnosis requires that other etiologies that produce similar alterations be discarded. These include ingestion of caustics, other toxics or carbon; infections; radiation therapy and metastatic melanoma. (3, 10) Findings can range from whitish membranes, which when removed leave a grayish or blackish mucous membrane, to diffuse necrosis with adherent yellowish exudates. The majority of cases feature ulceration and blackish or grayish appearance demarcated by the gastroesophageal junction, with the cardiac region having its usual appearance. Our cases fit this description. The spectrum of associated lesions is wide and includes gastric hemorrhages, duodenal hemorrhages, ulcerations and perforations. In the general case series there are ten cases of duodenal ulcers (4%), two cases of gastric ulcers (1%), two cases of duodenal ischemic necrosis (1%), four cases of active bleeding (2%), three cases of esophageal perforations (1.3%) and one case of duodenal perforation (0.5%) (Table 1).

Outcomes varied greatly. It was favorable for the second of our patients whose esophageal mucosa had normalized

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
11. Abed J et al.	80/M	Diffuse abdominal pain, melena	3/3	Ulcerated, black, necrotic mucosa	Extensive necrosis, severe inflammation, absence of epithelium	Cured		Ulcerative colitis, GERD, antacids and bismuth subsalicylate
12. Abu-Zaid A et al.	40/M		2/3	Black esophagus, necrotic mucosa, multiple superficial ulcerations	Focal inflammatory infiltrate, ulceration, necrosis, hemorrhage	Cured		
13. Akkinepally S et al.	60/M	Unconscious, melanemesis and melena	1/2	Black esophagus, severe hypertensive gastropathy, ischemic erosions in the duodenum		Died due to hepatorenal syndrome and sepsis		Alcohol abuse, upper digestive bleeding, cirrhosis and hypotension
14. Altenburger DL et al.	45/F		3/3		Diffuse acute inflammatory infiltrate, lipofuscin pigmentation due to ischemia	Autopsy: black esophagus, ischemic mucosa and submucosa, muscular necrosis		Cocaine and alcohol
15. Ambrosio MR et al.	18/M	Streptococcal toxic shock syndrome	3/3		Total circumferential black esophagus	Death-autopsy		
4. Augusto F et al.	23/M 6/F 40 to 91 years. Avg. 75.2	Hematemesis or melena Eight patients with hemodynamic instability	2/3 in 17 3/3 in 10 1/3 in 1 29 cases	Black esophagus		10% to 34% die from base disease		24 (82.3%) with severe base disease, DM-II and HT
16. Barnes T et al.	53/M	Melanemesis on day 15 of Cefazolin		Necrotizing esophagitis		Cured		Septicemia and femoral osteomyelitis due to Staphylococcus aureus. PT: 89.2 and INR: 8.11
17. Bremholm L et al.			3/3	Diffuse black esophagus		Dies at 48 hours		Hemorrhaging and hypoperfusion
18. Cameron PA, Schweiger F	62/M	Unconscious, hypovolemia, hypothermia, acute renal failure, NGT*, Coffee grounds	3/3	Black esophagus	Acute esophageal necrosis and diffuse brown pigment	Cured		Sclerosing cholangitis. Coronary disease, HBP, DM-II, alcoholism

