Study of Prevalence and Risk Factors for JCV Antibody Seroconversion in MS Patients from the UMass Memorial MS Center

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BACKGROUND

- Multiple sclerosis (MS) is an autoimmune inflammatory demyelinating disease of the central nervous system (CNS) that is a leading cause of disability in young adults. Treatment directed at the rapid, aggressive progressive phase of MS is typically difficult. Natalizumab is an effective drug for the treatment of relapsing-remitting multiple sclerosis (RRMS). However, in rare cases, its use is associated with the development of progressive multifocal leukoencephalopathy (PML), a potentially fatal complication caused by the John Cunningham virus (JCV).[1] It is thought that the JCV infects the tonsils or kidneys, but cannot replicate well in the cells of these organs. The virus can subsequently infect B-cells and travel to the central nervous system (CNS). Glial cells in the CNS are permissive to JCV replication, which contributes to the development of PML.[3]
- It is estimated that the majority of adults are positive for JCV antibodies. Studies on MS patients have reported a prevalence of 46-60% and an association between JCV antibody status and age, gender, national origin, and length of immunosuppressive therapy.[2,4,5]
- Risk factors for infection with the JCV are not well understood. Environmental factors may play a role.

OBJECTIVES

- To identify risk factors associated with JCV antibody status in a cohort of MS patients followed at the UMass Memorial MS Center.
- To determine if there is an association between family members' and MS patients' JCV antibody status.
- To determine if there is an association between a set of environmental exposures and JCV antibody status.

METHODS

- We identified patients who have been tested for antibodies to JCV and performed chart review to determine if there is a difference in terms of gender, age, area of residence, marital status, or smoking status between patients who tested positive and those who tested negative for JCV antibodies. We are reporting those results here.
- The R statistical programming language was used to analyze the data. We applied Chi-Square , Fisher's Exact, and t tests to determine statistical significance. The Levene test was applied to assess normality of numerical data. The Agresti & Coull method was used to calculate a 95% CI (displayed as error bars in the graphs) around our observed counts of JCV antibody status. We had a 24.4%, 96.7%, and 99.9% chance of detecting small, medium, and large differences between groups, respectively.
- Family members will be tested for JCV antibodies to determine if there is an association between family member JCV antibody status and patient JCV antibody status.
- We developed a questionnaire asking about environmental exposures. This questionnaire will be administered to patients with available JCV serology results to determine if there is a difference in exposures between groups.

