A Case of Recurrent Fungal Meningo-encephalitis

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Presentation of Current Illness

9-year-old Hispanic female

Two month history of symptoms

- Headache
- Photophobia
- Difficulty with balance
- Nausea/emesis

Increasing in frequency over past two-five days
Past Medical History

• Otitis media

• Urinary tract infections

• Candidal infections
  – Recurrent oral thrush since birth
  – Vertebral osteomyelitis, diskitis, and paraspinal abscess (2010)
  – Meningitis (dx 6/2012) with persistence of disease (2/2013)

• Meds: Fluconazole daily

• Immunizations: UTD

• NKDA

• Social History: Born in NY, two healthy older sibling, poor school performance due to missed days, no tobacco exposure

• Family History: Mother with migraines; grandfather with heart disease
Physical Exam, Labs and Imaging

- Physical Exam: Afebrile, dilated pupils (5mm), 3+ disc edema with blurred margins, unsteady FTN bilaterally, decreased UE strength, flat affect

- Na 145, K 3.7, Cl 113, Bicarb 19, BUN 3, Cr 0.41, Gluc 94

- **16.7** >12.9/38.1 <319 (**ANC 14.6, ALC 1.6, AEC 0.14**)

- **Fungitell** >500pg/mL (<80 pg/mL)

- **CSF - Nuc cells 372** (7%N, 69%L, 20%M), RBC 304, prot 472, gluc <20
  - Atypical & plasmacytoid lymphs
  - Routine cultures negative

- Brain MRI- Cont **diffuse leptomeningeal enhancement** from 2/2013 and **progressive ventriculomegaly**
Abnormal Studies

– Response to tetanus/diphtheria post vaccination
  
  • Diphtheria titer 0.1 IU/mL (6/2012) → 0.16 IU/mL (3/2013)
  • Tetanus titer 0.04 IU/mL (6/2012) → 0.12 IU/mL (3/2013)

– Antigen proliferation to candida and tetanus
  
  • Viability of lymphs 85.4% \[>=75\]
  • % CD45 of CA 0% \[>=5.7\]
  • % CD3 of CA 0% \[>=3\]
  • % CD45 of TT 0.3% \[>=5.2\]
  • % CD3 of TT 0.2 \[>=3.3\]

– Candida skin test - nonreactive
Diagnosis and Summary

- Genetic testing ultimately reveals homozygous \textit{CARD9} mutation, most likely consistent with autosomal recessive \textit{CARD9} deficiency.
- \textit{Card9} plays a critical role in the development of Th17 responses to \textit{Candida} and loss of function in this adapter protein is associated with increased susceptibility to fungal infections.

McDonald DR. J Allergy Clin Immunol 2012;129:1429-35