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature. *Continued*

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
19. Caravaca-Fontán F et al.	65/M	Dyspepsia, nausea, retrosternal burning and melanemesis	3/3	Diffuse circumferential black esophagus		Cured		24 h after renal transplantation, pulmonary edema and cardiac arrest, aortic stenosis, aortic balloon and transcatheter valve replacement
20. Castaño-Llano R et al.	68, 69 and 82 years	Hematemesis	2/3 3 cases	Black esophagus	Biopsies show ischemia	Two improve One Dies due to multiorgan failure		Hepatic cirrhosis/mastectomy due to cancer, liver metastasis
21. Choi EJ et al.	48/M	Hematemesis	3/3	Diffuse, friable black esophagus	Inflammatory infiltration, necrotic tissue	Cured		
3. Day A, Sayegh M	68.4 years (19-91) 88/M 22/F. 2?	UDB 65%, epigastric pain 8%, dysphagia 7%, melena 5%	112 cases, the majority 1/3 to 2/3	Friable black esophagus, yellow exudates and ulceration, clear cardiac demarcation	Severe mucosal and submucosal necrosis and inflammation of the muscle fibers	Death: 38.4% Resolution: 49.1% Stenosis: 7.1% Unknown: 3.6% Other: 1.8%		Shock/hypotension: 20%; Hepatic failure: 15%; neoplasia: 11%; infection: 7% Unknown: 26% Others: 21%
22. De Palma GD et al.	82/M	Melanemesis	3/3	Circumferential black esophagus				Coronary artery disease, HBP, DM
23. Edling P, Thomsen H		Hematemesis		Acute esophageal necrosis		Cured		Diabetic ketoacidosis
		Hematemesis		Acute esophageal necrosis		Cured		Diabetic ketoacidosis
24. Eren B et al.	17/F	Abdominal distention and vomiting				Died at 6 hours, Autopsy found black esophagus		
25. Fernández R et al.	87/F	UDB after spinal anesthesia		Black esophagus with active bleeding		Died		HTA, atrial fibrillation
26. Fernández-Carrillo C et al.	94/M	Melanemesis	1/3	Distal necrotic plates		Cured		Angina, arterial hypotension fractured femur, chronic atrial fibrillation
27. Galanopoulos M et al.	80/F	Melena	1/2	Circumferential black esophagus	Epithelial necrosis with non-specific inflammatory exudate	Cured		1 week 1600 mg/d Ibuprofen, and iron-deficiency anemia (Hb 9 g%)

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature. *Continued*

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
28. Galtés I et al.	54/M	Unconscious	3/3	Acute esophageal necrosis		Died		Alcoholism, polytoxicomania, DM-I
29. Garas G et al.	89/F	Epigastric pain, nausea, vomiting, hematemesis and melena	2/3		Ischemia, hemorrhaging, necrosis	MOF, Died	Large hiatal hernia, gastric volvulus	AAA and thrombosis
30. Gómez AA et al.	67/M			Black esophagus		Stenosis, SEMS*		DM and ketoacidosis, atrial fibrillation, chronic renal failure, severe sepsis
10. Gómez LJ et al.	82/M	Hematemesis, epigastralgia	3/3	Black esophagus	Erosion or ulceration, extensive necrosis, vascular thrombosis in 5 of 7	Cured		Cardiopathy, valvular heart disease, chronic atrial fibrillation, warfarin
	87/F	Hematemesis and rectal bleeding	2/3	Black esophagus		Cured		DM, HBP, atrial fibrillation, Warfarin
	71/F	Melanemesis, vomiting, epigastralgia	3/3	Black esophagus		Died, MOF		Cardiopathy, DM and ketoacidosis
	77/M	Melanemesis, vomiting, epigastralgia	2/3	Black esophagus and duodenal ulcer		Cured		Kidney failure
	83/M	Hematemesis	3/3	Black esophagus		Cured		Kidney failure
	63/M	Melanemesis, vomiting, dyspepsia	2/3	Black esophagus and two duodenal ulcers		Cured		COPD
	94/F	Melanemesis, vomiting	3/3	Black esophagus		Die don 28th day, MOF and sepsis		HH, esophagitis G-IV, renal failure
31. Gómez V et al.	50/F	Dysphagia	3/3	Diffuse greyish and black esophageal discoloration	Acute esophageal necrosis with dispersed inflammatory cells with bacteria and yeast	Diffuse deep ulceration and distal stenosis of 3 mm, 1/2 less than 10 weeks. Dilations without result	SEMS, middle third fistula, esopha-gectomy	42 days after liver transplantation, 10 days post-rupture of inferior phrenic artery with hemorrhagic shock
32. Groenveld RL et al.	68/F	MOF, perforation Pneumomediastinum drainage and pneumothorax	1/3	Circumferential black esophagus, perforation at 32 cm		Stenosis + dilations		

