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COMMENT & CRITIQUE

A case of early multiple system atrophy unveiled by antidepressant administration

Affective symptoms can be the initial manifestation of Parkinsonism. In some cases, it is difficult to distinguish dull facial expression and psychomotor retardation associated with depression from the masked face and bradykinesia seen in Parkinsonism. We here report a patient with anxious depression who, after selective serotonin reuptake inhibitor (SSRI) treatment, developed progressively obvious extrapyramidal symptoms (EPS). Multiple system atrophy (MSA) was later confirmed.

A 52-year-old female patient (BS) with no personal or family history of psychiatric illness presented with depressed mood, anxiety, multiple somatic discomforts (dyspnoea, chest tightness, palpitations and burning sensation of the limbs), insomnia, poor appetite and weight loss of 7 kg in 4 months (47.5 kg at evaluation). BS visited several psychiatric clinics and was treated with multiple different SSRIs, including fluoxetine, sertraline and escitalopram. She was admitted briefly to the psychiatric ward on one occasion. When taking SSRIs, she displayed akathisia and other EPS, including aggravated psychomotor retardation, rigidity, distal tremor and unsteady gait. The EPS always improved with discontinuation of antidepressants and hindered her from using SSRIs for more than 1 week. Her anxiety and depression were not alleviated. The EPS occurring with SSRI therapy was progressively more evident over time. BS visited our clinic after approximately 6 months of doctor shopping. Our assessment revealed that her respective scores of Hamilton Rating Scale for Depression (HAM-D) and Hamilton Rating Scale for Anxiety (HAM-A) were 30 and 40 (1,2). Duloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI), was prescribed to BS for several days, but again was discontinued because of intolerable EPS. BS was referred to neurological ward under the working diagnosis of Parkinson's disease (PD).

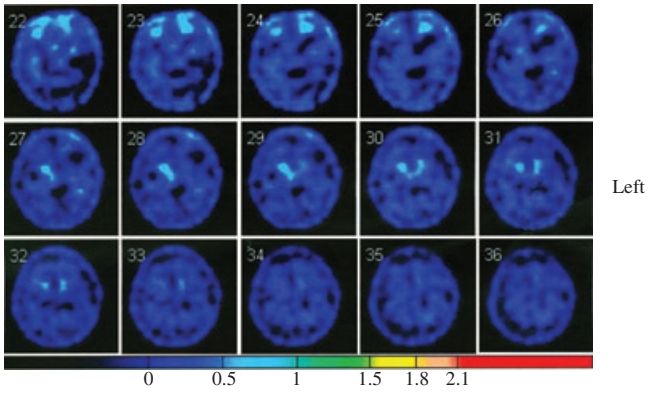

Fig. 1. The dopamine transporter brain image (SPECT; in radiological orientation) was performed 4 h after 25mCi of Tc-99m TRODAT. The colour bar reflects the availability of dopamine transporter, which indexes the density of dopamine neuron, with a score above 1.8 rated as normal and the score below 1 rated as abnormal. There was severe decreased uptake of radioactivity involving the bilateral striatum, more prominent on the left.

Dopamine transporter scan by single photon emission computed tomography (SPECT) examination was performed with the ligand Tc-99m TRODAT (Fig. 1). Results showed obvious decreased uptake of radioactivity involving the bilateral striatum, in particular the putamen. The loss of pre-synaptic dopamine transporter activity was more prominent over the left side. Brain computed tomography (CT) showed senile cortical atrophy and small hypodensities at bilateral striato-capsular regions. Laboratory analyses including differential blood counts, electrolytes, hepatic enzymes, creatinine, urea nitrogen, creatine kinase, thyroid hormones, cortisol and urine analysis were all within normal limits, as were plain films of the chest and electrocardiogram. Antinuclear antibody was negative. Physical examination revealed borderline orthostatic hypotension, mild unsteadiness and urine incontinence. On the basis of these findings, multiple system atrophy with Parkinsonism (MSA-P) was diagnosed. The prescribed medication included levodopa 300 mg, selegiline 10 mg, pramipexole 0.75 mg, clonazepam 3 mg, propranolol 30 mg and trazodone 150 mg. After treatment for 6 months, her psychiatric and neurological symptoms improved, with HAM-D and HAM-A scores of 16 and 22, respectively, and body weight restored to 56 kg.

The interaction between cerebral serotonin (5-HT) and dopamine systems is widely acknowledged. It is proposed that 5-HT2A antagonism would enhance dopaminergic transmission, which is one of the mechanisms accounting for the atypical features of new generation antipsychotics [serotonin-dopamine antagonists (SDA)]. SDAs are associated with less EPS and cognitive impairment compared with typical antipsychotics (dopamine receptor type 2 antagonist) (3). Accordingly, it is reasonable to assume that enhanced serotonin level, in this case mediated through SSRIs, may act through the 5-HT2A hetero-receptor on dopamine neurons to reduce dopaminergic transmission. This pathway might also account for the occasional observed side-effects of akathisia and EPS with

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SSRIs (4). Serotonergic antidepressants thus may result in decompensation of the hypo-dopaminergic brain of our patient, unveiling the underlying Parkinsonism which subsequently resulted in her poor compliance. Several studies support a role of the dopaminergic system in depression (5). The improvement of BS's depression and anxiety could be a result of the synergistic effects of dopaminergic agents, propranolol and trazodone, with the latter having 5-HT2A antagonist activity.

Depression is a common problem in patients affected by PD or MSA-P. The optimal choice of antidepressant for patients with PD or degenerative disease with Parkinsonism is still uncertain (6). Recently, Menza et al. (7) compared nortriptyline and paroxetine and showed that paroxetine was not efficacious in the treatment of depression in PD. Another double-blind, randomised, placebo-controlled study of PD found that noradrenergic antidepressant induced a stronger therapeutic effect than SSRIs (8). The observed superiority of antidepressants with noradrenergic properties could be because of (a) reduced interference with the dopaminergic system, and (b) reduced dopamine clearance in the cortex (9). Although BS was treated with SSRIs and SNRI, premature termination of therapy prevented us from determining whether SNRI use is better than SSRI in MSA-P depression. Given the role played by the dopaminergic system in PD-associated depression (5), the above-mentioned studies prompt doubt as to whether SSRIs are the optimal antidepressants in hypo-dopaminergic conditions. In addition, the patient presented here highlights the potential for SSRIs to worsen EPS in Parkinsonism and suggests that SSRI-induced EPS could be an early indicator of MSA-P. More studies are warranted to elucidate the best choice, regarding both treatment efficacy and complication profile, of antidepressants for PD or neurodegenerative diseases with Parkinsonism.

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