The Bing-Neel Syndrome: Clinical observations on nine new cases and the literature

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Waldenström's macroglobulinemia produces peripheral neurologic complications in over half of patients but rarely involves the dura, leptomeninges, brain, and CSF. To aid the WMS in creating diagnostic criteria for these occurrences (Bing-Neel Syndrome [BNS]) we have reviewed our experience and those reported by others to accumulate 31 examples of BNS. We divide these Group A with evidence of lymphoplasmacytoid (LMP) cells within the CNS and Group B with LMP cells absent for whom we posit an autoimmune mechanism. We provide illustrative examples. Fifty-five percent of cases received WM therapy and 21 patients had stabilization of IgM levels and 9 had stable WM at BNS onset. Sixty one percent had BNS in setting of progressive WM. Median of 36 months separated WM from BNS diagnosis but 26% had coincident occurrence. Cortical dysfunction (42%) manifested as memory deficits and behavioral changes had MRI correlates of white matter changes (54%), but FLAIR changes in five patients (16%) also appeared without cortical dysfunction. WM **after** neurologic symptom in 26% included visual field deficits, optic nerve lesions, cranial nerve sensation changes and amnesia. Spinal cord changes in 67% of BNS included cauda equine, meninges, dura, and intramedullary sites. Thirty-five percent had diagnostic biopsy of brain or dura or meninges with LMP cells staining for IgM. Surprisingly BNS patients did not have CSF (16%) studies but when performed usually contained over 3 leukocytes/mm^3 rarely followed by molecular studies and immunohistochemical analysis for CD19 and/or CD20 surface markers (n = 6). The CSF contained no LMP cells in eight patients but four of these had WM cells on biopsy. Four patients with acellular CSF did not undergo biopsy.

Sixty-five percent of BNS had abnormalities on brain MRI: white matter (5 of 31), enhancing lesions (7 of 31), or both (8 of 31). Of 13 with white matter hyperintense T2/FLAIR changes, five harbored "non-specific" changes. Isolated brain lesions were observed in 10 patients. Treatment offers hope of response as forty-two percent of responders sustained a response from 6 months to 4 years while three non-responders patients succumbed within 8 months. Nine patients died four months after PR or PD.

Since the epinomonic reports of Bing and Neel and collaborators (Bing and Neel, 1936), the diagnosis "BNS" has been applied without discretion to many central neurologic conditions in WM patients. We will provide criteria for the diagnosis of Group A BNS wth LMP infiltrates as well as for Group B for whom local IgM deposits may be responsible for white matter lesions. These criteria, in the setting of a relevant clinical history and staging of WM, include CSF flow cytometry and/or immunohistochemistry and light chain quantification, and contrast-enhanced MRI.