AN ADULT WITH PANCYTOPENIA AND SUSCEPTIBILITY TO VIRAL INFECTIONS

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History of Present Illness

24 year old male who recently returned from a trip to Wyoming was admitted to the ICU with fevers, headaches, confusion, progressively deteriorating mental status, rash for two to three days, nausea, vomiting, diarrhea, and cogwheel movements.

- **Immunizations**: Did not receive most vaccines, except perhaps tetanus. He contracted chickenpox in the past and was able to clear the infection spontaneously without hospitalization.

- **Medications**: None.
Past Medical History

- Born full term in California without complications.
- Recurrent warts on fingers, hands, arms, toes, feet, and legs since 7 years old, which recur despite multiple attempts for removal.
- 4-6 pneumonias since 9 years old (once requiring hospitalization at age 12 years); 10 bronchitis; 3-4 sinusitis, resolved after antimicrobials.
- No recurrent oral ulcers, oral thrush, abscesses, otitis media, meningitis.
- In 2007-08, he received a workup at UC Davis Hematology and Chico Allergy for persistent leukopenia (1500-2000s), neutropenia (700-900s), lymphopenia (200-900s), monocytopenia (20s), intermittent thrombocytopenia (100-200s). He had elevated total IgG 3000-4500s; IgG1 2300s; IgG3 300s; SPEP with polyclonal gammaglobulins of 3.5; UPEP with detectable total proteins, albumin, alpha1, alpha2, beta, gammaglobulins; ANA+ 1:40; Scl-70 Ab 1.3. He had normal IgG2 397, dsDNA, anti-RNP, SM Ab, CH50, C3, C4, vitamin B12 level, alpha 1 antitrypsin level, high resolution chest CT in 10/2007.
- Bone marrow biopsy in 2007: reduced myeloid precursors with marked left shift, and decrease in megakaryocyte. He had no other cell line problem or lymphoma. These findings may represent evolving aplastic anemia.
Family History and Physical Findings

**Family History:**
- Mother had a few pneumonias since 30 years of age and intermittently has warts since 4 years ago, which resolve spontaneously.
- Father developed a brain abscess leading to chronic epilepsy at age 29 years old. He died at 48 years old from complications due to influenza pneumonia. The patient’s paternal grandfather also died at age 50 years from influenza pneumonia.
- Sister has hyper and then hypothyroidism, with mild arthritis at her back.
- Maternal grandmother with rheumatoid arthritis. Maternal grandfather with throat cancer and rosacea. Maternal aunt with SLE.

**Vital signs:** Temp (max) 38.8° C, HR 104 BPM, BP 109/65 mmHg, RR 33 BPM, SpO2 98% on room air.

**General:** Drowsy, confused, belligerent.

**Skin:** Erythematous rash on nose and cheeks. Warts on fingers, hands, forearms, elbows, toes, feet, and lower legs bilaterally.

- Chest x-ray, head CT, MRI of the brain, EEG were normal.
**Initial Labs**

- **Serum WNV IgG**: 1.18 (normal <=1.29)
- **Serum WNV IgM**: 5.23 (normal <=0.89)
- **CSF WNV IgM**: 1.11 (normal <=0.89)
- **Serum WNV RNA**: detected
- **HIV Ab**: neg
- **Serum HIV-1 DNA and RNA**: neg
- **CSF WEE IgG and IgM**: neg
- **CSF Lyme Ab**: neg
- **WEE IgG and IgM IFA**: negative
- **CSF HSV PCR**: neg
- **CSF CrAg**: neg
- **CSF latex agglutination (H flu, N meniningitides, S pneumoniae)**: neg
- **CSF VDRL**: non-reactive
- **CSF Lyme (B. Burgdorferi) ELISA**: neg
- **CSF/Blood/Urine/Resp/Parasite culture**: no growth
- **C diff toxin**: neg
- **Infectious mononucleosis screen**: neg
- **Influenza A and B antigen screen**: neg
- **Leptospira Ab**: neg
- **Hantavirus Ab**: neg
- **Serum CMV PCR**: neg
- **Borrelia hermsii IgG**: neg
- **Borrelia hermsii IgM**: neg
- **Hantavirus IgG and IgM**: neg
- **Leptospira Ab**: neg
- **Urinary Legionella Ag**: neg
- **RMSF IgG and IgM**: neg
- **R typhi IgG and IgM**: neg
- **3 smears for intracellular organisms**: neg
- **ANA**: neg
- **dsDNA**: neg
- **Complete metabolic panel**: normal
- **Urinalysis with microscopy**: neg
Initial Labs

- **Cell counts:**
  - White blood cells (WBCs): 4.9 k/uL
  - Absolute neutrophil count: 4.44 k/uL
  - Absolute lymphocyte count: 0.42 k/uL
  - Absolute monocyte count: 0 k/uL
  - Absolute eosinophil count: 0.01 k/uL
  - Absolute basophil count: 0 k/uL
  - Total lymphocyte: 251 /uL
  - CD3 lymphocyte: 228 /uL
  - CD3/4 lymphocyte: 161/uL
  - CD3/8 lymphocyte: 68 /uL
  - CD4/45RA lymphocyte: 45 /uL
  - CD4/45RO lymphocyte: 350 /uL
  - CD19 lymphocyte: 8 /uL
  - CD16/56 lymphocyte: 13 /uL
- **Immunoglobulins:**
  - IgG 2180 mg/dL, IgG1 1780 mg/dL, IgG2 203 mg/dL, IgG3 140 mg/dL, IgG4 2.2 mg/dL
  - IgA 185 mg/dL, IgM 82 mg/dL, IgE 8 kU/L
- **Titers (all after IVIG):**
  - Measles IgG: <0.9 (before IVIG), VZV IgG: 2.14
  - Tetanus IgG: 0.4 IU/mL, Diphtheria IgG: 0.12 IU/mL, H flu IgG: 1.56 IU/mL, S pneumoniae 23 serotypes: 10/23 >1.3 mcg/mL
  - HSV-1 IgG: 8.02, HSV-2: 0
  - HBsAg, HBsAb, anti-HBC Ab, anti-HCV Ab: neg
- **T cell phenotyping:**
  - There is an increase in the relative distribution (%) of CD8 central memory (Tcm) T cells as well as a large expansion of total CD4 memory (CD45RO+) T cells, with an increase in % effector memory (Tem) CD4 T cells. The only other remarkable finding is the population of CD25dim CD4- T cells. This subset is 9.6% of total lymphocytes. Gating on the CD4+25bright subset, there is a significant increase in activated CD4 T cells, which is often seen in active inflammation/infection.
- **B cell phenotyping unable to be performed due to low B cell numbers.**