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Baclofen-induced Frontal Lobe Syndrome: Case Report

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Summary

An 81-year-old man with cervical spondylotic myelopathy developed an acute frontal lobe like syndrome with prominent perseveration and an abnormal electroencephalogram after being given seven doses (70 mg) of baclofen for spasticity. The clinical symptoms cleared up in 72 hours after the medication was discontinued.
Key words: *Baclofen; Cervical spondylotic myelopathy; Spasticity; Confusional state.*

Baclofen, an analogue of aminobutyric acid, has been used for the treatment of spasticity in patients with spinal cord lesions (Sachais *et al.*, 1977; Young and Delwaide 1981). It appears to act primarily at the spinal cord level, but in large doses may also act at supraspinal sites. Transient drowsiness is the most common neurological side effect with therapeutic doses of this drug. We report here a patient who developed an acute frontal lobe syndrome with prominent perseverative behaviour after being treated with relative low doses (10 mg t.i.d.) of baclofen.

Case History

An 81-year-old man was admitted in July 1989 for progressive weakness and numbness of both upper and lower extremities for one and a half years. He had no history of psychiatric diseases. Neurological examination revealed marked spasticity and weakness of both arms (grade 3) and legs (grade 3 on the right and grade 2 on the left), with a sensory level at T3. His mentality was normal. A cervical myelogram with computed tomography (CT scan) showed cervical spondylosis with severe spinal stenosis and disc herniation at the C5–6 level. He then had a total laminectomy from C3 to T1, with slight improvement of muscle strength,

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especially fine movements of both hands. Three weeks later, he was given baclofen 10 mg t.i.d. for spasticity. After 7 doses of this drug he became confused, with periods of agitation, and disorientation for time, place and persons. Although he was awake, alert and articulated, he had mild paraphasia. The most striking features were his euphoric mood and prominent perseverative behaviour. His legs became flaccid and paraplegic, but the strength of both arms remained unchanged. His electrolytes, blood sugar, liver and renal functions were all within normal limits. A CT scan of the brain with contrast on the same day was normal. On the following day, a ^{99m}Tc hexamethyl-propyleneamine oxime (HMPAO) and single photon emission tomography (SPET) of brain was normal. Electroencephalographic (EEG) tracings showed bilateral frontal intermittent rhythmic delta activity and diffuse background slowing of theta and delta activity. Notably an EEG tracing 9 months previously showed only mild background slowing. Baclofen was discontinued. His mentality gradually returned to normal within 72 hours, and the strength of both legs also returned to baseline. Two days later, he was restarted on a smaller dose of baclofen 5 mg t.i.d. for 1 week, and then 10 mg t.i.d. for the following 3 weeks without the side effects of acute mental confusion. Repeated EEG 3 months later revealed only mild background slowing.

Discussion

The pharmacokinetics and metabolism of baclofen have been previously investigated (Faigle and Keberle, 1972; Knuttson, Lindblom and Martensson, 1974). Baclofen is absorbed well by the gastrointestinal tract and reaches peak blood level within 2 to 3 hours, with a half-life about 3·5 hours. Baclofen mainly undergoes renal excretion with only 15% being metabolised by the liver. With therapeutic doses of baclofen, the side effects of transient drowsiness and other mental symptoms, including hallucinations, euphoria, mental excitation, depression, confusion or anxiety, occur most commonly in patients with a history of psychiatric or some other brain disorder; also in geriatric patients (White 1985; Yassa and Iskandar, 1988). Transient EEG abnormalities due to baclofen, such as bursts of triphasic waves (Abarbanel *et al.*, 1985) and periodic sharp waves (Hormes *et al.*, 1988), have been reported.

Our 81-year-old patient was certainly at risk from developing side effects of the central nervous system even with therapeutic doses. However, the unusual feature in our patient was the frontal lobe like syndrome with striking perserverative behaviour, and the flaccid paraplegia and bilateral frontal intermittent rhythmic delta activity on EEG tracing further supported the presence of a bifrontal lesion. These prompted an examination of the brain by CT and by a HMPAO SPET scan, which were normal. Confusion, disorientation and perseveration may be associated with several metabolic disturbances. There were no metabolic disturbances in our patient to account for the syndrome. Rapid resolution of the neurological changes and later the EEG changes, confirmed our diagnosis.

Baclofen acts as an agonist at the presynaptic aminobutyric acid (GABA) receptor, and it causes neuronal hyperpolarisation and decreases the release of neurotransmitters such as glutamate, catecholamines, and substance P (Bowery *et al.*, 1980). Regarding glutamate decarboxylase activity, an index of GABAergic innervation, its enzymatic activity is noticeably high in the prefontal, orbitofrontal

and temporal pole cortex (Javoy-Agid *et al.*, 1989). Although the pathogenesis of the baclofen-induced frontal lobe syndrome is unknown, it is possible that the inhibitory effect of baclofen on the GABA receptor-rich frontal lobes may have caused the frontal lobe symptoms.

Baclofen is probably the safest and most effective agent currently available for the treatment of spasticity, but our experience demonstrates that a frontal lobe like syndrome may develop in the elderly with therapeutic doses. We emphasise that baclofen should be started with a smaller dose in the elderly to allow for physiological accommodation to the drug.

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