
Parkinsonism Associated with Interferon Alpha Therapy for Chronic Myelogenous Leukemia

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Abstract

A 79 year-old man was treated with Interferon alpha for chronic myelogenous leukemia and developed severe parkinsonism that resolved after Interferon alpha was stopped. Carbidopa-levodopa was associated with early improvement, but discontinuation did not result in worsening of the parkinsonism.

Introduction

Two forms of recombinant interferon (IFN) alpha, IFN alpha 2a and IFN alpha 2b, are used in a variety of disorders, including hairy-cell leukemia, hepatitis, AIDS-related Kaposi's sarcoma, chronic myelogenous leukemia, and melanoma.¹ Reported adverse neurological effects of IFN alpha have included tremor, mental deterioration, mood and behavioral changes, cortical blindness, leukoencephalopathy, Bell's palsy, and coma.²⁻³⁻⁴⁻⁵ We report a patient who developed severe parkinsonism that resolved after treatment with IFN alpha 2b was stopped.

Case History

A 79 year-old man was treated with IFN alpha 2b, 3 million units subcutaneously daily for chronic myelogenous leukemia with the Philadelphia chromosome. His past medical history included prostate cancer, hypertension, hypercholesterolemia, peptic ulcer disease, and gout. His other medications included omeprazole, hydrochlorothiazide, lisinopril, allopurinol and tolterodine. Early side effects of IFN included mild nausea, anorexia and weight loss. These symptoms abated with a transient reduction in dose. IFN was subsequently increased to 6 million units daily. At eight weeks of treatment (cumulative IFN dose of 324 million units), the patient developed a resting tremor, followed by mild confusion and difficulty with ambulation. At twelve weeks of treatment (cumulative IFN dose of 486 million units) the resting tremor had worsened. He developed greater difficulty walking and fell frequently. He required help with activities of daily living. His dosage was again reduced but no improvement in symptoms was noted.

After twelve weeks of treatment (cumulative IFN dose of 498 million U), he was unable to stand independently and was confused, and was hospitalized. He was alert but inattentive, with soft, indistinct speech. His verbal responses were confused and tangential. He required assistance to sit, stand, and walk. He demonstrated a parkinsonian gait, bradykinesia, cogwheel rigidity, and a prominent tremor of the arms present at rest and with action and sustained posture. Strength was intact. Examination of the cranial nerves, sensation, and reflexes was intact. Serum electrolytes were normal. BUN and creatinine were 39 and 1.5 respectively. Magnesium, phosphorus and calcium were within normal limits. Non-contrast CT scan of the brain revealed mild cerebral atrophy, and a small old infarct in the left basal ganglia. MRI scan of the brain revealed mild cerebral atrophy, a small old right pontine infarct, and a small infarct in the left basal ganglia. Thyroid function tests and ammonia level were normal. HTLV-1 by ELISA was negative.

Interferon was stopped. Carbidopa-levodopa 25/100 mg three times daily was started. After several days the patient's mentation, tremor, and ambulation had improved. He continued to improve as an outpatient. Carbidopa-levodopa was stopped after two weeks without worsening of symptoms. One month after stopping IFN the patient felt he had returned to his pretreatment baseline. On examination he showed no confusion. Speech was normal. He had mild cogwheel rigidity and a postural tremor, but no resting tremor. His gait was mildly slow and stiff, which his wife said was his baseline.

Discussion

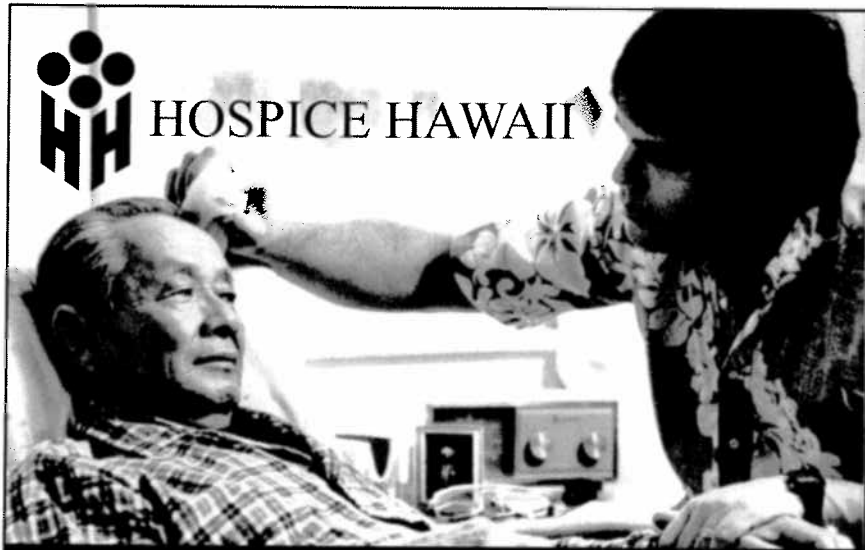
Our patient developed parkinsonism after eight weeks of IFN alpha treatment. The motor and cognitive dysfunction progressed to the point of severe disability. These problems resolved after IFN alpha was discontinued. Early treatment with carbidopa-levodopa was associated with clinical improvement, but there was no worsening when it was stopped. This effect of IFN alpha has not been emphasized in the medical literature. Mizoi and colleagues published a Japanese-language report of parkinsonism in a 52-year-old woman treated for six months with IFN alpha therapy for chronic hepatitis C. This patient benefited from carbidopa-levodopa.⁶ Meyers and colleagues reported four patients who developed parkinsonism after IFN alpha treatment for various malignancies. All patients benefited from carbidopa-levodopa.⁷ Talpaz and colleagues reported two patients who developed extrapyramidal symptoms with IFN alpha.⁸

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"Parkinsonism...", Continued from p. 48

Shuto and colleagues found that repeated administration of IFN alpha in mice was associated with a 10% decrease in brain dopamine levels, and an 18% decrease in 3,4-dihydroxyphenylacetic acid levels.⁹ They concluded that repeated administration of IFN alpha inhibits dopaminergic neuronal activity. In susceptible patients, such as those with underlying parkinsonism, a partial reduction in dopaminergic activity by IFN alpha therapy may be enough to produce an overt Parkinsonian disorder. Our patient had mildly impaired gait at baseline. It is possible that he has mild underlying parkinsonism making him more susceptible to IFN alpha toxicity. Merimsky and colleagues suggested that neurological effects of interferon may occur in cancer patients earlier than patients with other diseases, and that the incidence of interferon toxicity on the central nervous system may be related to the dose and the age of the patients.²

Clinicians should be aware of the possibility of drug-induced parkinsonism in patients treated with IFN alpha, especially those who already have parkinsonian symptoms or signs.

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