

Multifocal inflammatory leukoencephalopathy induced by accidental consumption of levamisole: A case report

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Keywords

Levamisole, Leukoencephalopathy, Magnetic Resonance Imaging

Abstract

Levamisole is an anthelmintic agent and also immunostimulant drug which is used to treat colorectal cancer. The present study aimed to show accidental consumption of levamisole alone induced multifocal inflammatory leukoencephalopathy. A 53-year-old male was admitted to the Neurology Department of Farabi Hospital (Kermanshah, Iran) with walking inability and recognition disorder. Following clinical examinations, the patient diagnosed as multifocal inflammatory leukoencephalopathy following levamisole consumption. The patient was treated with intravenous methylprednisolone followed by prednisolone. The magnetic resonance imaging (MRI) was done 1 month later and did not show a reduction or remission in the lesions. History of the patient showed that he had accidentally consumed levamisole 8 months ago. It seems that the consumption of levamisole can induce multifocal inflammatory leukoencephalopathy and delayed

treatment of the patient with corticosteroid cannot diminish the neurotoxicity of levamisole. In addition, the cytotoxic dose of levamisole induces irreversible multifocal inflammatory leukoencephalopathy.

Introduction

Levamisole, an anthelmintic agent that targets the nicotinic acetylcholine receptors, is usually used as an immunostimulant in combination with 5-fluorouracil (5-FU) to treat colorectal cancer since 1990. It has been shown that combination of these two drugs decrease the risk of clinical recurrence and to increase survival in patients with stage III adenocarcinoma of the colon.¹⁻³

The neurotoxic effects of levamisole therapy have been rarely reported. In this report, we describe multifocal inflammatory leukoencephalopathy in a patient with accidentally consumption of levamisole after 8 months of gastric lavage of the drug.

Case report

A 53-year-old man was admitted to the Neurology Department of Farabi Hospital (Kermanshah, Iran)

with walking inability and recognition disorder. Patient history showed that he had referred to hospital with vomiting, vertigo and headache 8 months before after consumption of two sachet of levamisole (for veterinary use) which each sachet contained 1.5 gram of levamisole hydrochloride. One month later, he had been stricken by progressive walking inability and recognition disorder up to administration to our hospital. The patient had not any previous illness.

On neurologic examination, he was confused and did not establish a good relationship with the bystander. On mental and cognitive power examinations, using the Mini Mental State Examination (MMSE), he earned 17 points (out of a total score of 30) with no signs of meningeal irritation (such as stiffness of neck). In addition, cranial nerves were normal. The power of limbs was within normal range but deep tendon reflexes in all of four limbs had increased in conjunction with extensor plantar response and reduced abdominal skin reflex. The patient had primitive reflexes including grasp, snout and palmomental. On cerebellar examination, finger to nose test and heel to shin was impaired and the gait was ataxic.

On the initial laboratory tests, complete blood count (CBC), blood sugar, urea, creatinine, and liver enzymes were normal. In cerebrospinal fluid analysis, color, pressure, cells, and sugar were normal but protein was increased (69 mg/dl). Oligoclonal band (OGB) was negative.

On electroencephalography (EEG), bilateral paroxysmal slow waves were seen. In visual evoked potential (VEP), there was a bilaterally prolonged P100 latency. Brain magnetic resonance imaging (MRI) showed mild cerebral atrophy and multiple focal lesions distributed in periventricular and cerebellar white matter and also in pons and midbrain (figure 1). These lesions had low-signal intensity on T1-weighted images and high-signal intensity in fluid-attenuated inversion recovery (FLAIR) view and T2-weighted images.

Following clinical examinations and ruling out of other causes, including infectious and vascular causes, trauma and metabolic, central nervous system (CNS) vasculitis and paraneoplastic syndromes; and according to the patient's history, the patient was diagnosed as multifocal inflammatory leukoencephalopathy following levamisole consumption. The patient did not give consent for brain biopsy.

The patient was treated with intravenous methylprednisolone (500 mg) every 12 hours for 7 days followed by two weeks oral consumption of the prednisolone (50 mg/day) during hospitalization. No change was noticed in cerebellar signs and gait disorder but a brief improvement was seen in mentality and cognition after 1 and 3 months. After a month of treatment, MRI did not show a reduction or remission

of the lesions. (figure 2)

Discussion

This paper reported the clinical features and MRI changes that were occurred suddenly after consumption of high dose levamisole and 8 months later. Clinical investigations and also MRI imaging showed the drug induced toxicity in the brain after 8 months of treatment.

