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LETTER TO THE EDITOR

Dramatic improvement by levodopa treatment in a patient with vascular parkinsonism

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Sir,

Herein, a-60-year-old female patient is described who attended to neurology clinic due to complaints of walking difficulty and postural instability. Upon history taking, it was learnt that the complaints of the patient had started 3 years ago, which had become rather evident following a stroke characterized by dysarthria and left lower extremity paralysis. In the following course, gait problems had insidiously deteriorated. Of note; no prodromal symptoms of Parkinson's disease (PD) such as hyposmia, constipation, and REM sleep behavior disorder were defined. The patient did not define complaints of memory impairment or hallucinations. She had no symptoms of dysautonomia such as orthostatic hypotension or gastroparesis. On neurological examination, she was evaluated as orientated and fully cooperated. Her speech was dysarthria. Remarkably, her walking was characterized with small steps and she had difficulty particularly during turning which was compatible with lower body parkinsonism (Video 1). Ocular examination revealed normal pursuit and saccadic eye movements. Motor, sensory, and cerebellar examination were in normal ranges. Besides, deep tendon reflexes were hyperactive in the lower extremities (more prominent in the left side). Babinski's sign was present on the left and a mild muscle stiffness on her left lower extremity (compatible with spasticity) was present. Vital signs revealed mild hypertension. Laboratory investigations including hemogram, biochemistry, lipid profile, thyroid, b12, and folic acid were in normal ranges. She scored 22 on mini-mental state examination. Cranial MRI showed bilateral, multiple, T2 hyperintense lesions in the periventricular areas, subcortical white matter, and basal ganglia (Fig. 1). Clinical history (acute onset and lack of prodromal symptoms of PD) as well as neurological examination (absence of extrapyramidal signs in the upper extremity) was atypical for PD. Cranial MRI had not showed the imaging sings of marked enlarged lateral ventricles, disproportional size of basal, Sylvian fussires, etc. rather excluding NPH. Besides, bradykinesia in the lower extremities were apparent and the clinical onset was characterized by an insidious progression following rather an abrupt onset manifesting with an ischemic stroke which also ruled out primary lateral sclerosis. Taken together, the diagnosis of vascular parkinsonism (VP) was established and levodopa/benserazide (100/25 mg) tb was initiated (gradually increased from 4 × 1/4 tb to 4 × 2 tb). A significant improvement in her walking speed and step width was achieved at 4 × 1 tb dosages. A mild, further improvement was observed following increment to the 4 × 2 tb dosages (Video 2). Further etiological investigations of the vascular lesions including CT angiography of the neck and brain, echocardiography and electrocardiography were in normal ranges. Susceptibility weighted imaging showed millimetric, hypointense lesions prominently in the bilateral basal ganglia and brain stem which was compatible with microhemorrhages (Figs. 1 and 2). The patient was diagnosed as VP in the setting of hypertension-related cerebral small-vessel damage and she was discharged on treatments of 4 × 200/50 mg levodopa/benserazide and 5 mg amlodipine for hypertension.

Discussion

Basically, VP can be defined as a form of secondary parkinsonism resulting from cerebrovascular disease [1]. It has been reported to account 2.5–5% of parkinsonism cases [2]. The clinical picture of VP is heterogeneous and differential diagnosis as well as discrimination from Parkinson's disease (PD) may be challenging. Clinically, symmetrical gait difficulties, postural instability, falls, dementia, pyramidal signs, pseudobulbar palsy,

