Progress report

Acute haemorrhagic gastritis: Modern concepts based on pathogenesis

Acute haemorrhagic gastritis is one of the most frequent causes of severe upper gastrointestinal haemorrhage. In series in which a positive diagnosis is made by endoscopy or laparotomy the incidence is approximately 25%. It is frequently related to recent aspirin ingestion and is also seen after major surgery or trauma ('stress' ulcers), but may occasionally appear in the absence of any apparent cause.

Acute haemorrhagic gastritis is a condition of acute diffuse superficial erosions (not extending deeper than the muscularis mucosae) or multiple petechial haemorrhages of the mucosa of the stomach usually confined to, or predominant in, the fundal region. Gastroscopically, the mucosa of the body of the stomach is uniformly red and oozing blood. This picture may change rapidly so that 24 to 48 hours after bleeding has stopped the mucosa may appear normal. A similar appearance is seen in severely ill patients after major surgery or trauma. In the latter case, the gastric lesions have often been referred to as 'stress ulcers', a term which has caused some confusion with classical Cushing's (neurosurgical) or Curling's (burns) ulcers in which there is a deeper lesion resembling a normal peptic ulcer. Patients with neurosurgical lesions or burns may, however, bleed from acute haemorrhagic gastritis. Acid output in acute haemorrhagic gastritis is decreased. In Cushing's or Curling's ulcer it is either increased or normal, suggesting a different pathogenesis for the two conditions.

Even in the presence of other radiologically demonstrable lesions acute haemorrhagic gastritis must be excluded (by gastroscopy) as the cause of bleeding. In a review of 618 patients already known to have a potentially bleeding lesion in the upper gastrointestinal tract when the current haemorrhage began, 40% were bleeding from some other lesion. In a recent series from the Boston City Hospital of 18 patients with acute bleeding and demonstrable varices, bleeding from gastritis was the most common finding (60%). Varices were the cause of bleeding in only 20%. This will not be recognized unless a positive diagnosis by gastroscopy is sought in all cases of acute upper gastrointestinal tract bleeding.

In patients bleeding massively from acute haemorrhagic gastritis (defined in one series as serum Hb < 8.0 g % and average transfusion requirement of 21 units blood) the mortality is upwards of 50%. If surgery is required then in many cases radical surgery ranging from hemigastrectomy to total gastrectomy is required. There have been some enthusiastic reports of the results of vagotomy and pyloroplasty but this has not proved satisfactory in all hands.

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Pathogenesis

We are faced with the possibility of a total gastrectomy as the only means of stopping exsanguination. What lessons may be learnt from animal and human studies on the pathogenesis of acute haemorrhagic gastritis? What is the application of these to the management of this potentially lethal condition? In attempting to find a relationship between gastric acid and gastric mucosal damage clinicians have long been puzzled by the absence of acid in gastric aspirates in these patients. Only recently has it been appreciated that gastric acid output is dependent on both acid secretion and acid absorption. Davenport has clearly shown in the dog that salicylates increase the absorption (back diffusion) of hydrogen ions across the gastric mucosa. This is associated with profuse bleeding. Acetylsalicylic acid has a pKa value of 3.5 and exists predominantly in the lipid-soluble, undissociated form at pH < 3.5. Above pH 3.5 salicylic acid exists mainly in the non-lipid-soluble, dissociated state which is less readily absorbed by mucosal cells. Bleeding due to salicylates is dependent on the amount of acid present in the gastric contents as it does not occur at neutral pH but occurs at pH < 3.5 in the presence of adequate concentrations of HCl.

As in the dog, the gastric mucosal barrier in man can be impaired by varying agents, and is impaired in disease states such as gastric ulcer and chronic gastritis. Ivey et al. have demonstrated marked back diffusion of hydrogen ions after intragastric instillation of bile salts. Salicylic acid also impairs the gastric mucosal barrier in man. Overholt and Pollard found an increased flux of sodium ions into the gastric mucosa after instillation of 20 mM acetylsalicylic acid. They were unable to show an increased loss of hydrogen ions but attributed this to increased acid secretion stimulated by acetylsalicylic acid. In unpublished studies, by reducing gastric acid secretion with intravenous atropine, we have confirmed Overholt and Pollard’s findings and have shown an increased back diffusion of hydrogen ions following intragastric instillation of salicylates. Our results confirm the findings of Geall et al. who used changes in potential differences to show that the gastric mucosal barrier was broken after instillation of aspirin in man.

As early as 1953 Chandler et al. stressed the association of achlorhydria with acute upper gastrointestinal bleeding associated with aspirin ingestion and suggested the use of nocturnal achlorhydria as a guide to the diagnosis of this condition. In his studies in the dog, Davenport used a glycine buffer to show that gastric acid secretion actually could occur but was masked by increased loss through the mucosa damaged by salicylates. The same phenomenon is almost certainly occurring in man.

