Parkinsonism can be cured

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SUMMARY

This case describes a woman with a history of rheumatoid arthritis with secondary vasculitic skin ulcers, Sicca syndrome and idiopathic Parkinson's disease that was diagnosed by a neurologist in 2005. The patient's parkinsonian symptoms were difficult to control, despite the use of antiparkinsonian medications. During a regular clinical review in 2011, the patient's rheumatologist had prescribed cyclophosphamide infusions to help with the vasculitic skin ulcers. Over the following 2 months, the patient's parkinsonian symptoms completely resolved.

BACKGROUND

This case report will focus on the possible underlying cause for this patient's symptoms and highlight the important lesson of idiopathic Parkinson's disease being a clinical diagnosis, and that further investigations and/or reconsideration of the diagnosis should be considered in patients who present with atypical symptoms, and particular consideration should be taken in patients with underlying connective tissue disease.

CASE PRESENTATION

A 67-year-old woman was reviewed by her rheumatologist in February 2011. She had a background history of seropositive rheumatoid arthritis, Sicca syndrome, hypertension, previous stroke in 2007 and idiopathic Parkinson's disease diagnosed by a neurologist in a different hospital in 2005. Her medications at the time included methotrexate 20 mg weekly, folic acid, arcoxia 90 mg once a day and solpadol (co-codamol). For her Parkinson's disease, the patient was on Stalevo (carbidopa, levodopa and entacapone) 150 mg four times a day, rasagiline 1 mg daily and amantadine 100 mg twice a day. The patient had previously been on dopamine agonists but was stopped secondary to the development of visual hallucinations (although the patient has milder hallucinations on her current medications). Her rheumatologist had been having difficulty with an ulcer on the right shin which had been spreading over the last 6 months. It appeared to be vasculitic in nature (likely rheumatoid vasculitis). The rheumatologist increased her methotrexate dose to 25 mg weekly and introduced 10 mg of prednisolone. He also commenced her on a course of pulsed IV cyclophosphamide. Over the next 2 months, the patient's parkinsonian symptoms had improved substantially, so much so that the patient was able to write her first letter to her daughter in 3 years. She is now able to hold cups, open jars and tins, which she was unable to do before and her speech improved as well.

INVESTIGATIONS

Bloods

Initial autoantibody tests in 2003 revealed rheumatoid factor (RF) level of 91 IU/ml, and negative antinuclear antibody (ANA).

Autoantibody tests revealed (at time of review before commencement of cyclophosphamide therapy) showed RF level of 65 IU/ml, anticyclic citrullinated protein antibody positive and C reactive protein of 18 mg/l, with negative ANA and anti-neutrophil cytoplasmic antibody. Viral hepatitis antibodies (hepatitis A, hepatitis B and hepatitis C) were also negative.

Imaging

In 2007, the patient had an MRI of the brain with MR angiogram (MRA) after presenting with deterioration in speech and mobility. The MRI showed evidence of a focal ischaemia in the left middle cerebellar peduncle. There was also significant scattered small vessel ischaemic change identified throughout the right and left parietal deep white matter regions. MRA at the time did not show any abnormality.

A repeat MRI brain and MRA was performed in August 2011 (about 6 months after start of cyclophosphamide) because of dramatic clinical response of the patient's parkinsonian symptoms. This showed bilateral small chronic infarcts in the inferior cerebellar hemisphere. In comparison with the 2007 scan, the small vessel ischaemic changes were more extensive in cerebral white matter (figure 1) and the MRA revealed a new 2 cm narrowing of the distal left vertebral artery (figure 2). Both the 2007 and 2011 scans did not reveal abnormality in the basal ganglia region.

DIFFERENTIAL DIAGNOSIS

Idiopathic Parkinson's disease—this patient was initially diagnosed and treated as idiopathic Parkinson's disease in 2005 by a neurologist from a different hospital. Her current neurologist had been suspicious that her parkinsonian symptoms were due to causes other than idiopathic Parkinson's disease, even before the use of cyclophosphamide. This is because of the atypical features that were present—frequent falls, myoclonus and hallucinations. The dramatic response to cyclophosphamide and non-recurrence of symptoms despite being off all her Parkinson medications now makes this diagnosis unlikely.