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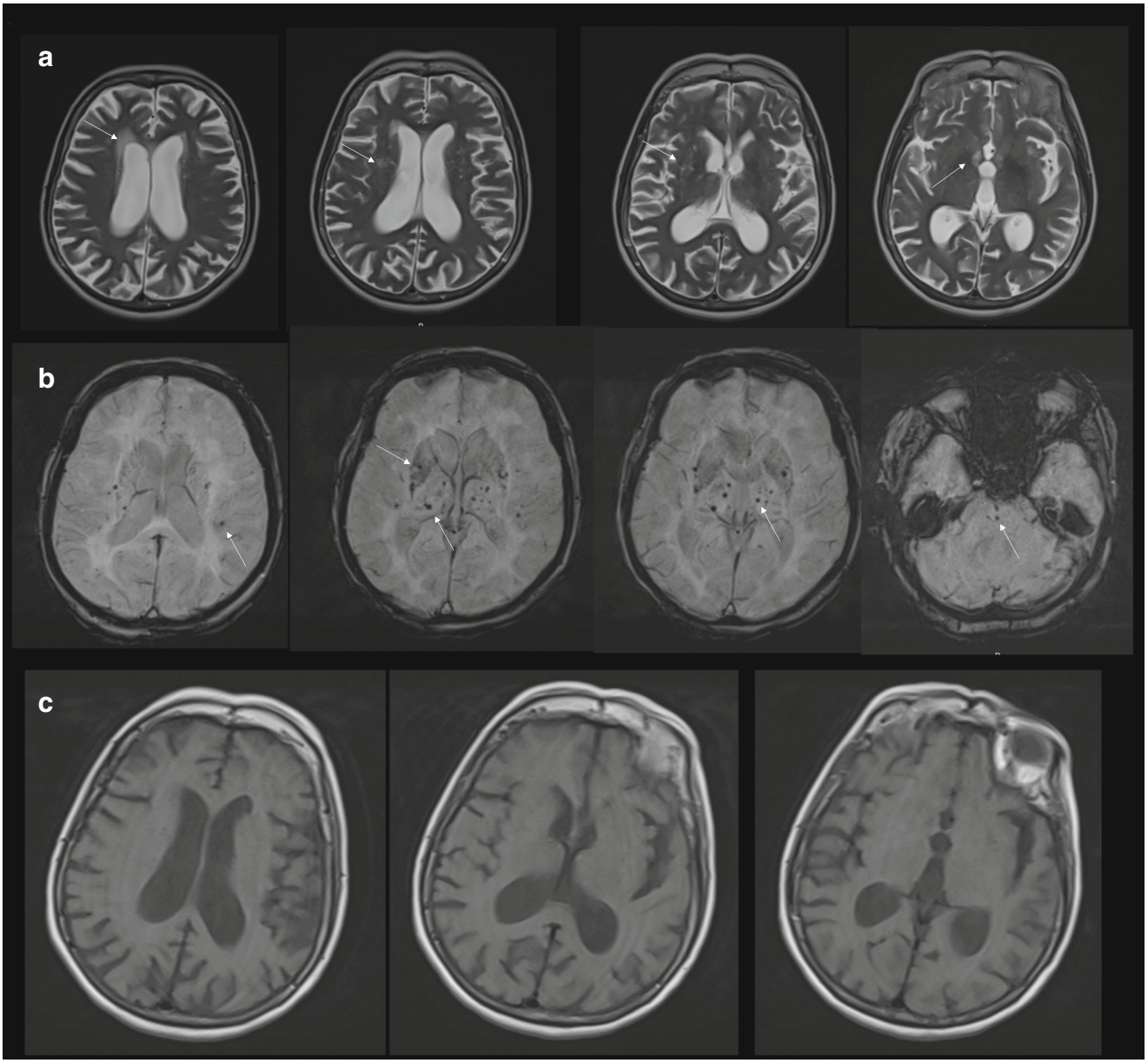

