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ORIGINAL COMMUNICATION

Parkinsonism following bilateral hypoxic-ischemic lesions of the striatum

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Abstract A 40-year-old white male received cardio-pulmonary resuscitation after cardiac arrest due to an epileptic status. Four months after the incident he developed an akinetic-rigid syndrome and a postural tremor more pronounced on the right side of the body. Brain imaging revealed bilateral lesions of the putamen and caudate nucleus. Levodopa improved bradykinesia and muscular rigidity, but not the postural tremor.

Keywords Cerebral hypoxia · Akinetic-rigid syndrome · Movement disorders

Introduction

Parkinsonism due to basal ganglia lesions caused by hypoxic-ischemic brain injury is exceedingly rare [1–3]. In contrast, parkinsonism associated with carbon monoxide or cyanide poisoning and stroke associated parkinsonism (after either an ischemic or hemorrhagic lesion) is much more frequent [4]. Parkinsonism is most commonly caused by lesions of the lenticular nucleus [4], or, in case tremor is a dominant clinical feature, by lesions of the thalamus [5]. Parkinsonism after striatal lesions (involving both the putamen and caudate nucleus) has only scarcely been described [3, 4]. Here we report a case of akinetic-rigid parkinsonism developing 4 months following bilateral hypoxic-ischemic lesions of the striatum.

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Case report

A 40-year-old white male with a 6 year history of temporal lobe epilepsy with complex focal seizures suffered an epileptic status causing cardiac arrest. He received 15 min of preclinical non-professional cardio-pulmonary resuscitation until being hospitalized on an acute neurological intensive care unit. At age 34 years he had developed right temporal lobe epilepsy. Diagnostic work-up at this time revealed limbic encephalitis of the right mesial temporal lobe associated with anti-Ma2-antibodies due to an embryonic carcinoma of the right testis. After right-sided orchiectomy and right-sided hippocampectomy he was set on antiepileptic treatment with levetiracetam and lamitrigine and his epilepsy was stable for the following 6 years. Two weeks prior to the epileptic status leading to cardiac arrest, he experienced several non-convulsive temporal lobe seizures.

At the day of admission to the acute intensive care unit an endotracheal intubation became necessary and he received assisted ventilation over a 4 week period. His clinical course was complicated by ventilator-associated pneumonia with *Escherichia coli* and *Klebsiella pneumonia* species and intensive care unit-acquired weakness. Four weeks after admission to the acute neurological intensive care unit he was transferred to our neurological intensive care unit for rehabilitation.

On admission to our hospital, he was under antiepileptic treatment with levetiracetam (3,000 mg per day), lacosamide (200 mg per day) and lamotrigine (300 mg per day). He was under assisted ventilation via a tracheal canula. He

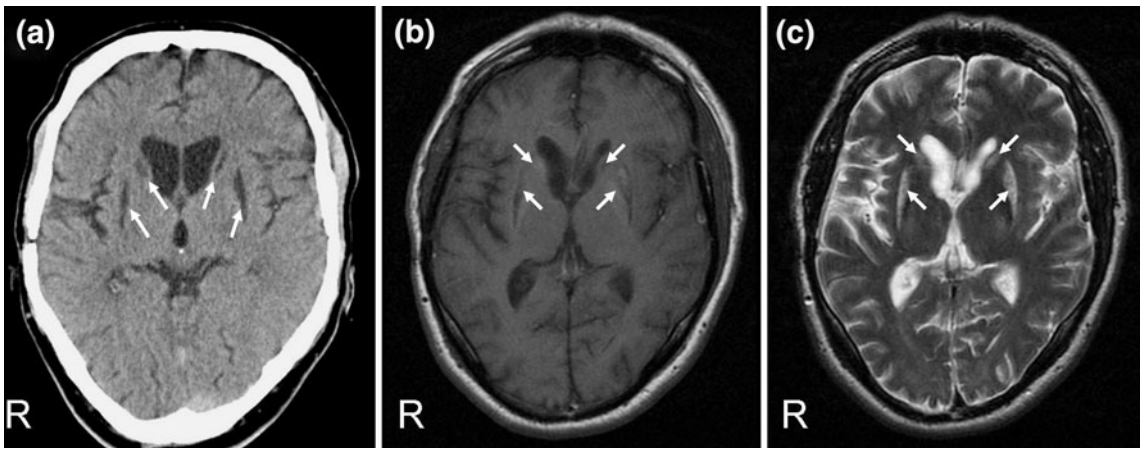

Fig. 1 Axial computed tomography (**a**), T1-weighted (**b**) and T2-weighted (**c**) magnetic resonance imaging scans at the level of the basal ganglia (*arrows*). Circumscribed lesions of the caudate nucleus and putamen are evident, which are hypodense on computed tomography scans, hypointense on T1-weighted and hyperintense on T2-weighted magnetic resonance imaging scans

was awake, oriented and responded well to verbal instructions. His neurological examination revealed tetraplegia (Medical Research Council score grade 2–3) [6] most prominent at the shoulder and limb girdle, reduced sensation to touch at the distal upper and lower extremities, symmetrical reduction of deep tendon reflexes and mild dysphagia. Electroneurography and electromyography confirmed the diagnosis of critical illness polyneuropathy and myopathy. Assisted ventilation was terminated 2 weeks after admission and the tracheal canula was removed. At this time he was transferred to our intermediate care unit. The tracheostomy was surgically closed and he received intensive physiotherapy, occupational therapy and swallowing therapy over the following 10 weeks. He did not experience any medical problems over this period; in particular, no epileptic seizures occurred. EEG recording showed a continuous generalised slowing without evidence for non convulsive epileptic status and/or cortical myoclonus.

