Occurrence of Herpes Zoster in Multiple Sclerosis Patients Treated with Natalizumab
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BACKGROUND
Herpes zoster (HZ) is caused by reactivation of the varicella-zoster virus (VZV). Risk factors include immunocompromised status, immunosuppressive treatment and age-related waning of cell-mediated immunity. It is estimated that 2.2 to 4.8 per 1,000 persons per year develop zoster.

VZV primary infection leads to varicella or chicken pox, which typically occurs among children. More than 90% of the adult population has had varicella but no immunologic parameters have been identified to distinguish who will develop zoster.

Viral reactivation is thought to be a result of aging-related waning of cell-mediated immunity. It may occur decades after initial infection causing herpes zoster and requires the spread of the virus to neighboring neurons within the ganglia.

Acute lymphocyte counts are decreased in patients with MS on natalizumab therapy and remained decreased six months after therapy cessation. The CSF CD4/CD8 ratios from MS natalizumab treated patients were similar to those observed in HIV-infected controls.

The prevalence of zoster among MS patients has not been described to differ from that of normal individuals. It seems that glatiramer acetate and interferon immunomodulatory treatment has no impact on HZ incidence.

METHODS
Review of medical records of MS patients on natalizumab in our center.

RESULTS

CASE 1. A 34 year old woman with RRMS diagnosed in 2006. Prior to natalizumab, therapy included interferon beta 1a IM and glatiramer acetate. After 11 doses of natalizumab she developed herpes zoster on the left T-6-T-9 level. Natalizumab was withheld for 3 months and 1 gram of valacyclovir daily was prescribed as long term prophylaxis therapy. She developed post-herpetic neuralgia.

CASE 2. A 43 year old woman diagnosed with RRMS in 1991. Prior to natalizumab she was treated with interferon beta 1b. She developed herpes zoster after the 3rd dose of natalizumab and was placed on long term prophylaxis with 1 gram of valacyclovir daily. The peripheral blood baseline CD4+ count was 1680/cumm and CD8+ count was 2400/cumm. No history of exposure was mentioned.

All the patients were women with RRMS with a median age of 43. They were previously treated with interferon beta and three of them had also used glatiramer acetate.

At the time of HZ, the patients had received 3, 4, 5 and 11 doses of monotherapy. One patient had experienced a remote episode of HZ and was recently diagnosed with RA. One of the patients developed post-herpetic neuralgia. No severe complications developed.

CONCLUSIONS
The occurrence of HZ among natalizumab treated MS patients in our center was higher than that of the general population.

Various observations can be made from our patients’ demographics; unfortunately our small sample size limits the power of such. There did not seem to be a trend for increased HZ incidence with an increasing number of natalizumab doses, previous disease modifying therapy or number of years since diagnosis.

The patients that developed HZ within the first 5 months of treatment were older when compared to the patient that developed it after the 11th dose. It is possible that age may be an independent risk factor toward development of HZ as occurs in the general population.

Peripheral baseline CD4 and CD8 values in our patients were no different from that of the general population; yet the patient with the lowest concentration of CD8+ in peripheral blood developed HZ earlier in the course of treatment.

The distribution of lesions in two of our patients involved more than one dermatome. No serious complications were reported but one patient experienced post-herpetic neuralgia.

In natalizumab clinical trials a small excess of herpes infections was reported. The post-release monitoring disclosed one case of fatal herpesvirus encephalitis and one nonfatal case of herpesvirus meningitis while on therapy.

In view of a higher HZ incidence in MS patients treated with natalizumab and the serious complications reported, we consider long term antiviral prophylaxis appropriate after HZ diagnosis in patients continuing to receive natalizumab.

5. Worthing JF. Herpes zoster: Epidemiology, natural history, and common complications.