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature. *Continued*

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
33. Gurvits GE et al.	75/M	7/8 patients with UDB	8 patients 1/3	Distal esophagus; some, proximal extension. Duodenal commitment in 50% of cases		Stenosis in 2/8 patients, 1/8 died due to underlying disease		Alcohol abuse, HBP, DM in 7/8, dyslipidemia, MNT anemia 7/8, vasculopathy, hypoalbuminemia 8/8, IRC 7/8
34. Hejna P et al.	53/F	Unconscious	3/3		Autopsy: complete epithelial necrosis, focal muscular mucosa, dense infiltrate leukocytes and ulceration	Died		Suicide with antipsychotics dies: haloperidol, zotepine and chlorprothixene
35. Hermet A et al.	72/M	Hematemesis and epigastralgia 1st postoperative day		Black esophagus		Cured		Hip replacement with hemodynamic compromise. Coronary disease, vasculopathy MM II, DM, HT
36. Hong JW et al.	85/M	Alcohol abuse> 100 grams and hematemesis	2/3	Whitish exudates suggestive of candidiasis, 2/3 distal black mucosa, edema and multiple erosions duodenal bulb	Epithelial necrosis with inflammatory exudate and ulceration. Not candida	Cured		HTA, DM, alcohol abuse, gastric ulcer and ECV sequelae
37. Iorio N et al.	63/F	Abdominal pain, diarrhea, nausea, vomiting. Palpable purpura in extremities Tissue	3/3	Ulcerated necrotic esophagus, necrotic duodenitis up to third portion	Granulation due to ulceration. Duodenal ischemic vasculitis of the mucosa and submucosa	Cured		Kidney transplant, DM-II, peripheral arterial disease, GMN and tubular lesion due to Henoch-Schönlein purpura
38. Ishibashi Y et al.	4 patients	UDB	3/3	Black esophagus		Cured in three One died		Ketoacidosis in three. DM in two
39. Kanaparthi C et al.	76/F	Nausea, epigastric pain, melanemesis and melena	2/3	Black esophagus with circumferential necrosis and ulceration. Multiple gastric and duodenal ulcers with necrosis	Inflammatory infiltrate, necrosis, exudate, acute and chronic duodenal inflammation	Cured		Coronary artery disease, CCI, CBE, DM-II, HT, asthma and dementia

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature. *Continued*

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
40. Karaahmet F et al.	81/F	Hematemesis	3/3	Extensive and diffuse black esophagus with friable mucosa		Improvement		HTA, DM-II, heart failure, colon cancer
41. Kim IK et al.	34/M	Hematemesis	2/3	Black esophagus, friable, 3 to 4 cm below the cricopharyngeal to the cardia	On the 6th day: necrosis of submucosa and candidiasis	Esophageal stenosis at 2 months, 3 dilations, subtotal esophagectomy and esophago-gastrostomy		Diabetic ketoacidosis with hypotension, hyponatremia, hyperkalemia, prerenal ARF
42. Kim YH, Choi SY	53/M	Hematemesis	2/3	Black esophagus up to the gastro-esophageal junction		Improvement		
43. Köksal AS et al.				Black esophagus		Cured	Perforated duodenal ulcer	
44. Kwon H-J et al.	67/F	Hematemesis	2/3	Black esophagus, macerated mucosa, distal circumferential necrosis with adhered clot		Cured		Coronary artery dissection during catheterization with acute hypotension
45. Lahbabi M et al.	60/M	Hematemesis, Septic shock	2/3	Circumferential black esophagus with exudate and diffuse bleeding	Local inflammatory response, mucosal and submucosal necrosis	Died at 6 hours due to septic shock		Ischemic and suppurated necrosis of the stump
46. Lin MC et al.	70/M	Melena and hematemesis for 2 days	2/3	Black esophagus and extensive ulceration		Cured		HBP, DM, CRF, atrial fibrillation, sick sinus syndrome and prostate cancer
47. Maher MM, Nassar MI	63/M	Melanemesis	2/3	Black and friable mucosa	Focal necrosis, hyalinosis of small vessels	Died		DM-II, HTA, COPD, ARDS, ARI, shock
48. Maroy B	81/M	Hematemesis	1/2	Varices grade 3 with black mucosa and necrosis between 30 and 40 cm. Ligation		Cured		Right hepatectomy and segment IV due to hepatoma and veno-occlusive disease of segments II and III by I131 Lipiodol
49. McLaughlin CW et al.	62/F	Nausea, melanemesis, retrosternal pain	1/2	Necrotic distal esophagus		Cured		Gastroesophageal reflux and large hiatal hernia