Twelve weeks after admission to our hospital, his weakness had improved markedly. He was able to stand and walk unassisted and performed most activities of daily life with only minor assistance. At this time, however, he developed akinetic-rigid parkinsonism with preponderance of the right hemi-body. He had difficulties in performing fine manual activities, such as using tools or performing crafts with his right more than with his left hand. Neurological examination showed moderate hypomimia, moderate hypophonia with festination of speech, a postural tremor of the right more than the left hand (frequency of 7 Hz, amplitude oscillations of up to 5 cm) and moderate bradykinesia as well as cogwheel muscular rigidity, which were most pronounced at the right side of the body. Froment manoeuvre deteriorated rigidity. Myoclonus was not evident on clinical examination, electroencephalography or electromyography. Primitive reflexes (glabella reflex, grasping reflex and palmo-mental reflex) were absent. The motor part of the Unified Parkinson's Disease Rating Scale (items 18–32) [7] was 25 points. At this time, computed tomography and magnetic resonance imaging (before and after intravenous administration of gadolinium-DTPA) scans of the brain revealed bilateral lesions of the caudate nucleus and putamen (see Fig. 1). Control EEG recordings showed slight improvement of continuous generalized slowing.

A course of levodopa (300 mg per day, three daily doses, in combination with 25 mg of carbidopa and 200 mg of entacapone) was initiated. On neurological examination 2 weeks after initiation of levodopa treatment, hypomimia, hypophonia, speech festination, bradykinesia and muscular rigidity were markedly improved. The motor part of the Unified Parkinson's Disease Rating Scale (items 18–32) was 18 points at this time. The postural tremor of the upper limbs improved only mildly. The addition of gabapentin (600 mg per day, three daily doses) caused a significant improvement of the upper-limb postural tremor. Three months after initiation of levodopa his akinetic-rigid syndrome was stable and the motor part of the Unified Parkinson's Disease Rating Scale (items 18–32) was 18 points. Also, the postural tremor remained stable and he was independent in all activities of daily living.

Discussion

Movement disorders following hypoxic-ischemic brain injury are estimated to occur in up to 40% of affected individuals [8, 9]. Myoclonus is definitely the most

common movement disorder after hypoxic-ischemic brain injury accounting for up to 30% [8]. Although the basal ganglia are thought to be especially vulnerable to hypoxia, probably mediated through excitatory amino acid glutamate and N-methyl-D-aspartate-receptors [9], parkinsonism following ischemic-hypoxic brain injury is rare. Lesions of the putamen appear to be associated with dystonia, while lesions of the globus pallidum cause an akinetic-rigid syndrome [9]. Parkinsonism caused by striatal lesions has only occasionally been described [2, 3].

The pathophysiology of movement disorders related to hypoxic-ischemic damage to the basal ganglia is thought to result from inadequate disinhibition of thalamic projections to the motor cortices [8]. I-123-IBZM-SPECT showed a marked loss of striatal D2-receptor binding, while I-123-β-CIT-SPECT (labelling striatal dopamine transporters) was normal, in a case of parkinsonism following hypoxic-ischemic bilateral lesions of the striatum [3]. The degree of postsynaptic loss of striatal D2-receptors should correlate with the amount of clinical improvement following levodopa administration [2, 3, 9, 10]. The fact that the akinetic-rigid syndrome (with the exception of postural tremor) in our patient improved significantly with levodopa implies only an incomplete loss of postsynaptic striatal D2-receptors. Carbon monoxide or cyanide poisoning is a much more common cause of parkinsonism related to striatal lesions [1]. The toxic effects of carbon monoxide poisoning have been attributed to its reduction in the oxygen transport capacity of haemoglobin, mediated by its binding to haemoglobin. Striatal damage is thought to be related to the formation of free radicals and damage to the electron transport chain. The toxic effects of cyanide poisoning are related to interference with the cytochrome oxidase system [11].

A delay in the onset of parkinsonism after hypoxic-ischemic brain injury is common [1, 8, 10]. Following a period of clinical stability, the akinetic-rigid syndrome can also increase in severity and spread to primarily uninvolved body areas [1, 10]. In our patient the akinetic-rigid syndrome developed 4 months after the hypoxic-ischemic brain injury. Why movement disorders after hypoxic-ischemic brain injury typically occur with a latency of weeks to months after the acute incident is unclear. It has been hypothesized that the latency reflects the time required for remyelination, ephaptic transmission, inflammatory changes, synaptic re-organisation, neural degeneration or denervation sensitivity to evolve [10].

In conclusion, akinetic-rigid parkinsonism after hypoxic-ischemic injury to the striatum is rare [12]. The pathophysiology of the syndrome is probably related to lesion-induced plastic changes within the basal ganglia network and the clinical syndrome corresponds to postsynaptic loss of striatal D2-receptor efficiency [10, 12]. Our case illustrates that levodopa may improve rigidity and bradykinesia, but not postural tremor. The efficiency of levodopa may be related to the degree of postsynaptic striatal D2-receptor loss [12].

Conflict of interest None.

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