

Case Report



A rare case of idiopathic cluster of differentiation 4⁺ T-cell lymphocytopenia presenting with disseminated tubercular infection

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Abstract

Idiopathic cluster of differentiation 4⁺ (CD4⁺) T-cell lymphocytopenia is a rare heterogeneous clinical syndrome characterized by low absolute CD4 counts on two different occasions without any evidence of other known cause of immunodeficiency including human immunodeficiency virus (HIV), infections or drugs associated with fall in CD4⁺ count. Also referred to as severe unexplained HIV seronegative immune suppression by the World Health Organization, it was first described by Centers for Disease Control in 1992 in patients with opportunistic infections who were negative for HIV but had low CD4 counts. Patients typically present with opportunistic infections, malignancies, or autoimmune disorders. There have been case reports on opportunistic infections such as cryptococcal meningitis or non-*Mycobacterium tuberculosis* infections in these patients. However, no case of disseminated *M. tuberculosis* has been reported as such in Indian literature. We present a case of disseminated tuberculosis with low CD4 counts without any evidence of HIV infection.

Keywords: Cryptococcal meningitis, disseminated tuberculosis, idiopathic cluster of differentiation 4⁺ T-cell lymphocytopenia, immunodeficiency, opportunistic infections

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Introduction

Idiopathic CD4 cell Lymphocytopenia (ICL) is a rare disorder leading to depletion in cell mediated immunity. Such patients are at increased risk of opportunistic infections. Being rare, it is less sought after, in patients who present with opportunistic infections who do not show any obvious reason for depressed immunity such as HIV, malignancy, drugs etc. We report a case of one such patient who presented with disseminated tubercular infection and was evaluated to have Idiopathic CD4⁺ cell lymphocytopenia.

Case Report

A 45-year-old male with no previous co morbidities, presented in outpatient department with of low-grade fever associated with evening rise since 1-month. There

was no respiratory or neurological complaint. However, history of loss of appetite and weight was present. His general physical examination was essentially normal. Investigations showed mild leukocytosis and high erythrocyte sedimentation rate of 35 mm. Urine routine showed 10–15 pus cells but culture was sterile. His Widal, mantoux, Brucella antigen, and cytomegalovirus serology were also negative. He was admitted for further evaluation. The chest X-ray was normal but contrast enhanced computed tomography chest showed multiple miliary nodules in bilateral lung fields suggestive of tuberculosis [Figure 1]. The patient was started on anti-tubercular therapy (ATT), four drug

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regimen. The patient improved symptomatically and was discharged.

The patient was fine until after 3 weeks when he presented with weakness of all four limbs and altered sensorium. On examination, he had irrelevant talks, and meningeal signs were present. All routine investigations were normal. The magnetic resonance imaging (MRI) brain was done which revealed multiple areas of T₂ hyperintensities suggestive of perilesional edema. However, cerebrospinal fluid (CSF) analysis was deferred in view of extensive brain edema. Anti-edema measures were started. Neurology consult was taken and contrast enhanced MRI brain was done which showed multiple tuberculomas with perilesional edema [Figure 2a and b]. Human immunodeficiency virus (HIV) (by ELISA and Western blot) was negative, but CD4 counts were low (absolute CD4 count - 32 cell/cumm). Bone marrow aspiration and biopsy were done which showed multiple granulomatous lesions suggestive of tuberculosis. ATT was continued. His sensorium and quadriplegia improved gradually. His repeat CD4 count was 51 cell/cumm. The patient was started on Septran DS for primary prophylaxis. The patient improved and was discharged in stable condition. On follow-up, repeat MRI showed resolution of edema [Figure 3a and b].

Discussion

Idiopathic CD4⁺ T-cell lymphocytopenia (ICL) is a rare heterogeneous clinical syndrome defined by decreased number of circulating CD4⁺ T-cell lymphocytes (<300 cell/cumm or < 20% of total T-cells) on more than one occasion. Though World Health Organization recognizes it as severe unexplained HIV seronegative immune suppression. It was first described by Centers for Disease Control^[1] in 1992 in patients with opportunistic infections who were negative for HIV but had low CD4 counts. To diagnose ICL, there should be no laboratory evidence of other known cause of immunodeficiency including infections or drug therapy associated with fall in CD4 count. Patients with ICL typically present with opportunistic infections, malignancies, or autoimmune disorders. No evidence of any transmissible agent has been described.^[2] Zonios *et al.*^[3] in their study of 39 patients with ICL described *Cryptococcus* and non-*Mycobacterium tuberculosis* as the main presenting opportunistic infections. It's still an enigma whether immunodeficiency leads to opportunistic infections or it's vice versa. Our patient satisfied the criteria for ICL, he was HIV negative and CD4 counts low on two separate occasions. Opportunistic infection in terms of *M. tuberculosis* was confirmed by the bone marrow.



