Immune Suppression and Epstein Barr Virus

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Introduction

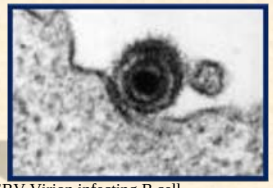
Infectious mononucleosis is a common viral illness affecting mostly teens and young adults. For most patients who have it, it is a self limited process without significant complications and with a favorable prognosis. Supportive treatment is often all that is needed. However, a small minority of the patients who have this infection can have more serious reactions to it that require specialized management.

Presentation:

•Typical triad of fever (98%), pharyngitis (85%), and adenopathy
•Myalgia, malaise, and fatigue (often prolonged) also present
•Splenomegaly in 50-60%
•Hepatomegaly in 10-30%
•Generalized petichial, urticarial, or macular rash after amoxicillin or ampicillin

Causes/Differential Diagnosis:

EBV, CMV, HIV, toxoplasmosis, viral hepatitis, HHV-7 or 8, Non Hodgkin's and Hodgkin's Lymphoma, Leukemias

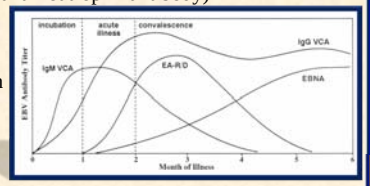


EBV Virion infecting B cell

Lab Findings:

•Heterophile antibody test (Monospot) positive
•Atypical lymphocytes
•ANC from 2K-3K around 3rd or 4th week in 50-80% of cases
•ANC <1K in <3% of cases (related to anti neutrophil antibody)

•Viral serologies such as IgM and IgG for Viral Capsid Antigen and IgG for Early Antigen peak at different times in the course of the illness whereas Epstein Barr Nuclear Antigen persists for life, shown to the right



Graph of EBV viral serologies over time showing various peak times of each serology

Treatment:

Is typically only supportive care (rest, fluids, etc)
Advice avoidance of contact sports for 4 weeks to avert splenic rupture
Corticosteroids may be indicated in cases of airway compromise or immune mediated anemia and thrombocytopenia

Case

An 18 year old previously healthy female presented to her PCP with a 5 day history of fever, sore throat, malaise, chills, myalgias, increasing fatigue and large tender lymph nodes in the neck. She started taking amoxicillin for presumed strep throat and subsequently developed a fine macular rash. A monospot test collected by the patient's PCP was positive. The patient received supportive care with subsequent resolution of her symptoms. Three weeks later, however, her fever and lymphadenopathy returned. A repeat CBC revealed neutropenia, so she was admitted to the hospital. She was febrile at 39.3 degrees and had tender lymphadenopathy of the anterior cervical and submandibular nodes. Also present was a diffuse gingivitis with some mild bleeding of the gums. She had no organomegaly, no rash, and her exam was otherwise normal. WBC count was 1.55 with 4.4% neutrophils giving an ANC of 68. The rest of the CBC was normal along with coagulation, and chemistries.

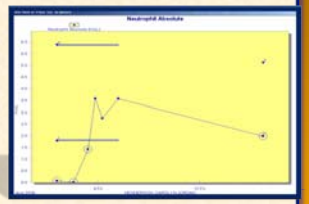
Admission Labs

	12.6	
1.55		252
	37.8	

139	106	9		80
3.8	29	0.9		

14.6	35.7
	1.1

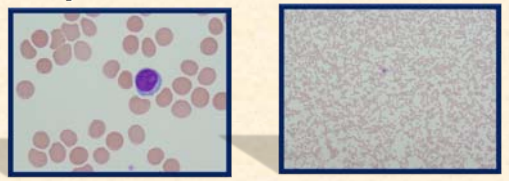
Neutrophils 4.4%
Lymphocytes 77.8%
Monocytes 15.4%
Eosinophils 1.8%
Basophils 0.6%
ANC 68



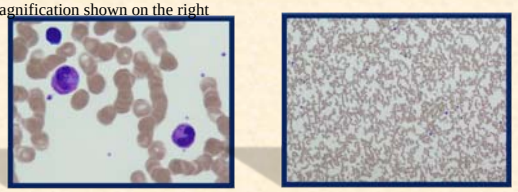
Graph of ANC over time showing resolution of neutropenia

Vancomycin, ceftazadime, and clindamycin were started for empiric coverage. Urine, blood, and throat cultures for HSV and strep were ultimately negative. The next day, the ANC dropped to 17, and G-CSF was then initiated. CMV IgM was positive while IgG and CMV PCR were negative. Anti parvovirus B19 IgM and IgG were 1:64 and 1:10 respectively. HIV ELISA was negative. EB viral capsid antigen IgM and IgG were positive while EBV nuclear antigen was negative. EBV PCR was mildly positive. The patient's WBC count improved and the neutropenia resolved along with her symptoms within a few days. She was discharged and follow up CBC's after discharge revealed no further neutropenia. Granulocyte agglutination assay, granulocyte immunofluorescence assay, and monoclonal antibody immobilization of neutrophil antigens were all negative.

Peripheral Blood Smears



Peripheral blood smear at 100x magnification showing single neutrophil on hospital day 2 during neutropenia shown on the left; 20x magnification shown on the right



Peripheral blood smear at 100x magnification on the left showing a greater abundance of neutrophils on hospital Day 4 after G-CSF was given; 20x magnification on the right.

Discussion

This case illustrates that febrile neutropenia is a potential serious complication of acute EBV infection which requires hospitalization. Obtaining bone marrow to workup the neutropenia is generally not advised because it can mislead one to a false diagnosis of leukemia because these patients often have an abundance of immature forms like myelocytes and promyelocytes. There are also risks of infection and nerve damage along with the pain associated with the procedure. G-CSF can be given to these patients to achieve a faster resolution of neutropenia, however, there are not data to prove definitively that giving G-CSF leads to improved outcomes such as decreased mortality. The neutropenia in these patients is a self limited process even without G-CSF. One could also make the argument that giving this drug increases the risk of a myelodysplastic syndrome. Furthermore, it puts the patient at risk of splenic rupture and anaphylaxis. Given the emerging risks of G-CSF administration, careful consideration must be given in the decision to use it in such patients.