Human Immunodeficiency Virus Infection in a Patient with Systemic Lupus Erythematosus

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Abstract

We describe a 47 years lady with systemic lupus erythematosus (SLE) who was infected with human immunodeficiency virus (HIV), due to transfusion either by blood or platelet concentrate. There was a near remission in the disease and during the course of follow up she developed cryptococcal meningitis. The approach to the diagnosis of HIV infection in a patient with SLE, the effect of SLE on the virus and vice versa and some management issues in this setting are discussed.

Human immunodeficiency virus (HIV) infection and systemic lupus erythematosus (SLE) share a number of clinical features that include fever, lymph node enlargement, skin rash and a host of renal, neurologic and hematologic manifestations. This problem is compounded by the fact that there may be weakly positive antinuclear antibodies (ANA) in HIV infected patients and false positive tests for HIV infection in patients with SLE.1

The occurrence of HIV infection in a patient with SLE is rare and to the best of our knowledge only 15 adults have been described with this occurrence.2,3 We have previously described one such case from our institution.4 The exact influence of HIV infection on SLE and vice versa are difficult to determine due to the rarity of the situation. Some reports have indicated that HIV infection may produce amelioration in the manifestations of SLE, especially when the CD4 count gets low. A corollary of the above is that deterioration in the manifestations may occur with anti-retroviral therapy and consequent improvement in CD4 counts.5 In this report we describe our second patient with concomitant SLE with HIV infection and discuss some of the diagnostic and therapeutic problems.

CASE REPORT

A 47 years female who presented to us in 1997 was diagnosed in another institution as having SLE in 1986 when she presented with bilateral symmetrical polyarthritis, fever, malaise, photosensitivity, hair loss and malar rash. Her ANA was positive. She was treated with prednisolone in a dose of 40 mg daily. The dose was titrated according to the disease activity. In 1997 she developed leucopenia and thrombocytopenia with the total leukocyte count of 3,400/mm² and a platelet count of 7,000/mm³. The latter led to epistaxis and haematemesis and required two units of whole blood and four units of platelet concentrate. Each of the donors was screened for HIV and hepatitis infections and had tested negative. At this stage she presented to us and her prednisolone dosage was increased to 60 mg/day and in four weeks time the counts normalized. Over the next two years her dosage of prednisolone was gradually tapered to 10 mg/day. She remained well until 28.12.99 when she had an episode of focal seizures affecting the left upper limb, without generalisation, unconsciousness or incontinence. She was treated in an outside institution with intravenous phenytoin but developed a second episode of left focal seizure with secondary generalization. A CT scan was normal and she was discharged on phenytoin in a dose of 300 mg/day. When she presented to us she was conscious, oriented, and afebrile and had a pulse rate of 70/min and the BP was 130/80 mm Hg. The rest of the systemic examination was normal. The urine examination was normal, as also the electrolytes, urea, creatinine and liver function. The cerebrospinal fluid showed 100 cells/mm³ with a differential count of 60% neutrophils and 40% lymphocytes. The proteins were 210 mg/dl and sugar was 50 mg/dl. The India ink preparation showed presence of Cryptococcus and cryptola antigen was positive in a dilution of 1:16. The culture showed growth of yeast species consistent with C. neoformans. MRI examination of the brain was normal. In view of the presence of cryptococcal meningitis and past history of transfusions HIV serology was performed and was positive. To rule out the possibility of a false positive result a qualitative RT-PCR was done and...
it, too, was positive. A serum sample drawn in March 1997 and kept in the serum bank also tested positive for anti-HIV antibodies. The CD4 count was 41/mm³, with CD8 count of 560/mm³ and CD4/CD8 ratio: 0.07. She tested negative for ANA at this admission. She denied any high-risk behaviour. Her husband tested negative for anti-HIV antibodies.

She was managed with standard doses of amphotericin B for a total duration of six weeks and after that she continued to be on fluconazole prophylaxis. Her HIV load was 2,11,181 copies/mm³ and she was started on zidovudine, lamivudine and saquinavir. Two weeks later she developed leucopenia and zidovudine was omitted. Six months later her viral load was 21,200 copies/mm³ and the CD4 count was 114/mm³. The prednisolone dosage had been tapered to 5 mg/day but by this time there was a recurrence of early morning stiffness and joint pains. These have so far been under control with anti-inflammatory medications. She was later on found to be anti-HCV antibodies positive and this was confirmed using an RT-PCR. She was administered a six month course of interferon-α and ribavarin, but this was unsuccessful as the RT-PCR remained positive at the end of therapy. Saquinavir was substituted with efavirenz at the time interferon was administered due to financial reasons. Currently she is asymptomatic on a combination of lamivudine, stavudine and efavirenz.

**DISCUSSION**

This patient highlights the course of a patient with SLE who develops AIDS, as defined by the presence of HIV infection and cryptococcal meningitis as the AIDS defining illness.

