Abstract


Unexplained chronic cough and vitamin B-12 deficiency.


Departments of Clinical Pathophysiology and Biomedical Science and Human Oncology, University of Turin, Turin, Italy, and the Unit of Pneumology, Consorzio Provinciale Antitubercolare, Local Health Agency Turin 2, Turin, Italy.

BACKGROUND: Chronic cough is characterized by sensory neuropathy. Vitamin B-12 (cobalamin) deficiency (Cbl-D) causes central and peripheral nervous system damage and has been implicated in sensory neuropathy and autonomic nervous system dysfunction.

OBJECTIVE: We evaluated whether Cbl-D has a role in chronic, unexplained cough.

DESIGN: Laryngeal threshold (histamine concentration that provokes a 25% decrease in the midinspiratory flow), bronchial threshold (histamine concentration that provokes a 20% decrease in the forced expiratory volume in 1 s), and cough threshold (histamine concentration that causes ≥5 coughs) in response to an inhaled histamine were assessed in 42 patients with chronic, unexplained cough [27 Cbl-D patients and 15 patients without Cbl-D (Cbl-N)] before and after intramuscular injections of cobalamin for 2 mo. Laryngeal, bronchial, and cough hyperresponsiveness was diagnosed when histamine concentration thresholds were ≤8 mg/mL. Seven Cbl-D and 3 Cbl-N patients underwent an oropharyngeal biopsy before treatment.

RESULTS: Cbl-D patients had a higher prevalence of laryngeal hyperresponsiveness than did Cbl-N patients (92.6% compared with 66.7%; P = 0.03), a thinner oropharyngeal epithelium [133.7 μm (95% CI: 95, 172 μm) compared with 230.8 μm (95% CI: 224, 237 μm); P = 0.002], a lower number of myelinated nerve fibers [2.25/mm(2) (95% CI: 1.8, 2.7/mm(2)) compared with 3.44/mm(2) (95% CI: 3, 3.8/mm(2)); P = 0.05], and a higher immunoreactive score for nerve growth factor (NGF) [6.7 (95% CI: 6, 7.3) compared with 2.8 (95% CI: 2.5, 3.1); P = 0.02]. After cobalamin supplementation, symptoms and laryngeal, bronchial, and cough thresholds were significantly improved in Cbl-D but not in Cbl-N patients.

CONCLUSIONS: This study suggests that Cbl-D may contribute to chronic cough by favoring sensory neuropathy as indicated by laryngeal hyperresponsiveness and increased NGF expression in pharyngeal biopsies of Cbl-D patients. Cbl-D should be considered among factors that sustain chronic cough, particularly when cough triggers cannot be identified.

PMID: 21248188