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Clinical Course Of A Patient With Agammaglobulinemia Caused by *SLC39A7* Defect

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Introduction

- Defects in transmembrane transporters can cause immunodeficiency, such as calcium and magnesium
- Zinc is essential for several key proteins and dietary deficiency can cause lymphopenia
- Downstream effects of *SLC39A7,* which encodes zinc transporter ZIP7 is not well understood when it comes to immunological function
- We discuss the clinical course of a patient who was found to have *SLC39A7* defect and agammaglobulinemia.

Initial Presentation

At 18-months of age, patient was admitted due to failure to thrive and pneumonia

Past Medical History: Failure to thrive (FTT), *E.coli* urosepsis (8 months), croup (11 months), recurrent otitis media complicated by ruptured tympanic membranes (15 months), and bacterial pneumonia (17 months)

Immunizations: Unimmunized by parental choice

Family History: No recurrent infections or primary immunodeficiency

Initial Labs

Total T Cells (CD3+)	7899 mm3
T Helper Cells (CD4+)	2633 mm3
T Cytotoxic Cells (CD8+)	5178 mm3
Total B Cells (CD19+)	0
NK Cells (CD16+ and CD56+)	527 mm3
Zinc	63 mcg/dL
Immunoglobulin G	<33 mg/dL
Immunoglobulin A	28 mg/dL
Immunoglobulin M	<7mg/dL
Immunoglobulin E	<2 kU/L
BTK	No duplication, deletion, or pathogenic variants

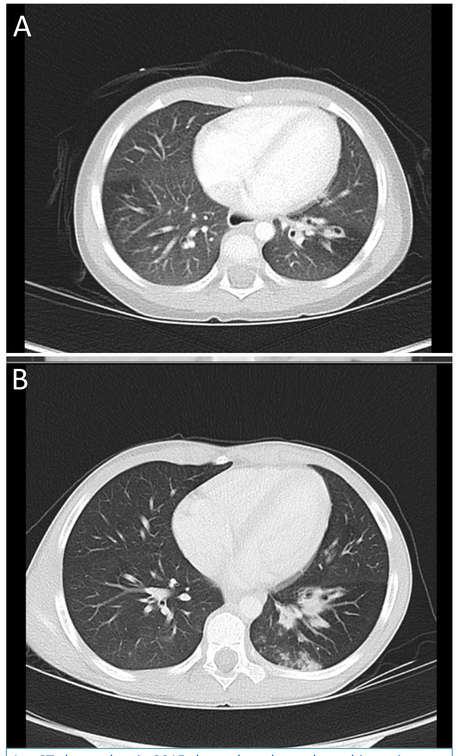
Clinical Course

- He received antibiotics for pneumonia and started immunoglobulin replacement therapy (IgRT)
- Despite being on IgRT, he continued to have chronic rhinosinusitis and cough
- At 3 years of age computed tomography (CT) scan of the chest showed bronchiectasis
- He was started on inhaled corticosteroids and twice a day airway clearance with high frequency chest wall oscillation vest and albuterol. This regimen is increased during acute illnesses

Course Continued

- Repeat CT scans of his chest and sinuses at 6-years of age showed pansinusitis and bronchiectasis with continued mucoid impaction
- He had a functional endoscopic sinus surgery (FESS) and bronchoscopy, which grew non-typeable *Haemophilus* and was then treated with Augmentin
- At 10-years-of age, the patient continued to have a chronic cough. Respiratory sputum culture grew many *Streptococcus pneumoniae*, *Haemophilus influenzae* non-typeable, and other normal oropharyngeal flora
- Another CT scan was done which showed worsening bilateral bronchiectasis and increased opacification of the paranasal sinuses
- Family became agreeable to starting prophylactic anti-microbial therapy, but discontinued due to concern of rash
- Our patient consistently grew below the 3rd percentile, while his mid-parental target height was close to the 50th percentile. He was started on growth hormone with improvement
- Exome sequencing showed compound heterozygous variants in the *SLC39A7* (c.54G>A(p.Trp18Ter and c.421G>A(p.Ala14Thr)

Figure 1



A. CT chest taken in 2015 showed moderate bronchiectasis primarily in the left, with evidence of air trapping and minimal disease in the right lower lobe
B. CT chest taken in 2022 showing increased opacifications in both the left and right lower lobe secondary to mucous plugging. There is also worsened air trapping compared to 2015

Discussion

- Variants in *SLC39A7* result in an autosomal recessive agammaglobulinemia-9, a primary immunodeficiency syndrome characterized by recurrent bacterial infections associated with agammaglobulinemia and absence of circulating B cells
- Other cases report FTT, bacterial infections, bronchiectasis, and short stature similar to our patient. Other clinical findings include blistering dermatitis, thrombocytopenia, and liver dysfunction
- In patients with recurrent infections despite IgRT, starting prophylactic antimicrobials earlier may be helpful in reducing lung injury and preventing infections

References

Anzilotti et Al. An Essential Role for the Zn2+ transporter ZIP7 in B cell development. *Nat Immunol*. 2019 March; 20(3): 350-361

Erdos et Al. A novel mutation in SLC39A7 identified in a patient with autosomal recessive agammaglobulinemia: The impact of the J project. *Pediatr Allergy Immunol*. 2022 Jun;33(6):e13805

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