

Uncommon Neurological Complications of Levamisole

A 33-year-old female presented to neurology outpatient clinic with complaints of fatigue, generalized weakness, and unsteady walking of 4 days duration. On physical examination, the patient was found to have mild gait ataxia. Rest of detailed clinical neurological exam was normal. There were no significant past medical history except for the recent diagnosis of verrucae planae by her dermatologist. The patient was started on levamisole 150 mg thrice a week for 5 weeks followed by a weekly dose. However, the routine labs results of the patient were unremarkable. Magnetic resonance imaging (MRI) of brain showed bilateral, multifocal subcortical white matter lesions suggestive of demyelination. [Figures 1 and 2] MRI of whole spine did not reveal any other demyelinating lesions. In addition, the patient denied any preceding infections or vaccinations. Therefore, we diagnosed levamisole-induced multifocal leukoencephalopathy (MIL) and started her on high-dose methylprednisone for three days. Her gait ataxia fully resolved with treatment.

Although levamisole has been in use since 1989, initially it was used as only as an antihelminthic and only more recently has been used as an immunomodulator drug in dermatology. It alters polymorphonuclear leukocyte (PMN) chemotactic responsiveness, increases NK cells, and activates T cells. It is used extensively for viral infections like warts and molluscum contagiosum. It has many adverse effects but the key effect is agranulocytosis which occurs in about 0.08–5% of cases.^[1] The earliest reported levamisole-induced leukoencephalopathy was in 1996. In a series of 31 patients identified by medline search, the most common symptom was gait ataxia. Most MRI lesions were supratentorial and close to periventricular region. Brain biopsy of levamisole-induced lesions demonstrates active

demyelination including myelin loss and accumulation of perivascular lymphocytes. Early discontinuation of levamisole and treatment with steroids yielded good recovery.^[2] Acute disseminated encephalomyelitis (ADEM) closely mimics MIL. However, patients with MIL rarely have constitutional symptoms, such as fever, malaise, myalgia, or nausea, preceding the neurologic symptoms.^[3]

Although the United States Food and Drug Administration (US FDA) approved its use along with 5% fluorouracil in the treatment of advanced colon cancer, it was later withdrawn from the US and Canadian markets in 2000 and 2003, respectively, due to the risk of serious adverse effects and the availability of more effective replacement medications. More recently, reports of MIL have been reported among cocaine users. Levamisole is a common adulterant found in up to 65% of cocaine samples and is believed to enhance the euphoric effects of cocaine.^[4] An immune mediated mechanism has been postulated for development of MIL following levamisole intake. Even a single dose can cause MIL with a delay in symptom onset ranging from one day to several weeks.^[5]

In conclusion, MIL is an uncommon complication of levamisole therapy. Health care professionals need to be aware of this complication. Immediate discontinuation of levamisole therapy, the use of steroids, immunoglobulin, and plasma exchange are known to hasten recovery.

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Conflicts of interest

There are no conflicts of interest.

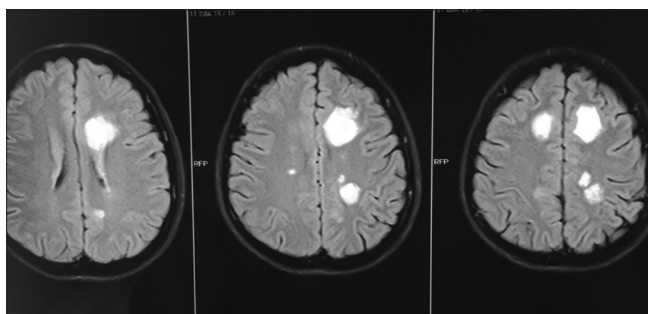


Figure 1: MRI FLAIR Sequence showing bilateral, multifocal subcortical white matter lesions

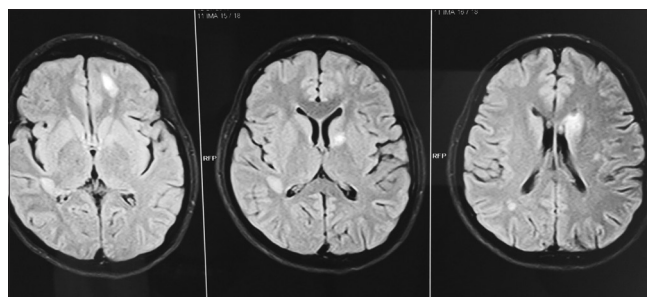


Figure 2: MRI FLAIR Sequence showing bilateral, multifocal subcortical white matter lesions

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