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A SEVERE CASE OF EPIGASTRIC PAIN, DIARRHEA AND COFFEE GROUND VOMITUS

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Introduction

Prof. Porta

Dear colleagues,

We discuss today the unusual presentation of a critical condition developed in an elderly patient admitted to our Internal Medicine ward. Will Dr. Marinucci please present the case?

Case presentation

Dr. Marinucci

An 86 year-old woman was admitted to the Internal Medicine ward for epigastric pain, diarrhea and coffee ground vomitus. She reported weekly bouts of diarrhea over the past year, hypertension and osteoporosis but was otherwise in good general conditions. On admission, vital parameters were normal and the patient only referred upper abdominal pain with a negative Blumberg sign.

Laboratory findings were: White blood cells (WBC) 14.69 x 10^9/L (reference range 4.00-11.0 x 10^9/L), C-reactive protein (CRP) 3.9 mg/l (< 3 mg/L), amylase 2500 U/L (40-140U/L), AST 878 U/L (6-40 U/L), ALT 437 U/L (20-60 U/L), fasting glycaemia 185 mg/dl (72-100 mg/dl); hemoglobin, electrolytes and renal function were normal. At haemogasanalysis pH was 7.33 and bicarbonates were markedly decreased at 17 mmol/l (22-29 ml/l) with low ionized calcium at 0.88 mmol/l (1.1-1.4 mmol/l).

Chest X-ray showed meteoric bowel distension, and an abdominal ultrasound scan showed irregular swelling of the pancreas with peripancreatic, subhepatic and parietocolic fluid collections and no evidence of biliary duct dilatation or cholelithiasis.

A CT-scan revealed nearly complete subversion of the pancreas (about 70% of the gland tissue), minimal left parietocolic and pelvic fluid effusion, thrombosis of the splenic and upper mesenteric veins, and mild intra- and extrahepatic biliary tree dilatation (Fig.1).

The patient was treated by fasting and hydration, proton pump inhibitors (PPI) and empirical antibiotics. Antitrombothic treatment was not administered because of the recent bleeding. Indeed, melena appeared on the following day, so that an urgent esophagogastroduodenoscopy (EGD) was performed.

Dr. Musso (endoscopist)

Endoscopic examination revealed diffused black, wash-resistant pigmentation of the esophageal mucosa, sparing only the upper 3 cm of the organ and extending down to the lower esophageal sphincter (LES) (Fig. 2 and 3). This was associated with LES incompetence, hiatal hernia and stasis

of dark material, probably due to gastroparesis (Fig. 4). The gastric and duodenal mucosae were normal. This endoscopic finding was characteristic of acute esophageal necrosis (AEN). My advice was to increase hydration and the dosage of PPI.

Prof. Porta

What are exactly the endoscopic features and the differential diagnosis of AEN? Are there any treatment protocols?

Dr. Musso

An endoscopic staging of this presentation, as proposed by Gurvits, includes: pre-necrotic esophagus (Stage 0), black esophagus (Stage 1), 'chess-board' esophagus (Stage 2) and re-epithelized esophagus (Stage 3) [1].

A possible explanation proposed in the literature for the fact that the gastric mucosa is spared is that, when injured, it repairs faster (within hours) than that of the esophagus (which takes days) [2,3], although gastric reflux is a likely additional cause of esophageal damage.

Dr. Zardo

Differential diagnosis is with other conditions with similar endoscopic presentation of the esophagus, such as melanosis, melanoma, acanthosis nigricans and caustic ingestion injuries. The differential diagnosis should be based on histology, anamnesis and clinical findings. For example, EGD in melanoma shows a localized and discontinuous extension, whereas in caustic ingestion typical findings are deep ulcers of the mucosa and/or severe hemorrhage. Neither has the typical extension of black pigmentation as in AEN.

Dr. Marinucci

In consideration of the high risk involved in this serious condition, we also requested a surgical consultation.

Dr. Strignano (surgeon)

I was consulted immediately after EGD for the suspicion of esophageal necrosis.

Esophageal necrosis can progress to perforation with consequent acute mediastinitis. This severe clinical condition usually needs urgent esophagectomy because of its very high mortality rate [4].

In this patient, the entire esophageal mucosa appeared necrotic but a CT-scan did not show any sign of perforation/mediastinitis. In other words, in this patient, AEN involved the mucosal layer but seemed to spare the muscular esophageal wall.

Considering the overall picture of advanced age and coexistent severe morbidities such as acute pancreatitis, splenic and mesenteric vein thrombosis, esophagectomy was not indicated.