Toxicity of levamisole is generally mild, even when levamisole is used alone, and is negligible in a series of patients in whom it is associated with 5-FU (\pm leucovorin). The spectrum of side effects (partly dose-dependent) includes myalgia, arthralgia, fatigue, fever, chills, skin rash, nausea, vomiting, anorexia and neurological symptoms. The latter mainly consist of depression, anxiety, insomnia, difficulty in concentration, headache and vertigo.^{4,5}

Clinical investigations of the patient showed memory loss, confusion, ataxia, dysarthria, and hyperreflexia that cannot be considered as the side effects of the drug alone but are the main symptoms of multifocal inflammatory leukoencephalopathy. Here, it seems that if a case subjected to only one but high dose of levamisole, the catastrophic effect is such prominent that may induce multifocal inflammatory leukoencephalopathy.

On the other hand, MRI imaging showed inflammation in many parts of the brain that led us to diagnose the patient as multifocal inflammatory leukoencephalopathy. Multifocal inflammatory leukoencephalopathy, a central nervous system disorder characterized by demyelination with perivascular inflammation, has recently been reported in several patients treated with the combination of fluorouracil and levamisole chemotherapy.^{6,7}

It has been suggested that the neurotoxicity derived by combination of these two drugs was mainly due to 5-FU rather than levamisole alone.^{4,5} However, some authors confirmed that multifocal inflammatory leukoencephalopathy could be induced by levamisole alone.^{8,9} In parallel with these studies, we also suggest that levamisole alone can induce multifocal inflammatory leukoencephalopathy.

On the other hand, in previous studies, levamisole was administered as a drug choice and there was no document in the literature for monitoring the effect of this drug following accidental consumption. In addition, gastric lavage followed by delayed treatment of the patient with methylprednisolone cannot diminish the neurotoxicity of levamisole. These data highlights the fact that the drug must be unavoidable to children and the usage of the drug must be used vigilantly.

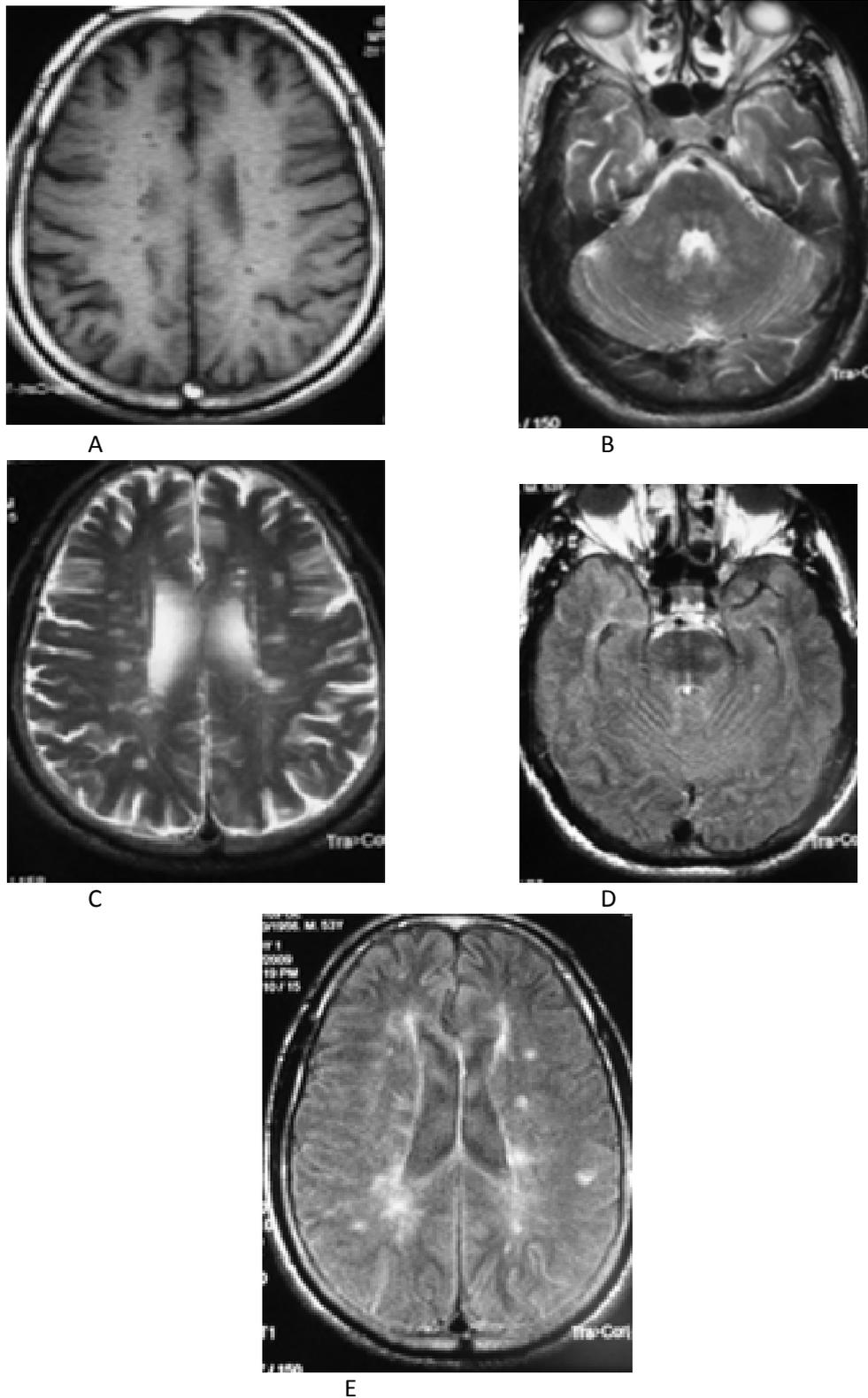
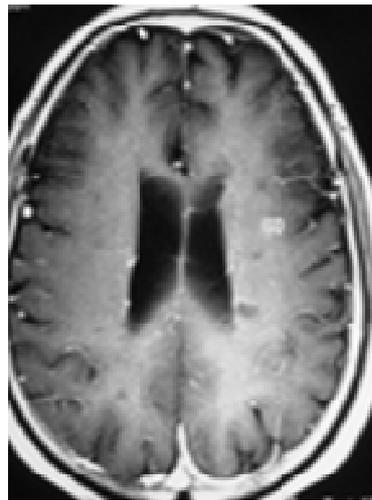


