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Life-threatening fluvoxamine overdose in a 4-year-old child

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Sir: We would like to report a case of life-threatening fluvoxamine overdose in a 4-year-old boy which resulted in profound coma, hypotension and aspiration pneumonitis. Fluvoxamine is an anti-depressant drug which acts as a selective inhibitor of neuronal uptake of 5-hydroxytryptamine [1]. Fluvoxamine maleate is available throughout Europe and the United States and is marketed under the names Faverin, Floxyfrol, Luvox and Dumyrox. Cases of deliberate overdose have been reported previously in adults, and deaths have occurred following simultaneous ingestion with other drugs [2]. However this is the first report of an overdose with this drug in a child.

A 4-year-old boy was found unconscious by his mother having accidentally ingested 400 mg of fluvoxamine tablets. This dose could be accurately verified since four tablets were found missing from an unopened packet of his mother's medication. On the arrival of the emergency services he was deeply comatose with a Glasgow Coma Score of 3/15, systolic blood pressure of 60 mmHg, heart rate of 76 bpm, respiratory rate of 20 bpm and axillary temperature of 34.7 °C. He was intubated and transferred to the local hospital where he received gastric lavage with activated charcoal, 3 boluses of atropine for persisting bradycardia, and 600 ml of intravenous fluid to support his blood pressure. Resuscitation was continued with intravenous dopamine and adrenaline via a central line. A short generalised seizure was controlled with 2.5 mg of intra-venous diazepam.

He was transferred by helicopter to a Paediatric Intensive Care Unit. During the flight, he required 3×0.1 mg boluses of adrenaline to maintain his blood pressure. His first documented arterial blood gas in 60 % inspired oxygen showed a pH 7.16, pO_2 56 kPa, pCO_2 5.6 kPa, HCO_3^- 17 mmol/l and base deficit 9 mmol/l. An ECG showed some ventricular premature beats, a right bundle-branch pattern and a prolonged QT interval of 0.4 s, but a normal Qtc interval. An echocardiogram was normal. Unfortunately no fluvoxamine assay was available although full urine toxicology screening revealed no evidence of any additional drug ingestion.

During the next 24 h he remained persistently hypotensive and required substantial inotropic support with adrenaline (up to 0.1 mcg/kg per min) and dopamine (up to 25 mcg/kg per min). His chest X-ray showed appearances compatible with aspiration at or prior to the time of intubation. After 24 h his clinical condition improved such that he was able to be extubated. Unfortunately, he subsequently deteriorated requiring re-intubation and his chest X-ray now showed diffuse bilateral infiltrates compatible with ARDS. He required mechanical ventilation for a further 5 days, but subsequently made a good recovery, was successfully extubated and later discharged from hospital.

This case report serves to remind emergency doctors and paediatricians that fluvoxamine can have potentially fatal side-effects when taken accidentally in relatively small quantities by children. In adults, overdoses less than 1000 mg are usually benign, although frequently there is little correlation between the plasma concentration of the drug and the clinical presentation [2]. Due to the long elimination $t_{1/2}$ patients suspected of taking a significant overdose should undergo standard cardiovascular monitoring for at least 48 h. Hypoventilation, hypotension and seizures require specific supportive treatment. Gastric lavage with activated charcoal may be usefully undertaken up to 24 h after ingestion. There is no specific antidote and extra-corporeal elimination methods are likely to be ineffective due to the large volume of distribution of the active drug [2].

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Nontraumatic seizure-associated bilateral fractures of the head of the humerus

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Sir: Status epilepticus is a life-threatening condition often requiring orotracheal intubation and pharmacological sedation. In the emergency situation, detailed examination of the patient is not possible. We report on a patient with convulsive status requiring intubation and sedation. After pharmacological interruption and extubation, nontraumatic seizure-associated bilateral fractures of the heads of the humeri were diagnosed.

A 59-year-old woman experienced a progressive status epilepticus, initially presenting aphasic symptoms and clonic movements of the right facial and upper limb muscles. This condition occurred in bed in the morning. Because two similar self-limiting seizures had occurred 1 month and 6 months earlier, treatment was not called for. After a short cessation, repeated seizures occurred, finally generalizing to grand mal status epilepticus. The emergency doctor found the patient unconscious with tonic-clonic limb movements, severe cyanosis, a bleeding tongue and persistent impairment of oxygen saturation. Orotracheal intubation was perfomed and treatment with midazolam and fentanyl initiated. On admission, the patient was intubated and mechanically ventilated. The neurological examination was normal. Computed tomography revealed a left supratentorial lacunar lesion due to a former lacunar stroke. Laboratory findings including cerebral spinal fluid were normal despite elevated creatine kinase (CK) (496 U/l; normal < 80 U/l; normal CK-MB and CK-BB) and slight leucocytosis (10 700/mm^3; normal < 8000/mm^3). The patient was not taking any drugs. Despite arterial hypertension, no underlying diseases – particularly of the bone – were known.

