CASE REPORT

IDIOPATHIC CD4 LYMPHOCYTOPENIA WITH ADRENAL HISTOPLASMOSIS

Tony Ete[1], Sumantro Mondal[2], Debanjali Sinha[2], Taso Beyong[1], Synrang B Warjri[1], Jyotirmoy Pal[3], Alakendu Ghosh[2]
[1] Department of Medicine, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India
[2] Department of Rheumatology, Institute of Post Graduate Medical Education and Research, Kolkata, West Bengal, India
[3] Department of Medicine, Institute of Post Graduate Medical Education and Research, Kolkata, West Bengal, India

Correspondence to: Tony Ete (tetepete@gmail.com)

DOI: 10.5455/ijmsph.2014.170920144 Received Date: 09.08.2014 Accepted Date: 17.09.2014

ABSTRACT
Opportunistic infections like cryptococcus, mycobacteria, pneumocystis carini, candidiasis and cytomegalovirus were reported to complicate idiopathic CD4 lymphocytopenia (ICL). However, a few cases of histoplasma infection has been reported in ICL. Here we are reporting a case of adrenal histoplasmosis in a patient presented with vague abdominal pain and weight loss who was later diagnosed to be a case of idiopathic CD4 lymphocytopenia.
Key Words: Idiopathic CD4 Lymphocytopenia (ICL); Adrenal Histoplasmosis; Histoplasma Infection

Introduction

Idiopathic CD4 lymphocytopenia (ICL) is a condition characterized by the decrease in CD4 count with consequent opportunistic infections. It was described for the first time in 1992. Both HIV and idiopathic CD4 lymphocytopenia are immunocompromised states - but they do differ with respect to CD8+ level and hypergammaglobulinemia. Fungal infections with Cryptococcus, Pneumocystis jiroveci, Candida are common in both HIV and ICL. Histoplasmosis, a fungal infection caused by soil-based fungus histoplasma capsulatum, is commonly found in immunodeficient individuals such as AIDS, transplant patients and patients with haematological malignancies. [1] Only few cases of histoplasmosis due to ICL has been reported.

Case Report

A 38 years old male, non-diabetic, hypertensive, and non-alcoholic, presented with complaints of vague abdominal pain in the right upper quadrant and weight loss for three months. The pain in abdomen was dull aching in nature with no relation to intake of food and passage of stool. Appetite was preserved. The patient had no fever. There was no past history of tuberculosis or symptoms suggestive of hepatitis. No history of any major illness and surgery in the past was elicited. The patient was unmarried, and had no history of multiple unprotected sexual intercourses. On examination, the patient was afebrile, alert, conscious, and with normal vitals. Examination of the respiratory system, cardiovascular system, nervous system and lymphoreticular system revealed no abnormality. However, a firm, non-tender liver with well-defined margin was palpable 3 cm below right costal margin with no bruit and rub. Routine blood count revealed haemoglobin- 11.4 gm/dl, RBC count- 4.49 million/cmm, total leucocyte count- 4600/cumm, adequate platelets, ESR of 30 mm. Liver function test revealed total bilirubin- 0.68 mg/dl, total protein- 7.08 gm/dl, albumin- 4.30 gm/dl, globulin- 2.78 gm/dl, SGPT- 29 U/L, SGOT- 37 U/L, serum GGT- 35 U/L. Serum creatinine was 0.9 mg/dl, urea- 23 mg/dl. Blood for HIV 1 and HIV 2 antibody was negative. Sputum examination was negative for bacteria on Gram- and acid fast-staining on two occasions. Blood screen for HIV1 and HIV 2 antibody was negative. Routine sonography of abdomen showed an enlarged liver, and a mass on the upper pole of both kidneys. CT scan of abdomen was carried out with contrast, which showed enlarged adrenal glands with heterogeneous echogenic shadows. CT guided biopsy of the adrenal gland was carried out and sample was sent for histopathological examination. Report revealed presence of histoplasma in the substance of adrenal glands. As the patient had no other features suggestive of immunosuppression, no history of taking immunosuppressive drugs, and no history of multiple unprotected sexual intercourse, it was difficult to explain the presence of histoplasma infection in a minimally symptomatic individual. Blood for CD4 count was sent - keeping in mind the probability of non HIV AIDS. Blood for CD4 was 216 /micro litre. The patient was started on antifungals and discharged in stable condition. Blood test for CD4 count was repeated after 6 weeks, which showed a CD4 count of 210 /micro litre. Patient was diagnosed as a case of idiopathic CD4 lymphocytopenia with adrenal histoplasmosis.