Recently, Skillman et al. studied the back diffusion of hydrogen ions in a group of severely ill patients prone to ‘stress ulcers’. They found a group of patients, 12 of 26 studied, with an abnormal loss of hydrogen ions across the mucosa up to 11 m-equiv/15 minutes. These patients had been frequently hypotensive and were more severely ill than the remaining patients with normal mucosal permeability. The authors then studied the effect of haemorrhagic shock on mucosal permeability in the rabbit. In all cases, this resulted in damage to the gastric mucosal barrier with increased back diffusion of hydrogen ions. At necropsy immediately after the study 90% of rabbits had multiple superficial gastric erosions. Thus it appears that haemorrhage severe enough to cause shock from any cause will itself damage the gastric...
mucosal barrier. This may explain the high incidence of 'stress ulcers' after major surgery or trauma. In further studies in the rabbit a buffer solution instilled into the stomach during haemorrhagic shock reduced back diffusion of H+ ions and resulted in only a 10% incidence of erosions. Similarly, buffer solution instilled into the stomach before and after but not during haemorrhagic shock resulted in normal mucosal permeability after the shock and no erosions were reported in this group.

Thus both Davenport's studies with aspirin-induced lesions in the dog and those of Skillman et al during haemorrhagic shock in man illustrate the importance of neutralizing intragastric acidity. Acid output is the difference between acid secretion and acid absorption. The absence of acid in gastric aspirates of patients with acute haemorrhagic gastritis may mask active acid secretion due to increased acid absorption by the abnormal mucosa. Absorption of hydrogen ions produces further mucosal damage so perpetuating the bleeding.

Management

On the basis of this experimental and clinical evidence, management of severe upper gastrointestinal bleeding involves accurate diagnosis by gastroscopy at the time of the patient's admission to hospital or as soon as he has been resuscitated. This should precede radiological examination. Barium may cover gastric folds while water-soluble contrast media such as Gastrografin or Hypaque have such high osmotic pressures that they produce a marked flux of fluid into the gastric lumen covering the lens of the gastrocope and seriously interfering with the examination. Use of hyperosmotic water-soluble contrast media in exsanguinated patients is contraindicated as the loss of fluid into the gut may precipitate collapse and death.

On the hypothesis that bleeding due to acute haemorrhagic gastritis in man is due to increased back diffusion of hydrogen ions, a programme aimed at complete neutralization of intragastric contents should be started once a positive diagnosis has been made. As the lesions are acute, the time involved is limited in making such a programme feasible unlike similar attempts in patients with gastric ulcer. It should be emphasized that a milk drip frequently recommended in the treatment of acute upper gastrointestinal bleeding does not bring about neutralization of gastric juice. In fact, in Doll's studies, using continuous intragastric milk drip in chronic gastric ulcer, the pH could not consistently be raised above 4 and in some cases above 2. Allowing for gastric emptying and the likelihood that acetylsalicylic acid may stimulate gastric secretion (as reported by Davenport in the dog and Overholt and Pollard in man) continuous intragastric infusion of an effective, readily available alkali such as sodium bicarbonate solution (eg, 1 m-equiv/ml at the rate of 1,000 m-equiv/24 hours) should be given. Even in those cases where bleeding is not due to haemorrhagic gastritis this might prevent such lesions developing secondary to haemorrhagic shock. Precautions must be taken against the development of systemic alkalosis but in a small number of patients so far treated in such manner at Royal Prince Alfred Hospital this has not yet proved a problem.

The hypothesis that acute haemorrhagic gastritis is initiated and/or perpetuated by increased back diffusion of hydrogen ions explains why vagotomy (and pyloroplasty) may be effective, particularly in less severe
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cases, by reducing acid secretion. A secondary effect may be reduced mucosal blood flow. Davenport has shown that vagal stimulation (intravenous injection of acetylcholine), produces copious bleeding in dog pouches after intragastric instillation of salicylates which he attributed partially to increased mucosal blood flow.

In more severe cases where presumably a greater amount of acid is diffusing back, or alternatively a lesser amount is producing greater damage, more radical surgery up to total gastrectomy is required to reduce acid secretion, which in turn reduces acid absorption.

Summary

Acute haemorrhagic gastritis is responsible for 25% of all severe upper gastrointestinal tract bleeds. Massive bleeding is associated with a mortality of >50%. It can be produced by salicylates and by acute haemorrhagic shock in the presence of adequate concentrations of acid, and in both situations is associated with increased back diffusion of hydrogen ions across the gastric mucosa. Neutralization of gastric contents prevents the development of bleeding and erosions. Rational management requires complete neutralization of gastric contents. If this fails acid secretion may be adequately reduced in less severe cases by vagotomy and pyloroplasty but most cases will require partial to complete gastrectomy.

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