Letters

Cerebral convulsion after enfluran anaesthesia and occupational exposure to tetrahydrofuran

Sir: Epileptic seizures as a complication of normal anaesthesia are infrequent. When encountered in previously neurologically healthy patients, a search should be initiated to detect any underlying diseases affecting the nervous system. The following case describes an association between status epilepticus, anaesthesia, and occupational exposure to tetrahydrofuran, a solvent.

The patient was a 45-year-old man who had earlier been healthy. He had had no birth or head trauma, or neurological disease. He was admitted straight from his workplace because of suspected acute appendicitis. A appendectomy was performed immediately, and the appendix was found to be gangrenous but not perforated. Upon awakening from the enfluran anaesthesia the patient had several generalised convulsions which were treated with benzodiazepine and thiopental. The convulsions subsided during the night, and the next day the patient was in good clinical condition. After examining the patient and after interviewing his wife, the consulting neurologist suspected the possibility of occupational intoxication and suggested further examinations. The first EEGs showed generalised irritation which subsequently improved; CT scan was normal. Psychological tests given because of his exposure to organic solvents revealed minor changes in visuomotor functions. The liver enzymes, which were slightly elevated after operation, returned to normal levels within two weeks.

Occupational history revealed that for the past ten years the patient had run his own one-man business, insulating the insides of water supplies with materials containing a PVC polymer. The insulation procedure involved the use of a solvent, tetrahydrofuran. While working in Saudi Arabia in the late 1970s he had an episode of apparent tetrahydrofuran intoxication. His symptoms included headache for a few days, fatigue, and a transient rise in liver enzymes. No other history of severe acute intoxication was obtained. He did not use personal protective devices because they were uncomfortable. For about two weeks before his appendectomy the patient had been working in particularly poor conditions without ventilation and using electric heaters to dry the water from the inside.

The volume of the containers varied from 800 to 1000 m³, and the tetrahydrofuran was concentrated at the bottom of the containers, where the patient worked. The estimated consumption of the solvent per container was 10 litres, about 2 l per day. In the week just before admission to hospital the patient had felt unusually tired and had had a headache that he associated with exposure to tetrahydrofuran. It should be mentioned that the patient had not drunk alcohol in large amounts for several years.

Tetrahydrofuran is a potentially narcotic and irritating colourless liquid with a molecular weight of 72.1. Its odour is similar to acetone, and it has a pungent taste. Its boiling point is 65–66°C, its vapour pressure 114 mm Hg at 15°C, its specific gravity 0.891, its flash point 1°F, and it is water-soluble. The synonym for it is cyclo-tetramethylene oxide. It has been used in industry as a solvent for resins and in the formation of lacquers. It has been suggested that the maximum allowable concentration be fixed between 100 and 200 ppm. In experimental animals it can cause a drop in blood pressure, narcosis, emesis, and the irritation of mucous membranes. It also penetrates the skin easily and accumulates in the body. The data on human toxicology are scant; it has been reported to cause headaches.¹ There has been one case report that tetrahydrofuran potentiated the nervous system effects of methyl-ethyl-ketone.²

Enfluran is a halogenated ethyl-methyl-ether with the same properties as halothane. It is a common anaesthetic gas cross-sensitive to other halogenates gases. Side effects (mainly cerebral convulsions) have been reported for high concentrations of this gas and with hyperventilation. As with halothane, hepatitis due to hypersensitivity may be a complication of use of this substance.³ Enfluran is an agent that can activate the liver microsomal mixed-function oxidase system.⁴ Theoretically, tetrahydrofuran may have a potentiating effect on enfluran by enhanced metabolism and an increased amount of toxic metabolites. Both the dosage of enfluran and the blood level of carbon dioxide were normal throughout the anaesthesia. This suggests that the blood concentration of enfluran should have been at the level which, under normal conditions, would not have provoked convulsions. The transient rise in liver enzymes reflects either the well-known hypersensitivity to liver damage ("halothane hepatitis") caused by enfluran or the joint effects of tetrahydrofuran and enfluran. It is also possible that the patient

had become tolerant to tetrahydrofuran and had a withdrawal phenomenon or that some active metabolite of tetrahydrofuran that could affect the irritability of the brain was formed. Nevertheless, there are several factors to suggest that occupational exposure to tetrahydrofuran was the main contributing factor in the development of cerebral convulsions in this patient: (1) The patient was unequivocally exposed to exceptionally high concentrations of tetrahydrofuran during the preceding two weeks, and his body burden of this chemical was probably exceptionally high during enfluran anaesthesia. (2) The patient had never had epilepsy or neurological disease before, and his clinical status and CT were normal. Minor psychological disturbances and unstable, slightly irritative EEGs were comparable with both his exposure to the solvent and with enfluran anaesthesia. (3) The toxicological and pharmacological data on tetrahydrofuran and enfluran show that they may potentiate each other. Furthermore the dosage of the latter was that normally used and should not have provoked convulsions under normal conditions.

The present case history suggests that the interactions of tetrahydrofuran and enfluran may provoke epileptic seizures. It is therefore important to consider the occupational history of recent exposure to some solvents as a risk factor for anaesthesia.

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