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A Rare Case Of Lymphomatoid Granuomatosis Complicating Ataxia Telangiectasia- An Early Presentation

Dr. Rakesh Inturi
(Extern, Department of Hematology Oncology)
Dr. Kusuma Chowdhary Ravulapalli
(Extern, Department of Hematology Oncology)
Dr. Ranjith Kumar CS
(Consultant, Hematology Oncology, American Oncology Institute)
Dr. Anil Aribandi
(Senior Consultant, Hematology Oncology, American Oncology Institute)

Abstract: *A 3year 6 months old male child presented to our hospital with symptoms of fever, and cough 2 to 3 episodes per month for the last 4 months. His past, Computerized tomography revealed enhancing mass in the right upper lobe with encasement of SVC. Biopsy specimen has revealed Pleuropulmonary blastoma and underwent Right upper lobectomy on 21/06/21. Histopathology examination has revealed Lymphomatoid granulomatosis Grade 3.Epstein - Barr virus (EBV) DNA PCR quantitative was positive with 55882 copies/ml. Lymphomatoid granulomatosis is an angiodestructive B-cell lymphoproliferative disease which is usually associated with EBV. It mostly presents in middle adulthood. Lungs are most commonly involved. Pediatric populations are not usually effected, but can be seen in immunocompromised patients. The patient is since then treated with chemotherapy, and now on maintance with Rituximab.*

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I. Introduction

Ataxia telangiectasia(A-T) is an autosomal recessive condition caused by mutations in the ATM gene, which codes for a serine/threonine kinase involved in the physiological response to double-stranded DNA breaks.[2,8] It is characterized by ataxia, oculocutaneous telangiectasia, combined immunodeficiency's, and increased predisposition to malignancies, particularly EBV-associated lymphoma. The immunological deficit seen in AT patients is frequently insufficient to account for the higher frequency of EBV-related cancers.

The lytic cycle of EBV takes place in the oropharyngeal epithelium, whereas the latent cycle takes place in B cells from the lymphoid tissues.[9] In immune-competent people, chronic infection is usually asymptomatic because the virus is kept in a dormant form.[7] In immune-compromised people, control of persistent EBV infection may fail, resulting in lympho-proliferative diseases and lymphomas.[9]

Lymphomatoid granulomatosis (LG) is an uncommon lymphoproliferative disorder first described by Liebow and colleagues in 1972.[5] LG is a proliferative angiocentric and angiodestructive disease that mainly affects the lung,[5] but other organs such as the central nervous system (CNS) may also be affected.[4] Histologically, LG is staged into 3 grades based on the presence of cytologic atypia, the extent of necrosis, and the retention of polymorphous cellular infiltrate.[6] It occurs sporadically in otherwise immunocompetent patients. However, many cases have been reported in patients with other conditions, including HIV, acquired and congenital immunodeficiency states, lymphomas (both Hodgkin's and non-Hodgkin's), ulcerative colitis, tumors of the gastrointestinal system and breast, infectious hepatitis, psoriasis, and sarcoidosis.[3]Patient first exhibits a waxing and waning clinical history that eventually advances to an aggressive disease with a high mortality rate.[1] A rare disease, pediatric LG appears to be more often seen in leukemia patients, as well as immunocompromised patients. The disease has a high mortality rate. This disease is a confounding entity due to its lack of identifiable clinical, laboratory, and imaging characteristics

II. Case Report

A 3year 6 months old male child presented to our hospital with symptoms of fever, and cough 2 to 3 episodes per month for the last 4 months. His past, Computerized tomography revealed enhancing mass in the right upper lobe with encasement of SVC. Biopsy specimen has revealed Pleuropulmonary blastoma and underwent Right upper lobectomy on 21/06/21. Histopathology examination has revealed Lymphomatoid granulomatosis Grade 3.

Epstein - Barr virus (EBV) DNA PCR quantitative was positive with 55882 copies/ml. He later developed a high-grade fever associated with cough, on testing blood cultures showed Acinetobacter sepsis for which he was treated.

Our first clinical examination revealed a sick child with short stature, below the 1th percentile for height (86cm) and weight (9 kg) which is also below 1th percentile. Small head (49 cm) between the 3rd percentile and 50th percentile for head circumference. These findings suggest chronic malnutrition. Morphologically, an absent toe on the right foot and telangiectasia in the eye were found. Neurological development was normal. General physical examination revealed that a Chest auscultation showed Rhonchi on the right side of the lung. The liver is palpable below the costal margin. Serology of immunoglobulin's revealed low levels of serum IgA, and immunological workup showed combined immunodeficiency. There were reduced neutrophils and B lymphocytes. Bone marrow biopsy showed cellular marrow with myeloid hyperplasia and absent iron stores suggestive of inflammatory or infective pathology. Genetic analysis revealed a pathogenic variant mutation (absence of ATM protein) and uncertain significance mutations were detected (table).

GENE	LOCATION	DISEASE	CLASSIFICATION
ATM gene	Intron 27	Ataxia Telangiectasia	Pathogenic
DNAJB13 gene	Exon 4	Primary Ciliary Dyskinesia	Uncertain Significance
SCNN1B gene	Exon 3	Bronchiectasis with or without elevated sweat chloride	Uncertain Significance

Epstein - Barr virus (EBV) DNA PCR quantitative was positive with 55882 copies/ml. PET CT was done which showed a moderate to intense FDG uptake (SUVmax 10.6) it was noted to be a heterogeneous enhancing mass like consolidation involving right middle lobe and also multiple well-defined soft tissue nodules are noted in the right lower lobe. A mild to moderate FDG uptake (SUVmax 8.0) is noted in multiple well-defined soft tissue attenuation nodules are noted in the right lower lobe (largest ~1.8*1.6 cm). Also, increased FDG uptake (SUVmax 10.5) is noted in few enlarged precarinal, subcarinal and right paratracheal nodes (largest ~1.9*1.6cm). He was since then on chemotherapy. He received chemotherapy consisting of 4 cycles of R-CHOP and 2 cycles R CVP. He is currently on monthly maintenance therapy with inj. Rituximab.PET CT showed a near complete metabolic and morphological response to therapy, with Deauville score of 2.

III. Discussion

Lymphomatoid granulomatosis is an angiodestructive B-cell lymphoproliferative disease which is usually associated with EBV. It is mostly presents in middle adulthood. Lungs are most commonly involved. Pediatric populations are not usually effected but can be seen in immunocompromised patients. Lymphomatoid granulomatosis complicaticating AT is extremely rare. AT is commonly associated with B- cell lymphomas, but association with lymphomatoid granulomatosis has not been seen often. Thorough search of the available literature showed a case of AT complicated by lymphomatoid granulomatosis in a 10-year-old. Our patient, who is 4-year-old is diagnosed with AT complicated with lymphomtoid granulomatosis making it the earliest known presentation based on the available literature.

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