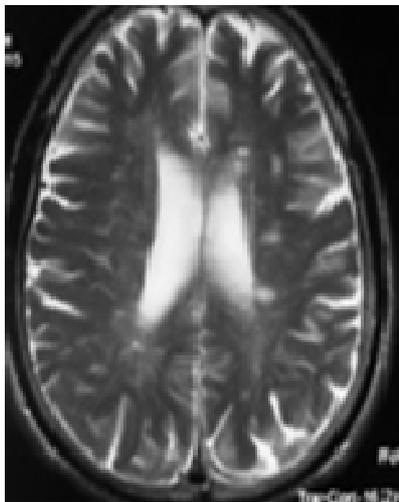
Figure 1. Initial brain MRI in the patient with multifocal demyelinating leukoencephalopathy after accidental consumption of levamisole; A: Brain MRI on T1WI revealed multifocal subcortical white matter lesions in the periventricular; B and C: Brain MRI on T2WI revealed multifocal subcortical white matter lesions in the periventricular, cerebellar and pons; D and E: Brain MRI on FLAIR revealed multifocal subcortical white matter lesions in the periventricular area, cerebellum and pons



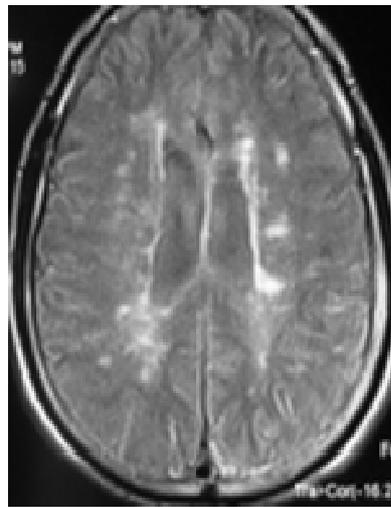
A



B



C



D



E



F

Figure 2. The follow-up brain MRI in patient with multifocal demyelinating leukoencephalopathy, after 1 month treatment with methylprednisolone disclosed no recovery of the subcortical white matter lesions; A: Brain MRI on T1WI revealed multifocal subcortical white matter lesions in the periventricular area; B: Brain MRI on T1WI with contrast revealed multifocal subcortical white matter lesions in the periventricular area and no evidence of enhancement; C: Brain MRI on T2WI revealed multifocal subcortical white matter lesions in the periventricular area; D, E and F: Brain MRI on FLAIR revealed multifocal subcortical white matter lesions in the periventricular area, cerebellum and pons

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