The high blood flow volume through gastrorenal or splenorenal shunts results in a rapid loss of the sclerosant into the systemic circulation during sclerotherpay. Furthermore, gastric varices are too large to ligate endoscopically.

Surgical portosystemic shunt is a method to decrease the high portal pressure and subsequently decompress the esophageal and gastric varices. In particular, the Hassab operation, which includes davascularization of the upper half of the stomach and esophagus and splenectomy, can eliminate gastric varices (Surgery 1967; 61:169-176). However, patients with gastric varices usually have cirrhosis of the liver and are in a compromised condition. As a result, the mortality rate is 42-56% for elective surgery and higher for emergency procedures (Am J Surg 1986; 152:290-293).

Percutaneous transhepatic obliteration is an effective, non-surgical procedure for treating esophageal and gastric varices, but is more invasive than balloon-occluded retrograde transvenous obliteration and difficult to perform repeatedly. In addition, intrahepatic hemorrhage may occur hwn hemorrhagic diathesis is present.

Transjugular intrahepatic portosystemic shunt (TIPS), first reported by Rosch et al in 1969 (Radiology 1969; 92:1112-1114), involves percutaneous decompression of portal hypertension. Complications, such as stent dislocations, hemoperitoneum and hepatic encephalopathy, sometimes occur and the 30-day mortality rate is 21% (JAMA 1995; 273:1824-1830).

Conversely, balloon accluded retrograde transvenous obliteration is less invasive than surgery, percutaneous transhepatic obliteration or TIPS. Balloon occluded retrograde transvenous obliteration causes the gastric varices to coagulate due to stoppage of the voluminous blood flow in the varices. The mechanism of treating gastric varices seems to be similar to that induced by endoscopic injection sclerotherapy. Collateral veins, such as the inferior phrenic, hemiazygos, or pericardial veins, should be occluded, for a grade of collateral development greater than 2.

Aggravation of esophageal varices is the most important complication of this method. Obliteration of the gastrorenal shunt causes portal venous pressure to increase and new collateral veins to the esophageal varices to develop. In such cases, endoscopic injection sclerotherapy is effective to preclude rupture of esophageal varices.

One of the patients in this study developed cardiogenic shock, immediately after injection of 10ml of the sclerosing agent. Cardiogenic shock is the first time to be reported as a complication of intravenous administration of the sclerosant.

Other complications reported are pulmonary edema, hemothorax and disseminated intravascular coagulation. Migration of the embolic coil at the inferior phrenic vein was another complication caused by a reversal of the direction of the blood flow. Partial obstruction of the renal vein, followed by gross hematuria, was caused once, due to dislocation of the balloon part of the catheter. Hemolysis and, consequently, renal tubular disturbance and renal insufficiency, due to ethanolamine oleate, were prevented, as haptoglobin was administered (one unit of haptoglobin binds 1mg of hemoglobin).

Follow-up results showed successful treatment of gastric varices. These midterm results also showed that the effect persisted for more than a year without aggravation. Additionally, the clinical symptoms of the three patients with encephalopathy improved remarkably. Even though the hemodynamics of balloon-occluded retrograde transvenous obliteration requires future investigations, this method offers good control of gastric varices in patients with gastrorenal shunts and has minimal complications.

E. LIAPI

Epidemics of diarrhea caused by a clindamycin-resistant strain of clostridium difficile in four hospitals

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Clostridium difficile is recognized as a major nosocomial pathogen throughout the world. Epidemics of C. difficile-associated diarrhea are often linked to a single strain capable of causing disease. Large outbreaks of diarrhea caused by a newly recognized strain of C.

difficile in four hospitals located in different parts of U.S.A. between 1989 and 1992 made S. Johnson and his colleagues to study them.

