HIV Infection with Myasthenia Gravis


Abstract
A soldier presented in Jan 2002 with features of proximal myopathy and diplopia. Clinically he had features of myasthenia gravis, which was confirmed by significantly positive neostigmine test, decremental response on electrophysiological study and raised acetylcholine receptor antibody titres. He also tested positive for HIV during evaluation of a cervical lymph node detected incidentally. He responded well to neostigmine and has remained asymptomatic on follow up.

INTRODUCTION
HIV infection and myasthenia gravis are common disorders but their association is rare. Only a few case reports exist in the literature. Their coexistence may be related to the involvement of thymus, which is central to the pathogenesis of both these conditions or it may represent a chance coexistence. A literature search in Medline/Pubmed has not revealed this documentation in India. We believe that ours may be the first such case.

CASE REPORT
A 48 year old soldier presented in Jan 2002 with features of proximal muscle weakness of both upper and lower limbs of 3 weeks duration and episodic diplopia of a few days duration. There were no symptoms pertaining to sensory system, cranial nerve involvement, or bowel/bladder disturbance. General examination was unremarkable except the presence of solitary cervical adenopathy left side (2 cm size). Neurological assessment revealed proximal muscle weakness (Grade 4-/5) and easy fatigability on clinical fatigue testing (Single Breath Count, Breath Holding Test). Myasthenic features could be established by a significantly positive neostigmine test and a decremental response on electrophysiological study (Fig 1). Acetylcholine receptor antibody titers were raised (0.63 nmol/l). CT scan of chest and muscle enzymes was normal. He also tested positive for HIV by ELISA during evaluation of the cervical lymph node. Western blot confirmed the HIV status. His CD4 count was 350/cmm and CD4:CD8 ratio was 0.23. The cervical lymph node on biopsy was reported as reactive adenitis.

He denied history of high-risk behavior or blood transfusion. He had received open injuries during Kargil operation (1999) and had carried injured colleagues, who were bleeding, to safety. Hence there did exist the possibility of transcutaneous transmission.

He was started on treatment with Neostigmine (15 mg 6 hourly) and Probanthiline (15 mg TDS) to which he showed an excellent response. Steroids were withheld keeping in mind his immunosuppressed status and the excellent response he showed to Neostigmine alone. He was doing well on follow up after 6 months.

DISCUSSION
Skeletal muscle involvement in HIV is quite common and may occur at all stages of HIV-infection including being the first manifestation of the disease in some patients. It usually manifests as HIV associated myopathy (a myopathy that meets the criteria for polymyositis in a majority of patients, and of acquired nemaline myopathy in some cases) or as Zidovudine myopathy (a reversible mitochondrial myopathy). The
other causes of muscle involvement include HIV wasting syndrome, opportunistic infections, tumour infiltrations, vasculitis and rhabdomyolysis. Myasthenic weakness in HIV infection is rare and has been documented to occur as part of the HIV seroconversion syndrome. The association may be explained by thymus gland dysfunction leading to altered immune response. Alternatively, it may represent a chance co-occurrence of two disorders rather than any true association.

The true thymus does not fill up with inflammatory cells in myasthenia gravis. Rather, cellular infiltrates and adipose tissue fill the perivascular space around true thymus lobules, with eventual collapse of the epithelial component of the thymus. Studies have shown that, just as in myasthenia gravis, most of the lymphocytic infiltrate in HIV-1 infected thymuses is located within the perivascular space surrounding the thymic epithelium and contains peripheral CD8 CTL effector cells. The human thymus thus can be thought of as a chimeric organ comprised of both central and peripheral lymphoid tissues. The thymus morphology shows the presence of thymitis with B-cell germinal centers in the thymic medulla in early HIV-1 infection, and calcification and thymic atrophy with epithelial collapse in the late stages of HIV infection. It is postulated that the thymic epithelial atrophy and decrease in thymopoiesis that occurs in myasthenia gravis and HIV-1 infection may in part derive from cytokines or other factors produced by peripheral immune cells within the thymic perivascular space. In view of the similarity that these two disorders share histologically, their coexistence may suggest a hitherto unknown immunopathogenetic mechanism which comes into play in some cases of HIV infection leading to the development of myasthenia gravis.

Case reports exist documenting the improvement of myasthenic symptoms over time as the HIV infection progressed. In a patient with HIV infection, the cellular and humoral immune responses were studied longitudinally from the onset of generalized myasthenia gravis. Progressive decline in CD4+, CD45R+ and CD4+, CDw29+ T-cells, cellular immune responses to alloantigen and mitogen stimulation, and acetylcholine receptor antibody titers were associated with clinical improvement of all myasthenic symptoms.

The management is not markedly different in a case of myasthenia with HIV from a case with only myasthenia gravis. Steroids can be given as and when indicated as they have been used extensively in HIV infection for other indications like PCP infection. Steroids have been documented to increase the risk of opportunistic infections slightly in HIV infection, therefore when used are best used along with HAART regimes. The role of immunomodulatory therapy is not clearly known. Thymectomy did not preclude long-term survival or prevent the presence or rise of naive-phenotype peripheral T cells after HAART in a study of three patients who were thymectomized either before or during primary HIV infection. However, there is not enough data on the use of immunosuppressive drugs and thymectomy in HIV and hence they are best avoided.

When confronted with muscle weakness in HIV infection, it is well worthwhile to look for a coexisting myasthenia gravis.

References