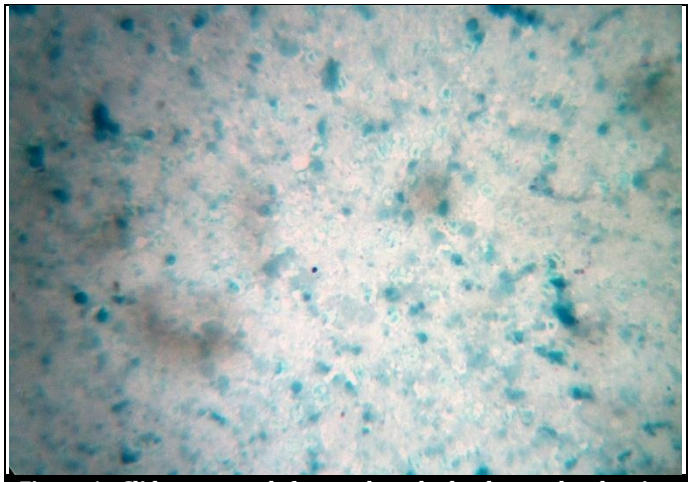

Figure-1: Slide prepared from adrenal gland sample showing histoplasma

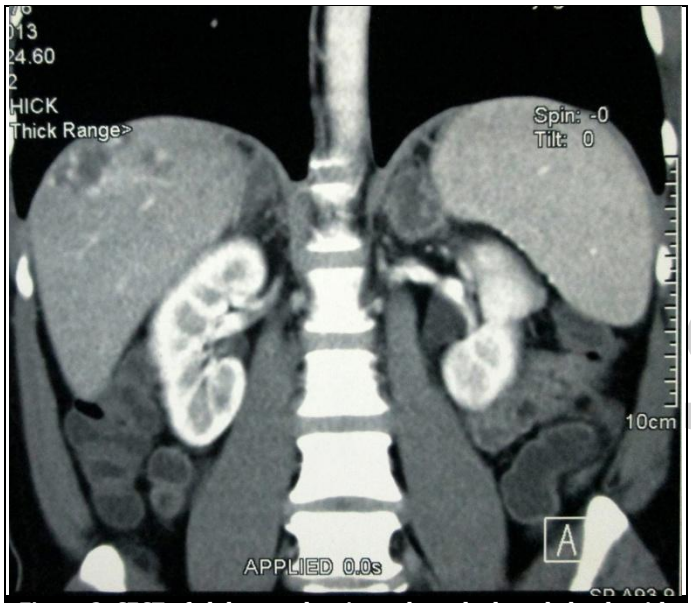

Figure-2: CECT of abdomen showing enlarged adrenal glands with heterogeneous echogenic shadows

Discussion

Idiopathic CD4 lymphocytopenia for the first time was described in the year 1992 by the CDC, as cases which demonstrated depressed (<300/cumm) numbers and proportions of CD4 count (<20% of total T cells), on at least two consecutive occasions, with no laboratory evidence of HIV-1 and HIV-2 infection, HTLV-1 or HTLV-2 infection, and the absence of any primary or secondary immunodeficiency disease, or treatment associated with depressed level of CD4 levels. By mid-1993,100 patients had been described. As no clustering of cases were documented, CDC concluded that although an unknown infectious agent of immunodeficiency cannot be ruled out definitively, data did not suggest the condition to be caused by transmissible agent. Persons donating blood to the affected patients, or in sexual contacts, were clinically well and had normal CD4 counts. There was no apparent predilection to one geographical area. 259 cases were reviewed, and the mean age was 40.7 years. Most of the patients were diagnosed upon development of opportunistic infections, without the presence of identifiable underlying immunocompromised status. Male to female ratio was 1.8:1.[2] Idiopathic CD4 lymphocytopenia (ICL) was a possible cause of opportunistic infections in the so-called immunocompetent host, unless they are screened with CD4 Counts after an HIV negative report. However, It was unclear whether idiopathic CD4+T cell lymphocytopenia develops as a consequence to an infection, or the infection is the cause of low CD4 +T cell count.[3] Two factors related to CD4+ lymphocyte function play a role in development of ICL. Firstly, the increased activation of CD4 can have a role, which may result from stimulation by an unidentified pathogen that results in a persistent decrease in the number of CD4+ lymphocytes. Secondly, the apoptosis of CD4+ lymphocyte may be associated with enhancement of expression of Fas and Fas ligand.[4] Clinical spectrum of Idiopathic CD4 lymphocytopenia ranges from an asymptomatic laboratory abnormality to life threatening complications. Opportunistic infections including Cryptococcus, Mycobacteria, Pneumocystis carini, Candida and Cytomegalovirus were reported to complicate idiopathic CD4 lymphocytopenia. Cryptococcal and non tuberculous mycobacterial infections are major presenting opportunistic infections of ICL.[5] The most important differential diagnosis of ICL is HIV infection. The decline of CD4 cell counts of the patients with idiopathic CD4 lymphocytopenia is slow or even absent over time as compared to HIV infection. ICL patients usually do not have increased numbers of CD8+ T lymphocytes, unlike HIV patients who do have an early increase in CD8+ T cells in response to the infection. Infectious agents such as bacteria, virus (Ebstein-Barr virus and cytomegalovirus), parasite and fungus can depress CD4 counts, and the changes associated are usually transient.[4] Common variable immunodeficiency can present with low CD4 counts and opportunistic infections, but it is usually associated with low levels of immunoglobulins, differentiating this condition from Idiopathic CD4 lymphocytopenia.[6] Reviewing of literature shows that ICL can be associated with any opportunistic infection associated with AIDS.[7] Histoplasmosis infection is very common in patients with AIDS. However, only few cases of histoplasmosis due to ICL have been reported: e.g. one case of disseminated histoplasmosis, a single case of pulmonary histoplasmosis[8], one case of mediastinal