Fig. 1 Cranial MRI showing bilateral, multiple, T2 hyperintense lesions in the periventricular areas, subcortical white matter and basal ganglia (arrows) (**a**). Susceptibility-weighted imaging showing multiple microhemorrhages in the bilateral basal ganglia and brain stem (**b**). T1 sequences (**c**)

and urinary incontinence have been remarked as manifestations which are more commonly encountered in VP, rather than PD [1]. Besides, presumed lack of levodopa response has been emphasized as a crucial feature of VP, distinctly from PD. Nevertheless, there are also researchers reporting substantial and noteworthy benefit to levodopa treatment in patients with VP [3, 4]. Among these reports, the results of the unique study by Zijlmans et al. were impressive [4]. The authors particularly investigated the presence of nigrostriatal pathology and its possible association with levodopa response. In conclusion of their study, they found that the presence of lesion in or near the nigrostriatal pathway (macroscopically visible in the putamen, caudate nucleus, and globus pallidus, or microscopic substantia nigra loss) was the only predictor of good levodopa response in patients with VP [4]. They hypothesized that a positive response in VP patients might be explained by the remaining pool of striatal dopaminergic nerve terminals which remains adequate to convert exogenous L-dopa into dopamine and thus compensate the dysfunctional nigrostriatal pathway [4]. Herein, I report a remarkable patient of VP, at whom the lesion sites included basal ganglia and levodopa therapy provided a significant improvement in the patient's clinic. Based on the discussions mentioned above, I think that the presentation of this sample case, which was strictly illustrative, may give substantial perspectives in this regard. Via the illustration of this patient and related limited literature, I point out the possible

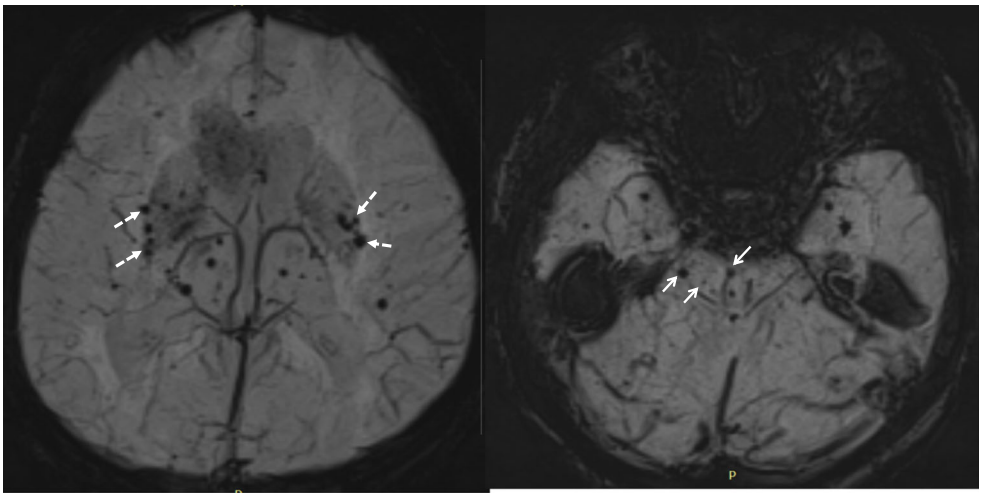

Fig. 2 Susceptibility weighted imaging showed millimetric, hypointense lesions prominently in the bilateral basal ganglia (scattered arrows) and brain stem (arrows) which was compatible with microhemorrhages

importance of localization of the lesion site in VP patients as different pathomechanisms might be playing role according to the affected lesion site which was previously hypothesized by Zijlmans et al. [5].

Remarkably, VP is an extremely heterogeneous entity, including a wide range of vascular pathology that might result in VP. Such that, there have been attempts to divide VP patients to several groups since 1929. A crucial classification suggested by Zijlmans et al. was that there may be two types of VP: one with an acute onset, possibly associated with basal ganglionic infarctions, and the other of insidious onset, associated more with diffuse subcortical white matter lesions [4, 5]. We think that clarification of the hypothesis of possible differing levodopa responses according to the affected lesion site (basal ganglia or other regions of thalamocortical pathways) may add substantial contributions to our currently understanding of VP pathophysiology as well as classification criteria of VP. Future reports focusing on the association between lesion sites and clinical outputs in VP are surely warranted to clarify these discussions.

Compliance with ethical standards

Conflict of interest The author declares that there is no conflict of interest.

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