Drop attacks in the elderly: effect of pyridostigmine

Sir,

Elderly people are prone to sudden unexplained falls, usually categorized as 'drop attacks', a definition excluding those in whom the falls are accompanied or preceded by changes in the level of consciousness or by vertigo.[1,2] The event is unpredictable and hence potentially dangerous, and constitutes the major type of home accident amongst people over the age of 65.[3] The basic abnormality to which the falls may be attributable has not so far been clarified, but is not usually considered to be connected with the frequent cardiac or cerebral vasculopathy common in the age group.[2]

An approach to the question of the underlying pathophysiology of the disorder was put forward by Weiner *et al.*[4] who found postural reflex impairment in 44% (severe) and 24% (moderate) of 34 such patients. The possibility of the immediate cause of the fall being a failure to generate tension in the quadriceps muscles sufficiently quickly to maintain erect posture has also been mooted.[5] This concept of a causal momentary failure in the peripheral neuromuscular circuit is somewhat reminiscent of the familiar clinical sign in spastic paraparesis characterized by sudden collapse of muscle resistance to passive stretching.

Preventive treatment has so far been limited to various means of special attention to daily care of susceptible individuals[3,6] with medication limited to that required for coexistent disorders (success has recently been reported[7] following treatment of hypothyroidism). The concept referred to above of impaired maintenance of quadriceps tension, prompted a trial of the anti-cholinesterase pyridostigmine, as a possible means of somehow aiding maintenance of the neuromuscular contraction mechanism.

This agent has been prescribed in six individuals (three men, three women) aged 65–73 with typical drop attacks as defined, occurring several times a month. Two patients suffered from moderate hypertension; at the onset of therapy none had any abnormal neurological findings, but one female followed for 2 years subsequently developed signs and symptoms compatible with multiple system atrophy. In this patient, the two other females and one male, drop attacks ceased with onset of therapy. The male patient agreed to suspend medication in advance of electromyography studies for possible myasthenia gravis (which were negative); attacks returned 2 weeks later and ceased once more on resumption of treatment. Two females refused to stop therapy. All patients were started and kept on a dosage of 60 mg pyridostigmine twice daily and none of them reported any undesirable side effects on this regime. In those responding favourably, benefit resulted from the onset of treatment and was subsequently maintained, the longest period being 4 years to date.

This limited series may not justify conclusions at present, but I believe the drug to be worth trying in patients whose falls cannot be attributed to any clear aetiological causation.

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Splenic abscess due to *Eikenella corrodens*

Sir,

Eikenella corrodens is a slow-growing, aerobic and facultatively anaerobic Gram-negative rod, which is a normal inhabitant of the human oral cavity, and upper respiratory and gastrointestinal tracts.[1] The diseases associated with this organism range from periodontitis and human wound infections to more serious infections.[2] This report describes our experience of a splenic abscess caused by *E. corrodens.*

A 40 year old man with history of antrectomy with Billroth II anastomosis was admitted because of fever, chills and left-sided lower thoracic pain for 5 days. The patient was febrile. His breath sound on auscultation at the right base was diminished and there was a tenderness on deep pressure in the left costovertebral area. Laboratory data revealed a leucocyte count of 12.6×10^9/l with 77% neutrophils. Chest, X-ray showed elevation of the left hemidiaphragm and a left-sided pleural effusion. Antibiotic therapy with erythromycin was administered. After 6 days of treatment, ultrasonographic examination of the abdomen revealed an enlarged spleen and perisplenic fluid collection, which was confirmed with computed tomography as a subcapsular spleen abscess. After that, the patient was treated with radiologically guided percutaneous drainage and clindamycin (2.4 g/day) plus gentamicin (240 mg/day), and he became afebrile in 24 hours. Seventy-two hours later, the antibiotic therapy was switched to ampicillin (12 g/day) because the culture of purulent material yielded *E. corrodens.* The results of blood cultures remained negative. The therapy was prolonged for 10 days and amoxycillin orally was continued until 25 days of therapy were completed.

Splenic abscesses are unusual; the incidence is between 0.2–0.7% in a population-based autopsy study.[3] The most common organisms are Gram-positive cocci, anaerobes, aerobic Gram-negative rods and *Candida* spp.[3] To our knowledge *E.corrodens* as a causative agent of splenic abscess has been reported only once before.[4] In the case presented here, the microorganism might have reached the spleen by either haematogenous dissemination from oral cavity some weeks or months after the surgery into the subcapsular blood collection caused by operation, or spread from stomach to traumatic haematoma via the splenic vein or direct extension in the surgery.

