SIDE EFFECTS OF DRUGS

Vertical gaze palsy in barbiturate intoxication

Paralysis of conjugate gaze is not a well-recognised sign of barbiturate intoxication in the conscious patient.[1 2] We describe here the occurrence of a vertical gaze palsy in a patient intoxicated with a medium-acting barbiturate.

Case report

A 28-year-old Australian woman (75·5 kg) presented with a four-day history of right frontal headache, drowsiness, photophobia, ataxia, anorexia, and vomiting. She denied ingestion of drugs, other than prednisone (5 mg/day) and theophyllin when required for her asthma, and there was no history of drug intoxication. There was no family history of adverse drug effects. She was afebrile and the general examination showed nothing abnormal. There was mild neck stiffness. She was drowsy and mildly dysarthric but could co-operate fully with the examination. There was mild engorgement of retinal veins in the right eye. Pupil size and reaction were normal. Horizontal gaze was full with bilateral fine gaze-evoked nystagmus in the supine position, which was unsustained when she sat up. Convergence was absent. Conjugate upward gaze was completely absent and no upward movement of the eyes occurred on forceful eye closure or with the oculocephalic manoeuvre. Downward gaze was full. The remainder of the examination showed nothing abnormal apart from generalised depression of deep tendon reflexes and mild ataxia of gait.

Investigations showed a normal blood picture, serum electrolytes, liver function tests, skull, and chest *x*-rays. The electroencephalogram showed widespread theta activity, which was more prominent in the right fronto-temporal region, with only a mild excess of beta activity. A brain scan of the cranium with an EMI scanner showed possible early ventricular dilatation and a possible right temporal lobe abnormality. Carotid and vertebral angiograms were normal. A lumbar puncture showed normal pressure and cerebrospinal fluid content. The serum butobarbitone concentration was 80 μmol/l (1·7 mg/100 ml) on the second day in hospital. Other barbiturates, bromide, and phenothiazines were not detected.

The patient subsequently admitted taking up to 60 butobarbitone (Butisol Sodium) tablets (100 mg) for her headaches in the three days before admission to hospital. No treatment was started, and on the fifth day she was alert, ocular movements were completely normal, and she was no longer ataxic. The serum butobarbitone level had fallen to 10 μmol/l (0·21 mg/100 ml).

Comment

Paralysis of upward gaze is usually regarded as a sign of midbrain tectal dysfunction and results most commonly from intrinsic or extrinsic structural lesions in the upper brain-stem region.[2] It may also be a manifestation of raised intracranial pressure or hydrocephalus.[2] Initial investigations in the present case were directed towards excluding an inflammatory or space-occupying lesion, and consideration of a possible drug intoxication was delayed because of the denial of drug ingestion and the finding of the vertical gaze palsy. The relatively high level of butobarbitone in the blood, and subsequent clearing of the abnormal eye signs within days of withdrawal of barbiturates confirmed their causal role.

The effects of barbiturates on the ocular motor system are well-documented. Cogwheel irregularities of pursuit movements may occur even in therapeutic doses, whereas saccadic movements are much more refractory to barbiturate intoxication.[3 4] Convergence is often impaired early.[4] A rapid low-amplitude vertical or horizontal gaze-evoked nystagmus then appears, which, when horizontal, may be greater in the abducting eye. A sustained horizontal positionally-induced nystagmus unaccompanied by vertigo may also occur. As intoxication proceeds towards narcosis, optokinetic nystagmus disappears, and the fast phase of induced vestibular nystagmus is eliminated.[2] Finally, when the patient is in deep coma, all ocular responses to caloric stimulation may be absent.[5]

The present case indicates that conjugate vertical gaze palsy may be present as an additional eye sign in the conscious barbiturate-intoxicated patient. The recognition of this fact is of some practical importance as it may avoid unnecessary neuroradiological investigation in such patients.

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[3] Rashbass, G, and Russell, G F M, *Brain*, 1961, **84**, 329.
[4] Bach-Y-Rita, P, and Collins, C C, *Control of Eye Movements*, p 478. New York, Academic Press, 1971.
[5] Blegvad, B, *Archives of Otolaryngology*, 1962, **75**, 506.

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Allergy to diazepam

There have so far been no reports of anaphylactic reactions to diazepam. This report describes a patient who suffered such a reaction.

Case report

A 28-year-old Swedish housewife, weighing 55 kg, was admitted for suspected cancer of the cervix. She gave a history of being allergic to peaches, raw onions, flowers, cats, nuts, dust, wool, and drugs including chlordiazepoxide, sorbitol, and clorazepate dipotassium. Allergic attacks had consisted of difficulty in swallowing due to swelling of the throat, swollen lips, and urticaria. There was no family history of allergy.

Treatment—She received an injection of Stesolid, which is a diazepam preparation manufactured by Dumex. It was injected intramuscularly and the dosage was 10 mg. This is the usual premedication prescribed for the gynaecological cases here. She took no other drugs at the time.

Adverse effect—Within two minutes after the intramuscular injection she complained of tingling in her fingers and toes. The whole buttock became covered in macular exanthema. Cramps in arms and legs rapidly intervened and the patient lost consciousness. No blood pressure was measurable, but the electrocardiogram showed sinus tachycardia. Cortisone and ephedrine injections with oxygen administration gradually restored normal vital signs. Consciousness returned after one and a half hours. The erythema turned into urticarial weals, which gradually faded over several hours.

Comment

Hypersensitivity reactions to the benzodiazepine derivatives have not been reported, although the drugs are known to be tissue irritants as well as having histamine-releasing properties. It would be interesting to measure their effect on cyclic adenosine monophosphatase phosphodiesterase and their anaphylactic release of histamine in sensitive patients. It is unthinkable that these drugs, which are probably the most commonly prescribed drugs today, are free from anaphylactic reactions, as we are led to believe from current reports.

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