

FATAL MEMBRANOUS STAPHYLOCOCCAL ENTERITIS IN SURGICAL PATIENTS*

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ANTIBIOTIC THERAPY HAS been a boon to the patient. The development of new antibiotics and the use of two or more antibiotics in combination have proved valuable in the prophylaxis and treatment of infections, in a large majority of cases. In exceptional circumstances such treatment, as ordinarily administered, may conversely cause possible harm. One such uncommon situation may occur when, following the use of several antibiotics, the normal flora of the intestinal tract is altered or destroyed, allowing a resistant strain of a pathogen to grow unchecked, with or without toxin production.

Membranous or pseudomembranous enteritis or enterocolitis have been observed particularly after surgical operations.^{1, 2} The sudden postoperative onset of severe shock often has suggested that a myocardial infarction or pulmonary embolism has occurred. Or membranous enteritis may simulate an acute surgical abdominal emergency³ either with or without any prior operative procedure. Other authors have invoked adrenal cortical failure or neurogenous imbalance to explain the dramatic breakdown of homeostatic forces.

Three fatal cases with autopsies have occurred recently at this institution. They are presented as examples of a small, but apparently increasing, group of postoperative fatalities due to staphylococcal membranous enteritis. Two of these cases have been

separately reported from the viewpoint of gastroenterology.⁴

Case 1. A man, 43 years old, had ulcerative colitis for 12 years. On his last admission, for completion of a three-stage total colectomy, he developed an upper respiratory infection with fever to 104°, and was treated with chloramphenicol, a total dose of 6.25 Gm. in 4 days. Penicillin, 400,000 units intramuscularly, was given on the fourth day. A rash developed and thereafter Gantrisin® replaced the previous therapy, 1.0 Gm. every 6 hours. On the ninth day fever had subsided, and on the twelfth day his colectomy was completed, leaving an ileostomy. There was postoperative fever and copious watery ileostomy drainage. Streptomycin, a total of 5.5 Gm. in 3 days, and terramycin, 0.5 Gm. intravenously on the fifth postoperative day were given. The patient went into profound shock on the fifth postoperative day, and died the next day.

At autopsy, 10½ hours later, the chief finding was a fibrinous membrane lining the jejunum and ileum. Culture showed hemolytic *Staphylococcus aureus* and *Pseudomonas aeruginosa*. A culture of blood taken from the heart contained hemolytic *Staphylococcus aureus*. Microscopically the membrane overlay mucosal necrosis (Fig. 1), and contained staphylococcal colonies buried in the fibrin network. Surgical closures were all intact. Other final pathologic diagnoses were fibrous and fibrinous peritoneal adhesions; atelectasis, right lower lobe; gastro-esophagomalacia and fatty metamorphosis of liver.

Case 2. A woman, 62 years old, received aureomycin, dose unknown, Banthine®, and an ulcer regime for vomiting and right upper quadrant pain. Her gallbladder and appendix had previously been removed. Following readmission for recurring pain and vomiting, she had a gastroenterostomy performed with exploration of the common duct.

Postoperatively she developed progressively severe shock, with fever of 101 to 105°. Transfu-

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TABLE I. Case 3: Chemotherapy and Temperature Chart.

	Dec. 3	Dec. 4	Dec. 5	Dec. 6	Dec. 7	Dec. 8	Dec. 9	Dec. 10	Dec. 11	Dec. 12
Temperature	98°	100.5	100.2	100.8	101.5	102	99	102	101.8	
Operation							Diarrhea		Shock	Death
Antibiotic Therapy:										
Penicillin	200,000u in wound						100,000u (IM)noon, 6 p.m. & midnight	100,000u 3, 6, 9 AM 8 PM and midnight	100,000u 3, 6, 9 AM and 6 PM	100,000u 3 AM
Crysticillin	300,000u 6 PM (IM)	300,000u 6 AM and 6 PM	300,000u 6 AM and 6 PM	300,000u 6 PM	300,000u 6 AM		300,000u 6 AM and 6 PM	300,000u 6 AM and 6 PM	300,000 6 AM and 6 PM	
Gantrisin						P. O. 0.5 gm. 6 AM and 1.0 gm. 12 noon	0.5 gm. 6 AM, 0.5 gm. noon and mid- night	0.5 gm. 6 AM	0.5 gm. noon	
Streptomycin						P. O. 0.5 gm. 6 P. M.	0.5 gm. 6 AM and 6 PM	0.5 gm. 6 AM and 6 PM	0.5 gm. 6 AM and 6 PM	
Terramycin							1000mgm. in 1000 cc. 5% D/W	1000mgm. in 1000 cc. 5% D/W		

