Hepatic Failure After Halothane

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A 54 year old white patient was admitted for cellulitis of the left foot. Diabetes mellitus and Laennec's cirrhosis had been diagnosed in another institution, one year before. Until that time, he had been a vagrant and a heavy drinker. He denied recent exposure to poisons, transfusions or drugs, except oral medication for diabetes.

He was emaciated, with spider nevi, gynecomastria and palmar erythema; a hard, nodular liver was palpable 10 cm. below the costal margin, on the midline. Total bilirubin was 1.1 mg./100 ml., Bromosulfalein test 19 per cent, alkaline phosphatase 14 to 31 King-Armstrong units, glycemia 120–150 mg./100 ml. Prothrombin time, direct bilirubin, thymol turbidity and cephalin flocculation tests, and albumin/globulin ratio were normal. A barium meal revealed no esophageal varices. After two weeks of local therapy and intramuscular antibiotics (7 days of Terramycin and 7 days of Chloromycetin), debriement and partial amputation were performed under sciotic block (20 ml. lidocaine 1.5 per cent). This was repeated after a week.

Nine days after the second amputation, the patient developed symptoms of acute spinal cord compression at tenth thoracic level, and laminectomy was proposed. For various reasons, the gravity of the cirrhosis was overlooked by the anesthesiologists. The patient's trachea was intubated after 80 mg. methohexital and 80 mg. succinylcholine intravenously and anesthesia maintained by 4 liters N₂O-2 liters O₂/minute and halothane for the 225 minutes required for a decompression laminectomy (T9–11) with stripping of an epidural tumor. Respiration was controlled with a Bennett respirator; we have no reason to believe that hypoventilation occurred at any time. Soon after induction, the pressure fell from a preoperative 120/80 to 85–90/60–70 while the pulse raised from 80 to 100–110/minute. Halothane was turned off, then kept at concentrations compatible with surgery, while 1,000 ml. of 5 per cent Albumisol and 1,000 ml. blood were administered; both measures produced no amelioration of the vital signs. On leaving the operating room, the patient was conscious, with good respiratory exchange; pulse and pressure had returned to their preoperative levels.

Twelve hours postoperatively, the patient became lethargic, slightly hypotensive and tachycardic; the vital signs responded favorably to 500 ml. blood. From the fifteenth hour on, he refused to take fluids and was kept on intravenous 5 per cent dextrose-water, with vitamin K. He was placed on intramuscular Aureomycin and Chloromycetin. On the thirty-second hour, nausea and vomiting occurred and persisted through the second postoperative day, while lethargy increased. One emesis contained a small amount of bright red blood. On the forty-eight postoperative hour, jaundice appeared; a few hours later, the patient passed a large tarry stool, with a new hypotensive episode corrected by 500 ml. blood.

On the third postoperative day, the patient became more lethargic, then confused and agitated, and developed distended abdomen, tremor and fetor hepaticus; jaundice deepened and respiration became labored. Several tarry stools brought new hypotensive episodes, again corrected by blood administration. In spite of massive transfusion, toward the seventy-fifth hour, the vital signs deteriorated progressively, the patient sunk into a deep coma and expired 80 hours after surgery.

Hemoglobin oscillated between 10 and 10.5 g./100 ml. during the postoperative course; on the second postoperative day, the prothrombine time was 23 seconds (normal 15 seconds) and alkaline phosphatase 28 King-Armstrong units. Urinary output and urinalysis remained normal until the last few hours; then anuria occurred. The temperature reached 100° F. the first 24 hours, then fell to 98–99° F. until 6 hours prior to death (97° F.).

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Autopsy was performed 10 hours after death. The 2,260 g. liver, of hobnail appearance, showed rare regenerative lobules of 1–4 mm. diameter, between large amounts of scar tissue; multiple microscopic slides confirmed the diagnosis of advanced generalized Laennec's cirrhosis, with a profusion of connective tissue, rich in biliary ducts, many of them dilated and containing a deeply stained inspissated bile. The parenchymal lobules, rare and of irregular size, contained normal cells, except for a few deeply bile stained or edematous areas; no cell showed necrosis or fatty metamorphosis. The kidneys were normal. The esophageal walls disclosed extensive ulcerations where the mucosa had been replaced by a thick necrotic membrane infiltrated with neutrophiles. The veins were very dilated. The gastrointestinal tract was filled with about two liters of bright red blood; the gastric mucosa showed innumerable pinpoint ulcerations. The epidural mass resected at operation was malignant and probably metastatic, but the primary lesion could not be found.

It is impossible to elicit the precipitating factor which led to the fatal hepatic failure. The time of onset of symptoms, however, points toward anesthesia rather than blood, antibiotics or another drug. Halothane, and its hypotensive effect on a probably hypovolemic patient is a prime suspect. The absence of zonal necrosis and fatty changes is worth emphasizing. In the 16 fatal cases reviewed by Blackburn (Anesthesiology 25: 270, 1964) and two others reported by Burns (Brit. Med. J. 2: 483, 1957) and Chamberlain (Brit. Med. J. 1: 1524, 1963), severe necrosis, usually with fatty changes were repeatedly present. Did the rapid evolution bring biochemical failure before the appearance of any morphological lesions? Or was the precipitating stimulus too small to cause pathological changes, while sufficient to produce functional failure in a diseased liver? This must remain speculative, but it suggests that severe biochemical damage may occur without histological changes and that liver biopsy may be misleading. Indeed, careful review of the chloroform literature discloses numerous fatal cases with minimal microscopic lesions, in spite of the insistence of many textbooks to describe a "classical central necrosis."

It is also possible that regenerative liver cells, although functionally sensitive, offer a morphological resistance to halothane. This abnormal response has been described with chloroform (McNider, J. Pharm. Exp. Ther. 59: 393, 1937).

Postoperative (Pressure) Alopecia

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Abel and Lewis1 reported 8 cases of a new type of alopecia, occurring only in women who had undergone prolonged gynecological operations. The alopecia always appeared over the vertex or the upper occiput. In 5 of the 8 patients there was pain, swelling, or serous discharge from the affected scalp within 72 hours after the operation. Hair loss began is this affected area in 3 to 28 days. It developed into a patch of alopecia, usually total, 2 to 8 cm. in diameter, resembling alopecia areata. By the time the hair loss occurred, the scalp appeared normal. Complete regrowth of hair occurred in all cases, usually starting within 90 days. Histopathological studies of the scalp in 6 cases showed the cardinal feature to be an obliterative vasculitis involving the vessels of the deep cutis and the fat. Two cases showed moderate panniculitis and two cases showed a mild perivascular lymphocytic infiltrate. Thomson and Estrelado2 recently reported a series of three cases

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