There are a number of pertinent issues in a case like this. These include the expanding spectrum of clinical autoimmunity among individuals with HIV infection. These include polyclonal hypergammaglobulinaemia, circulating immune complexes, and a host of autoantibodies that include ANAs, IgG, and IgA rheumatoid factor, and anti-phospholipid, anti-platelet, anti-RBC, anti-lymphocyte surface antigen, anti-neuronal, anti-neurotransmitters and anti-myelin associated antibodies. In a study where 151 consecutive patients with AIDS and AIDS-related complex were screened, 19 were positive for ANAs. Seventeen had low titer of 1:20 and two had titers of 1:160.6 False positive anti-HIV antibodies are known to occur in patients with SLE. In a situation where there is a doubt of the presence of HIV infection in a patient with SLE the diagnosis of HIV infection would need the detection of HIV antigens and one of the PCR analysis or a p24 capture assay will be needed to settle the diagnosis. In this patient a qualitative PCR was carried out to detect the presence of the viral antigens.

What are the effects of one on the other? SLE improved clinically and serologically with the occurrence of HIV infection. Previously studies have demonstrated improvement in SLE with a decline in CD4 counts. That does appear the case in our patient. She was in virtual remission at a CD4 count of 41/mm³. This notion also supports the contention that activated CD4+ lymphocytes play an important role in SLE. Studies in our case too support this belief since the percentage of CD4+CD25+ cells declined from 36 to 24 in a five-month period following anti-retroviral therapy. It is also possible that HIV may suppress activity of SLE soon after seroconversion even when the CD4 count is normal. This can be on account of the fact that HIV produces many immune effects that include polyclonal B cell activation and reduced antibody responses to various specific immunogens. Alternatively, there may be qualitative dysfunction before the start of CD4 cell depletion, which is manifested by reduced responsiveness of the CD4 cells to monocyte presented soluble antigens. A corollary to the above findings is that once the CD4 counts improve there may be a recurrence of symptoms related to SLE. There has been the reappearance of morning stiffness and joint pains with an increase in CD4 counts to 114/mm³. Significantly, ANA had become negative at the time of development of cryptococcal meningitis.

The effect of SLE on HIV infection is speculative and the studies published previously have suggested that SLE may accelerate the progression of HIV infection.4 Prednisolone may have been partly responsible for the acceleration in the course of HIV infection. Further, SLE has increased T cell activity and high levels of T cell activation results in accelerated HIV replication.

The issues of management of these patients has not been adequately addressed. Earlier reports have used zidovudine alone for treatment. That is inadequate therapy by present day standards. It would be reasonable to assume that optimum treatment of HIV infection be given using current guidelines. Using the combination recommended for the treatment of HIV infection there has been an increase in the CD4 count and a significant decline in the viral load in this patient. What remains uncertain is the management in case there is a further increase in CD4 counts and there is a recurrence of manifestations of SLE. We have so far successfully managed the patient with anti-inflammatory drugs alone, but if there develops a major organ involvement then a therapeutic decision shall have to be made according to the circumstances. This, then, could be the first reported case where a patient having both SLE and HIV infection has been administered the standard triple drug anti-retroviral regimen and where along with an increase in CD4 counts there has been a return of some of the minor manifestations of active SLE.

**REFERENCES**


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**Book Review**

**Borderlands of Epilepsy**

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Edited by: Ambar Chakravarty

**Foreword**

I am honoured to have been asked to write a foreword for the book ‘Borderlands of Epilepsy’ edited by Professor Ambar Chakravarty.

The first and foremost question to be answered in the management of epilepsy is: does the patient have epilepsy? A significant number of patients with so-called ‘intractable seizures’ have non-epileptic events. It would be a mistake to treat a non-epileptic event as epilepsy. By the same yardstick it would be erroneous not to diagnose a seizure disorder if the patient presents with atypical manifestations. This book serves precisely to answer this fundamental question.

The first chapter is a tribute to the eminent British neurologist Sir William Richard Gowers, from whose book ‘The Borderland of Epilepsy’ (written in 1907) the title of the present book is borrowed. The second chapter deals with the unusual manifestations of seizures. The next fourteen chapters deal exhaustively with non-epileptic episodic events that may be mistaken for epilepsy. The topics covered include syncope, cardiac events, drop attack, sleep phenomena, migraine, dizzy spells, psychogenic seizures and other events. The significance and limitations of electro-diagnostic procedures like EEG and video-EEG monitoring have been lucidly dealt with. The final chapter by the editor himself is a useful commentary summing up the various issues involved in making a positive diagnosis of epilepsy.

I would like to compliment Prof. Ambar Chakravarty for having invited well known neurologists from India and abroad to contribute chapters for this book. The trust reposed in him by the Association of Neuroscientists of Eastern India (ANEI) has been amply justified. By bringing out this monograph, the ANEI has done a useful service for the medical community. I am sure that neurologists, psychiatrists, physicians, pediatricians and all those who care for patients with epilepsy will find this book extremely valuable.

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