Vasculitis:

- Rheumatoid vasculitis—tend to get a vasculitic neuropathy, as a result of infarction of individual peripheral nerves by vasculitis in the vasa nervorum. Rheumatoid vasculitis affecting the central nervous system (CNS) is rare and may present with seizures, dementia, hemiparesis, cranial nerve palsy, blindness, hemispheric dysfunction, cerebellar ataxia or dysphasia.^{1 2}

To cite: Lobo R, Fraser A, Kiely P, et al. *BMJ Case Reports* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-008057

Figure 1 MRI scan in fluid attenuated inversion recovery in 2007 (left) and 2011 (right) showing focal and confluent T2 high signal change in cerebral white matter, consistent with small vessel disease. When compared with the previous scan in 2007, there is more extensive and confluent T2 white matter abnormality.

- Sjögren's vasculitis—can present with a range of CNS findings, from focal central lesions to dementia. Sjögren's syndrome, may mimic multiple sclerosis and present as a relapsing-remitting or primary progressive neurological dysfunction.³ Movement disorders have been noted by previous authors as a CNS manifestation in primary Sjögren's syndrome.^{4 5}
- Infectious cause of vasculitis—especially important because of the use of immunosuppressants. In particular, there have been increasing reports of CNS vasculitis associated with hepatitis C virus without underlying cryoglobulinaemia.⁶ Again, the dramatic response to cyclophosphamide and negative viral hepatitis screen makes this diagnosis unlikely.

Granulomatous angiitis of the CNS—a form of primary central nervous system vasculitis—this condition presents in a variety of ways, and it is usually suspected in patients with a long history of unexplained diffuse neurological dysfunction or spinal cord dysfunction.⁷ It is not associated with symptoms of systemic vasculitis (eg, the vasculitic skin ulcer seen in this case).⁷

Benign angiopathy of the CNS—also known as reversible cerebral vasoconstriction syndrome—is a disease of preponderance in women that is characterised by reversible multifocal narrowing of the cerebral arteries heralded by sudden, severe (thunderclap) headache, with or without focal neurological deficits. Most importantly, the angiographic findings are reversible (reverts in 4–12 weeks).⁷ Our patient's chronic and indolent progression of symptoms does not fit well with this diagnosis.

Figure 2 MR Angiogram in 2011 demonstrating a mild 2 cm long area of narrowing of the distal left vertebral artery (red circle) which could be the result of the vasculitic process.

OUTCOME AND FOLLOW-UP

Over the progressing months, the patient's parkinsonian symptoms continued to improve and the patient was weaned off her Parkinson medications. Unfortunately, her vasculitic ulcers had not improved, and hence cyclophosphamide was switched to intravenous rituximab in July 2011. As of July 2012, the patient's parkinsonian symptoms had completely resolved and she was not on any Parkinson's disease medications. A repeat MRI scan would have been ideal to assess progression or resolution of the previous MRI findings, but was not performed as it would have been academic and not resulted in any change in management.

DISCUSSION

This was a case of parkinsonian syndrome that mimicked idiopathic Parkinson's disease that was probably caused by presumptive vasculitic cerebral vasculopathy. The previous stroke was probably due to a vasculitic infarct. A comparison of the MRI had shown progression with a new area of stroke within 4 years of each other (unilateral cerebellar area in 2007 and bilaterally in 2011). The MRI also showed progression of white matter ischaemic changes.

Parkinsonism secondary to vasculitis is rare. A search of PubMed at the time of writing of this article revealed five cases—one case secondary to Behcet's disease⁸ two cases secondary to primary Sjögren's syndrome^{9 10} one case secondary to temporal arteritis¹¹ and one case of presumed vasculitis of unknown cause.¹²

Conventional cerebral angiogram was not performed in this case. MRI is better at identifying tissue structures but inferior at outlining cerebral vessels versus conventional cerebral angiogram.¹³ Serial studies have also shown that CNS vasculitis that responded to treatment is more likely to be evident on conventional angiograms than on MRI.¹⁴

We postulate that there was probably vasculitis/vasculopathy affecting basal ganglia (which would have caused the patient's symptoms), even though there was no evidence seen on both MRI scans. There have been demonstrated cases where patients may have vascular narrowing that was sufficiently small but with no infarct, which would give a negative MRI, but a positive cerebral angiogram.^{13 15}

With regard to the use of rituximab, it has been used in neuropsychiatric systemic lupus erythematosus therapy and the results seem promising.⁷ Rapid improvement of CNS-related manifestations, particularly acute confusional state was described in a case report.¹⁶ It would seem that the use of rituximab may also be beneficial in this case.

Learning points

- ▶ Idiopathic Parkinson's disease is a clinical diagnosis—there are false positives.
- ▶ An unusual history that is not consistent with typical idiopathic Parkinson's disease (eg, frequent falls, myoclonus) should prompt further investigation and/or reconsideration of diagnosis.
- ▶ Be wary of patients with connective tissue diseases presenting with neurological symptoms—think of a disease-related cause.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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