

Immune Reconstitution Inflammatory Syndrome – Kochs

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Abstract: Immune Reconstitution Inflammatory Syndrome (IRIS) is defined as paradoxical deterioration in clinical status after Anti Retroviral Therapy (ART) initiation despite improved immune function due to inflammatory response against infectious agent, which may or may not be diagnosed at initiation of ART. Tuberculosis is most common opportunistic infection in HIV patients. Though it can present at any stage of HIV infection, it appears more commonly when CD4 count is around 350 cells/microL. In advanced stages of AIDS, tuberculosis remains quiescent and may not present clinically or radiologically. With initiation of ART, tuberculosis may appear as IRIS. We report a case of tuberculosis presenting as IRIS in HIV-1 infected patient who had no previous history of mycobacterial infection. The patient was kept on ART with a baseline CD4+ count of 63 cells/microL. Ten days after initiation of ART patient had massive pericardial effusion leading to cardiac tamponade with pleural effusion and fever. His repeat CD4 count increased to 100 cells/mm³. On analysing pericardial and pleural effusions, a diagnosis of tuberculosis was made and patient was started on anti-tuberculosis therapy (ATT) along with ART and systemic steroids. Tuberculosis is commonest opportunistic infection presenting as IRIS.

Keywords: HIV, Immune reconstitution inflammatory syndrome, Tuberculosis.

Key Message: In a resource poor setting like India, tuberculosis is endemic and is one of the most common opportunistic infection in HIV infected individuals which can be a common presentation of IRIS.

I. Introduction

Immune Reconstitution Inflammatory Syndrome (IRIS) is defined as paradoxical deterioration in clinical status after Anti Retroviral Therapy (ART) initiation despite improved immune function due to inflammatory response against infectious agent, which may or may not be diagnosed at initiation of ART¹. Previous infections in individuals with IRIS may have been previously diagnosed and treated or they may be subclinical and later unmasked by the host's regained capacity to mount an inflammatory response². Mycobacterium tuberculosis (TB) is one of the commonest pathogen known to cause IRIS with reported incidence varying from 8 to 43%^{3,4,6,7}.

Several risk factors for the development of paradoxical TB-IRIS are – shorter delay between commencing tuberculosis treatment and ART, low baseline CD4+ cell count, higher baseline viral load, rapid reduction in viral load on ART and disseminated tuberculosis. The majority of the cases develop IRIS within initial few weeks (more common in first two to three weeks) to six months or it may occur in even up to one year of ART initiation^{1,5,6,8}. The patient usually presents with worsening or appearance of new clinical or radiological features. With this background, we are presenting a case of HIV patient on ART, who developed massive pericardial effusion with cardiac tamponade and minimal pleural effusion as IRIS.

II. Case Report

A 40 years old male was diagnosed as HIV-1 positive with baseline CD4 cell count of 63 cells/microL. He was started on ART with Zidovudine, Lamivudine and Nevirapine regimen at govt. general hospital on 12th July 2013. The patient was screened for any focus of tuberculosis, X-ray chest had no evidence of any active or latent focus of infection before initiation of ART. Ten days after the initiation of ART, he presented with chest pain, high temperature, difficulty in lying down and altered level of consciousness. The patient was hospitalized and was investigated accordingly. On radiological examination, X-ray chest (Figure-1) was suggestive of massive cardiomegaly with minimal pleural effusion. 2D-echo showed massive pericardial effusion and cardiac tamponade. With the help of physician, pericardial effusion was aspirated and analyzed, which showed numerous lymphocytes. As Koch's infection is the most commonest cause of pericardial effusion and the aspirate yield was lymphocyte predominant. His repeat CD4 count increased to 100 cells/mm³ suggesting TB presenting as IRIS. Without interruption of ART the patient was started on Anti-Tuberculous Treatment (ATT) with Isoniazid, Pyrazinamide, Rifampicin and Ethambutol along with oral Prednisolone of 1.5mg/kg body weight for two weeks. The patient was gradually relieved of all symptoms except fever. As the fever was persistent, we repeated X-ray chest (Figure-2) which showed an increase in the amount of effusion in the pleural cavity which was aspirated. A repeat chest X-ray (Figure-3) five days later, suggests moderate cardiomegaly and there was minimal pleural effusion. He was discharged after tapering the steroid dosage with 0.75mg/kg body weight for 2 weeks along with ATT and ART and the patient history was uneventful till date.

III. Discussion

Initiation of ART, will reduce the viral load and improves the immunological status of the patient. With this improvement in the immunological status, patient feels better and gradually recovers from opportunistic infections and the patient should not succumb to any infections. On the contrary, in IRIS with the introduction of ART the patient's general condition may worsen which at times may be lethal. Common clinical conditions which usually present as IRIS are – Tuberculosis (both pulmonary & extra-pulmonary) and Mycobacterium Avian Complex(MAC) constitute 30%⁸, Pneumocystis jiroveci pneumonia, and Cytomegalovirus(CMV) retinitis, of which CMV retinitis is the most dreaded, as patient will end up in loss of vision with initiation of ART. For these reasons, it is mandatory to investigate thoroughly for any undetected Koch's/CMV infections and treat the opportunistic infection before initiation ART.

