Subacute Combined Degeneration as the Initial Manifestation of Folate Deficiency

Degenerescência Combinada Subaguda como Manifestação Inicial da Deficiência de Folato

Keywords: Folic Acid Deficiency; Peripheral Nervous System Diseases; Subacute Combined Degeneration
Palavras-chave: Deficiência de Ácido Fólico; Degenerescência Combinada Subaguda; Doenças do Sistema Nervoso Periférico

Neurological complications of folate deficiency are uncommon but may closely mimic those of cobalamin deficiency, particularly subacute combined degeneration (SCD).[1,2] It results from demyelination of the dorsal and lateral columns of the spinal cord and manifests clinically with symmetrical loss of vibration and proprioception, impaired tactile discrimination and sensory ataxia.[2,3] Although strongly associated with vitamin B_{12} deficiency, isolated folate deficiency can produce a similar myeloneuropathic pattern (that is, a pattern on the spinal cord and peripheral nerves), a fact that is often overlooked in clinical practice.

We report the case of a 55-year-old man with moderate alcohol intake who presented with one month of ascending paresthesias from the feet to the hips, followed by tingling in the fingertips and increasing gait unsteadiness. Examination revealed preserved upper-limb strength and mild distal lower-limb weakness (Medical Research Council grade 4/5), without proximal involvement. Sensory testing revealed impaired light touch and pinprick up to the knees, with complete loss of vibration sense to the same level. Deep tendon reflexes were absent in the lower limbs. Romberg sign was positive, suggesting sensory ataxia.

Laboratory evaluation demonstrated a markedly low serum folate level, with normal vitamin B_{12}, methylmalonic acid and homocysteine (Table 1). Magnetic resonance imaging of the cervical and thoracic spine demonstrated symmetrical T2-weighted hyperintensity of the dorsal columns, without evidence of compressive lesions. Cerebrospinal fluid, infectious, autoimmune and paraneoplastic studies excluded alternative etiologies. Nerve-conduction studies revealed severe sensory axonal polyneuropathy.

High-dose folate (10 mg/day) and intramuscular vitamin B_{12} were initiated. Vitamin B_{12} was administered empirically, as folate replacement alone may mask a subclinical cobalamin deficiency and allow progression of neurological damage. The patient improved steadily, achieving independent ambulation and near-complete sensory recovery at six months. Follow-up laboratory evaluation showed normalization of serum folate levels and partial electrophysiological improvement.

This case highlights a rare but meaningful presentation: SCD-like features arising despite normal vitamin B_{12} levels. The combination of proprioceptive loss, sensory ataxia, ascending paresthesias and sensory axonal neuropathy is uncommon in isolated folate deficiency. After exclusion of

Table 1 – Complementary diagnostic studies during hospitalization

Category	Tests/markers	Result
Vitamins	Serum folate	1.5 ng/mL (reference > 5)
	Vitamin B_{12}	474 pg/mL (normal)
Amino acids	Methylmalonic acid	Normal
	Homocysteine	10.2 µmol/L (reference < 15)
Autoimmunity	ANA, RF, anti-SS-A, anti-SS-B	Negative
	Anti-ganglioside antibodies	Negative
	Anti-MAG (myelin-associated glycoprotein)	Negative
	Paraneoplastic antibodies (serum)	Negative
Cerebrospinal fluid	Culture/microscopy	Negative
	Herpes simplex virus types 1 and 2 PCR	Negative
	Varicella-zoster virus PCR	Negative
	Brucella spp Serology	Negative
	Rickettsia spp Serology	Negative
	Borrelia burgdorferi (Lyme) Serology	Negative
	VDRL Serology	Negative
	Neurotropic virus PCR panel	Negative
	Paraneoplastic antibodies (CSF)	Negative
Other investigations	Thoraco-abdominopelvic CT	No neoplastic findings
	Nerve-conduction studies	Severe, length-dependent sensory axonal polyneuropathy

ANA: antinuclear antibodies; CT: computed tomography; MAG: myelin-associated glycoprotein; PCR: polymerase chain reaction; RF: rheumatoid factor; SS-A/SS-B: soluble antigens A and B; VDRL: Venereal Disease Research Laboratory

other metabolic, infectious and immune-mediated causes, folate depletion remained the most plausible mechanism, although alcohol-related neuropathy cannot be fully excluded, as alcohol is a recognized cause of toxic neuropathy. Folate deficiency was considered likely secondary to chronic alcohol use.

Folate deficiency disrupts S-adenosylmethionine-dependent methylation, which is essential for myelin integrity.[4] It should be considered in subacute sensory neuropathies, particularly in patients with alcohol use or malnutrition, as early treatment may allow substantial neurological recovery.[3]

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AUTHOR CONTRIBUTIONS

JSV: Writing of the manuscript.
MSR, PRS: Data collection.
MA, MFD: Critical review of the manuscript.
All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

CONFLICTS OF INTEREST

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Joana SOUSA VARELA [1], Patrícia SANTOS [1], Miguel SIMÕES RODRIGUES [1], Mário AMARO [1], Maria Francisca DELERUE [1]
1. Internal Medicine Department. Hospital Garcia de Orta. Almada. Portugal.
✉ **Autor correspondente:** Joana Sousa Varela. jccsv1996@gmail.com
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