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CASE REPORT

Case Presentation: Large Diffuse B-cell Lymphoma Developing in the Context of Primary Immunodeficiency

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ABSTRACT

Ataxia Telangiectasia (AT) is a rare, autosomal recessive neurodegenerative disorder characterized by immunodeficiency. Clinically, it is known to be associated with progressive cerebellar ataxia starting in early childhood, oculocutaneous telangiectasia, cellular and humoral immunodeficiency, and an associated increased risk of cancer. A 9-year-old female patient diagnosed with ataxia telangiectasia presented to the immunology outpatient clinic with complaints of difficulty breathing and snoring. Examination revealed an ulcerative vegetative mass obstructing the airway in the palate. The patient also presented with white plaques on her tongue, raising the possibility of fungal infection or lymphoproliferative disease. A biopsy of the palatal lesion was performed, and the patient was diagnosed with Diffuse Large B-Cell Lymphoma. Cultures from the biopsy also revealed simultaneous Candida albicans growth. This case highlights the increased risk of lymphoproliferative disorders in patients with primary immunodeficiency due to Ataxia Telangiectasia, which may present with a range of clinical manifestations. In this patient group, there is a potential association with invasive infections and malignancy, underscoring the need for clinicians to consider further investigations and, if necessary, perform a biopsy to support the diagnosis in cases of clinical suspicion.

Keywords: Ataxia Telangiectasia, Diffuse Large B-Cell Lymphoma, Fungal Infection

INTRODUCTION

Cancer registry data (ICR) include information about the types of malignancies reported by patients with Ataxia Telangiectasia (AT). The largest category of malignancies in these patients comprised non-Hodgkin lymphomas and leukemias (64%), followed by other solid tumors (26%) and Hodgkin's disease (10%) (1). Recognizing the underlying immune deficiency in these patients is crucial because it may necessitate modifications to chemotherapy and radiation therapy protocols, making accurate diagnosis highly important.

Individuals with primary or secondary immunodeficiencies experience a significantly increased risk of infections and malignancies. Other syndromes associated with such increased risks include Wiskott-Aldrich Syndrome (WAS), common variable immunodeficiency (CVID), and severe combined immunodeficiency (SCID). Among these, patients with AT exhibited the highest incidence of malignancy, followed by CVID and WAS. According to cancer registry data, non-Hodgkin lymphoma is the most common malignancy among these disorders (2). Lymphomas in patients with AT form a highly heterogeneous group based on histological subtypes. Morphologically and in terms of cellular markers, these lymphomas more closely resemble those seen in children without immune deficiency than in patients with WAS and SCID.

The definitive diagnosis of AT is made by identifying homozygous or compound heterozygous mutations in the ATM gene. Supporting diagnostic findings include elevated serum AFP levels and reduced IgA and IgG levels. Cerebellar atrophy on MRI is another important diagnostic feature, whereas the presence of telangiectasias on physical examination is considered pathognomonic for AT.

In patients with congenital, acquired, or iatrogenic immunodeficiency, the risk of lymphoproliferative diseases is higher than that in the general population. Immunodeficiency-related lymphoproliferative diseases are categorized separately in the World Health Organization classification of hematopoietic and lymphoid system malignancies. These diseases exhibit clinical and pathological characteristics that differ from those of malignancies

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in the general population, depending on the underlying cause. Lymphomas, which are most commonly of B lymphocyte origin, typically display aggressive histopathological features and are frequently associated with Epstein–Barr virus (EBV). In immunodeficient patients, an insufficient cytotoxic T lymphocyte response to EBV leads to uncontrolled proliferation of EBV-infected B cells. In addition, inherited or acquired genetic alterations in oncogenes and tumor suppressor genes, chronic antigenic stimulation, and oncogenic viral infections can contribute to the development of lymphoproliferative diseases in immunodeficient individuals. Written consent was obtained from the parents.