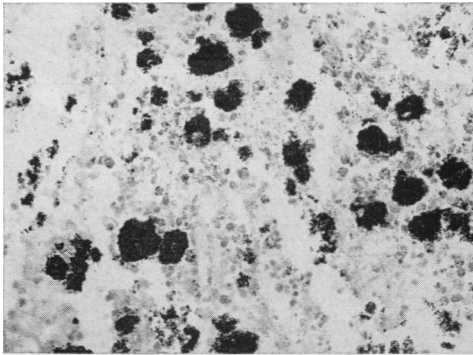


FIG. 1

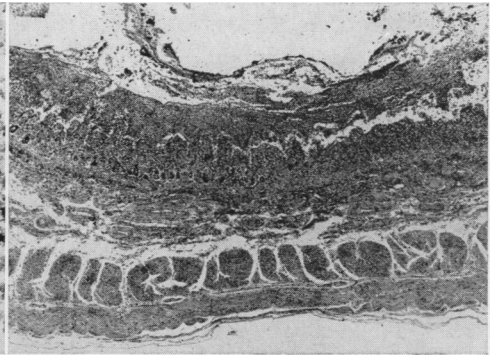


FIG. 2

FIG. 1. Gram stain of fibrinous enteric cast from Case 1, demonstrating numerous colonies of *Staphylococci* (x 171).

FIG. 2. Small intestine from Case 2, with fibrinous cast and destruction of upper portion of mucous membrane. Hematoxylin and eosin (x 18).

sions were administered. Chemotherapy administered postoperatively included 2.75 Gm. of terramycin by vein; 250,000 units of penicillin every 6 hours; streptomycin 0.5 Gm. every 6 hours, and 0.25 Gm. of aureomycin subcutaneously. She died on the third postoperative day.

The autopsy, nine and one-half hours postmortem, showed a 2 cm. penetrating duodenal ulcer with focal adjacent peritonitis and about 100 cc. of clear ascitic fluid. There was a tan-pink fibrin cast in all except the upper 10 cm. of small intestine beyond the gastro-enterostomy. Bacteriologic study of intestinal cast material demonstrated nonhemolytic *Streptococci* and *B. proteus*, and gram stains

showed many staphylococcal colonies in the fibrin (Fig. 2). Heart blood culture contained *Staphylococcus aureus* and non-hemolytic *Streptococci*. The same organisms had been found in the abdominal wound shortly before death. Other final pathologic diagnoses included focal hemorrhage in right lobe of liver with fatty metamorphosis and necrosis, petechiae and ecchymoses of epicardium, focal atelectasis and congestion of lungs, and arteriosclerosis.

Case 3. J. P. D. (142869). A 46-year-old, white, male clerk, with a 10-year history of peptic ulcer, entered the hospital in December, 1952, because of recurrent attacks of severe epigastric

FATAL MEMBRANOUS STAPHYLOCOCCAL ENTERITIS

pain, weight loss of 30 pounds in 1 year, nausea, vomiting and pyloric obstruction. There was no history of melena or hematemesis. Physical examination was negative except for slight epigastric tenderness on deep pressure. Blood pressure was 108/80.

Roentgen examination reported a chronic duodenal ulcer, partially obstructing, and a chronic inflammatory disease of the left lung base.



FIG. 3. Cross-section of small intestine from Case 3, showing membranous cast, partly attached and partly free in lumen.

On the third hospital day (Dec. 3) a partial gastric resection was performed for a posterior penetrating ulcer of the stomach which was adherent to the pancreas. The postoperative course was uneventful except for a low grade fever which had reached 102° on the fifth postoperative day (Dec. 8). Chest roentgenogram revealed a probably resolving atelectatic process on the left, also the possibility of some similar process on the right, but to a lesser degree.

He was placed on increased doses (Table I) of crysticillin, streptomycin, Gantrisin® (Dec. 8) and terramycin (Dec. 9). Sputum culture was reported as showing pure growth of hemolytic *Staphylococcus aureus* (Dec. 11). After two days of therapy, his temperature dropped to normal but he developed a gastro-intestinal upset characterized by vomiting and diarrhea. The terramycin was stopped, but the patient had an immediate elevation of temperature to 102°. On the ninth postoperative day, the patient became irrational and confused. He was found on the floor in profound shock. He died 6 hours later (Dec. 12).

