A 2 YEAR OLD BOY WITH SEVERE PNEUMONIA

Katie Nelson, MD
Stanford University
CIS School
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OUR CASE

22 month old male presents with 11 days of high fevers and progressive respiratory distress.

- Previously healthy, no sick contacts
- On exam: ill-appearing, tachypneic, hypoxic, decreased breath sounds over R posterior lung field
- Chest X Ray: RML and RLL infiltrates
- Chest CT scan: RML & RLL consolidation with calcifications, RLL cavitary necrosis
CLINICAL COURSE

- Treated with multiple parenteral antibiotics, no improvement
- Extensive infectious workup negative including cultures from bronchoalveolar lavage fluid and chest tube drainage
- Transferred to Stanford from community hospital due to progressive deterioration in respiratory status and persistent fevers.
DIAGNOSTIC TESTING

- CRP: 30.8
- IgA: 386, IgM: 122, IgG: 1143
- T and B cell subsets: normal
- Tetanus and diptheria titers: normal
- Dihydrorhodamine testing: 73% oxidation-positive neutrophils at 24 hours.
- Review of flow cytometry plots demonstrated clearly diminished oxidative burst vs. control
**DIAGNOSIS: CGD**

- Analysis of gp91-\textit{phox}, p22, p47 and p67 expression yielded low-undetectable levels of p22 and gp91 vs. control.

- Genomic DNA sequencing of CYBB gene revealed A>G nucleotide substitution in exon 1 encoding gp91-phox.

- Maternal CYBB sequencing negative for mutation.
DISCUSSION

- 65% of CGD is due to CYBB mutations on X chromosome, missense mutations in exon 1 have been described
- Lack of maternal carrier status
  - Not identified in 10% of patients with CYBB mutations
  - Maternal germline mutation vs. maternal germline mosaicism
- Pitfalls of dihydrorhodamine testing
  - Importance of reporting not only positive oxidative burst, but also mean fluorescence intensity
THANK YOU!

References