Figure 1: Computed tomography chest showing miliary pattern

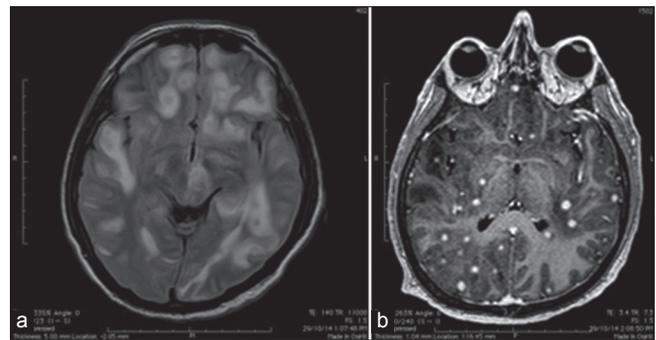


Figure 2: (a) Contrast enhanced magnetic resonance imaging showing perilesional edema. (b) Contrast enhanced magnetic resonance imaging showing multiple tuberculomas

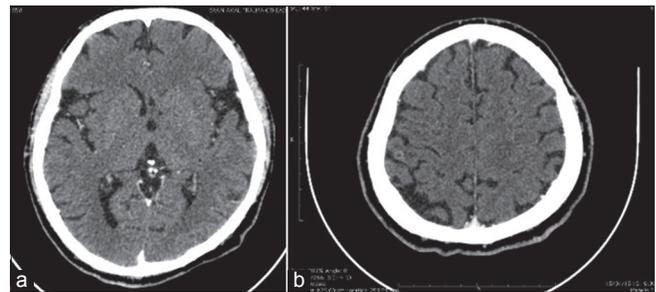


Figure 3: (a) Magnetic resonance imaging showing resolution of edema. (b) Magnetic resonance imaging showing resolution of edema

The distribution of ICL is ubiquitous with no apparent geographical predilection. Most patients diagnosed of ICL are adults, however, few case reports in children have also been described. In the literature review done by Ahmad *et al.*,^[4] mean age of diagnosis was 40.7 ± 19.2 years with male predominance. The most common opportunistic infection was *Cryptococcus neoformans* followed by *M. tuberculosis* (MTB). In their review of 258 patients, 44 patients had tuberculosis (19-MTB, 17-*Mycobacterium avium* complex and 8 others).

The etiology appears to be multifactorial. Various mechanisms have been described in the literature regarding the development of ICL. Lee *et al.*^[5] hypothesized abnormal translocation of microbial products from the intestinal wall as the underlying etiology after they found increased levels of serum lipopolysaccharide and other markers of CD4 cells activation in patients with ICL. Furthermore, the possibility of genetic factors in the pathogenesis of ICL has been studied. Zonios *et al.*^[3] found higher proportions of HLA-DR⁺CD4 cells in ICL patients as compared to controls.

Patients with ICL are more prone to opportunistic infections on other hand various infections, malignancies, and certain medications are known to depress CD4 counts. Transient CD4 lymphocytopenia has also been documented in healthy individuals.

Long-term follow-up of patients with ICL has shown the persistence of low CD4 counts in the patients for several years. In a few cases, resolution was also seen. Lymphocytopenic patients had a more severe course of disease in mycobacterial infections. Disseminated tuberculosis has been reported in the literature.^[6] However, miliary tuberculosis with bone marrow involvement, as in our patient, has not been reported to the best of our knowledge.

There is no treatment for ICL. Infections need to be treated. CD4 cell counts should guide about starting prophylaxis. Regular monitoring should be done for ICL patients, especially on prophylaxis treatment as an increase in CD4 counts seen in some patients can help stop the treatment. Interleukin 2 has been shown to increase CD4 counts and possible improvement in immunological function.^[7,8]

Conclusion

High clinical suspicion should be maintained to diagnose ICL. Patients usually present with infection. Any active infection, malignancy or autoimmune disease should be actively sought out and managed accordingly.

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Conflicts of interest

There are no conflicts of interest.

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