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature. *Continued*

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
50. Messner Z et al.	45/M	Melena, abdominal pain	1/3	Black esophagus with massive bleeding		Improvement	Eso-phageal Stent DANIS SEAL	
51. Nikolić S, Zivković V	76/M	Sudden death			Autopsy: Acute esophageal necrosis. Acute gastroduodenal erosion	Death due to UDB		Old ECV-immobility
52. Pastuszak M, Groszewski K	87/F	Upper gastrointestinal bleeding, hypotension		Black esophagus		Cured		Hemodynamic disorders, GOR symptoms
53. Pereira O et al.	62/F	Melena, acute anemia 8.4 g	2/3	Extensive candidiasis, Black esophagus		1/3 distal stenosis, dilations and cured		Alcoholic hepatitis, DHT, arterial hypotension, MNT, folate deficiency anemia
54. Pierini A et al.				Black esophagus		Cured		
55. Plaza-Santos R et al.	47/M	Hematemesis for 3 days Improvement	2/3	Ulcerated, necrotic, circumferential mucosa, with fibrin exudate		Improvement		Diabetic ketoacidosis, ARF, alcoholic drinker> 100 g/d
56. Pramparo SE et al.	80/M	Dysphagia, hiccups, melanemesis	2/3	Esophageal necrosis	Ischemic necrosis	Died		DM-II, HTA. peripheral vascular disease, aortic valve replacement, smoking
9. Ramos R et al.	68 to 87 years. Avg. 76.2 9/M. 2/F	Melenas, hematemesis, vomiting, abdominal pain	1/3 to 3/3 11 cases	Black esophagus	6 biopsies: mucosal and submucosal necrosis	Seven die Four improve		Nine with CHF Two with liver cirrhosis
57. Rigolon R et al.	50/M	Dysphagia, vomiting, fever, epigastric pain	2/3	Circumferential necrosis from 24 to 40 cm of the dental arch	Tissue necrosis, granulation tissue, leukocyte infiltration and hemosiderosis	Dysphagia, distal stenosis of 10 cm by 1 cm, 3 dilations, Cured		HTA, Diabetic ketoacidosis, dehydration, with hypotension and tachycardia on admission
58. Rodrigo M et al.	77/M	Hematemesis	2/3	Autopsy: Acute necrotizing esophagitis, ruptured aorta aneurysm	Ischemic mucosa from 30 cm and necrotic to 38 cm			Use of NSAIDs
59. Román-Fernández A et al.		Massive bleeding, hypotension		Black esophagus				Subarachnoid anesthesia for partial hip arthroplasty
60. Salem GA et al.	62/F	Hematemesis, hypothermia		Acute esophageal necrosis		Cured		Alcoholism

