Case Report

A rare case report of idiopathic CD4 lymphocytopenia in an Indian male with nasal Rhizopus fungal polyp with drug-induced acute kidney injury

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ABSTRACT

Idiopathic CD4 lymphocytopenia (ICL) is a rare entity of immune deficit of CD4+ T cells (below 300/mm^3) which was first defined in 1992, unrelated to human immunodeficiency virus (HIV) syndrome without predefined clinical presentation and natural history. The etiology, pathogenesis, and management of ICL remains poorly understood and inadequately defined. The clinical presentation can range from serious opportunistic infections to incidentally diagnosed asymptomatic individuals. Cryptococcal and nontuberculous mycobacterial infections and progressive multifocal leukoencephalopathy are the most significant presenting infections, although the spectrum of opportunistic diseases can be similar to that in patients with lymphopenia and HIV infection. The prognosis is influenced by the accompanying opportunistic infections and response to the treatment. This rare disease invites uncountable opportunistic infections sometimes leading to lethal outcome. We report a case of ICL in an immunocompetent 18-year-old male with a history of intermittent epistaxis, fungal nasal polyp diagnosed to have Rhizopus with drug-induced acute kidney injury during the course of treatment, a rarest diagnosis as underlying main disease entity. To the best of our knowledge, ICL presenting with opportunistic infection of Rhizopus is the first case to be reported here from a tertiary care center of India, a developing country where a major population lives with poor hygiene and low socioeconomic status.

Key words: Drug-induced acute kidney injury, idiopathic CD4 lymphocytopenia, nasal polyp, Rhizopus

INTRODUCTION

Idiopathic CD4 lymphocytopenia (ICL) is a rare entity of immune deficit of CD4+ T cells (below 300/mm^3). It is a syndrome without certain pathogenesis, prognosis,

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and treatment and may lead to devastating outcome in a healthy adult. It was first defined in 1992 by Centres for Disease Control and Prevention (CDC), and since then, ICL has been described as a rare heterogeneous syndrome in the absence of any infectious etiology or without any immunosuppressant drugs. This rare entity can be incidentally diagnosed in an asymptomatic individual and may present with serious opportunistic infections. Sporadic cases have been reported time to time from different corners of the world. The meta-analysis of reported cases and literature shows that the spectrum of opportunistic diseases can be similar to the patients with lymphopenia and human immunodeficiency virus (HIV) infection, although cryptococcal, nontuberculous mycobacterial infections, and progressive multifocal leukoencephalopathy are the most common reported infections. Usually, it was diagnosed in middle age as happened in our case.[1]

India is a developing country with major population living with poor hygiene and low socioeconomic status where any type of opportunistic infection can be acquired and may present with different spectrum of this disease. Registry system is also not appropriate. As this disease is a diagnosis of exclusion, underdiagnosis of this disease will always be there at primary and secondary care center. Cost factor will always be a major factor during evaluation and treatment of serious opportunistic infection and immunotherapy of this disease entity. To the best of our knowledge, no case has been reported of Rhizopus fungal infection with nasal polyp as an opportunistic infection in a patient with ICL. Here, we attempt to summarize the salient features of this condition in our case on the basis of available literature to date.

CASE REPORT

An 18-year-old male Indian male with farming background from a remote area presented to the department of otorhinolaryngology outpatient department with chief complaints of bleeding from the nose on and off and nasal obstruction for 1 year. Initially, bleeding was on average 1–2 episodes per month. However, in recent month, it increased to 1 to 2 episodes per week. There was no history of trauma, significant bleeding from other site, or any ecchymotic patches on the body. There was no history suggestive of tuberculosis, sarcoidosis, connective tissue disorder, hypertension, diabetes, high-risk behavior, allergy or repeated blood transfusion, or any treatment with immunosuppressive medications or steroid. No family history of bleeding disorder, diabetes, and hypertension present. There was no history of recurrent infections in childhood. On general examination, he was hemodynamically stable, no pallor, no icterus, no edema, no lymphadenopathy, and overall systemic examination was normal. His investigations are mentioned in Table 1. There was negative serology for HIV 1 and 2, hepatitis B surface antigen, anti-hepatitis C virus, and antinuclear antibody. Epstein–Barr virus and cytomegalovirus were also negative. HIV 1 and 2, repeated at interval of 4 weeks and 12 weeks and found negative. Absolute CD4 count was done and was found to be 265 cells per mm^3, and absolute CD8 count was 258 cells per mm^3. CD4/CD8 ratio was 1.03. Nasal endoscopy was performed and a small polyp was found in the posterior nasal wall [Figure 1a and b], from where biopsy was taken and sent for histological examination. On microscopic examination periodic acid–Schiff stain (×100) showed broad septate fungus with fragmented buds, which was suggestive of Rhizopus as shown in Figure 2a and b, which was consequently confirmed on culture. The patient was managed with injection liposomal amphotericin B (5 mg/kg); however, after receiving three doses of liposomal amphotericin B, the patient developed deranged kidney function on investigation and was transferred to the department of nephrology. After thorough investigation from nephrology point of view, no other significant causative factor for acute kidney injury was defined. As in culture, the causative organism was also sensitive to voriconazole, liposomal amphotericin B was stopped, and tablet voriconazole was started. Kidney

