By the age of 43 the patient noticed progressive gait disturbance—he mentioned diminished arm swing and trouble turning. At the same time, he developed bilateral asymmetrical action tremor (predominantly on the left side) and bradykinesia. He was prescribed levodopa/carbidopa and achieved partial improvement of the tremor and gait. When evaluated at our movement disorders unit, patient was taking levodopa/carbidopa 200/50 mg, half a tablet five times a day. From the beginning he presented with dyskinesias. His Hoehn-Yahr stage was 2, his UPDRS score was 18, and the Schwab and England Activities of Daily Living was 90%. General physical examination was unremarkable. On neurological examination there was moderate bilateral weakness of ankle dorsiflexion (he had an electroneuromyography in 2002 which revealed bilateral L4–S1 radiculopathy and left fibular nerve neuropathy; lumbosacral spine computed tomography showed spinal stenosis at L3–L4; such abnormalities had been attributed to GD), cogwheel rigidity of both upper and lower limbs, mild bilateral kinetic tremor, lower limb dyskinesias, and loss of ankle reflexes. The patient was prescribed pramipexole 0.25 mg three times daily and obtained mild symptomatic improvement.

Comment
Recent reports have emphasised the association between GD and parkinsonism. In 1985 McKeran et al described a 55 year old patient with type 1 GD diagnosed at the age of 17, who developed a parkinsonian syndrome, only initially responsive to levodopa.7 Neudorfer et al reported six patients with GD and parkinsonism.7 Four patients were followed up and a poor response to levodopa was observed. In 1999, Machaczka et al reported another patient with parkinsonism preceding the clinical manifestations of GD by 12 years.7 More recently, Bembi et al described four patients with GD and parkinsonism.7 The age of onset was younger than in classical Parkinson’s disease, but the clinical picture was indistinguishable. Two patients had been diagnosed with type 1 GD at an early age and developed parkinsonism several years afterwards. Enzyme replacement was effective for systemic symptoms, but had no effect on the parkinsonism. The patient we report here developed parkinsonism at a young age (43), like most cases described in published reports. This seems to be a consistent feature of patients with type 1 GD who develop parkinsonism. Another interesting point is that the patient presented with parkinsonian symptoms while receiving enzyme replacement therapy, confirming previous published data about the ineffectiveness of this specific GD treatment for correcting neurological manifestations of the disease. He had bilateral signs from the start and so a substantial response to levodopa therapy, which would not be expected in classical Parkinson’s disease.

The nature of the association between GD and Parkinson’s disease remains to be elucidated. The mechanism involved in the development of parkinsonism in carriers of GBA mutations may be related to protein misfolding. Studies indicate that glucocerebroside accumulation induces apoptosis in cultured neurons and that neurons with high levels of glucocerebroside have a higher sensitivity to agents that lead to cellular death.8

In spite of the association described, most patients with GD never develop parkinsonism, suggesting the involvement of other factors, genetic or environmental, in the disease process. It has been increasingly recognised that parkinsonism may be a clinical feature of type 1 GD and may even precede this diagnosis, so GD must be considered in the differential diagnosis of parkinsonism in subjects with early onset and poor response to levodopa. The basis for this association remains unknown. The treatment of parkinsonism in these cases is similar to classical Parkinson’s disease. However, it is usually less effective. Enzyme replacement therapy is an important advance in controlling the systemic manifestations of GD, but its impact on neurological symptoms is limited.

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References

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BOOK REVIEW
Head injury, pathophysiology and management, second edition

Traumatic brain injury is one of the most difficult and challenging management problems facing clinicians. The last 20 years have seen major advances in the prevention and treatment of head injury, resulting in a substantial decrease in associated mortality. In the 1970s, 50% of patients with severe head injuries died as a result. In the 21st century mortality rates of around 25–30% are commonly reported. There has been a decreasing number in the number of good to moderately disabled survivors as opposed to those left severely disabled or vegetative. This improvement is due to several factors, including better patient retrieval and resuscitation, enhanced emergency facilities and early surgery. However, head injury remains a major health and social problem both for developed and developing nations. Research is increasingly clarifying the underlying physiological mechanisms involved in neurological damage, offering the chance of better methods of diagnosis and treatment. There has been particular interest in the development of neuroprotective agents.

This is a comprehensive and extensively updated guide to the management of severe head injury. It provides a complete management framework for traumatic brain injury and is divided into three sections covering mechanisms of injury, quantification and monitoring, and treatment of the injury. There is detailed coverage of the relevant basic sciences, which then leads on to more clinical aspects with particular emphasis on the rapidly evolving areas of neuromonitoring and neuroprotection.

It is extensively referenced and well-illustrated. The contributors come from a wide range of clinical and scientific disciplines with an international perspective, resulting in a balanced contemporary review of the current knowledge and understanding of head injury. Some of the illustrations suffer from being outdated in style but this is compensated for by a section of colour-plates.

It would be a useful reference addition to the library of neurosurgeons, trauma surgeons and intensivists responsible for the care of head injured patients.

J Grieve