

An interesting cause of fever with acute respiratory distress syndrome

Abstract

Fever with Acute respiratory distress syndrome (ARDS) is a common emergency presentation seen in tropical countries like India. Aetiology of ARDS varies depending on regional prevalence, environmental factors and host factors like immunosuppression. Immunosuppression increases the hosts' susceptibility to opportunistic infections like *Pneumocystis jirovecii* pneumonia (PJP). We report a 19-year-old HIV negative boy who presented with fever with ARDS, was diagnosed with PJP, and had a CD4 count of 212 cells/mm³. The patient's CD4 count was found to be low on repeat measurement with a normal hematological profile, bone marrow evaluation along with a repeat ELISA negative for HIV. Hence, the diagnosis of Idiopathic CD4 lymphocytopenia, a rare clinical condition was made.

Keywords: PJP pneumonia, CD4 count, human immunodeficiency virus, Idiopathic CD4 lymphocytopenia

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Abbreviations: ICL, idiopathic CD4 lymphocytopenia; GCS, glasgow coma scale; HIV, human immunodeficiency virus

Introduction

PJP pneumonia is a common opportunistic infection in HIV positive patients especially at CD4 count less than 200 cells/mm³. Unusually, it can also present in HIV negative patients who have some other cause for immunosuppression: like immunosuppressive drugs, diabetes and malignancies like leukemia. When no such cause can be identified, patients with CD4 counts less than 300 are labelled to have Idiopathic CD4+ T-lymphocytopenia (ICL) – a rare clinical condition. Such patients also have increased risk of all the opportunistic infections similar to those found in HIV. Only a few reports of this disease entity have been published reports from India. We present a case of ICL with PJP pneumonia in a 19-year-old boy and review the literature.

Case

A 19 year old boy presented to the emergency with complaints of fever for 2 weeks, dry cough for 1 week and breathlessness for

5 days which had worsened in 2 days. There was no history of sputum, hemoptysis, and chest pain. There was no history of alcohol consumption, Diabetes mellitus, malignancy, chemotherapy or any other immune suppressive medications or known HIV infection. The patient had received high doses of parenteral antibiotics prior to presentation but his fever had persisted. On examination, the patient was conscious but not oriented to time, place and person with a Glasgow coma scale (GCS) of 9. He was emaciated, dehydrated and febrile with temp of 104.2F in the right axilla. His pulse rate was – 128/minute regular, Blood Pressure– 90/62 mm of Hg and respiratory rate 40 breaths/min. Pallor was present and there was no cyanosis, icterus or clubbing. He had bilateral crackles on auscultation. Rest of the physical examination was unremarkable. The blood investigations of the patient are summarized in Table 1. The patient was incubated and put on mechanical ventilation in respiratory ICU with lung protective ventilation strategies. In view of negative blood cultures and persistent fever despite broad spectrum antibiotics, serology for *Leptospira*, kala azar and brucella were sent which were negative (Table 2).

Table 1 Laboratory Investigations

Alt-Alanine Transaminase, Ast- Aspartate Transaminase

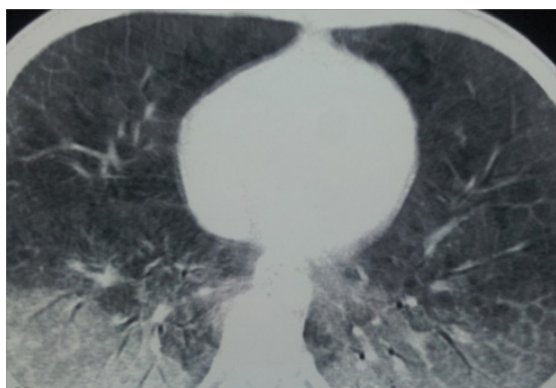
Haemoglobin	8.1 g/dl	B.UREA	35 mg/dl	ALT/AST	28/35 IU
Total leucocyte count	4370cells/mm ³	S.Creatinine	0.8 mg/dl	Alkaline phosphatase	93 IU
Differential Count(polymorph/lymphocyte)	62/34	Sodium	138 meq/l	Total protein/Albumin	7.9/3.2 gm/dl
Platelet count	1.9 lac/mm ³	potassium	3.8 meq/l	Calcium/Phosphate	9/4.5 mg/dl
ESR	19MM/hour	CRP	Positive	Total bilirubin	0.5mg/dl
Blood culture	No growth	Urine culture	No growth	Central line tip culture	No growth