Tuberculosis is usually spread from person-to-person through the air by droplet nuclei that are produced when a person with pulmonary or laryngeal tuberculosis coughs, sneezes, talks or sings. Transmission generally occurs indoors, in dark, poorly ventilated spaces where droplet nuclei stay airborne for a long time. Once infected, the progression to active disease is dependent on the immune status of the individual⁷.

People with suppressed immunity are more likely to develop active TB than those with normal immunity. The annual risk of TB in an HIV positive person is 10% compared to a lifetime risk of 10% in a healthy individual⁷. Infection with HIV increases the risk of progression of recent M. tuberculosis infection, reactivation, relapse and re-infection. Reactivation of latent infection occurs as weakening of the immune system by HIV infection acts as a trigger⁷. In advanced stages of HIV even the unusual sites like bone marrow, liver and spleen become favorable sites for multiplication of mycobacteria.

HIV is responsible for a large increase in the proportion of patients with smear-negative pulmonary and extra-pulmonary TB. These presentations are most common in advanced stages of HIV which are difficult to diagnose as they are sputum negative and cannot be detected radiologically. These patients have inferior treatment outcomes, including excessive early mortality, compared with HIV-positive, smear-positive pulmonary TB(PTB) patients. It is due to late presentation, diagnosis and initiation of treatment in smear – negative patients. This delay in diagnosis is now resulting in dreadful complications with IRIS on initiation of ART as tuberculosis is first presentation of IRIS. Therefore rapid diagnoses of not only smear positive PTB but smear-negative pulmonary and extra-pulmonary TB and early initiation of treatment is key to reduction of TB mortality in people living with HIV⁷.

Smear microscopy has good specificity for TB but has very low sensitivity in detecting TB in patients with non cavitary pulmonary disease or low bacillary load in sputum (e.g. HIV positive patients) who are sputum negative⁷. In a resource poor setting country like India mycobacterium culture is not easily available, so could not be done. Viral load levels at initiation and following initiation of ART could not be done due to financial constraints. There is a need for prolonged durations of treatment with ATT in case of disseminated infection in HIV patients.

The present case was completely asymptomatic clinically and even after investigations both radiologically and hematologically at the start of ART with low CD4 counts of 63cells/mm³. After 10 days of starting ART, general condition of the patient deteriorated with complaints of fever, chest pain and difficulty in lying down. His repeat CD4 count increased to 100 cells/mm³ from 63 cell/mm³. The knowledge of IRIS comes into play in situations like this as it readily clinches the diagnosis on taking into account of patient's condition and his CD4 count.

As X-ray was suggestive of massive cardiomegaly, pleural effusion and 2D-echo showed cardiac tamponade, we have managed the patient with the help of physician. Koch's infection is the most common cause of pericardial effusion, in our country where TB is highly endemic. Along with specific therapy of ATT, steroids were employed in this patient to surmount the overwhelming symptoms and recurrent accumulations of fluid in pericardial and pleural cavities due to IRIS. Steroids played a great role in recovery of this patient. Unless steroids were employed as in this case we cannot tide over life threatening complications of IRIS.

Tuberculosis can develop during various stages of immune depletion. With the advancing immune depletion, extra-pulmonary TB occur with greater frequency. This unmasking IRIS can develop also in patients with no previous history of opportunistic infections, since the restored immunity might respond to the subclinical opportunistic infection or other yet undefined antigens^{8,9}.

We present this case report, as it clearly depicts the very nature of IRIS, which is life threatening resulting in morbidity and mortality where timely diagnosis and intervention play a major role. In developing country like India, tuberculosis is endemic in the community which is the most common opportunistic infection and infects every part of the body and is the most common presentation of IRIS, as in this case, where we start ART at low levels⁹. Here we can appreciate the severity of IRIS. We can expect more cases of IRIS in our country as access to ART is increasing and patients are more likely to have advanced immunosuppression with undiagnosed opportunistic infections at the initiation of ART^{10,11}. So we must be vigilant and diligent efforts must be made to diagnose and treat opportunistic infections before initiating ART.

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Figures and legends:

Figure -1: X-ray chest PA view showing pleural effusion and cardiomegaly.

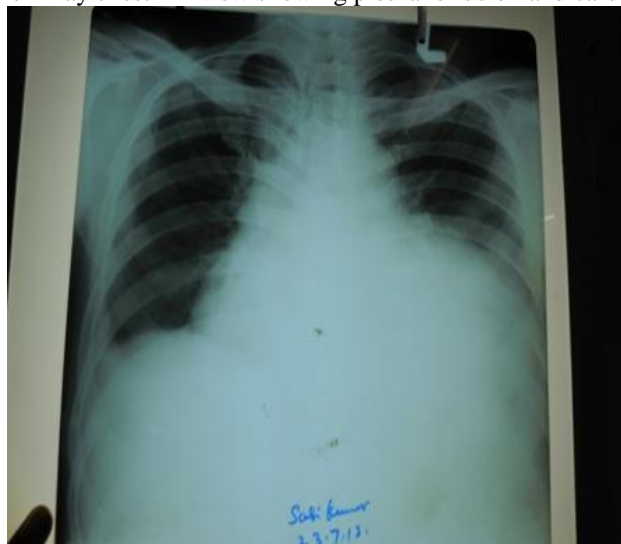


Figure-2: X-ray chest PA view showing increase in the amount of effusion in the pleural cavity.



Figure-3: X-ray chest PA view showing decrease in the amount of pleural effusion