The frequent use of clindamycin seemed to be associated with the outbreak in one of these hospitals, so authors evaluated the association of diarrhea from this strain with the use of clindamycin, the resistance of this strain to clindamycin and the genetic basis for resistance to clindamycin. Case control studies were performed at the New York, Arizona and Massachusetts hospitals to evaluate the relation between exposure to clindamycin and diarrhea due to the epidemic strain of C. difficile. Within each institution clindamycin use was a more frequent cause of diarrhea due to the epidemic strain than of diarrhea due to nonepidemic strains. Overall, 35 of 83 cases of diarrhea (42 percent) due to the epidemic strain were associated with clindamycin use, as compared with 12 of 99 cases (12 percent) due to nonepidemic strains ($p<0,001$). In contrast, the use of other antibiotics was not associated with diarrhea due to the epidemic strain. Similarly, hospitalization in a surgical ward was not a risk factor for diarrhea due to the epidemic strain.

All 85 isolates of the epidemic strain of C. difficile were highly resistant to clindamycin. The representative isolates of epidemic strains from each hospital outbreak were also highly resistant to erythromycin, as was the clindamycin resistant strain that was used as control. The majority of nonepidemic strains from each outbreak were susceptible to clindamycin. Both clindamycin-susceptible control strains were susceptible to clindamycin. High-level resistance to clindamycin was present in 15% of the nonepidemic strains.

DNA dot blot hybridizations were carried out on chromosomal DNA prepared from the epidemic strain of a C. difficile and control strains under highly stingent conditions, with use of an ermB-specific probe derived from C. difficile strain 630. Erm is called a group of highly related genes that have been found in gram (+) and gram (-) organisms which encode a 23s ribosomal RNA methylase. This methylase confers resistance to macrolide-lincosamide-streptogramin (MLS) antimicrobial agents such as erythromycin and clindamycin. DNA from all the representative isolates of the clindamycin-resistant epidemic strain at each hospital showed strong hybridization with the probe, indicating that the isolates contained an ermB gene. The control strains, which were susceptible to MLS antibiotics, did not hybridize to the probe.

Next, they conducted PCR for each of the isolates analyzed by dot blot hybridization, to confirm that the gene present in the epidemic strains was closely related to strain 630. They found that it was indeed. No PCR products were obtained from the MLS-susceptible control strains.

The investigators concluded that the use of clindamycin was a specific risk factor for diarrhea due to the highly-clindamycin-resistant strain of C. difficile and that resistance to clindamycin further increases the risk of C. difficile-associated diarrhea. They thought that their results shed new light on the relation between antibiotic use and C. difficile-associated diarrhea. The role of the antimicrobial agent has been assumed to be to disrupt the normal intestinal flora, particularly anaerobes, of the host, which is an important resistance factor with respect to infection with C. difficile. The relatively high likelihood of C. difficile-associated diarrhea after exposure to clindamycin is not just a consequence of effects on the resident flora but it may also be linked to the susceptibility profile of the organism.

They also suggest that this strain or genetically related stains may have an even broader geographic distribution than it is suggested from the four outbreaks. A comparison with the use of PCR ribotyping indicated that the epidemic strain from one hospital was the most common strain among hospitalized patients in England and Wales and was responsible for a large outbreak in England involving 175 patients and 17 deaths of one hospital. The dissemination of resistance to MLS antibiotics among clinical isolates of C. difficile, especially in hospitals could be mediated by elements such as plasmids or transposons or other mobile genetic elements located on chromosomes.

C. difficile-associated diarrhea is unknown in the absence of use of antimicrobial agents, and the risk of illness among hospitalized patients increases with the use of clindamycin and the presence of clindamycin-resistant strain of C. difficile.

COMMENTS

Pseudomembranous colitis (PMC) is an inflammatory process mediated by toxins and characterized by plaques or pseudomembranes attached to the surface of the inflammed colonic mucosa (N Eng J Med 1994; 330:257-262). The term "antibiotic-associated colitis" is similar to pseudomembranous colitis because many of patients develop the disease after using antimicrobials and at least on biopsy have microscopically visible pseudomembranes.

