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THE ENTITY OF PARKINSONISM AND ASSOCIATED LIPOMATOSIS

The recognition of syndromic associations is important for identifying new disorders. Parkinson disease (PD) is usually a sporadic disorder; however, in approximately 5% of the cases, it can be familial.¹ In some genetic forms of PD, the phenotype may closely resemble sporadic PD; however, in others, the syndrome is more complicated and includes neurologic or systemic features that are unusual for sporadic PD.¹ We describe a new association of parkinsonism clinically resembling PD with multiple lipomatosis.

Methods. The study was approved by the UCLH/ethics committee (06/N076), and informed consent was obtained. Clinical data and investigations of family 1 are given in the Results (see additional cases on the *Neurology*[®] Web site at Neurology.org).

Results. *Family 1.* The index patient (II-5) is a 58-year-old Indian woman who developed a left-sided akinetic-rigid syndrome and severe depression at age 49 years (figure). She started treatment (8 mg/day ropinirole, 300 mg/day levodopa) at age 52 years, which led to significant improvement of her motor symptoms; depression and anxiety showed mild response to treatment with duloxetine and amitriptyline. One year after treatment, she developed “wearing-off,” moderate dyskinesias, and episodes of functional whole-body tremors. Apomorphine injections caused paranoid ideation and delusions of reference and were discontinued. On examination at age 58 years, she had a left more than right hypokinetic-rigid syndrome, with dystonic posturing of the left side (video). She had experienced multiple painless lipomas of the trunk and upper and lower limbs since age 30 years (video). MRI and muscle biopsy results were normal. Skin biopsy of the lipomas revealed benign angiolipomas.

The 68-year-old brother of the index case (patient II-2) developed difficulties using his left foot and depression at age 61 years. He was started on levodopa (300 mg/day) with improvement of his motor symptoms. Some months later, ropinirole (up to 8 mg/day) was added, upon which he developed Pisa syndrome and excessive daytime sleepiness. On examination at age 68 years, he had hypomimia, left more

than right akinetic-rigid syndrome, Pisa syndrome, and camptocormia. He had multiple lipomas in both upper limbs and trunk since age 40 years.

His 43-year-old daughter (patient III-1) developed slowness in her left leg at age 39 years, was diagnosed with PD, and showed excellent response to ropinirole (up to 12 mg/day) but early development of fluctuations. On examination, she had torticollis to the right, asymmetric bilateral bradykinesia and dystonia more on the left upper and lower limbs, depression, and multiple lipomas (video). Formal neuropsychometry showed no cognitive decline. MRI and muscle biopsy had normal results.

Genetic studies. Genetic studies in affected members from family 1 (II-2, II-5, and III-1), as well as other patients (supplementary material), included sequencing of *LRRK2* (G2019S), *SNCA* (Ala30Pro and exonic duplications/deletions), *VPS35* (Asp620Asn), *DCTN1*, *Parkin*, *PINK1*, and *DJI*, common mitochondrial mutations (m.3243A>G, m.8344A>G, m.8993t>G/C), large-scale rearrangements of mtDNA, and *POLG* (p.Ala467Thr, p.Trp748Ser, p.Gly848Ser and sequencing of the gene), and no mutations were found. *NF1* and *PTEN* mutations were excluded.

Discussion. We describe a new association of parkinsonism resembling PD and multiple lipomatosis in familial and sporadic cases and suggest that this may constitute a new entity. The majority of our patients were of Indian origin, implying a higher incidence in this ethnicity. In our cohort, the age at onset varied; parkinsonism was accompanied by early neuropsychiatric features and was levodopa-responsive, with early development of fluctuations and dyskinesias. Moreover, our patients were prone to develop neuropsychiatric side effects early and with low doses of dopaminergic treatment.

We could not identify the cause of this syndrome in our patients; however, one patient who presented with parkinsonism and lipomatosis has been described before,² and this was due to mitochondrial rearrangements; moreover, both parkinsonism³ and multiple lipomatosis⁴ may occur in mitochondrial disorders. However, we did not detect any mitochondrial mutations including *POLG* in our patients, and muscle biopsy had normal results. Moreover, paternal inheritance in both

Supplemental data
at Neurology.org

Figure Family pedigree (family 1)

There are 3 members with levodopa-responsive parkinsonism and multiple lipomatosis.

families would argue against a mitochondrial-encoded genetic defect in these cases.

Autosomal dominant familial multiple lipomatosis (FML) and its subgroup of familial angiolipomatosis are well-described; however, no genes have been identified. Patients have multiple painless subcutaneous lipomas over the torso and limbs, usually noticeable after the third decade of life, as in our patients.^{5,6} Since FML can be confused with hamartoma syndromes like neurofibromatosis and more importantly *PTEN*-related disorders, we excluded known *PTEN* and *NF1* mutations in our patients.

A causal relationship between these patients' parkinsonism and lipomas cannot be directly established. Additional families and genetic tests will be needed to unravel the possible underlying genetic etiologies of this syndrome, which may well be heterogenous.

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BIOPSY-NEGATIVE PET-POSITIVE GIANT-CELL ARTERITIS

Giant-cell arteritis (GCA) is the most common systemic vasculitis of the elderly, with a lifetime risk of 1% in women and 0.5% in men.¹ Failure to identify the early signs of GCA can result in treatment delay, predisposing patients to a number of potentially disabling and life-threatening complications, including anterior ischemic optic neuropathy, stroke, aortic aneurysm, and dissection.² We present a case of biopsy-negative GCA in which PET-CT revealed evidence of extensive large-vessel vasculitis.

Case report. A 64-year-old woman with a history of hypertension and dyslipidemia presented with a 2-month history of occipital headaches, horizontal diplopia, and 10-pound weight loss. Evaluation by her general practitioner, neurologist, and ophthalmologist revealed right temporal artery tenderness and an elevated erythrocyte sedimentation rate (ESR), raising suspicion for GCA. Oral prednisolone was empirically instituted, but then discontinued following a normal right-sided temporal artery biopsy (TAB). At this stage, the patient was reassured that GCA was unlikely. Two weeks later, however, the headache recurred together with new-onset jaw claudication,