The management of AEN can be divided into an acute and a chronic phase. Treatment of the former is based upon intensive care of the underlying causes and prevention of acute complications, such as esophageal perforation, mediastinitis and abscesses. As mentioned above, only these complications would require urgent esophagectomy or surgical/radiological drainage. The chronic phase is characterized by developing esophageal stricture, which can cause mechanical dysphagia. Esophageal stenosis would require either an endoscopic procedure, with balloon dilations or stenting, or surgery (esophagectomy or a by-pass operation) [5].

Indeed, AEN is very rare and its etiology often remains unknown. A study by Bonaldi et al. [4] reported on a case of AEN following pancreatoduodenectomy and presenting with acute upper gastrointestinal bleeding. Conservative treatment with blood transfusions, total parenteral nutrition and high-dose PPI was performed and no complications appeared at endoscopic follow-up.

Sakatoku et al. [4] described a case of esophageal stenosis after AEN, which was successfully treated by esophageal by-pass using a gastric conduit in a high-risk patient. Assessment of the general medical condition of patients prior to surgery is mandatory when planning a surgical strategy (esophagectomy or by-pass).

Dr. Marinucci

Therefore, we concluded that surgical treatment was both not indicated, for absence of acute or chronic complications of AEN, and contraindicated because of severe co-morbidities. Consequently, in agreement with the endoscopist and surgeon, we opted for intensive medical care.

Dr. Morra di Cella

Conservative treatment is not standardized because of the rarity of this condition and is based upon generous hydration, high dose proton pump inhibitors (PPI), parenteral nutrition and resolution of underlying causes [6].

Unfortunately, clinical conditions and laboratory findings rapidly deteriorated on the following day. Blood tests showed White Blood Cells 21.77 x 10^9/L, C-reactive protein 378 mg/l, creatinine 3.37 mg/dl (0.5-1.2 mg/dl), and progressive worsening of liver and pancreatic indices. In order to

investigate the underlying cause of AEN, coagulation and autoimmune screen panels were planned, but the clinical conditions did not permit to obtain a blood sample.

On the third day from admission, ileus paralyticus, hypotension and respiratory failure appeared, most likely due to sepsis or inhalation/aspiration of gastric fluids, leading to acute respiratory distress syndrome (ARDS). X-ray showed bilateral pleuric effusions and evidence of severe gastroparesis. Cardio-circulatory arrest occurred during the radiologic procedure and the patient died after unsuccessful cardiopulmonary resuscitation.

Prof. Porta

You have described a rare condition defined by endoscopic evidence of black circumferential pigmentation of the esophagus associated with mucosal necrosis on histology [7]. Who described first this clinical condition and what about its epidemiology?

Dr Zardo

The condition was first described in 1967 by Brennan [8] and Lee [9] et al. on post-mortem examination.

Men are more frequently affected than women with a 4:1 ratio and a peak in the sixth decade of life.

A literature search by Gurvits et al. from January 1965 to February 2006 showed a total of 88 patients, 70 men and 16 women with an average age of 67 years. The patients were generally admitted for gastrointestinal bleeding and cardiovascular event/shock and prognosis is often fatal with a high mortality rate (38%), depending on local and general patient conditions [1].

A study by Augusto et al. in 2004 reported 29 patients affected in a series of 10,295 patients undergoing esophagogastroduodenoscopy (EGD) over 5 years [10].

Prof. Porta

What are the possible causes and clinical presentation of AEN? Do you hypothesize a possible association between acute pancreatitis and AEN? What evidence is available from the literature?

Dr Zardo

The majority of patients present with coffee ground vomitus, epigastric/abdominal pain, hematemesis and/or melena, dysphagia, low-grade fever and syncope.

The etiology is multifactorial. Possible risk factors include the direct effect of acid gastric reflux in the presence of gastric outlet obstruction [11]. Another potential factor is the indirect effect of

decreased esophageal blood flow caused by acid-induced mucosal injury, which may account for frequent involvement of the distal third of the esophagus [12]. Several pathologies are potentially associated with AEN, such as gastric outlet obstruction, gastric volvulus, ischemia, shock and sepsis [7,13].

We suggest a possible role for circulating pancreatic enzymes in determining inflammation of the esophageal mucosa. There are only two reports in the literature on the possible association between acute pancreatitis and esophagitis in animals and a cause-effect relationship can only be hypothesized [14,15].

