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LETTER TO THE EDITOR

Reversible parkinsonism and cognitive deficits due to vitamin B_{12} deficiency

Ana Filipa Santos · Margarida Rodrigues · Pedro Abreu · Carla Ferreira

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Dear Sir,

Vitamin B_{12} deficiency is responsible for many neurological disorders and is normally sought in clinical practice in patients with dementia or ataxia [1, 2]. Parkinsonism secondary to B_{12} deficiency is exceedingly rare [2, 3] with only two previous reports, summarized in Table 1.

A 71-year-old woman with chronic gastritis developed a rapidly progressive gait disorder with very early falls within 1 month. She was slightly disoriented and presented asymmetrical parkinsonism with marked facial hypomimia, hypophonia, bradykinesia and rigidity (more evident on the left side and upper limbs), parkinsonian gait with postural instability (Unified Parkinson Disease Rating Scale part III—26). Frontal release signs and ideomotor apraxia were also present. She had no cerebellar nor pyramidal signs, her proprioception was normal and autonomic dysfunction, daily fluctuations, visual hallucination or delusions were not present. No new medication had been started and no exposure to neuroleptics, carbon-monoxide or toxics was recorded.

Levodopa was started, 150 mg/day for 2 weeks, then the dose was increased to 300 mg/day, at which point the patient became more disoriented, needing help to attain daily activities and ultimately bedridden, with more marked motor impairment. It was then suspended. At this time laboratory studies showed a serious deficit of vitamin B_{12} (83 pg/ml, normal >250 pg/ml). Hemoglobin level, mean corpuscular volume, folate level, thyroid function, autoimmune and serological screen were normal. She had no clinical signs or symptoms of myelopathy or neuropathy. Brain MRI revealed mild cortico-subcortical atrophy.

Vitamin B_{12} replacement was started with injections at a dose of 1000 mg/day for 7 days, than once a week for 4 weeks and monthly thereafter, with progressive clinical improvement. Nine months later she was totally independent from the functional point of view. She was able to take care of herself and her house chores including going shopping on her own. Neurological examination was normal with no frontal release signs.

The most likely cause of this patient's parkinsonism and cognitive deficits was, in our view, the serious B_{12} deficit documented, since we have observed full recovery with replacement therapy and excluded other possible causes. Pathophysiology of extrapyramidal symptoms in patients with vitamin B_{12} deficiency is far from clear. Vitamin B_{12} has fundamental roles in CNS, especially the methionine-synthase mediated conversion of homocysteine to methionine [4]. This amino acid is a major source of *S*-adenosylmethionine, the most important methyl donor in the brain and influences serotonin, norepinephrine, and dopamine synthesis [4]. A deficiency of vitamin B_{12} may lead to increased homocysteine levels. And there is evidence that increased homocysteine levels might accelerate dopaminergic cell death in Parkinson's disease (PD), through neurotoxic effects [4]. Other known enzymatic reaction which is dependent on vitamin B_{12} is the conversion of methylmalonic acid to succinyl-CoA, so vitamin B_{12} deficiency can lead to increased levels of serum methylmalonic acid. Also, the methylmalonic acidemia usually presents with acute extrapyramidal syndrome in infants and some cases respond to vitamin B_{12} replacement

A. F. Santos (✉) · M. Rodrigues · C. Ferreira
Serviço de Neurologia, Hospital de Braga, Sete Fontes, São Victor, 4710-243 Braga, Portugal
e-mail: filipasantos@hotmail.com

P. Abreu
Serviço de Neurologia, Hospital de São João, Faculty of Medicine, University of Oporto, Porto, Portugal

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Table 1 Description of reported cases of adults with reversible parkinsonism and B_{12} deficits

References	Age	Gender	Initial clinical presentation	Other neurological abnormalities beyond parkinsonism	Serum vitamin B_{12} level (pg/ml)	Evaluation for causes of vitamin B_{12} deficiency	B_{12} supplementation	Clinical improvement	Last follow up
Kumar [2]	55	Male	Bradykinesia and tremor of hands of 10 days duration	Myeloneuropathy	5	Atrophic gastritis	Started on vitamin B_{12} injections at a dose of 1000 mg/day for 7 days; than once a week for 4 weeks; monthly thereafter	Within 3 days	At 5 years: no neurological deficits
Sharrief et al. [3]	43	Male	Gait abnormality ("Stumbling") 3 months before hospitalization	Myeloneuropathy Impaired cognition	254	Autoimmune gastritis	Parenteral vitamin B_{12} therapy (not specified)	Within 1 week	Not specified

[2]. Brain imaging and autopsy studies of this autosomal recessive disorder have shown symmetrical involvement of basal ganglia [2]. Globus pallidus may be especially vulnerable because of its high energy requirements [3].

We alert that complicated extrapyramidal and cognitive manifestations may be, sometimes, due to B_{12} deficiency and this recognition is essential since we can easily and effectively treat these patients.

Conflict of interest The authors declare that they have no conflict of interests.

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