CASE PRESENTATION

Our patient is a 9-year-old girl, followed in the Pediatric Allergy and Immunology outpatient clinic with a diagnosis of Ataxia Telangiectasia (AT), which is a primary immunodeficiency and was receiving regular immunoglobulin support every 3 weeks. The patient is on prophylactic treatment with Trimethoprim-Sulfamethoxazole (TMP-SMX) for Pneumocystis jirovecii (PJP) and Fluconazole for fungal infection prophylaxis. Because of her primary immunodeficiency, she has a history of hospitalizations for pneumonia.

She presented to the Allergy and Immunology clinic with complaints of nasal congestion, difficulty breathing, and wheezing. On physical examination, a white plaque-covered mass was found on the soft palate, and a polypoid lesion was identified in the left nasal cavity (Figure 1). Given the differential diagnosis of malignancy and fungal infection, the patient was admitted for further evaluation. Laboratory results showed hemoglobin 12.3 g/dL, total leukocyte count 11,900 × 10^6/µL, absolute neutrophil count 9,200 × 10^6/µL, absolute lymphocyte count 600 × 10^6/µL, monocyte count 1,800 × 10^6/µL, lactate dehydrogenase (LDH) 288 U/L, uric acid 1.2 mg/dL, phosphorus 3.74 mg/dL, potassium 3.96 mg/dL, and creatine kinase 409 U/L. Epstein-Barr virus (EBV) DNA was negative, and immunoglobulin levels showed IgA at 4 mg/dL and IgG at 1,037 mg/dL. Given the defective DNA repair gene in AT, MRI was planned instead of a CT scan for imaging.

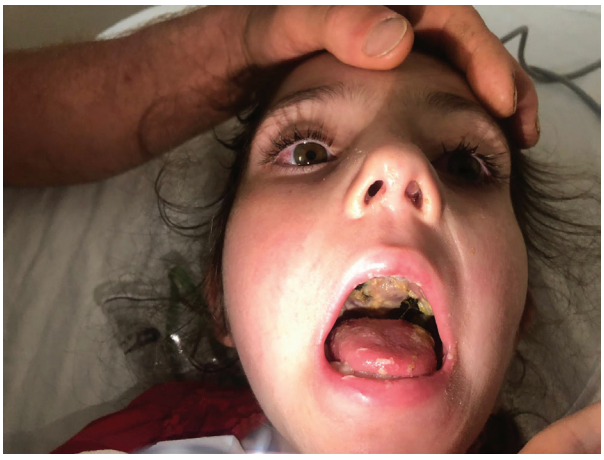

Figure 1: Bilateral telangiectasias in the sclerae and a vegetative mass appearance on the palate.

Imaging Findings

Magnetic Resonance (MRI) imaging revealed a mass that obliterated the nasopharynx, with infiltration into the ethmoid, sphenoid, and frontal sinuses. The lesion was hypointense on T1- weighted imaging and heterogeneously isointense on T2-weighted imaging. After intravenous contrast administration, the lesion showed homogeneous enhancement and significant diffusion restriction, which are highly indicative of lymphoma. Additionally, a fistulous lesion was noted connecting the oral and nasal cavities (Figure 2).

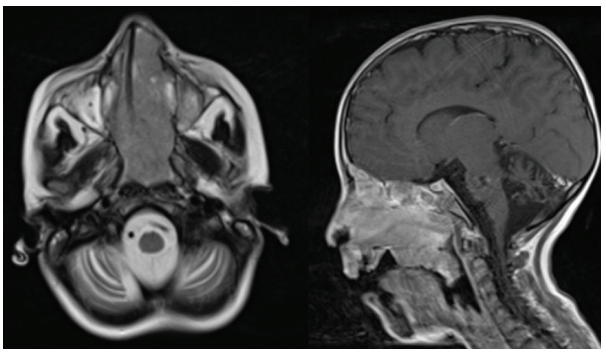

Figure 2: Pre-treatment MRI image of the lesion.

Microbiological and Histopathological Findings

Culture of the lesion site revealed *Candida albicans*. Galactomannan antigen testing, which was performed to assess for possible invasive fungal infection, was negative. To evaluate for lymphoproliferative disorders, Tru-cut biopsy was performed on the lesion, and the diagnosis of Diffuse Large B-Cell Lymphoma (DLBCL) was confirmed.

