CASE REPORT
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Angiocentric Nasal T-Cell Lymphoma in a Patient with Idiopathic CD4+ Lymphocytopenia

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ABSTRACT

Idiopathic CD4+ Lymphocytopenia is a rare combined immunodeficiency disease, characterized by low CD4+ T-cell count and increased susceptibility to opportunistic infections, autoimmunity and malignancies after exclusion of secondary forms of CD4 lymphocytopenia. Here we present a 13-year old boy who was referred to our center because of destructive ulceration of soft and hard palates with extension to nose and maxillary sinus starting at 6 months of age. He had a history of recurrent otitis media, chronic diarrhea, arthritis and herpetic lesions of eyes and mouth since the age of 5 years. Laboratory studies revealed very low number of CD4+ T-cells (<100 cells/mm^3). Secondary causes of CD4 lymphocytopenia, including HIV infection, were ruled out. Immunohistological studies of destructive lesions in oral and nasal cavity revealed angiocentric T-cell lymphoma. Unfortunately, the patient died in spite of treatment with a combination of irradiation and chemotherapy. This patient is the first reported case of lethal midline granuloma with origin T-cell lymphoma in idiopathic CD4+ lymphocytopenia.

Key words: Idiopathic CD4 lymphocytopenia; Granuloma; Lymphoma

INTRODUCTION

Idiopathic CD4+ Lymphocytopenia (ICL) is a rare primary immunodeficiency disease, characterized by decreased CD4+ T-cell count (<300 cells/mm^3 or <20% of the total T-cell count) on two occasions in the absence of HIV or HTLV infections and the absence of other known immunodeficiency diseases or therapies associated with reduced CD4+ T-cell count. Although most cases are adults, some children with ICL have been reported.[1,2] The patients with ICL usually experience opportunistic infections, including

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Cryptococcus infection, *Pneumocystis jirovecii* pneumonia, and mycobacterium infection, which are often the first manifestations of thethe disease.[1,3] Some patients with ICL develop autoimmune diseases and malignancies.[1,3,4]

Nasal type T-cell lymphoma, also known as angiocentric lymphoma, is a subtype of peripheral T-cell lymphoma that is defined as an aggressive lymphoma, which develops from mature-stage of T-cells and natural killer cells.[5-7] This type of lymphoma which is a rare subtype of non-Hodgkin's lymphoma was previously named as lethal midline granuloma.[8,9]

Here we report a case of ICL who was complicated with lethal midline granuloma with origin T cell lymphoma. To the best of our knowledge, this is the first case of ICL who experienced such a malignancy.

Case History

A 13-year old male was referred to our clinic with past medical history of recurrent episodes of otitis media, chronic diarrhea, arthritis and herpetic lesions of eyes and mouth since 5 years of age. He was the the fifth child of consanguineous parents (first cousins) with history of early death in a sibling due to infection and failure to thrive. He had one healthy sister and four healthy brothers at the time of admission. He has recently suffered necrotizing destructive ulceration of soft and hard palates with extension to nose and maxillary sinus (lethal midline granuloma). This extensive destructive lesion in oral cavity was apparent in physical examination.

Laboratory work-up revealed anemia and mild lymphopenia; autoimmune work-up, including RF, anti-dsDNA, ANA and ANCA were negative. Chest X-ray of the patient was normal. Abdominal sonography revealed normal liver and spleen diameters. Bone marrow aspiration and biopsy were also normal. Immunologic studies revealed normal serum immunoglobuline levels, normal complement and normal phagocytic system (Table 1). However, peripheral blood flowcytometery showed CD4+ T-cells of less than 200 cells/mm^3 and reversed CD4/CD8 ratio to 0/2. Decreased CD4+ T-cells count (<100 cells/mm^3) and reverse ratio of CD4+/CD8+ T-cells was confirmed in serial tests. HLA DR was present. Secondary causes of CD4 lymphocytopenia, including HIV infection, were excluded and there was not any alternative explanation for the CD4 lymphocytopenia; thus the diagnosis of ICL was made for the patient.

Immunohistological study of destructive lesion revealed angiocentric T-cell lymphoma with origin of lethal midline granulomas (Figure 1). The patient died in spite of treatment with combination of irradiation and chemotherapy.

Table 1. Laboratory findings of the patient with idiopathic CD4+ lymphocytopenia.

