Cerebellar degeneration and folate deficiency due to cough mixture abuse

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A 34-year-old Chinese man was admitted with unsteady gait and clumpsiness. Examination showed sensory peripheral neuropathy but accompanied by gross past pointing, dysdiadochokinesia and cerebellar gait. A computerized tomogram scan showed bilateral cerebellar degeneration (Figure 1A arrows) and thinning of folia (Figure 1B). There was mild macrocytic anemia (hemoglobin 10.6 g/dL, mean corpuscular volume 104.6 fl) and urinary dextromephorphan was detected. Although initial appearance did not show dental carries as a stigma of cough mixture abuse, careful examination showed total teeth erosion and full replacement by dentures (Figure 1C). He volunteered cough mixture binges of 500 mLdaily for two years. Further assays showed low vitamin B12: 130 ug/mL (normal 170-814) and red cell folate: 57 ug/mL (normal >164) levels. Metabolite screening showed grossly elevated serum homocysteine (HC) levels (102 umol/l, normal 5-12) but not methylmelonic acid (MMA) levels (0.19 umol/l, normal 0.05-0.6). This was compatible with severe folate deficit and low vitamin B12 level.[1] Since cerebellar toxicity was hitherto unreported and a lumbar puncture was performed. The cerebrospinal fluid (CSF) showed undetectable HC (normal <0.25 umol/l)[2] and near normal MMA levels (0.32 umol/l, normal 0.12-0.31).[3] After three months of physiotherapy and vitamin supplements, there was recovery in gait and dexterity with residual cerebellar signs. He defaulted further follow-up. Cough mixture abuse is a major health problem in many Oriental countries, and the neuropathic effects due to severe secondary folate deficiency were only recently recognized.[1] The biochemical mechanisms are unknown, but abusers (and their fetuses) may suffer from irreversible neurological damages, usually in the form of peripheral neuropathy. The reason for this first case of cough mixture related central nervous system toxicity is unclear. Cerebellar damage is a known consequence of folate deprivation in patients with seizures[5] or congenital metabolic disorders.[6] However, unlike high CSF levels of MMA and HC in severe B12 deficiency[7,8] or folate metabolic defects[9] the normal CSF levels in our case do not suggest direct neurotoxicity. In fact, dextromethophan is used as an NMDP receptor antagonist for the treatment of toxic CSF levels of HC.[10] It is possible that toxic impurities in the concoction and / or congenital predisposition may account for the novel cerebellar toxicity in our case.

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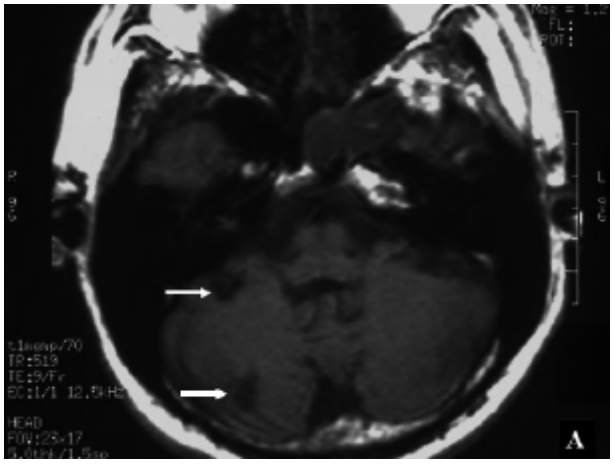

Figure 1 A.

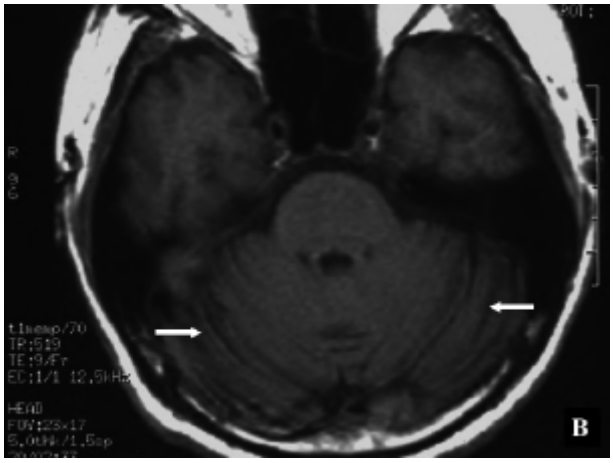

Figure 1 B.

Figure 1 C.

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