Silent Cholinesterase Gene—Report of a Family

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The enzyme, pseudocholinesterase (serum cholinesterase, acylcholine acylhydrolase, I.U.B. Commission on Enzymes 3. 1. 1. 8.), is found in many human tissues. Although the enzyme is genetically controlled, with no known biologic function, pharmacologically it hydrolyzes succinylcholine, shortening the action of this muscle relaxant. Genetically, the type and amount of pseudocholinesterase are determined by genes at two loci (E_1 and E_2). At locus E_1, with at least four alleles, there can be the usual or normal (E_1^u), the atypical (E_1^a),[1] the fluoride (E_1^f),[2] and the silent (E_1^s).[3] At locus E_2, the C_5^+ variant results in a 30 per cent increase in activity of the enzyme.[4]

The silent gene (E_1^s) was described in 1962.[3] Patients homozygous for the silent gene ($E_1^sE_1^s$) have no pseudocholinesterase activity.[5, 6] About 64 such cases have been reported, 48 of them in Eskimos.[7] Succinylcholine causes prolonged paralysis in these patients. The following case adds to those previously reported and demonstrates the importance of genetic typing of those patients suspected of having prolonged apnea resulting from succinylcholine.

REPORT OF A CASE

A 27-year-old Caucasian woman of northern European extraction was admitted to the hospital for anterior cervical fusion. Following two previous anesthesias, for lumbar laminectomy and hysterectomy, she had been very slow to awaken, and she was concerned that she might have received too much anesthesia. Although specifically questioned, the patient gave no history of problems with muscle relaxants.

The patient was thin. Physical examination and laboratory studies disclosed no abnormalities.

Anesthesia was induced with thiopental, 200 mg iv, followed by succinylcholine, 40 mg, to facilitate endotracheal intubation. Anesthesia was maintained with oxygen, 2l, nitrous oxide, 2l, and halothane, 0.5–0.75 per cent, through an in-line vaporizer (Fluotec). Vital signs were stable throughout the 90-minute procedure. However, the patient was apneic throughout the procedure, with ventilation being controlled for a total of three hours before adequate spontaneous ventilation was maintained. Because a decrease in succinylcholine hydrolysis was suspected, a blood sample was assayed for pseudocholinesterase activity, using the method of Garry.[8, 9] This method distinguished atypical (E_1^a) and fluoride (E_1^f) activity by buffer inhibition.

Review of the patient's previous anesthetic records disclosed that she had been apneic for 95 minutes (succinylcholine, 60 mg) at the lumbar laminectomy and for 75 minutes (succinylcholine, 40 mg) at the hysterectomy. A diagnosis of succinylcholine apnea had been made each time, once with laboratory confirmation, but the patient had not been informed.

No pseudocholinesterase activity was found in the patient's serum. Therefore, she is homozygous for the silent gene ($E_1^sE_1^s$).

The patient's family was tested for pseudocholinesterase activity. The results of the determinations and deduced genotypes are shown in table 1. A family tree is shown in figure 1. Subject III-2 is presumed to be $E_1^sE_1^s$. Subject IV-1 could be either $E_1^uE_1^s$ or $E_1^sE_1^s$. The patient and

TABLE 1

Generation	Subject	Pseudocholinesterase Activity, I.U.	Deduced Genotype
I	1	5.62	$E_1^uE_1^u$
II	1	2.29	$E_1^uE_1^s$
	2	2.95	$E_1^uE_1^s$
III	1	4.73	$E_1^uE_1^u$
	2	2.40	$E_1^uE_1^s$
	3	0.00	$E_1^sE_1^s$
	5	0.00	$E_1^sE_1^s$
IV	1	3.84	$E_1^uE_1^u$ or $E_1^uE_1^s$
	3	2.60	$E_1^uE_1^s$
	4	3.35	$E_1^uE_1^s$
	5	2.86	$E_1^uE_1^s$
	6	2.55	$E_1^uE_1^s$
	7	2.82	$E_1^uE_1^s$

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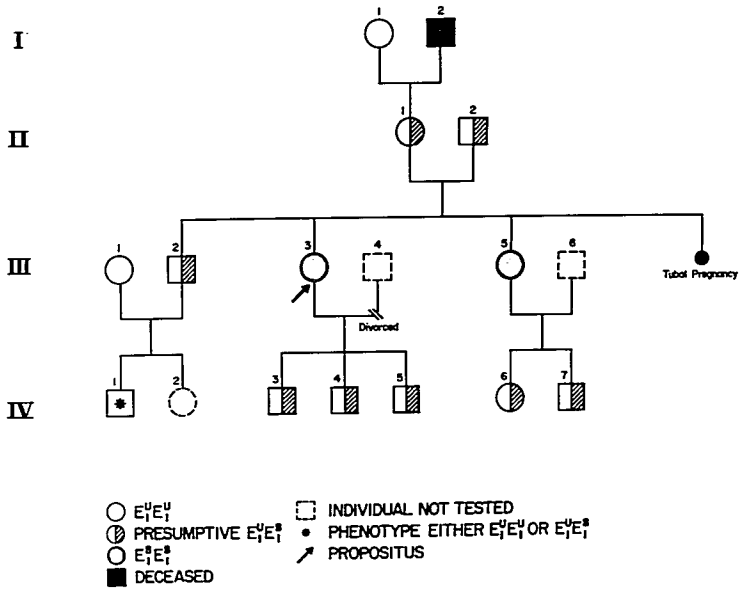

FIG. 1. Family tree of the patient (III-3), showing deduced genotypes for pseudocholinesterase in four generations.

her sister are $E_1^aE_1^a$. No atypical (E_1^a) or fluoride (E_1^f) activity was found in any sample.

Family testing of all patients with genetic deficiencies of pseudocholinesterase should be done, with counseling of the family. Some record for the deficient member, such as a letter or, preferably a medical warning bracelet, should prevent exposure to succinylcholine should the individual need anesthesia.

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