Table 2 Special investigations

CBNAAT- cartridge based nucleic acid amplification test, TB- tuberculosis

Leptospira serology	negative	Broncho- alveolar lavage (BAL) pyogenic culture	No growth
Brucella serology	negative	BAL for PCP	Positive in silver stain
Kala azar serology	negative	CBNAAT for TB	Negative
Elisa for HIV(done twice)	negative	BAL culture FOR M.TB	Negative

Chest X ray of the patient was suggestive of bilateral fluffy opacities. The CT chest (Figure 1) of the patient revealed bilateral, predominantly basal, ground glass haze with no pleural effusion; suggestive of Acute respiratory distress syndrome (ARDS). A Bronchoscopic lavage was sent which revealed oocyst of *Pneumocystis jirovecii* on silver stain. Stain for acid fast bacilli and fungal mount for KOH was negative. HIV test was negative by ELISA. Patient was started on injectable cotrimoxazole with steroids. Patient improved and was extubated on day 5 of admission. A repeat sample was analyzed for HIV status which was negative by ELISA. In view of no other cause found for immunosuppression, the CD4 count of the patient was sought which was 212cells/mm³. The patient was gradually allowed all oral feeds and was built nutritionally. A bone marrow biopsy was carried out which was norm cellular and normoblastic. A repeat CD4 count was 240cells/mm³ in follow up visit after 6 weeks.

**Figure 1** The CT of the patient chest.

Discussion

Idiopathic CD4⁺ T cell lymphocytopenia (ICL) is defined by persistent CD4⁺ T cell lymphopenia in absence of infection with HIV-1 or any other cause of immunodeficiency, with CD4⁺ T cell counts below 300cells/microl, repeated at least 6 weeks apart.¹ ICL is a disorder of unknown etiology. Even though first described in 1992, very little is known regarding its pathophysiology and etiology. Initially believed to be of viral etiology, research has recently focused on identifying abnormalities in various aspects of immune function. ICL is characterized by an increased predisposition to opportunistic infections. The typical clinical manifestations of ICL include cryptococcal, mycobacterial, PJP pneumonia and other opportunistic infections, malignancies, and autoimmune disorders. These conditions are all believed to result from immune dysregulation.² Due to the rarity of this condition, no specific guidelines exist for prophylaxis, monitoring, or treatment.³ Therefore; the management is based on the experience with HIV treatment where such opportunistic infections are common.⁴ A high index of suspicion is necessary for their identification so that early treatment can be started for the opportunistic infections. There are few case reports from India. In

these reports also, patients presented with diseases like cryptococcal meningitis and tuberculosis. Sharma et al reported a case of refractory cryptococcal meningitis with ICL with a CD4 count of 203cells/mm³ in Chandigarh.⁵ A similar case of cryptococcal meningitis successfully treated with intravenous amphotericin had a CD4 count of 235/mm³.⁶ Mukherjee et al.⁷ reported two cases of dermal candidiasis and disseminated tuberculosis infection.⁷

An international cohort study over 20 years comprising of forty patients done in France, revealed that around 60% of the ICL patients presented with opportunistic infections, 10% with malignancies and 35% with autoimmune features and rest were asymptomatic. Among infectious manifestations, PJP pneumonia was seen in 10%. Others included cryptococcal meningitis, atypical mycobacteria, no cardiac and similar opportunistic infections seen in AIDS patients. In the follow of these patients, it was found that patients presenting with infectious manifestations had low NK cell activity and low initial CD4 T-cell count <150/mm³ and low NK cell count (<100/mm³) were prognostic markers of increased mortality.⁸ Our patient had a CD4 count above 200/mm³ and showed dramatic recovery with treatment of the opportunistic infection. He was doing well till 6 months of follow up and submission of this case. For improving CD4 counts, treatment with IL-2 has been suggested.³ Even in the French cohort, around 6 patients were given recombinant IL-2, but it was eventually stopped in all due to side effect of injection intolerance, autoimmune effects and lack of efficacy in normalizing CD4 levels. However, in view of paucity of data there are no recommendations on how to treat such patients and due to unclear pathophysiology, it still remains a challenge to the practice of modern medicine.

Conclusion

Hence in immunocompetent patients who do not have HIV infection or other known immunosuppressive conditions that develop unusual opportunistic infections, a possibility of Idiopathic lymphocytopenia must be entertained.

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Conflict of interest

The author declares that there is no conflict of interest.

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