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature. *Continued*

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
61. Santos VM et al.	83/M	Vomiting, dysphagia, weight loss	1/3	Distal esophagus with stenosis, ulcer, black coloration	Acute necrotizing esophagitis	Improvement		DM-II, HTN, rectal cancer
62. Shafa S et al.	62/M	Hypotension and hypoxia despite intubation	3/3	Total black esophagus, large perforation at 35 cm		Died		Amputation due to necrotizing fasciitis, large pneumothorax right POP found by probe in right pleura
	63/M	Acute chest pain, nausea hematemesis	3/3	Diffuse esophageal necrosis, partial exfoliation, continuous bleeding, hemostasis with epinephrine		Improvement		CHF, COPD, alcohol abuse
	72/M	2nd degree DPO melena and 2 g Hb	3/3	Diffuse acute esophageal necrosis	Inflammatory exudate and necrotic tissue	Cured		Bilateral subrotulian amputation, with hemorrhaging
62. Shafa S et al.	25/M	Melena, acute anemia and dysphagia	3/3	Total esophageal necrosis, stenosis 1/3 middle of 5 cm long, non-extendable		Residual stenosis despite dilations		Diabetic ketoacidosis, HTA, alcohol, cocaine and marijuana
	64/M	Hematemesis and acute anemia, transfusion	3/3	Total esophageal necrosis, distal circumferential		Shock, MOF and rapid death		HBP, sequelae ECV, cholelithiasis and alcohol abuse
	49/M	Melena, MOF, acute anemia	1/3	Necrosis of distal third		Died from infection and MOF		Asthma, HBP, fever, weakness and syncope
63. Shimamura Y et al.	38/M	Hematemesis	1/3	Black columns, with disappearance of superficial vascular bed	Infiltration by leukocytes with hemosiderosis	Cured		Diabetic ketoacidosis
64. Singh D et al.	25/F	Nausea alterated consciousness 1/5, pneumomediastinum 1/5, ARF 1/5, hematemesis 1/5, GERD 1/5, epigastralgia 1/5, syncope 1/5, hypotension 1/5, vomiting 2/5, digestive bleeding 2/5		Black esophagus		2/5 Died		All with comorbidity, especially coronary heart disease, DM, renal failure
	49/F							
	50/F							
	60/F							
	36/F							

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature. *Continued*

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
65. Talebi-Bakhshayesh M et al.	34/M	Hematemesis, abdominal pain, nausea, vomiting	2/3	Black esophagus	Infiltration by lymphocytes, neutrophils and eosinophils, necrosis	Cured		Diabetic ketoacidosis
66. Tanaka K et al.	67/M	Vomiting, chest pain, On day 37 relapse upon suspension PPI	2/3		Diffuse exudate and necrotic debris			DM, HBP, angina pectoris
67. Tsao C et al.	73/M	Melanemesis the day after discharge caused by diarrhea due to antibiotics				Died on admission, autopsy: cachectic, acute esophageal necrosis, ischemic and pseudo-membranous colitis		Abdominal pain, bloody diarrhea, loss of 10 kg, HBP, COPD, hypovolemia and urinary tract infection
68. Tse A et al.	58/M	Severe hemorrhagic shock	2/3		Inflammation and acute, transmural necrosis in patches, inflammatory thrombosis and acute vasculitis	Cured	Necrosis 10 cm, mediastinitis, bilateral pleural effusion, pneumo-mediastinum, distal esophageal perforation	Alcohol abuse, epilepsy, refractory GERD with stenosis at gastrointestinal junction, two biodegradable stents in 20 months
69. Unuma K et al.	75/M	Found dead with melanemesis	3/3		Extensive mucosal necrosis	Autopsy: anemia, Black esophagus		Alcohol abuse
70. Usmani A et al.								Diabetic ketoacidosis
71. Venara A et al.	75/M	Sudden death			Esophageal necrosis	Autopsy		
72. Wallberg ME et al.	75/M	Vomiting, fever, shock, gastric aspirate coffee grounds	3/3	Black esophagus, areas of necrotic debris, antral erosions, blood remnants	Esophageal necrosis	Cured		HTA, urinary tract infection, septic shock due to E. coli
73. Watermeyer GA et al.	63/F		3/3	Diffuse black esophagus, friable, yellow exudate		Died due to liver failure		Toxic hepatitis due to anti-TBC

Table 2. Cases of necrotizing esophagitis (black esophagus) described in the medical literature. *Continued*

