Introduction

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system (CNS), characterized by multifocal areas of demyelination of varying sizes, distributed throughout the brain. It is the only known clinical manifestation of an opportunistic infection by JCV (John Cunningham virus, named after the patient from whom it was first isolated in 1971). PML is an AIDS defining condition that occurs when the CD4 count is <100/µL. PML-immune reconstitution inflammatory syndrome (IRIS) is a paradoxical worsening or unmasking of PML, which occurs following the initiation of antiretroviral therapy (ART). IRIS is caused by the rapid recovery of the immune system in the presence of the pathogen.

There are very few studies which have looked into the outcome of PML-IRIS in HIV-infected patients across the globe. Data on ART and AIDS-associated PML-IRIS from India is scarce.

In this paper, we describe the clinical findings and progress of the disease in an Indian patient with HIV having a CD4 count of 44/µL.

Case Report

A 47-year-old male presented to us in April 2017. He was apparently normal 20 days prior to presenting to us when he noticed excessive fatigue and weakness which was progressive. Five days after onset of initial symptoms, he started having increasing difficulty in walking. Around this time, he also developed difficulty in swallowing. On further questioning, his wife gave a history of progressive weight loss of 20 kg over 2 years. There was no history of tuberculosis, diabetes mellitus, hypertension, or blood transfusions. No previous...
Abraham, et al.: Is this PML or PML-IRIS?

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Our µ and (b) MRI T1 - weighted

The onset of PML-IRIS

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Hence, we continued ART but replaced Tenofovir

The literature suggests that continuing ART is associated

The mechanism via which treatment with ART

40 mg once a day was started and then tapered over a period

The patient was brought on a stretcher, though conscious he was

After a week, he was sent back to our center. He was unconscious

Magnetic resonance imaging (MRI) with contrast of the brain

After our center, he was unconscious and febrile (100 °F). Nystagmus was noted bilaterally and
cogwheel rigidity was present in all four limbs.

At our center, we were confronted with the following clinical
dilemmas. First, was his condition explainable by a diagnosis of
PML alone or was this PML-IRIS? Second, should we restart
ART or withhold it? Third, was there a role for steroids in his
management? And last, if we chose to start ART, should we
switch to a regimen with greater CNS penetration?

After reviewing the literature and internal discussion, we thought
this presentation was more likely due to PML-IRIS than PML
alone. We felt that the literature supported ART continuation
and hence continued ART. We chose to add steroids though
the literature was equivocal on its benefit. Prednisolone of
40 mg once a day was started and then tapered over a period of
4 weeks. We also switched his ART regimen from Tenofovir,
Emtricitabine, and Efavirenz to a combination of Zidovudine,
Lamivudine, and Efavirenz (Zidovudine has better blood brain
barrier penetration).

By the eighth day of switching ART and adding prednisolone,
patient started to show improvement. He was able to sit in a
chair and his speech was clearer and his temperature was back
to normal. After 40 days of initiating treatment, patient was fully
oriented, walking without support but has difficulty maintaining
balance, speech was coherent, and he was able to perform his
daily activities without help. He still had episodes of amnesia. He
was discharged from our centre on June 17 with advice for regular
follow-up. A review on July 20 showed further improvement in
his condition. He had gained 10 kg since his presentation at our
center. He walks with a steady gait, and speech is much clearer.
He contemplated returning to work as a civil engineer.

Discussion

A paradoxical worsening of pre-existing, untreated, or partially
treated opportunistic infections due to rapid recovery of the
immune system following ART initiation is called IRIS.\[9\]
PML-IRIS is usually seen in patients starting therapy with CD4
count <50/µL.\[8\] The mechanism via which treatment with ART
leads to PML-IRIS is not clearly understood, but it is postulated
that a sudden recovery of T-cell activity due to ART with a
high pathogen (JCV) load results in a massive inflammatory
response that damages the brain. This results in a T-cell mediated
encephalitis.\[8\] Occasionally, the damage can be so severe that
it leads to a massive swelling of the brain with herniation and
death.\[2\]

It is important to differentiate between the diagnosis of PML
and PML-IRIS as they differ in treatment and failure to choose
appropriate treatment might lead to the death of the patient.
PML-IRIS can be differentiated from PML by the following:
(a) clinical profile of worsening symptoms on initiation of
treatment is suggestive of IRIS\[8\] and (b) MRI T1-weighted
images of PML are hypointense and do not show enhancement
with gadolinium, whereas patients who develop IRIS may show
variable degrees of enhancement.\[3\] The onset of PML-IRIS
can vary from 1 week to 26 months after ART initiation.\[8\] Our
patient presented with worsening of symptoms 10 days after
initiating ART.

There is no recommended specific antiviral therapy against
JCV.\[2\] The literature suggests that continuing ART is associated
with better outcome in patients with PML. The prognosis of
patients without initiation of antiretroviral treatment is poor
with an average survival of 2–4 months for HIV-positive
patients.\[5\] Hence, we continued ART but replaced Tenofovir
with Zidovudine for better CNS penetration.\[8\]

Although there are no treatment guidelines that clearly
recommend the use of steroid in PML-IRIS, some studies note
a trend for lower mortality in patients with PML-IRIS with
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reports from India exposes the probability of under diagnosis
of PML-IRIS. Significant recovery of our patient with the
continuation of ART and steroidal support strongly advocate
the need for clinicians to have a high index of suspicion for
early detection of PML-IRIS and initiation of steroid therapy
with continued ART.

Declaration of patient consent
The authors certify that they have obtained all appropriate
patient consent forms. In the form the patient(s) has/have
given his/her/their consent for his/her/their images and other
clinical information to be reported in the journal. The patients
understand that their names and initials will not be published and
due efforts will be made to conceal their identity, but anonymity
cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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