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CD4 lyphocytopenia with an unusual presentation

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Abstract
A malnourished male child from rural West Bengal, India, presented with oral mucosal candidiasis, accompanied with iron deficiency anaemia which was not responding significantly to oral antifungals. CD4 count of the child was observed to be markedly low. We highlight recurrent episodes of oral non-albicans Candida infection in this child suffering from Nutritionally Acquired Immune Deficiency Syndrome. Few weeks of oral iron therapy and nutritional supplementation mediated reversal to immune competence supported by rise in CD4 count, increase in CD4: CD8 ratio, improved nutritional status and also cure of infection; without any further recurrence in the follow-up period.

Keywords: CD4 count, CD4:CD8 ratio, iron deficiency anaemia, Nutritionally Acquired Immune Deficiency Syndrome, oral mucosal candidiasis

1. Introduction
Combination of malnutrition induced immunosuppression and childhood infections is the leading cause of mortality. Immunological dysfunctions associated with malnutrition have been termed Nutritionally Acquired Immune Deficiency Syndromes (NAIDS) [1]. In India though malnutrition is extremely common, but cases of malnutrition induced recurrent oral candidiasis have not been reported till now. We report the case of a malnourished male child from rural India, presenting with recurrent oral mucosal candidiasis; accompanied with; iron deficiency anaemia and low CD4 count.

Case History
Six year old male child from Purulia, West Bengal, India, presented with history of recurrent intermittent high grade fever with chill and rigor for five months duration. Notably every time the fever was associated with recurrent oral mucosal ulceration, painful white patches over the tongue and difficulty in deglutition. Patient was treated elsewhere with various antifungal and antibacterial antibiotics only to respond for few days and the oro-pharyngeal manifestations reappeared in a matter of one to two weeks on discontinuation of therapy. His developmental history was normal and he was completely immunised. No similar history was found in the family. General survey of the patient was consistent with grade II malnutrition with mild pallor, raised temperature, mild tachycardia and tachypnea. There were painful white patches over the palates and tongue (figure 1). Examination of the respiratory, cardiovascular and gastrointestinal system was non contributory. Tongue scraping was sent to microbiology laboratory for fungal and bacterial culture and smear examination. Following this, patient responded to a prolonged course of oral fluconazole and injection amphotericin B lipid complex, only to recur in a matter of weeks.
He was investigated extensively. Hemogram showed hypochromic microcytic anemia (Hb: 9 gm%), low MCV (72 Fl), Serum ferritin: 6 ng/dl, TIBC: 480 micro mole/L, transferrin saturation:10%. T4, TSH, C-Reactive Protein, renal and liver function tests were within normal limits. Serum calcium, phosphate, magnesium studies were normal. Serum IgA, IgM, IgG were within normal limits, but serum IgE (2500 IU/ml) was raised. CD4 count was 567 cells/micro litre and and the CD4:CD8 ratio was low (0.38). Direct smear from the tongue scraping showed presence of fair number pus cells and budding yeast, and fungal culture showed growth of non-albicans Candida species. Repeated blood culture reports were negative and HIV serology was non reactive on multiple occasions. Mantoux test, Widal serology, peripheral blood smear for Malaria Parasite and Malaria Parasite Dual Antigen were negative. Stool and urine examination, were normal. Findings of chest x-ray, USG whole abdomen and Echo Doppler study were non contributory.
Patient was advised for management of malnutrition and iron therapy. Oral iron supplementation and nutritional therapy was started along with oral antifungal. The oro-pharyngeal lesions improved drastically over few days and fever did not recur this time. Antifungal was omitted after one week.
Patient was on regular monthly follow-up for one year. Throughout, tongue examination was painless and did not show any lesion. There was improvement in nutritional status and haemoglobin status (13 gm%). Also the CD4 count had increased to 838 cells/micro litre and CD4:CD8 ratio had increased to 1.67. Patient was advised to continue with oral iron and nutritional supplementation and in the follow-up visits for the next one year, no recurrence of the tongue lesions was observed. However, the patient was lost to follow-up and came back after one year with recurrence of fever and mucosal candidiasis. On questioning, there was history of discontinuation of therapy for 11 months. This time also the lesions improved with similar treatment.

Fig 1: white patches of candidiasis over the tongue mucosa

Discussion

Our patient presented with grade II protein-energy malnutrition, iron deficiency anaemia, low CD4 count and recurrent episodes of oral mucosal candidiasis. Protein-energy malnutrition or deficiencies of single nutrients that assist in nucleic acid metabolism generally lead to atrophy of lymphoid tissues, a state of anergy and dysfunctions/failure of cell mediated immunity(CMI) [1, 3]. Reduced CD4 count is a natural physiological effect of malnutrition and impaired immunity is a critical adjunct factor in malnutrition-associated infections [2, 3].

Immunological dysfunctions associated with malnutrition are termed Nutritionally Acquired Immune Deficiency Syndromes (NAIDS) [1]. Malnourished children may show decreased serum IgE levels, which is contrary to our case [4]. We did not find evidence of any parasitic infestation in the child. Rest of the serum immunoglobulin were normal as supported by Das I *et al*.[5]

Oro-pharyngeal lesions which had failed to show significant healing following antifungal therapy, showed drastic improvement following oral iron supplementation and nutritional therapy. Also his nutritional status improved within weeks of nutritional therapy. Iron supplementation and improved nutrition aided in restoration of normal immune response. Lower $CD4^+$ lymphocyte levels and the CD4:CD8 ratio in children with iron deficiency may contribute to the decreased CMI, which can be restored by iron supplementation [5]. Nawrot U *et al* has also mentioned remission of recurrent mucocutaneous candidiasis following restoration of cell mediated immunity [6].

Malnutrition and iron deficiency anaemia induced poor CMI may increase susceptibility to recurrent mucosal candidiasis. Reversal to immunocompetent state and cure of infection without future recurrence, following iron supplementation and nutritional therapy are the notable features in our case.

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