Immunohistochemical analysis showed negative EBV staining.

Further Investigations

Positron Emission Tomography-Computed Tomography (PET/CT) showed no hypermetabolic areas except for the nasal and oral cavities. Bone marrow aspiration and biopsy were performed, and no evidence of lymphoma involvement.

Treatment

Given the diagnosis of stage II non-Hodgkin lymphoma (NHL) on the basis of primary immunodeficiency, the patient was started on the R-CHOP chemotherapy protocol, administered every 3 weeks. She was also started on antifungal treatment with Amphotericin B for the treatment of widespread *Candida albicans* infection and prophylaxis. After three cycles of chemotherapy, follow-up magnetic resonance imaging (MRI) revealed a complete response to treatment. After six cycles of R-CHOP chemotherapy, the patient completed her treatment protocol, and the decision was made to discontinue further therapy based on her risk group (Figure 3).

DISCUSSION

Our patient, diagnosed with Ataxia Telangiectasia (AT) and chronic lung disease due to recurrent pulmonary infections,

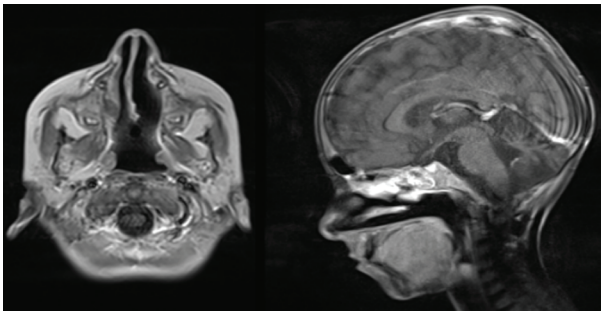

Figure 3: Post-treatment magnetic resonance imaging image.

tolerated the combination of rituximab and CHOP chemotherapy very well. Additionally, she did not experience long-term bone marrow suppression or severe febrile neutropenic episodes typically associated with chemotherapy, due to receiving regular intravenous immunoglobulin (IVIG) replacement therapy.

The combination of AT and lymphoma is extremely rare. In such cases, a personalized treatment approach is crucial. This underscores the importance of management by experienced teams with the potential for drug dose modifications when necessary. Consequently, our case highlights the need for an individualized approach for treating these complex patients (3). In patients with immunodeficiency, susceptibility to lymphoproliferative syndromes and EBV association should also be carefully considered. If serum EBV DNA levels are positive upon diagnosis, it is essential to monitor the trend of these levels during treatment (4).

In Ataxia Telangiectasia, defective cell cycle control leads to increased sensitivity to agents that cause DNA damage, such as radiation therapy and chemotherapy. This resulted in a higher propensity for malignancies, especially leukemia and lymphoma. Chronic lymphoproliferation due to antigenic stimulation following B and T cell activation, along with impaired apoptosis, contributes to the initiation of lymphoid proliferation (5).

The prognosis of lymphomas developing in the context of primary immunodeficiency is generally worse than that of immunocompetent individuals. In such cases, chemotherapy doses may need to be reduced to protect the patient from drug toxicity. However, this reduction can be concerning for clinicians because it may increase the risk of disease progression and relapse. Nonetheless, the primary goal remains to protect highly sensitive patients from the toxic effects of chemotherapy, thereby preventing complications related to increased infection frequency.

Although rare, Candida albicans can cause invasive fungal infections in immunocompromised individuals (6). It is important to remember that the natural course of infections may differ between immunodeficient and immunocompetent patients (7). In our case, chemotherapy was well managed and infection control was successfully achieved, providing a rare example of lymphoma development in the context of primary immunodeficiency. This case may serve as a valuable reference for clinicians managing similar cases of immunodeficiency–associated malignancy.

This case highlights the need for careful monitoring and management in immunocompromised patients, emphasizing individualized treatment plans that consider both the primary immunodeficiency and the risks of malignancy and infection.

Informed Consent: Written consent was obtained from the participants.

Peer Review: Externally peer-reviewed.

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Conflict of Interest: Authors declared no conflict of interest.

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