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Acute transient cerebral intoxication induced by low doses of baclofen

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We report a case of acute transient encephalopathy with confusion, drowsiness, myoclonic jerks, periodic triphasic sharp wave EEG patterns induced by low doses of baclofen. We discuss the pathogenesis and the differential diagnosis from the subacute spongiform encephalopathy of sudden onset.

Key Words: Baclofen — Lioresal — cerebral intoxication — periodic sharp wave EEG pattern

Introduction

Baclofen, a gamma-aminobutyric acid derivative, drug chosen for the treatment of spasticity [7, 9] is also used with limited success for conditions such as trigeminal neuralgia [5], stiff-man syndrome [2], Huntington disease [3]. Sedation, confusion and stupor have been reported in elderly persons with cerebrovascular diseases [8[.
An acute encephalopathy with unusual clinical and electroencephalographic findings caused by low doses of baclofen have very rarely been reported [1, 6].
We describe a patient who experienced an acute encephalopathy associated with a periodic sharp wave electroencephalographic patterns 48 h after starting treatment with 30 mg of baclofen per day.

Case report

A 72-year-old man was hospitalized because of spastic tetraparesis caused by traumatic myelopathy occurring eleven years previously.
48 h after starting treatment with 10 mg of baclofen 3 times daily, the patient became disoriented, confused, drowsy. Myoclonic jerks appeared in his arms and legs. A CT-scan was normal; brainstem auditory evoked responses (BAER) and somatosensory evoked potentials (SEP) were normal too. Study of the cerebrospinal fluid sample revealed no abnormalities. The values for blood glucose, urea, creatinine, ammonia, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, lactic dehydrogenase, alkaline phosphatase, bilirubin levels and electrolytes were all within the normal limits. Electroencephalographic (EEG) tracings showed periodic triphasic sharp wave discharges (Fig.1). EEG abnormalities were not modified by sensory, visual or acoustic stimulation. EEG recording during sleep was not performed. 24 h after baclofen discontinuation the EEG abnormalities improved. 72 h after the patient was alert and oriented, the myoclonic jerks disappeared completely and the EEG changes disappeared too (Fig. 2).

Discussion

In the case described the absence of coexisting brain lesions, the normal CT-scan, BAER, SEP, cerebrospinal fluid findings, the absence of any metabolic disturbances (notably hepatic or renal), the acute onset and rapid resolution of clinical and EEG abnormalities after discontinuing the drug suggest a direct cerebral toxic effect of baclofen.
The acute encephalopathy with confusion, drowsiness, myoclonic jerks, periodic sharp wave EEG pattern, is a very infrequent condition and

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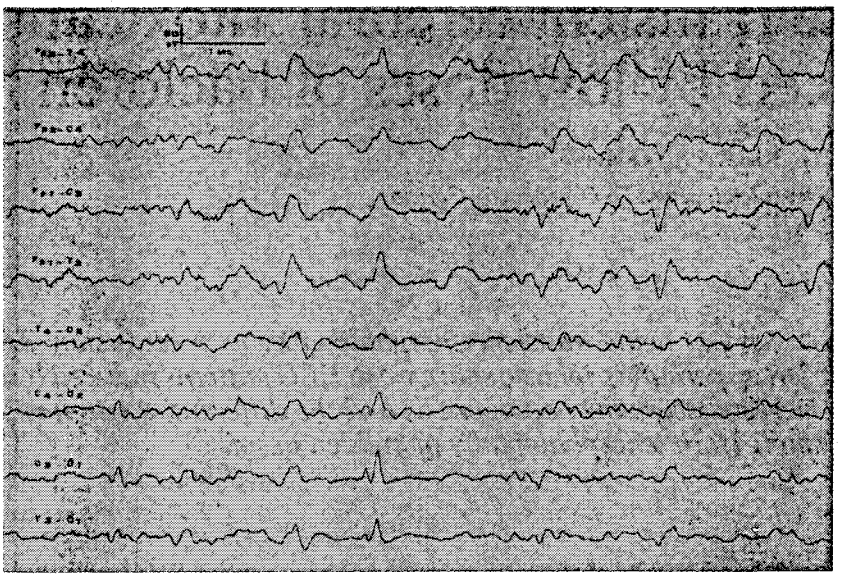
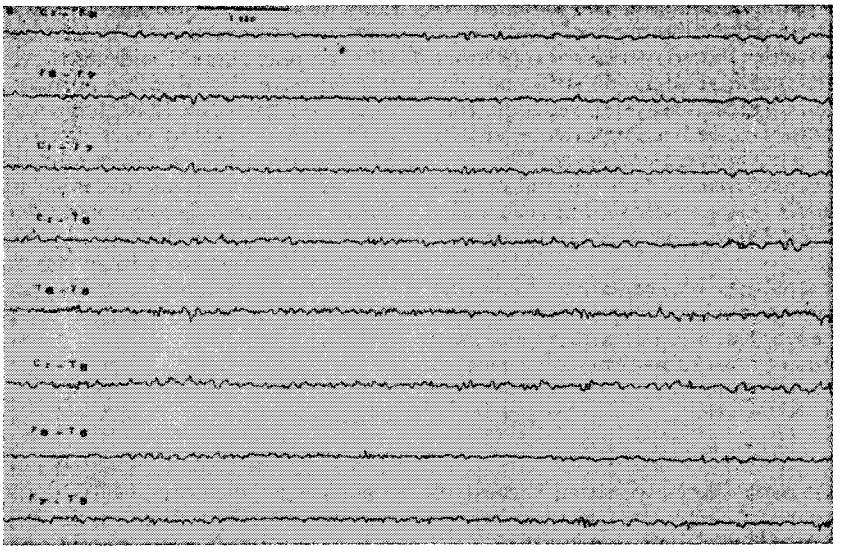


Fig. 1. *Periodic sharp wave discharges 48 h after the start of the treatment with baclofen*

Fig. 2. *Disappearance of the EEG changes 72 h after baclofen discontinuation.*



may masquerade as subacute spongiform encephalopathy (Creutzfeldt-Jakob disease) of sudden onset [1, 6]. The prognosis of this acute cerebral intoxication induced by baclofen is excellent after discontinuation of the drug, if it is recognized early.

However, when the dosage of the baclofen is high [10, 11] the clinical picture and the EEG findings

are those of a deep metabolic coma: the history very often suggests the diagnosis.
Baclofen is a gamma-aminobutyric acid (GABA) which incorporates a para-chlorophenyl radical in the beta position. Its half-life is approximately 3½ hours. After a single dose more than 85% of the drug is excreted unchanged by the kidney. The toxic dosage is near the therapeutic dosage in humans (1.2 mg/kg/day).
Baclofen acts as an agonist at the presynaptic receptor of the GABA-B (bicuculline-insensitive). Causing neuronal hyperpolarization and decreasing the release of neurotransmitters (catecholamines, glutamate, substance P) the drug has an inhibitory effect on the central nervous system [4].
It is not however clear which of these neurotransmitters has an important role in the pathogenesis of this encephalopathy and related EEG patterns. Moreover, it is not clear why low doses of baclofen cause this type of encephalopathy only in very few persons.

Sommario

Gli Autori descrivono il caso di un paziente con un'acuta transitoria encefalopatia caratterizzata da sonnolenza, confusione mentale, mioclonie, onde trifasiche periodiche allo EEG, indotta da basse dosi di baclofen. Viene discussa la patogenesi e la diagnosi differenziale verso l'encefalopatia subacuta spongiforme ad esordio improvviso

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