Reference and first author	Age-gender	Symptoms	Length of necrosis	Endoscopic findings	Histological findings	Outcome	Surgical treatment	Base diseases *
74. Worrell SG et al.	84/F	Melena and hematemesis	2/3	Black esophagus between 24 and 36 cm		Cured		Cirrhosis
	84/M	Nausea, chest pain, and hematemesis DM, HBP	1/3	Black esophagus		Cured with stenosis, 7 dilations		DM, HTA
	77/M	Hematemesis and diarrhea	3/3	Black esophagus with distal perforation		Died at day 17 due to small bowel ischemia and MOF	CT: pneumo-mediastinum, distal esophageal perforation, right pleural effusion, esoph-agectomy. Cervi-costomy	Cirrhosis and DM
75. Wu MH, Wu HY	67/M	Melena Femoral Sengstaken tube	2/3	Black esophagus, Gastric ulcer and duodenal ulcer		Esophageal perforation at 24 h and Died		Neck fracture, Hemodialysis due to hyperkalemia
	46/M	Epigastric pain, nausea and vomiting for 7 days, hematemesis and melena for 3 days resolution	1/3 distal, progres-sed to all esopha-gus	Black esophagus	Diffuse transmural necrosis with 1/3 distal exfoliation	6th day exfoliation of entire esophagus, pleural effusions, esophagectomy, esophago-gastrostomy fistula,		Gastric ulcer with frequent bleeding last 2 years, hemorrhaging duodenal ulcer
5. Yasuda H et al.	Avg. 62.5 years		16 patients 1/3	Distal necrosis and HH most frequent associated findings				All with comorbidity 8/16 with NSAIDs, 4/16 DM ketoacidosis
76. Zacharia GS et al.	62/F	Nausea, hematemesis and retrosternal pain	1/3	Black distal esophagus	Inflammatory subepithelial infiltrate with intense hemorrhaging and necrotic tissue	Cured		Insulin-dependent DM, HT
77. Živković V, Nikolić S						Died due to hypothermia, autopsy		Hypothermia

AAA: abdominal aortic aneurysm; NSAIDs: non-steroidal anti-inflammatory drugs; DHT: dehydration; DM: diabetes mellitus; DM-I: type I diabetes mellitus; DM-II: diabetes mellitus type II; MNT: malnutrition; CBE: cerebrovascular event; COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; MOF: multi-organ failure; GMN: glomerulonephritis; HH: hiatal hernia; HT: arterial hypertension; UDB: upper digestive bleeding; CHF: congestive heart failure; ARF: acute renal failure; CRI: chronic renal failure; MM II: lower limbs; ARDS: acute respiratory distress syndrome; NGT: nasogastric tube; CT scan: computerized axial tomography; TB: tuberculosis; SEMS: Self-expanding metallic stent

by the one month follow-up examination. Our third patient remained asymptomatic for ten weeks and then refused additional follow-ups. Nevertheless, we do not know how our other three patients evolved. In the general series, mortality reached 32% while 38% were cured. Partial resolution was achieved for the rest of the cases (Table 1). This included residual stenosis which was resolved in two thirds of the patients through dilations but required surgical treatment in 4% of these cases.

Associated comorbidity is a common finding in most cases in the literature. AEN occurs in high-risk patients. Risk is determined by the age of presentation, acute and chronic debilitating diseases, hemodynamic compromise and multiorgan dysfunction (Table 1). Also present in our patients were hyponatremia, hypochloremia and prerenal acute renal failure in Case 1; a giant hiatal hernia of 9 cm and severe gastroesophageal reflux disease with a history of bleeding in Case 2; baseline pneumonia, severe thrombocytopenia, exacerbated chronic renal failure and choledocholithiasis with obstruction of the bile duct in Case 3; and mesenteric thrombosis in Case 4. Table 1 shows comorbidity in the overall series. There were acute and severe diseases in 78% of 157 patients. The remaining 104 patients who are detailed had hemorrhaging, shock, arterial hypertension, heart disease, liver failure, diabetic ketoacidosis, renal failure, septicemia and alcoholism with more than one pathology in the majority of patients.