Table 1: Laboratory investigations

Parameters	Normal range	Patient's lab value	Patient's lab value at discharge
Hemoglobin (gm/dl)	13.3-16.2	8.7	10.1
Total leukocyte count (×10^3/μl)	4-10	5	5.2
Platelet count (×10^9/L)	165-415	147	197
Blood urea (mg/dl)	15-50	90	16
Serum creatinine (mg/dl)	0.5-1	2.1	0.8
Serum sodium (mmol/L)	136-146	141	140
Serum potassium (mmol/L)	3.5-5.0	3.4	4.1
Fasting blood glucose (mg/dl)	75-100	87	98
Serum bilirubin (mg/dl)	0.3-1.3	0.4	0.5
SGOT (U/L)	12-38	36	31
SGPT (U/L)	7-41	38	32
ALP (U/L)	44-147	100	95
Serum albumin (mg/dl)	4.0-5.0	3.5	3.7
Prothrombin time (s)	12.7-15.4	20	Normal
aPTT (s)/INR	26.3-39.4/	18/1.02	Normal

SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, ALP: Alkaline phosphatase, aPTT: Activated partial thromboplastin time, INR: International normalized ratio

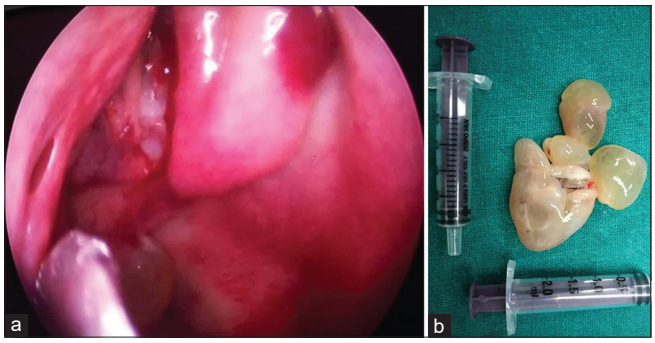

Figure 1: (a) Nasal endoscopy – A small polyp found in posterior nasal wall. (b) Dissected nasal polyp

function improved to normal as shown in Table 1 within 7 days and the patient was discharged with oral antifungal and trimethoprim–cotrimoxazole prophylaxis. CD4 and CD8 counts were repeated 1 and 3 months and were 272 cells per mm^3 and 280 cells per mm^3, respectively. At 3 months, he was asymptomatic and all routine investigations were within normal limit. The patient was lost to follow-up after 3 months.

There are no published guidelines for the management of this type of rarest entity. Hence, we followed the recommended prophylaxis treatment according to the CD4 levels in HIV-infected patients.

In view of the paucity of data, there are no recommendations on how to treat such patients, and due to unclear pathophysiology, it remains a challenge to choose an appropriate treatment strategy protocol for such atypical cases.

DISCUSSION

It is now clear that infection with HIV Type 1 and 2 can result in the depletion of CD4+ T-helper lymphocytes and the development of the acquired immunodeficiency syndrome. However, with progress of time, a rare phenomenon of low CD4 count in HIV-negative patients has puzzled the physician.

The entity called ICL, a disorder of unknown entity, was first defined in 1992 by the US CDC as:

- Depressed numbers of circulating CD4+ T cell lymphocytes (<20% of total T cells) on more than one occasion
- No laboratory evidence of infection with HIV-1 or HIV-2
- Absence of any defined immunodeficiency or therapy associated with depressed levels of CD4+ T cells.[1]

Evidence for possible etiologies of ICL is scarce. A viral etiology was initially suspected, but this has not been replicated.[2] Some studies have demonstrated evidence of increased activation and turnover of CD4 cells; excess

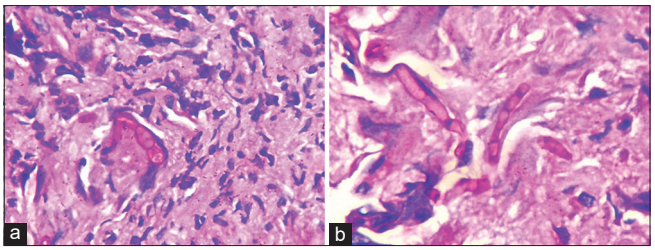

Figure 2: (a) Microscopic examination periodic acid–Schiff stain (×100). (b) Microscopic examination periodic acid–Schiff stain (×100) shows broad septate fungus with fragmented buds

CD4 apoptosis may be due to overexpression of Fas/FasL.[3] The underlying pathophysiology of the disorder is yet to be defined confidently.

Because of low CD4 count, patients are susceptible to opportunistic infections. There are many case reports of cryptococcal meningitis in idiopathic CD4 lymphocytopenia.[4,5] A recent meta-analysis of 258 ICL case reports since 1989 demonstrated that 87.6% of ICL patients had at least one opportunistic infection, with the most common being cryptococcus, mycobacteria, candida, and varicella zoster virus.[6] Limited data from those reports support IL-2 as a relatively safe and potentially effective treatment for ICL patients.[7] The CDC did not observe progressive decline in CD4-T cell count as occurs in HIV infection.

In our case, fungal infection in an immunocompetent individual fulfilling all the criteria provided the clue to reach the final diagnosis of ICL. In the present case, estimation of serum immunoglobulin levels and serology for HTLV I and II could not be done due to cost constraint. However, in this case, no sign and symptoms consistent with HTLV 1 and 2 infection were present. There was no history of recurrent infections in childhood that led us clinically to think and evaluate this case as ICL.

The occurrence of Rhizopus as opportunistic infection in such case is a very rare phenomenon. To the best of our knowledge, infection by Rhizopus in idiopathic CD4 lymphocytopenia is the first case.

CONCLUSION

The diagnosis of ICL should be considered in atypical infections in absence of any known immunodeficiency or drug-related immunodeficiency of CD4+ T cells. Early diagnosis of this rare disorder may help avoid lethal outcome for the patients. Despite extensive research, ICL remains a syndrome of uncertain pathogenesis, prognosis, and treatment including prophylaxis. Further intensive study of immunogenic basis of pathogenesis of this condition is a mandate of time in context of raising number of documented case reports.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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