The treatment of spleen abscess consists of appropriate systemic antibiotic and removal of pus by percutaneous catheter, splenotomy or splenectomy.[3,5] *E. corrodens* is usually susceptible to a broad-spectrum antibiotic such as ampicillin, cephalosporins, fluoroquinolones and thienamycins.[1,2,4] Finally, we choose radiographically guided percutaneous drainage for two reasons: the peripheral location of the abscess, which was easy to puncture for confirmation and placement of a drainage catheter, and is a successful procedure with very high cure rate and very low rate of complications (over 80% and less than 5%, respectively.[3,5]

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Acute serum lipid changes in a renal transplant recipient on intravenous cyclosporin upon administration of an intravenous lipid solution

Sir,

We wish to report an acute increase in serum lipids on the administration of intralipid in a renal transplant recipient on intravenous cyclosporin and steroids. A 53 year old male developed perforated diverticular abscess 3 months after a renal transplantation. He underwent a Hartmann's procedure. This was complicated by a paralytic ileus and parenteral nutrition was initiated to establish nutritional support. He was commenced on a peripheral regimen of Vitrimix (Kabi Pharmacia) consisting of 500 ml of 20% Intralipid (fractionated soybean oil 100 g, egg-yolk phospholipids 12 g, glycerol 22.5 mg/l), and 1,600 ml of 0.9% glucose. Within 24 hours, his blood sample was turbid in nature and his serum total cholesterol concentration rose from 5.2 mmol/l to 10.0 mmol/l, and serum triglyceride concentration rose from 4.2 mmol/l to 15.1 mmol/l concurrently. His serum lipid abnormality persisted and the Vitrimix was discontinued after 48 hours. He was then commenced on an alternative parenteral nutrition formulation consisting of 500 ml of 20% intralipid, 500 ml of 50% glucose and 1,000 ml of Vamin administered through a central vein. His lipid levels still remained moderately elevated with the serum appearance, however, becoming less turbid. Clinically, on day 4 he had become confused and on examination was generally hypotonic. On day 9 he developed recurrent grand mal seizures and his clinical condition deteriorated. He remained drowsy but responsive to verbal command, he suffered a fatal cardiac arrest on day 10.

Similar changes were reported in a renal transplant patient on intravenous methylprednisolone and intravenous cyclosporin, when on administration of propofol 10 mg/ml dissolved in Intralipid (fractionated soybean oil 100 g, egg-yolk phospholipids 12 g, glycerol 22.5 g in 1,000 ml water),[1] the patient's serum triglyceride rose from 3.16 to 6.01 mmol/l and cholesterol from 3.63 to 5.75 mmol/l.

Both cases had similar acute changes in serum cholesterol and triglyceride upon infusion of intralipid-based solutions concurrently with cyclosporin. However, while the patient in de Klippel's report had a sudden increase in his whole blood cyclosporin concentrations (250–997 ng/ml), in our patient his whole blood cyclosporin concentrations were within the range of 300–600 ng/ml and no sudden increase was demonstrated. This difference between the two patients may be spurious as de Klippel's patient had his whole blood cyclosporin concentrations measured using a non-specific assay, while we used a specific EMIT method. It is well established that metabolites of cyclosporin interfere with the measurement of cyclosporin in the non-specific assays, and it is recommended that the parent drug whole blood assay is preferred.[2]

Cyclosporin is lipophilic and 40% is taken up by erythrocytes and most of the rest is bound to lipoproteins with high (HDL) and low density lipoproteins (LDL), and very little binds to very low density lipoproteins (VLDL). The infusion of intralipid produces a sudden increase in VLDL, and fall in HDL and LDL, resulting in a rise in unbound cyclosporin concentration.[3] This unbound cyclosporin is postulated by de Klippel to have produced a cyclosporin-induced encephalopathy in his patient. Although our patient had some neurological symptoms similar to the described case, we were unable to perform a magnetic resonance imaging (MRI) scan and therefore unable to demontrate white matter changes on MRI of leukoencephalopathy. However, the common feature in both these cases is that they developed an acute mixed hyperlipidaemia on the administration of an intralipid solution whilst on cyclosporin.

We conclude that an interaction exists, which severely disrupted the patient's lipid metabolism. The altered neurological state observed was possibly mediated by abnormal distribution, and binding of cyclosporin and its metabolites. Until this interaction is fully understood, we believe that intralipid-containing solutions are best administered with caution in renal transplant recipients on intravenous cyclosporin.

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