Case Report

Idiopathic CD4+ T cell Lymphocytopenia (ICL): an Extremely Uncommon Presentation of ICL with PCP in an HIV Negative Patient

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INTRODUCTION

At the beginning of the HIV/AIDS epidemic in the 1980s, the medical community learned about a subset of patient population who presented with opportunistic infections, had severely depressed CD4 T cell counts, but to everyone's surprise these patients did not have HIV infection and there was no other explanation to account for their immunodeficiency [1-5]. Emergence of these anomalous findings lead to a review of 230,179 cases in the Center for Disease Control and Prevention (CDC) AIDS Reporting System from 1980s to the early 1990s and found 47 cases of Idiopathic CD4+ T cell lymphocytopenia (ICL) [6]. To our knowledge these 47 cases represent the largest pool of ICL patients and who were then studied prospectively between 1992 through 2006 to define the natural history of the disease [6-7]. Most of our understanding of the rare ICL syndrome comes from the findings obtained from these 47 patients [7].

CASE REPORT

We present the case of a 38 year old, previously healthy male with past medical history significant only for intravenous drug abuse. He initially presented to the emergency department with worsening shortness of breath and had to be supported on a mechanical ventilator for subsequent hypoxic respiratory failure. A chest XR is shown below. Patient was pancultured and a host of labs were sent for analysis. All cultures were negative except for the growth of Pneumocystis jirovecii in the sputum. Based on these findings, a diagnosis of Pneumocystis jirovecii pneumonia (PCP) was made and based on prevailing clinical experience the next logical step was to check for infection with HIV. Customary labs were sent for the diagnosis of HIV via DNA PCR along with the evaluation of CD4 T cell count. While the CD 4 T cell lymphocyte count was expectedly low at 74, the HIV test was surprisingly negative. Patient's hepatitis panel revealed Hepatitis C antibodies in the serum but the viral load was exceptionally low. Liver function tests including albumin and INR were both normal (Figure 1).

After a prolonged hospital course, the patient fully recovered and was discharged home. A follow up evaluation of the CD 4 T cell lymphocytes was stable at 72 and the patient remained persistently negative for the HIV infection.

DISCUSSION

ICL is a rare syndrome defined by chronically low CD4 T cell count, absence of infection with HIV and absence of any other explanation for the low CD4 T cell count on two different occasions. ICL is found all throughout the world and there does not seem to be gender preponderance either [8-12]. Adult individuals make up the majority of the ICL cases, although few and far between a handful of pediatric and elderly cases of ICL have also been reported in the past [8-12]. In spite of aggressive research, an etiology for this disease has not been established yet [13, 14]. Because of the higher proportion of IV drug abuse and high risk sexual activity in the original 47 patients [1, 15, 16], a transmissible cause was initially sought. A retrospective review of 1200 HIV-negative patients with history of IV drug abuse only found 4 cases of ICL [17] whereas separate studies on subjects with high risk sexual activity and a history of exposure...
to blood products also failed to show any statistically significant correlation with ICL [18]. These studies were especially helpful in aiding to rule out a contagious cause of ICL [19, 20]. Interestingly, our patient also had some of the similar characteristic found in the original 47 patients. He was not only a long term IV drug user, but was also involved in high risk sexual activity. These findings may explain the onset of hepatitis C in our patient, but based on the discussion above, the actual instigating factors for the onset of ICL remains elusive. Generally accepted pathophysiology of ICL involves increased apoptosis from crosslinking of the T cell receptors [21, 22].

Clinical manifestations of ICL vary greatly depending on the extent of the drop in CD4 T cell count and chronicity of this decrease [23]. Depending on the CD4 T cell count, ICL may be discovered in an asymptomatic patient on incidental routine labs to individuals who are exceptionally sick from opportunistic infections. ICL patients may present clinically similar to the HIV/ AIDS patients, but there are significant differences requiring special attention. Most notably, the ICL patients present with a better prognosis compared to the HIV patients [24-27]. Unlike the HIV patients whose CD4 T cell count can drop precipitously without treatment, the decline in CD4 T cell count in ICL patients is relatively slow and stabilizes at a chronically low level. This difference might account for the comparatively better outcomes associated with this syndrome [28]. Unlike HIV/AIDS, ICL is not sexually transmitted and this has been repeatedly shown by published works by several investigators [29,30]. Women constitute half the total ICL patient population compared to only one-third seen in HIV/AIDS. Patients also tend to have normal or decreased levels of immunoglobulin compared to the usual hypergammaglobulinemia seen in HIV/AIDS [31]. Furthermore, it was also shown that the two entities have different susceptibilities to opportunistic infections, with HIV/AIDS patients faring worse [32,33].

Majority of the reported cases have described infection with Mycobacterial or Cryptococcal disease and progressive multifocal leukoencephalopathy [34,35]. Other ICL related opportunistic comorbidities comprise a long list, ranging from viral, bacterial and protozoan infections to autoimmune disease to various malignancies [35]. Our patient represented this small subset of the already rare ICL patient population who are infected by Pneumocystis jirovecii.

While no standard treatment options exist, management is usually based on treating the underlying opportunistic infections. The general susceptibility to opportunistic infections is proportional to the extent of the drop in CD4 T cell count. It is necessary [37-42]. Stem cell transplantation carries its own risks and its use has not been well documented [43].

The prognosis depends on the severity of the opportunistic infections and by some accounts patient with a higher expression of HLA-DR on CD4+ T lymphocytes and a lower CD8+ T cell count appear to have a higher rate of mortality [44].

**CONCLUSION**

ICL is a very rare medical syndrome and the presence of Pneumocystis jiroveci pneumonia (PCP) in our patient makes this case even more unique. Smaller ICL patient population has always been a limiting factor for conducting research and a major hindrance in finding an etiology for the syndrome. Our case report adds to this small pool of ICL patients to assist in future investigations. The presentation of ICL varies tremendously and in its extreme form may mimic AIDS. It carries different prognosis and therefore the diagnosis of ICL should always be considered in the differentials while managing HIV negative patients with low CD4 T cell count. While the etiology of ICL remains a mystery, the advancements in genomic sequencing studies has opened access to newer frontiers and a breakthrough might just be around the corner.

**REFERENCES**

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