Biochemical Tests	Results	Immunological tests	Results
WBC (cells/mm^3)	7200	IgG (mg/dl)	1620 (NR: 748-2001)
Neutrophils (%)	88	IgM (mg/dl)	306 (NR: 99-550)
Lymphocytes (%)	6	IgA (mg/dl)	210 (NR: 54-217)
Hemoglobin (g/dl)	7.5	IgE (IU)	24
Platelets (cells/mm^3)	566000	CD3 (%)	70 (NR: 52-78)
ESR (mm/hr)	75	CD4 (%)	12.01 (NR: 25-46)
LDH (IU/L)	356	CD8 (%)	58.26 (NR: 9-35)
Calcium (mg/dl)	8.4	CD19 (%)	8.04 (NR: 8-24)
Phosphorus (mg/dl)	3.5	CD4/CD8	0.2 (NR: 0.9-34)
Alkaline phosphatase (IU/L)	114	NBT (%)	100
PT (seconds)	13.8	CH50 (%)	100
PTT (seconds)	29	C3 (mg/dl)	90 (NR: 55-120)
Cholesterol (mg/dl)	132	C4 (mg/dl)	52 (NR: 10-40)
Triglycerides (mg/dl)	118	RF	Negative
BUN (mg/dl)	7	LE cell	Negative
Creatinin (mg/dl)	0.46	ANA	Negative
SGOT (IU/L)	48	ANCA	Negative
SGPT (IU/L)	21	Anti ds DNA	18.5 (NR to 25)

NR: Normal range

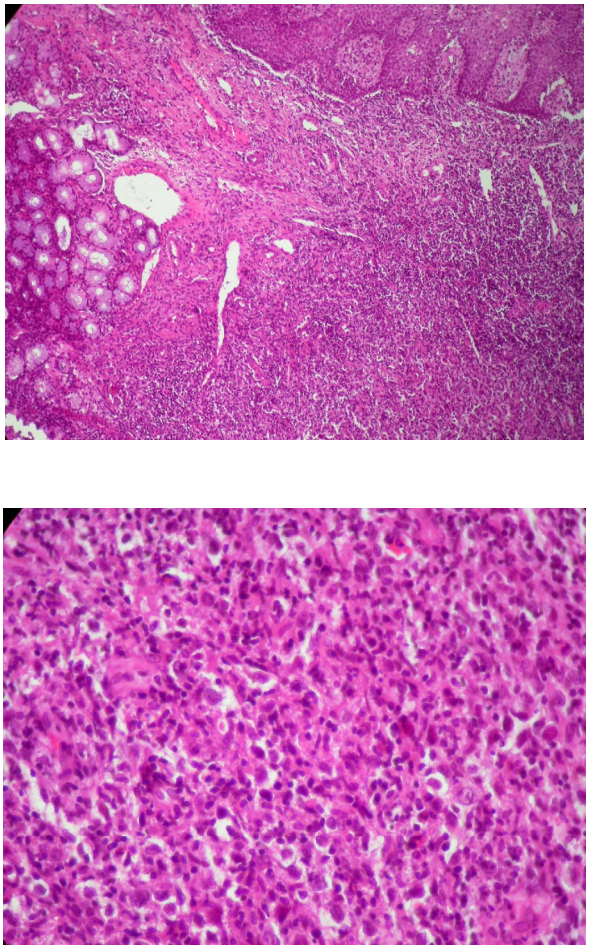

Figure 1. Angiocentric T-cell lymphoma with origin of lethal midline granulomas.

DISCUSSION

Neoplasitc disorders have been reported in a number of patients with ICL, similar to those described in advanced HIV patients and other chronically immunocompromised patients. Lymphomas is one of the malignancies that has been reported in some patients with ICL; and different types of lymphomas, including B-cell non-Hodgkin's lymphomas, cerebral intravascular lymphoma, diffuse large cell lymphoma, and burkitt's lymphoma have been reported in this group of patients.[1,4,10,11]

Our patient had destructive lesions of palate, nose and maxillary sinus. Immunohistological study of biopsy specimen revealed sinonasal malignant T-cell lymphoma (angiocentric) as origin of lethal midline granuloma in this patient. In clinical practice, the destructive processes of the facial midline appears as a symptom of various infective, malignant or autoimmune diseases, such as Wegener's granulomatosis.[12] In our patient, nasal type T-cell lymphoma (angiocentric) have been the origin of lethal midline granuloma, similar to other reports of this syndrome.[13,14] In fact, most nasal lymphomas seem to be associated with a T-cell phenotype, which are aggressive, locally destructive midfacial necrotizing lesions.[15-17] Nasal type T-cell lymphoma which is an extranodal non-Hodgkin's lymphoma of the nasal cavity presenting NK or T cell markers, makes less than 1% of cases of non-Hodgkin's lymphoma, but is more common in Asia and Latin America.[18-20]

Previous reported patients with nasal type T-cell lymphoma were not associated with underlying primary immunodeficiencies. The majority of lymphoma that was reported in ICL had B-cell origin, but our patient had nasal type T-cell lymphoma (angiocentric) which did not reported in other studies. Natural history of these lymphomas characterizes through a rapidly progressive course with a poor prognosis similar to our patient who died in spite of full treatment with chemotherapy and irradiation.

This report is the first case of lethal midline granuloma with origin T-cell lymphoma in ICL and because of its poor prognosis; this tumor should be included into the list of the differential diagnosis of lethal midline granuloma.

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