Experimental data, Macklin has proposed a causative mechanism for pneumothorax and pneumomediastinum. He showed that when the right lower lobe of the lung of a cat was hyperinflated alveolar rupture occurred. Subsequent dissection of air could occur along the pulmonary vascular sheath to the hilum, producing pneumothorax and pneumomediastinum.

In the patient presented the pneumothorax probably was due to the process described by Macklin. The pneumopericardium probably was also due to the same mechanism, with sufficient accumulation of air to cause cardiac tamponade. We have seen no reports of the latter complication in the literature, but with the increasing use of prolonged ventilation in treating infants it probably will be seen more frequently.

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Early Postoperative Death of a Child after Repeated Halothane Anesthesia

O. Z. LERNAU, M.D.,* E. LEVY, M.D., PH.D., F.R.C. PATIL,† S. NISSAN, M.D., F.A.C.S.‡

Since the first descriptions of hepatic failure following halothane (Fluothane) anesthesia, shortly after its introduction to clinical use, a connection between halothane and hepatic damage, often fatal, has been postulated in many reports. In the majority of retrospective and prospective studies carried out to try to establish a relationship, confirmation has not been obtained, but in recent examinations, including large-scale studies, investigators have concluded that this complication may occur at a very low incidence.

Since it is desirable, as recently stressed, to continue to accumulate data in the hope of further clarification of the problem, we record the case of a child who died a few hours after operation under halothane anesthesia.

References


Case Report

The patient was delivered normally after an uneventful 8 months' pregnancy. Birth weight was 2,580 g. He was the first child of an 18-year-old Tunisian-born mother. At the age of 5 days a diagnosis of esophageal atresia with a distal tracheoesophageal fistula was made. During surgical operation the next day an esphagostomy and feeding gastrostomy were established after ligation of the fistula. The patient underwent four additional operations. At the age of 16 months the ileocolic and right colic vessels were ligated in preparation for esphagostomy replacement by the right colon. Ten days later, at reoperation, an ileocolic intussusception was reduced. The fourth operation was a tonsillectomy and adenoidectomy. In the fifth and last operation, at the age of 2 years, ten months, when the child was well developed and weighed 14 kg, the esophagus was replaced by the right colon.

The patient was premedicated with atropine before each operation. On each of two occasions the large bowel was sterilized preoperatively with suxamethonium and neomycin. On five occasions anesthesia was induced and maintained with
a mixture of oxygen, nitrous oxide and halothane through a non-rebreathing T-piece system. Muscle relaxation was achieved three times with small doses of succinylcholine and, in the last operation, with d-tubocurarine. Respiration was assisted. There were no respiratory difficulties during or after the operations. There was no evidence of shock, and blood loss was minimal. During the last operation the child received 200 ml of whole blood, his pulse rate remaining below 120/min throughout the four hours of the procedure.

Postoperative course after the first operation was uneventful. Postoperative course after the second was complicated by intestinal obstruction; following reduction of intussusception there were two short spikes of fever reaching 39°C on the fourth and sixth postoperative days, with no jaundice or other complication. After adenoidectomy and tonsillectomy the child was kept in hospital for only one day.

No technical difficulties were encountered during the last operation. The liver was normal to inspection and palpation. An hour after the operation a pneumothorax developed on the left side, causing respiratory distress. It was diagnosed immediately and effectively treated by intercostal under-water-seal drainage. During the next few hours the child was conscious and talking. There was slight circumoral cyanosis only when he wept, which disappeared along with a few scattered rales over both lungs after deep intratracheal suction. During this time the child received 15 mg meperidine and intramuscular injections of penicillin and streptomycin. His course during this stage was evaluated repeatedly and found to be completely satisfactory.

About eight hours after operation, pronounced listlessness, accompanied by slight sweating and moderately dilated pupils, developed. There was a transient rise in body temperature to 38.9°C, which reverted spontaneously to normal within an hour. There were no signs of cardiovascular or respiratory difficulties, as evidenced by good color, normal pulse, and normal and fully-expanded lungs on chest x-ray. Nevertheless, the motor listlessness continued, and about ten hours after operation the patient had a sudden convulsion, with cessation of breathing. He died in spite of immediate vigorous resuscitation efforts.