RESULTS

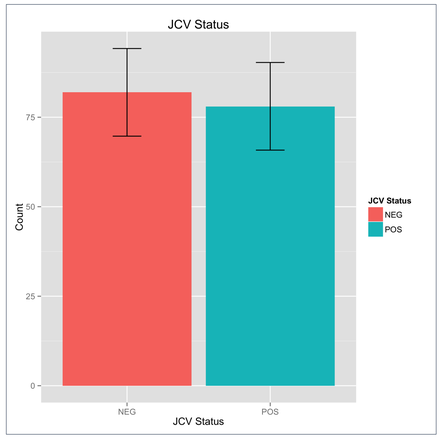

Figure 1

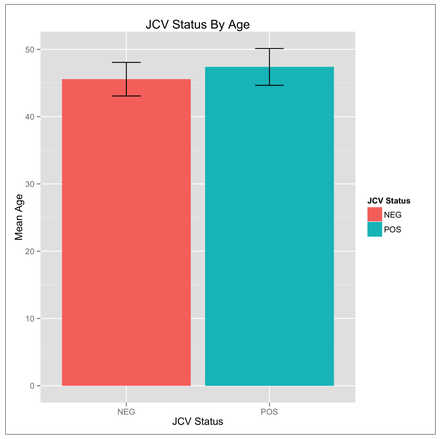

Figure 2

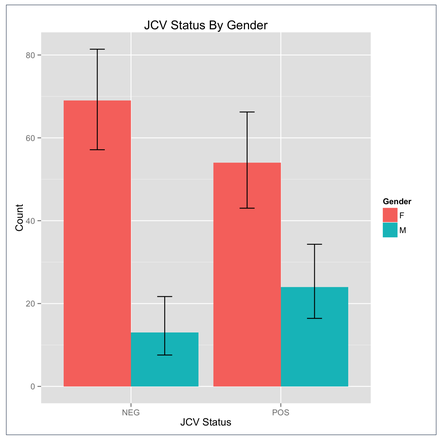

Figure 3

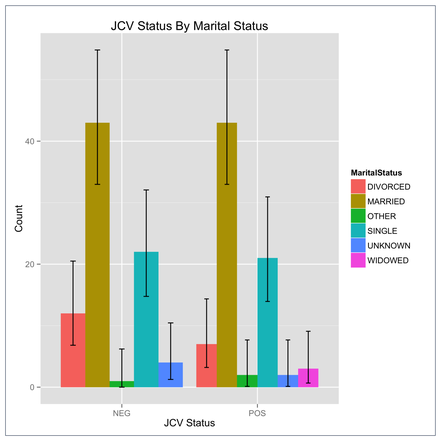

Figure 4

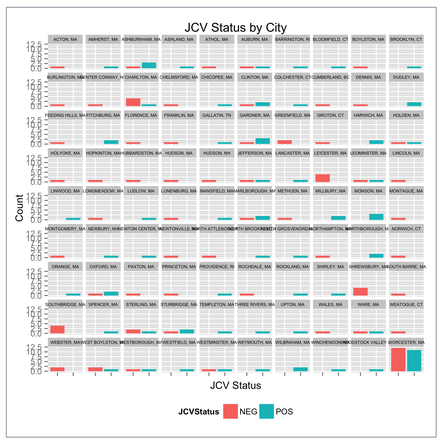

Figure 5

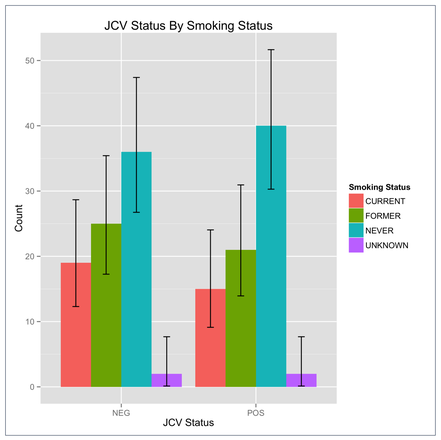

Figure 6

RESULTS

- 160 patients with JCV serology results were identified. 123 (76.9%) were female and 37 (23.1%) were male, with a mean age of 46.7 years.
- 78 (48.8%) of subjects were positive for JCV antibodies and 82 (51.2%) were negative (**Figure 1**).
- The mean age in the negative and positive groups were 45.6 and 47.4, respectively (p>0.05) (**Figure 2**).
- 69 (56.1%) and 54 (43.9%) of the women were negative and positive, respectively. 13 (35.1%) and 24 (64.9%) of the men were negative and positive, respectively (p<0.05) (**Figure 3**).
- 86 (53.8%) of patients were married and 74 (46.3%) were single, divorced, widowed, or other. There was no difference in JCV serology status between these groups (p>0.05) (**Figure 4**).
- Patients came from various locations in MA, RI, CT, NH, TN, and British Columbia. There were differences in JCV antibody status between the different areas of residence (p<0.01) (**Figure 5**).
- 34 (21.3%) and 46 (28.8%) of patients reported being current and former smokers, respectively. We did not detect a difference between smokers and non-smokers (p>0.05) (**Figure 6**).

CONCLUSIONS

- The 48.8% prevalence of JCV antibodies in this patient population is consistent with that of other studies. In our study, gender and area of residence were associated with JCV antibody status, whereas age and marital status were not. It is theorized that JCV infection occurs through an environmental exposure, so it stands to reason that area of residence may influence JCV antibody status. A greater number of men were positive for JCV. It is possible that occupational exposures are a factor in this result.
- We are in the process of enrolling patients and family members and administering our exposures questionnaire to patients who agree to participate in our study. This work is ongoing.

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REFERENCES

1. Bloomgren G, Richman S, Hotermans C, Subramanyam M, Goelz S, Natarajan A, Lee S, Plavina T, Scanlon JV, Sandrock A, Bozic C. Risk of natalizumab-associated progressive multifocal leukoencephalopathy. N Engl J Med. 2012 May 17;366(20):1870-80. doi: 10.1056/NEJMoa1107829. PubMed PMID: 22591293.
2. Bozic C, Richman S, Plavina T, Natarajan A, Scanlon JV, Subramanyam M, Sandrock A, Bloomgren G. Anti-John Cunningham virus antibody prevalence in multiple sclerosis patients: baseline results of STRATIFY-1. Ann Neurol. 2011 Nov;70(5):742-50. doi: 10.1002/ana.22606. PubMed PMID: 22162056.
3. Ferenczy MW, Marshall LJ, Nelson CD, Atwood WJ, Nath A, Khalili K, Major EO. Molecular biology, epidemiology, and pathogenesis of progressive multifocal leukoencephalopathy, the JC virus-induced demyelinating disease of the human brain. Clin Microbiol Rev. 2012 Jul;25(3):471-506. doi: 10.1128/CMR.05031-11. Review. PubMed PMID: 22763635.
4. Outteryck O, Ongagna JC, Duhamel A, Zéphir H, Collongues N, Lacour A, Fleury MC, Berteloot AS, Blanc F, Giroux M, Vermersch P, de Sèze J. Anti-JCV antibody prevalence in a French cohort of MS patients under natalizumab therapy. J Neurol. 2012 Nov;259(11):2293-8. doi: 10.1007/s00415-012-6487-5. Epub 2012 Apr 12. PubMed PMID: 22527227.
5. Warnke C, Dehmel T, Posevitz-Fejfár A, Chan A, Berthele A, Schmidt S, Haas J, Kronsbein HC, Seitz F, Tackenberg B, Mäurer M, Gerbershagen K, Limmroth V, Adams O, Hartung HP, Gold R, Hemmer B, Wiendl H, Kieseier BC. Anti-JC-virus antibody prevalence in a German MS cohort. Mult Scler. 2012 Jul;18(7):1054-5. doi: 10.1177/1352458511429955. PubMed PMID: 22740609.