Histopathology and etiology

In Case 2, biopsies of the distal esophagus showed acute esophagitis with extensive mucosal and submucosal necrosis with a viable muscle layer and reactive epithelial changes. Histological findings are obtained in only a few cases, 15% of the overall series, either in biopsies taken during diagnostic endoscopy, from a surgical piece, or at autopsy. (3, 10) Histological findings in the overall series demonstrate compromise of the submucosa and muscularis propria, deep compromise of the esophageal wall, necrosis in almost all cases, inflammation, thrombosis and ischemia not only of the esophagus, but also of the stomach and duodenum (Table 1).

The severity and depth of lesions were demonstrated by clinical evolution and associated complications such as esophageal perforations, mediastinal infection, abscesses, fistulas and esophageal stenoses. These resolved in only 40% of cases despite the dilations (Table 1). Of course, the mortality rate of 32% is high.

Based on the reported cases and the literature reviewed, the etiology is believed to be associated with hypoperfusion within the esophageal mucosa caused by decreased blood flow of various arterial branches. This gives rise to ischemia that leads to necrosis. Decreased blood flow is associated hemodynamic and electrolyte imbalances, hypersensitivity to medications such as antibiotics and NSAIDs, alcoholism, acid reflux, and to underlying diseases which can alter sensitivity and microvasculature. (3 , 7, 14) This is corroborated by associated comorbidities and frequent multiorgan and hemodynamic compromise aggravated by digestive bleeding that leads the patient to consult a physician (Table 1). In addition, findings of ischemia and thrombosis in histopathological studies favor this hypothesis. There are no experimental studies that prove these hypotheses.

Prognosis

Patients' prognoses depend on the severity of compromise of the patient's general health status and on the patient's age. In a group of patients who died, four did so in the first six hours, two died two days after admission, and there were six cases of sudden death or people found unconscious. The extension of necrosis seems to be related to fatal outcomes, since only two patients with a third or half of the esophagus compromised died, while the remaining 29 deaths occurred in people with two thirds or more of the esophagus compromised. The underlying disease was responsible for mortality in a large number of patients, and the authors described it as the main cause in 22 patients.

Risk factors include advanced age, male gender, extension of necrosis and associated comorbidities including hemorrhages, shock, sepsis, hypertension, heart disease, liver failure, kidney failure, diabetic ketoacidosis and alcoholism.

Treatment

The authors are emphatic and unanimous in stating that there is no specific treatment for necrotizing esophagitis in the absence of a defined etiology. Its association with multiple entities can lead to this situation. Interactions with associated comorbidities enhances the danger of esophageal injury with ischemia, thrombosis and necrosis of the mucosa and the esophageal wall. For these reasons, general support measures are recommended for management of the underlying diseases that trigger hypoperfusion (shock, sepsis, heart, kidney and liver failure and multiorgan failure). One key goal is to restore hemodynamic, acid-base and metabolic equilibrium. In cases of anemia, transfusions of packed red blood cells should be administered. Proton pump inhibitors can be administered intravenously to control associated acid-peptic lesions and aggravation of these lesions. (3, 7-11, 14) Stents can even be used to manage profuse active bleeding. In one case reported, this was used as a rescue method. (54) Naturally, the management of relevant medical and surgical complications such as superinfection, perforations and fistu-

las is important as are dilating stenoses and stenting in cases of poor response. (34, 35, 72) Even esophagectomies can be considered for patients with serious complications (Table 1). (3, 6-11, 14, 35, 45, 78, 79).

CONCLUSIONS

Necrotizing esophagitis is a rare and severe esophageal disorder with high mortality and complication rates. The high comorbidity that accompanies it is, apparently, the trigger and cause of mortality for a large group. Comorbidity, together with advanced age, male gender and the extent of necrosis are important risk factors. The therapeutic approach must therefore be interdisciplinary and must aim at restoring the hemodynamic, acid-base, metabolic and acid-peptic equilibriums while managing infectious complications. Serious complications occur frequently and require close evaluation and timely management due to the risk to the patient's life.

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Conflicts of interest

This study has not been presented in any meeting or sent to any other publication.

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