Postmortem examination revealed a pale yellow liver weighing 440 g. The cut surface was finely granular, with patchy yellow discoloration. The transplanted colon, with its anastomoses, was viable. The air passages were free and the lungs slightly congested.

Histologically, the normal pattern of the liver cords was disturbed, the cells being clustered in small groups, in an acinar-like structure. There was slight dilatation of the central veins and sinusoids, but the main feature was fine fatty vacuolization, with scattered foci of necrosis and ghost cells (Figs. 1 and 2). The changes were mainly centrilobular. A slight commencing polymorphonuclear sinusoidal reaction was present. The lungs showed congestion and early edema. No special macroscopic and microscopic features were found in the other organs.

**DISCUSSION**

It is not clear whether there was a relationship between halothane anesthesia, the patho-
logic changes in the liver, and the death of the patient. Attempts to characterize specific pathologic changes due to halothane have been made, with little success. The liver is described as being small and soft, and the histologic changes range from slight centrilobular acidophilic degeneration to massive necrosis of the entire hepatic parenchyma with coarse vacuolization and formation of ghost cells; there may be intrahepatic cholestasis or various degrees of fatty infiltration. The changes found in our patient correspond to the mild intermediate group described in the National Halothane Study. There are no accepted criteria for distinguishing these pathologic changes from those of viral hepatitis, so there is a tendency in the literature to ascribe such changes either to serum hepatitis following injection of blood given before or during operation or to coincident infectious hepatitis. In the absence of a laboratory test for diagnosing viral hepatitis with certainty, the question has to remain open.

The macroscopic and microscopic findings in the liver at autopsy, in contrast to the normal macroscopic findings of the liver during the operation, establish that hepatic damage took place immediately following operation. This appears to exclude a viral etiology, apart from the unlikely possibility that the onset of viral hepatitis coincided with the immediate postoperative period.

In the etiology of the hepatic damage the importance of recurrent exposure to halothane has been stressed. This was a prominent feature in the history of our patient. This factor, combined with the rarity of the condition, suggests that the pathogenesis may be an individual hypersensitivity reaction. The recent reports of hepatic injury occurring after occupational exposure to halothane support this hypothesis. If, indeed, hypersensitivity to halothane was an operative factor in our patient, it might be expected that some evidence of this would have developed at the fourth exposure, but on that occasion the patient was under observation in the hospital for only one day after the operation.

The listlessness and sudden convulsion preceding death might be explained by hypoglycemia as a manifestation of a rapid overwhelming insult to the liver, as described by others, so that there was no time for more than a relatively mild degree of morphologic change to occur; this would also explain the lack of clinical impression of hepatic involvement and the fact that liver-function tests were not carried out.

In a recent review of 89 case reports of fatal postanesthetic hepatic failure from the
literature, there was only one report of an infant, who died at the age of eight weeks from hepatic failure after halothane anesthesia for pyloromyotomy. The only other reported patient less than 10 years old had not received halothane. Among the 80 cases of massive hepatic necrosis reviewed from the pathologic and clinical aspects in the National Halothane Study there were no patients under the age of 10 years. It seems that in infancy and childhood a fatal outcome of halothane anesthesia is rare (although it should be pointed out that the percentage of patients in the infancy-childhood age range subjected to halothane anesthesia is not clear from the National Halothane Study). There are two possible contributing factors to this apparent rarity: the incidence of repeated exposure to anesthesia would be expected to be lowest in the young and to rise with increasing age, and there is evidence that, compared with adults, infants and children are less likely to show evidence of delayed hypersensitivity or allergy.

In the National Halothane Study, the most comprehensive inquiry into the subject, in which 10,171 postoperative deaths were reviewed, only those patients thought to have massive necrosis of the liver were selected for histologic screening. This deliberate exclusion of lesser degrees of hepatic damage precluded the possible detection of cases similar to that presented in this report.

It seems plausible that in hypersensitive patients acute hepatic damage may develop after repeated exposure to halothane, causing a rapid, severe biochemical injury which leads to death before definitive morphologic changes have had time to appear. A high clinical and pathologic index of suspicion, combined, perhaps, with modern histochemical and electronmicroscopic examination, might help to substantiate this suggestion.

REFERENCES