Autopsy, 5 hours postmortem, revealed dehiscence of the surgical wound including the peritoneum. The peritoneum adjacent to the wound was congested; elsewhere it was normal. About

100 cc. of clear yellow ascite fluid was present. The gastro-enterostomy was intact, with a widely patent stoma and no evidence of leakage or separation. The small bowel was dilated and contained much yellow fluid. The mucosa was covered with a yellow-brown membrane which easily stripped away. Microscopically the upper half of the small intestinal mucosa was replaced by necrosis and a membranous exudate composed of fibrin, large num-

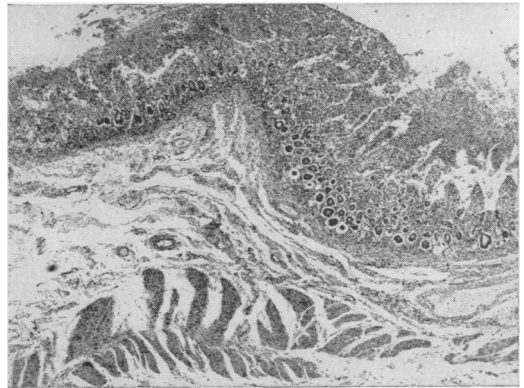


FIG. 4. Membranous staphylococcal enteritis with partial destruction of mucosa, from Case 3. Hematoxylin and eosin (x 18).

bers of polymorphonuclear leukocytes and bacterial colonies of *Staphylococci*. The gland crypts were infiltrated with *polymorphonuclear leukocytes* and showed focal necrosis. Portions of the membrane were also free in the lumen (Figs. 3, 4).

The left lower lung lobe had severe bronchiectasis and an extensive necrotizing pneumonitis with abscess formation. Culture of the left lung taken at autopsy was reported as hemolytic *Staphylococcus aureus*, *Streptococcus hemolyticus*, *Streptococcus anhemolyticus* and *Aerobacter aerogenes*. Culture of heart blood at autopsy was reported as hemolytic *Staphylococcus aureus*, *Streptococcus hemolyticus* and *B. proteus*. Sensitivity tests on the hemolytic *Staphylococcus aureus* from the lung swab revealed: penicillin, no sensitivity, 200 mg./liter; terramycin, no sensitivity; streptomycin, no sensitivity; neomycin, moderate sensitivity, 7 mm.; bacitracin, slight sensitivity.

DISCUSSION

These cases had several features in common. All three patients had undergone major gastro-intestinal surgery. All three developed profound shock, rapidly followed by death. They had received four or more antibiotic or chemotherapeutic reagents

postoperatively. On postmortem examination, each patient had a fibrinous membranous cast in the intestinal tract, from which hemolytic *Staphylococcus aureus* was isolated bacteriologically in two cases. *Staphylococcus aureus* was also cultured from the heart blood in all three cases, and identified by gram stain in large numbers in the intestinal fibrinous casts. In the one case where the organism was subjected to sensitivity studies, it was resistant to all the antibiotics used.

Management of persisting fever and gastro-intestinal symptoms in surgical patients receiving antibiotics would be assisted by relatively frequent sputum, nose and throat, or stool cultures. Report of a pure culture of hemolytic *Staphylococcus*, or possibly *Streptococcus*, would be an important danger signal. It would then be necessary to appraise the antibiotic therapy critically. Increasing the dosage of penicillin to maximum amounts would appear to be more desirable than multiplying the number of different chemotherapeutic agents employed. The usefulness of sulfonamides should not be forgotten. Newer drugs such as Neomycin, and others, are also apparently at present more often effective against resistant bacterial strains.

Lethal antibiotic-resistant hemolytic staphylococcal infections have not been limited to enteritis. Endocarditis,^{5, 6} septicemia and other types are known. Epidemiologic studies have showed the acquisition of insensitive Staphylococci to be due to hospital cross-infections in some patients.^{7, 8}

It is emphasized that, numerically, cases such as those reported have been very few. No reason for curtailment or abandonment

of antibiotic chemotherapy in surgical patients has been found in the present study.

SUMMARY

Three fatal cases of hemolytic *Staphylococcus aureus* membranous enteritis with septicemia have been reported. All occurred postoperatively in surgical patients receiving combinations of antibiotics. The Staphylococci were resistant or insensitive to the antibiotics employed. Means of preventing this uncommon serious complication in surgical patients are discussed.

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