A study by Naito et al. [15] suggested an association between trypsin and chronic esophagitis due to gastroesophageal reflux disease (GERD). Their *in vitro* study on mouse epithelial esophageal cells revealed increased release of inflammatory chemokines and prostaglandins induced by trypsin, possibly leading to chronic esophagitis.

Petrovic at al. [16] emphasized the potential etiological role of LES incompetence in the simultaneous occurrence of GERD and acute pancreatitis, suggesting a feedback mechanism involving the three conditions in a sort of vicious circle. Animals with pancreatitis developed LES incompetence, whereas those with esophagitis and LES incompetence developed acute pancreatitis. In addition, the authors selected a group of 10 patients (6 women and 4 men) with acute pancreatitis, assessing endoscopy and esophageal manometry that showed significantly lower mean pressure in both lower and upper esophageal sphincters compared to a control group of healthy subjects. The authors concluded for a pathogenic role of LES incompetence in both acute pancreatitis and esophagitis.

Dr Marinucci

Other hemorrhagic complications of pancreatitis, such as gastric and duodenal ulcer [17], rupture of pseudoaneurysms and intracystic bleeding from vessels within the pseudocyst wall, are potentially connected with vascular lesions caused by inflammation and enzymatic self-digestion in acute pancreatitis [18]. These factors may damage the esophagus in different ways, either acting directly on the mucosal barrier or indirectly with gastric and/or duodenal vessel erosion leading to localized ischemia. We propose that the same mechanism(s), in association with hypoperfusion and gastroparesis, may have led to acute esophageal necrosis during acute pancreatitis in our patient. Clearly, however, a demonstration of these hypotheses cannot be produced because of the scarce literature on the subject and the rarity of the condition.

Prof. Porta

I wish to thank you all for presenting this clinical case. A diagnosis of esophageal necrosis is a rare occurrence in our everyday practice, but should be kept in mind because of its potentially severe consequences, which unfortunately materialized in full in our patient. Future research should help to gain further insight into the pathogenesis of this severe condition and to develop effective therapies.

Compliance with Ethical Standards

Conflict of Interest: The authors declare that they have no conflict of interest.

Informed consent was obtained from the patient before applying the diagnostic and therapeutic procedures described.

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Figure legends

Fig.1. Subversion of pancreatic parenchyma in acute pancreatitis

Fig. 2. Esophagus showing a black pigmentation consistent with mucosal necrosis, starting 3 cm below the UES

Fig. 3. Mucosal necrosis abruptly interrupts at the GE junction, where a striking demarcation between oesophageal necrotic and gastric healthy mucosa is evident

Fig. 4. Dark brown fluid material adherent to gastric antral wall; after irrigation, the underlying mucosa looks normal

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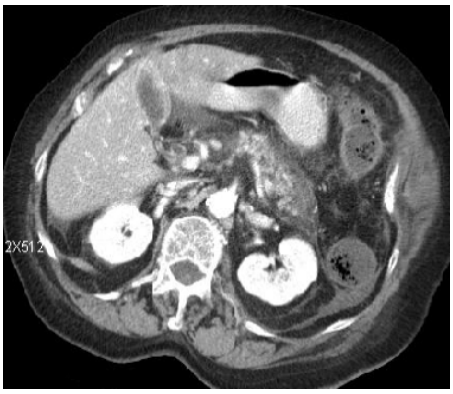

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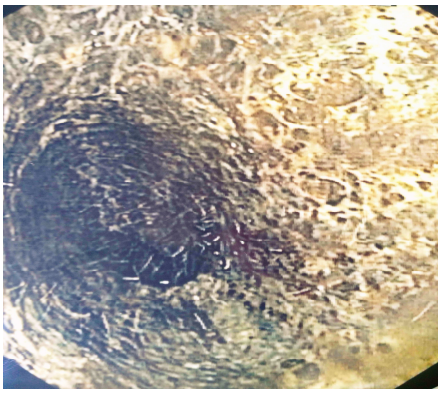

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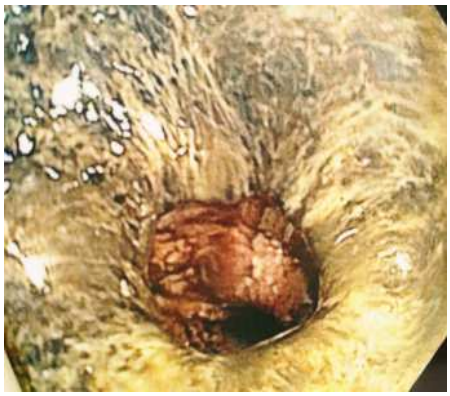

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