lymphadenopathy revealing histoplasmosis[7], one case of histoplasmosis-induced brain abscess and one case of extrapulmonary histoplasmosis[9], one case of histoplasmosis-related pleural effusion[10]. Here we are presenting a case of adrenal histoplasmosis, which presented with nonspecific symptoms of abdominal discomfort, in whom, HIV 1, HIV 2, HTLV 1 and HTLV 2 were excluded. CD4 count in blood was found to be lower than 300/cumm on two occasions separated by 6 weeks. Finally, the patient was diagnosed as a case of adrenal histoplasmosis in ICL. He was treated with Itraconazole 200 mg daily and discharged in a stable condition with an advice to follow up.

Conclusion

In summary, we present a case of adrenal histoplasmosis in a patient with ICL. Due to their poor response to therapeutic interventions, a high index of suspicion has to be maintained in their identification. Prophylactic antifungal treatment was given and continued as recommended.

References

1. Kauffman CA. Histoplasmosis: A clinical and laboratory update. Clin Microbiol Rev 2007;20:115-32.
2. Ahmad DS, Esmadi M, Steinmann WC. Idiopathic CD4 Lymphocytopenia: Spectrum of opportunistic infections, malignancies, and autoimmune diseases. Avicenna J Med 2013;3:37-47.
3. Augustine R, Khalid M, Misri ZK, Hegde S. Idiopathic CD4+ Tlymphocytopenia—adiagnostic dilemma. J Assoc Physicians India. 2010;58:45-7.
4. Zonios DI, Falloon J, Bennett JE, Shaw PA, Chaitt D, Baseler MW, et al. Idiopathic CD4+ lymphocytopenia: Natural history and prognostic factors. Blood 2008;112:287-94.
5. Walker UA &Warnatz K. Idiopathic CD4 lymphocytopenia. Curr Opin Rheumatol 2006;18: 389–95.
6. Rabab AA, Amjad HS & Fatih EM. Common variable immunodeficiency with CD4 T lymphocytopenia and overproduction of soluble IL-2 receptor associated with Turner's syndrome and dorsal kyphoscoliosis. Clin Pathol 1997;50: 876–9.
7. Spira TJ, Jones BM, Nicholson JK, Lal RB, Row T, Mawle AC, et al. Idiopathic CD4+ T-lymphocytopenia – An analysis of five patients with unexplained opportunistic infections. N Engl J Med 1993;328:386–93.
8. Confalonieri M, Aiolfi S, Gandola L, Scartabellati A, Colavecchio A, Cannatelli G, et al. Disseminated histoplasmosis and idiopathic CD4+ T-lymphocytopenia. An autochthonousItalian case. Press Méd 1995;24:459.
9. Tassinari P, Deibis L, Bianco N, Etcheveria de Perez G. Lymphocyte subset diversity in idiopathic CD4+ T-lymphocytopenia. Clin Diagn Lab Immunol 1996;3:611–3.
10. Kortsik C, Elmer A, Tamm I. Pleural effusion due to Histoplasma capsulatum andidiopathic CD4 lymphocytopenia. Respiration. 2003;70:118-22.

Cite this article as: Ete T, Mondal S, Sinha D, Beyong T, Warjri SB, Pal J, et al. Idiopathic CD4 lymphocytopenia with adrenal histoplasmosis. Int J Med Sci Public Health 2014;3:1562-154
Source of Support: Nil
Conflict of interest: None declared