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Atypical Serum Cholinesterase Eliminated by Orthotopic Liver Transplantation

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Plasma cholinesterase or pseudocholinesterase (PChE) hydrolyzes local anesthetics and succinylcholine. Although PChE is synthesized by functioning hepatocytes,[1] control of its production has not been elucidated.

Low PChE levels may be seen in many clinical situations, including liver disease.[2] When the PChE level is reduced to 20% of normal (i.e., 80% reduction), the duration of apnea following succinylcholine administration may be increased from a normal duration of 5 min to nearly 15 min.[3] Duration of neuromuscular blockade will be considerably longer in the presence of the homozygous atypical enzyme.

We describe a patient with end-stage liver disease secondary to alpha 1-antitrypsin deficiency who had correction of a PChE deficiency after Orthotopic Liver Transplantation (O.L.T.). At the time of the transplantation, this patient had a prolonged neuromuscular blockade after succinylcholine, and was subsequently documented to have a PChE variant. Following O.L.T., PChE levels became normal, as did the genotype of the enzyme. This finding suggests that determination of enzyme character may reside entirely within the liver.

CASE REPORT

A 14-yr-old girl with advanced hepatic cirrhosis was scheduled for O.L.T. Past medical history was remarkable for neonatal jaundice and congenital hepatitis. At age 10 yr, alpha l-antitrypsin deficiency was diagnosed based on an alpha l-antitrypsin level of 30 mg/dl (normal 85–213 mg/dl). Phenotype testing revealed a ZZ or a Z-null pattern. During the disease process, she suffered from hepatic encephalopathy, portal hypertension with ascites, and hypoxia secondary to intrapulmonary shunting and a diffusion defect. She had no previous surgery, and had not previously received general anesthesia. Family history was unremarkable for anesthesia-related problems, since no immediate family members had undergone surgery. Anesthesia was induced with iv thiamylal, after which succinylcholine, 1.0 mg/Kg was administered iv and the trachea intubated. Anesthesia was maintained with isoflurane, nitrous oxide, and oxygen. A peripheral nerve stimulator was employed to gauge the adequacy of muscle relaxation. No twitch response or post-tetanic facilitation was observed for 3.5 h following the succinylcholine. When the twitch finally did reappear, a single dose of metocurine 10 mg was administered. After surgery, the patient was transported to the Pediatric Intensive Care Unit.

Because of excessive intravascular volume and poor respiratory effort, ventilation was controlled for 36 h postoperatively. Her trachea was extubated once diuresis had been induced. Since the operation, the patient has maintained excellent liver function despite several episodes of acute graft rejection. In the 24 months since transplantation, no subsequent exposure to succinylcholine has occurred.

Because of concerns about the prolonged neuromuscular blockade noted intraoperatively, blood was analyzed for serum cholinesterase, both before revascularization and 5 and 9 months following transplantation (table 1). Liver function was concurrently evaluated (table 2). Enzyme analysis reveals a heterozygous atypical PChE (E^uE^a) prior to the liver transplant and a normal PChE (E^uE^u) following the liver transplant. Postoperative alpha 1-antitrypsin phenotype was noted to be type M and alpha 1-antitrypsin level was measured to 185 mg/dl (normal 85–213 mg/dl) 10 months following transplantation.

DISCUSSION

Prolonged response to succinylcholine was first attributed to low activity levels of PChE, which can be present during liver disease and exposure to medications. In 1958, Kalow[2] investigated apnea occurring in relatively healthy patients undergoing electroshock therapy. He determined several genetic variants of PChE based on inhibition of substrate hydrolysis by dibucaine. Since the enzyme is genetically determined, the PChE genotype remains constant throughout life.

Atypical PChE is not a rare disease. The incidence of a homozygous, dibucaine-resistant gene is 1/2,800. The heterozygous genotype has a frequency of 1:25. Patients with these variants do not exhibit any symptomatology unless given succinylcholine, resulting in a prolonged apnea. Usually, one would expect only a modest prolongation of paralysis in a patient with the E^uE^a genotype. We can only explain the 3.5 h of skeletal muscle paralysis as due to a combination of atypical genotype with depressed activity in this patient with liver failure.

Orthotopic liver transplantation is an accepted treatment for certain forms of end stage disease, and is being utilized with increasing frequency.[4] Liver disease due to alpha l-antitrypsin deficiency can be cured by liver transplantation.[5] The transplant recipient acquires the

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TABLE 1. Serum Cholinesterase Levels Pre- and Post-liver Transplant

	Pre-transplant	5 Months Post-transplant	9 Months Post-transplant	Normal
Serum cholinesterase (u)	40	113	175	90–160 u
Dibucaine number (%)	56	89	84	>80
Fluoride number (%)	50	81	73	>61

TABLE 2. Liver Function Tests Pre- and Post-liver Transplant

	Pre-liver Transplant	5 Months Post-liver Transplant	9 Months Post-liver Transplant
SGOT (units/l)	80	395	170
SGPT (units/l)	44	159	233
Alkaline phosphatase (units/l)	335	123	148
LDH (units/l)	262	251	248
Bilirubin (mg/dl)	3.7/1.9	3.3/2.1	2.3/1.4
Albumin (g/dl)	2.2	4.3	4.9
PT (pt/control) (s)	17.2/12.2	12.4/12.6	11.9/12.3
PTT (pt/control) (s)	37.8/33.6	29.1/31.1	34.5/32.3

SGOT = serum glutamic oxalacetic transaminase; SGPT = serum glutamic pyruvic transaminase; LDH = lactic dehydrogenase; PT = prothrombin time; PTT = partial thromboplastin time.

donor phenotype (from Pi ZZ to Pi MM).[6] Follow-up studies on these patients show no evidence for reversal to the original phenotype or diminishing alpha l-antitrypsin in the serum levels.[6] Our patient had a similar pattern. Laboratory results showed that the recipient alpha l-antitrypsin phenotype changed and became the same as the donor's when studied 10 months post-transplantation. This patient, in addition, has a new PChE genotype. PChE changed from E^uE^a to E^uE^u after liver grafting.

In summary, two genetic disorders (alpha l-antitrypsin and serum cholinesterase deficiency) were successfully treated by orthotopic liver transplantation. The role of the liver in the pathophysiology of both diseases is demonstrated.

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Sodium Bicarbonate Buffers Gastric Acid during Surgery in Obstetric and Gynecologic Patients

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Buffering gastric acid with nonparticulate oral antacid prior to induction of general anesthesia may reduce pulmonary damage if aspiration ensues. Previous studies in rabbits have shown that severe pulmonary dysfunction resulted from aspiration of acid fluid with a *p*H lower than 2.5, while aspiration of acid fluid with a *p*H of 2.5 or above caused little or no damage.[1]

Aspiration of emulsion type oral antacids, and suspensions of aluminum and magnesium hydroxide caused diffuse histologic changes in the lung tissue of dogs.[2] In contrast, the aspiration of hydrochloric acid (HCl, *p*H 4.5) buffered by a nonparticulate antacid such as Bicitra® caused only a transient decrease in Pa_{O_2} in rabbits.[3]

The ideal preoperative oral antacid should be nonparticulate, fast-acting, and highly effective at low volumes. Sodium bicarbonate ($NaHCO_3$), a clear liquid antacid with a *p*H of 7.5–8.0, meets these criteria. This study was designed to determine the volume ratio of

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