# Mediastinal Mass in Patient with HyperIgM syndrome AICDA mutation

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## Introduction

In this case report we are presenting a 21 year old male diagnosed with autosomal recessive type of Hyper IgM syndrome due to AICDA gene who presents with an extensive non-malignant mediastinal mass which has responded to therapy with 3 recombinant medications.

## Case description

A 21-year-old Caucasian male with autosomal recessive Hyper IgM syndrome due to AICDA mutation, diagnosed at 17 months, presented with a newly developed mediastinal mass. He receives routine IVIG therapy every 28 days. Routine surveliance tests that include complete pulmonary function tests (PFT's), chest x-rays, CBC and CMP are done once a year. At age 16, patient was noted to have cervical and inguinal lymphadenopathy. CT scan indicated left mediastinal, hilar and pleural lymphadenopathy with softtissue infiltration around the descending thoracic aorta and esophagus Biopsy indicated no evidence of a lymphoma or infection.

5 years after initial workup, routine PFT's showed a decline in diffusion capacity to 50% predicted. Patient displayed no clinical symptoms of chest pain, cough, dyspnea, dysphagia or reflux. CT scan of chest with contrast which revealed an extensive ill-defined soft tissue mass extending from the thoracic outlet to the level of the esophageal hiatus that encased vascular structures resulting in narrowing and occlusion of left upper lobe pulmonary artery and complete occlusion of the left lower lobe pulmonary arteries respectively. Imaging demonstrated homogenous ventilation to both lungs and absence of perfusion to the left lower lobe. Infectious workup was negative for atypical infections. Transesophagael biopsy revealed mixed cellular infiltrate with no predominant cell type or evidence of malignancy, consistent with previous lymph node biopsy 5 years prior. CD20 and CD3 stains revealed aggregates and scattered B-cells and T-cells. H&E stain slides indicated minute fragments of tissue with fibrosis and mixed inflammatory infiltrate comprising a few lymphoid follicles and scattered small lymphocytes, histiocytes, eosinophils and many plasma cells.

Removal of mass was proposed due to its extensive involvement in surrounding all vital structures in the mediastinum. However, due to the ambiguous borders and location, surgical excision was not possible. As there is no literature on how to manage this mass with Emperic therapy was started on the cell types based on the biopsy. This included 4 doses of Rituximab (100mg/m2 check this), 3 doses 10mg/kg pulse steroids 18 hours apart, and daily sirolimus (level was adjusted based on sirolimus level). After just one round of treatment with rituximab, 3 doses of pulse steroid therapy and daily sirolimus, a follow-up chest CT scan with contrast indicated significant interval improvement with 50-60% reduction of the soft tissue mass (reduction might be more).

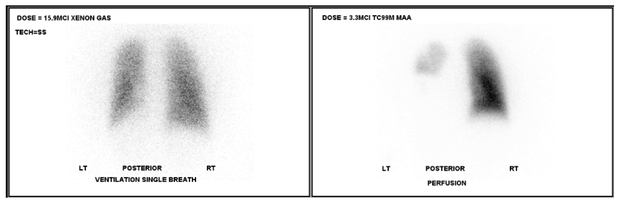



**Figure 1&2:** Initial V/Q scan upon discovery of mediastinal mass

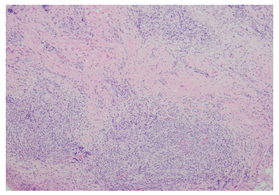


**Figure 3:** Transesophageal biopsy of mediastinal mass (2019 with extensive fibrosis and chronic lymphocytic infiltrate

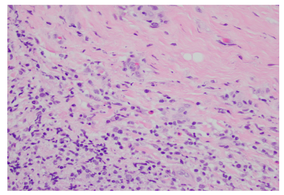
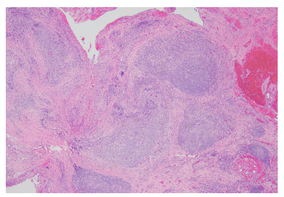


**Figure 4:** Transesophageal biopsy of mediastinal mass (2019 Infiltrate composed of small sized lympocytes, plasma cells, histiocytes and occasional eosinophils



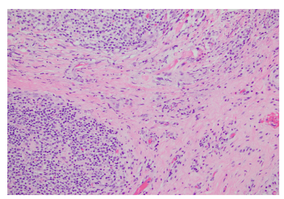


**Figure 5 & 6**: Lymph node biopsy from 2014 with surrounding fibrosis and chronic inflammation

## Discussion/Conclusions

HIGM with AICDA is one of multiple AR-HIGMs involved in the activation-induced cytidine deaminase (AID) gene repair mechanism. AID deficiency has a known link to lymphoid hyperplasia, but generally results in non malignant lymphoid proliferation. Studies show AR- HIGM Type 5, which is due to a Uracil-N glycosylase (UNG) enzyme deficiency, has been linked to Lymphoma[1]. Given our patient has an AID deficiency, the documented risk of lymphoma in HIGM with AICDA mutation is low. AID initiates deamination of cytosine in Ig genes resulting in a U:G mismatch. This mismatch is then processed through various mechanisms to result in Somatic hypermutation. One of the most prominent mechanisms for processing U:G mismatches is through UNG. UNG is involved in error-free base excision repair of AID induced lesions.

For this reason UNG deficiencies lead to lymphoma where as AID deficiencies are associated with non malignant lymphoproliferative disorders[4]. The pending concern with this patient's lymphoid hyperplasia is the actual burden of the mass encasing vital anatomic structures. This patient displayed decline in diffusion capacity and pulmonary vascular occlusion was visualized on chest CT; thus making it imperative to reduce the mediastinal mass.

Our Proposed treatment therapy was composed of Rituximab, Pulse steroid therapy and daily Sirolimus. Rituximab was chosen HyperIgM is an intrinsic B-cell defect. There are no documented cases of the use of rituximab to treat a benign lymphoproliferative mediastinal masses in a HIGM patient with AICDA mutation. There are, however, cases of successful treatment of autoimmune and lymphoproliferative complications of patients with intrinsic B-cell immunodeficiencies with Rituximab (one specific case documenting the resolution of elevated IgM as well as lymphoproliferation in a HIGM patient with AICDA mutation that stopped immunoglobulin therapy)[2].

Pulse steroids where chosen for the reduction of the inflammation. Sirolumus was used to suppress multiple T cell lines. Sirolimus can decrease non-malignant lymphoproliferation in patients with immunodeficiencies, however, the use of sirolimus in HIGM is not well documented. There was Significant reduction of the mass (40%) after receiving just one course of rituximab and 3 pulse steroid and daily Sirolimus, area calculated using imaging.

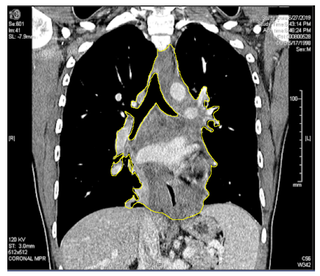


**Figure 7**: Initial MRI of mediastinal mass prior to treatment (6/27/2019)

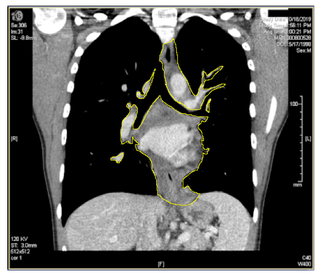


**Figure 8**: MRI conducted 3 months after 1 course of pulse steroids and Rituximab with daily Sirolimus (10/18/2019).

**Conflict of interest:** the authors declared that they have no conflict of interest

## References

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