The etiologic agent in nearly all instances is Clostridium difficile. The disease is caused by the two toxins of C. difficile, A and B (Dis Colon Rectum 1998; 41:1435-1449). About 75% of C. difficile isolates produce these toxins. Isolates that do not produce toxins do not cause colitis or diarrhea. Growth of the organism is promoted by poorly understood antibiotic-induced alterations in the normal intestinal flora. PMC is usually found in association with one or more underlying diseases, which especially involve the abdomen and require antibiotic therapy. Variations in the clinical severity of C. difficile infection in different patients are not solely-specific phenomena related to immunoblot type or to the production of cytotoxin or enterotoxin (Infect Immunol 1991; 59:2456-2462).

The incidence of PMC depends on the frequencies with which endoscopy and toxin tests on stools are performed to establish the diagnosis, on patterns of antimicrobial use, on antibiotic resistance patterns of the C. difficile isolates, and on epidemiologic factors favoring transmission of the organism (Infect Control Hosp Epidemiol 1995; 16:459-477).

C. difficile is now acknowledged to be the main cause of nosocomial diarrhea in USA as well as in Europe. Many observers have noted a steady increase in the number of cases over the past 15 years. The traditional association of PMC with exposure to clindamycin, a condition known as "clindamycin colitis", greatly reduced the use of this drug in the United Kingdom. During this same period of declining clindamycin use, C.difficile-associated diarrhea has increased, even in hospitals in which this drug is only rarely used. The chief risk factor for the disease is prior exposure to antibiotics. Nearly all antimicrobials have been implicated in PMC. Analysis of the available data suggests that use of second- and third- generation cephalosporins, clindamycin, ampicillin and amoxicillin is associated with the highest risk of C. difficile diarrhea. Quinolones, aminoglycosides, macrolides, vancomycin, and extended-spectrum penicillins are associated with lower risks, and trimethoprim, tetracycline, imipenem, and meropenem seem to carry an intermediate level of risk (N Eng J Med 1999; 341:1690-1691).

In the study of Johnson et al., treatment with clindamycin had a dual effect. It selected for the clindamycin-resistant epidemic strain of C. difficile, and the suppressive action of the drug on the patients' bowel flora facilitated overgrowth of the organism. The strain identified or a closely related one was responsible for outbreaks of diarrhea in geographically diverse hospitals in the USA and UK. The findings of the authors provide support to the earliest observations about the role of clindamycin in causing C. difficile diarrhea. There is no doubt about the reliability of the results because of use of high sensitive methods (PCR, dot blot hybridization) and positive and negative controls (N Eng J Med 1999; 341:1645-1651).

Several hospitals have noted an increase in the number of cases of C. difficile diarrhea after antibiotic restrictions were relaxed, thereby increasing access to newer antibiotics, including third-generations cephalosporins (Lancet 1997; 349:1176-1177). The literature is not definitive on the value of changing antibiotic policies, nor there is agreement on which drugs need to be restricted, since this varies depending on patterns of use. We need at least one large randomized trial comparing the epidemic strains of C. difficile which are responsible for outbreaks of diarrhea and their resistance to clindamycin and other antibiotics. However, altering antibiotic-prescribing patterns by instituting strict control measures is worthy of consideration when standard isolation and environmental policies are unsuccessful. Discontinuing all suspect antimicrobial agents is desirable especially when one confronts such situations as the epidemic of C. difficile diarrhea in hospitals. The problem to be solved is whether physicians are willing to make changes in their practices even if that means forsaking some of their favorite antibiotics (N Eng J Med 1999; 341:1690-1691).

EFI AGGELOPOULOU

The natural history of pain in alcoholic chronic pancreatitis

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According to the current literature, 27-67% of patients with alcoholic chronic pancreatitis (ACP), experience chronic pain severe enough to warrant surgical intervention. The choice of surgical procedure (drainage vs. resection) and its efficacy in relieving pain and maintaining pancreatic function are debated.