Familial predisposition in plasma cell disorders

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Hereditary cancer of virtually all varieties is replete with genotypic and phenotypic heterogeneity involving cancer at multiple anatomic sites wherein their "pattern recognition" may prove vital in diagnosis and management. In a large population-based, case-control study, Brown et al. (*Cancer 85*:2385-2390, 1999), calculated the odds ratio for multiple myeloma (MM) associated with having a MM-affected first-degree relative to be 3.7. There was a significantly increased risk of MM associated with a family history of any hematologic cancer (odds ratio = 1.7). Camp et al. (*N Engl J Med 359*:1734-1735, 2008) showed a significant excess of MM and melanoma in first-, second-, and third-degree relatives of MM affecteds (p = 0.039 to p = $1.7x10^{-9}$), with a significant increase in prostate cancer (PC) (p = 0.028). Eriksson and Hallberg (*Cancer Causes Control 3*:63-67, 1992) found an increased risk of MM in persons with first-degree relatives with any non-hematologic cancer (RR = 1.21), particularly PC (RR = 3.11) or brain tumor (RR = 6.61). In our earlier study of 39 MM-prone families (Lynch et al. *J Clin Oncol 23*:685-693, 2005), differing hematologic disorders, PC, and other solid tumors appeared to be integral to certain MM families. One notable African American family with a strong hereditary predisposition to MM and monoclonal gammopathy of undetermined significance (MGUS) showed an excess of PC (Lynch et al. *N Engl J Med 359*:152-157, 2008). Therein the 13q14 region of genetic loss in MM and PC merits attention (Sossey-Aloui et al. *Genomics* 80:5-7, 2002). Waldenström's macroglobulinimia (WM) occurred infrequently in our familial MM resource. Familial MM patients appear to be younger at diagnosis than their sporadic counterparts. Anticipation was suggested in a subset of our MM families. Collectively, these findings suggest common host susceptibility factors in concert with environmental perturbations in MM's and WM's etiology. McMaster et al. (*Clin Cancer Res 13*:5063-5069, 2007) and Renier et al. (*Cancer 64*:1554-1559, 1989) describe remarkable familial clusters of WM. Ögmundsdóttir et al. (*Clin Lymphoma Myeloma 9*:27-29, 2009) described an Icelandic family with multiple cases of MGUS and WM, and note that the medical literature reports approximately 130 families with two or more cases of MM, MGUS, or WM. In conclusion, plasma cell disorders merit intensive genetic and environmental interactive investigation.