After diagnosing secondary generalized grand mal status epilepticus, antiepileptic treatment with valproic acid was initiated, the analgosedation reduced stepwise and the patient extubated. One day later, the patient reported pain at endpoint elevation of both arms. X-rays of both shoulders re-

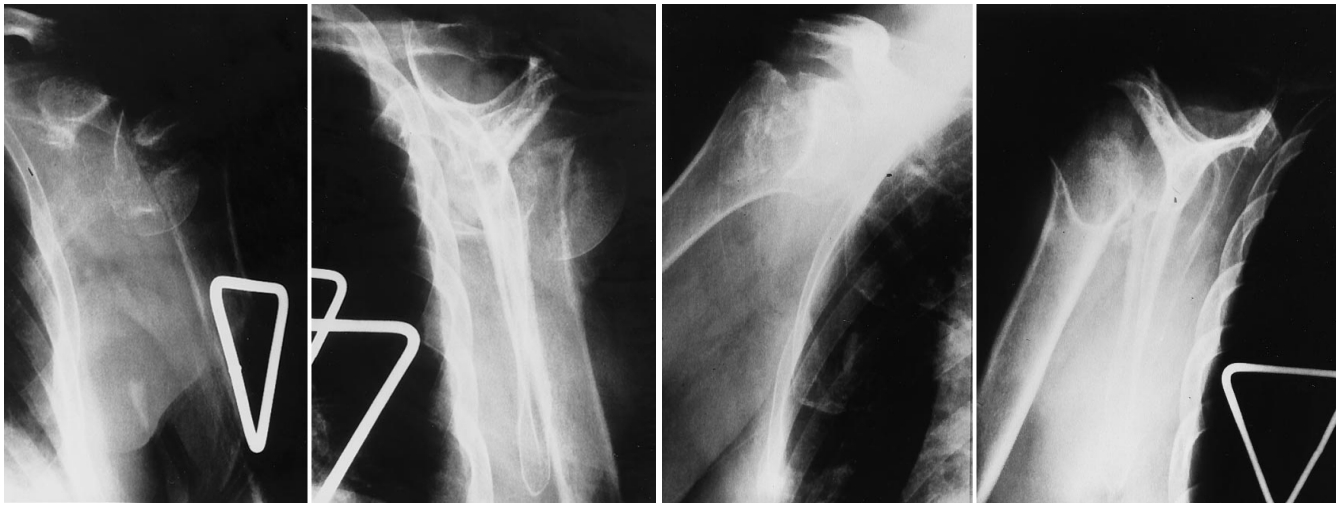

Fig. 1 X-rays of both shoulders demonstrating fractures and dislocation of the right (*right*) and the left (*left*) humerus

vealed posterior luxated fractures of the heads of the humeri (Fig. 1). The right fracture was reposed unsuccessfully and finally treated surgically. The left fracture was reposed and treated conservatively. The postoperative course was unremarkable and healing sufficient. Under treatment with valproic acid, the patient has been seizure-free for 6 months.

Our patient met the criteria of status epilepticus. The cyanosis, loss of consciousness and diminished protective reflexes presented made orotracheal intubation and the administration of sedative agents necessary to interrupt the status. In this situation and later during the first period in the intensive care unit, no abnormal limb configuration which would have suggested bone fractures was detectable. Retrospectively, primary care and transport were unremarkable, suggesting that the fractures did not occur as a result of manipulation or luxation.

It is estimated that 1.1 % of the patients admitted to the hospital with epileptic seizures reveal bone fractures, mostly, however, as a consequence of direct trauma during the seizure [1]. Most often, vertebral compression fractures occur [2], but nearly all types of fractures have been seen [3–8]. In these patients, an underlying bone disease, such as osteoporosis, osteomalacia, metastatic lesions, alcoholism or antiepileptic drug-associated metabolic bone disorder has usually contributed to the fracture.

The case history of our patient is interesting for three reasons. First, no risk factors for pathological bone fractures were present and direct trauma was not probable because the attack occurred while the patient was still in bed. It must be assumed that, during the tonic clonic seizure, a muscle contraction occurred which was violent enough to fracture the bone. Pathomechanically, it is speculated that during the seizure the humerus is adducted, rotated inward and bent while the muscles of the shoulder pull on the head of the humerus [8]. Second, signs and symptoms of bone fractures were initially absent and were detected later when the patient was extubated and reported pain during extreme joint movements. Third, seizure-associated bone fractures typically occur in patients with severe and frequent seizures [9]. Our patient, however, had had only two seizures previously, the fractures occurring during the third.

In conclusion, fractures of the bone following seizures are uncommon but may have serious consequences if not recognized. The simple ability to move the upper limbs does not rule out fracture. In contrast, the presence of pain at extreme upper limb elevation suggests shoulder pathology and should prompt X-rays to rule out or to confirm bone fracture as observed in our patient.

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