Bing Neel Syndrome: the French experience

Laurence Simon1, Benjamin Carpentier2, Jehan Dupuis3, Lauris Gastaud 4, Carole Soussain5, Béatrice Mahe6, Camille Payet-Revest7, Stéphane Lepretre8, Véronique Leblond9, Luc Fornecker1

1 CHU Strasbourg, France, 2 CHU Lille, France, 3 Hôpital Henri Mondor, APHP, Paris, France, 4 Centre Antoine Lacassagne, Nice, France, 5 Institut Curie, Saint-Cloud, France, 6 CHU Nantes, France, 7 CHU Besançon, France 8 CHU Rouen, France       9Hôpital Pitié-Salpêtrière, APHP, Paris, France

Background: Bing-Neel syndrome (BNS) is a rare complication of Waldenström Macroglobulinemia (WM) defined as the direct involvement of central nervous system (CNS) by neoplastic cells. Because of its rarity, few data are currently available in the literature, which is mostly based on case-reports descriptions. The prognosis remains poor and the management of these patients is challenging with no consensus about the best treatment strategies to use. Patients and Methods: We retrospectively analyzed 26 patients out of 9 French centers databases, treated for a BNS between 2003 and 2014. Results: The median age at the time of BNS diagnosis was 61,5 years. In 9 cases (34,6%), BNS was the first manifestation of WM. In others cases, median time between WM diagnosis and BNS was 84 months (range 8-204). The majority of patients (n=21/26, 81%) had an infiltrative form with only 5 patients presenting with a pseudotumoral involvement of brain parenchyma. The diagnosis was made on cerebrospinal fluid (CSF) analysis in the majority of cases (91%). The median interval between appearance of neurological symptoms and diagnosis of BNS was 6 months. The most frequent symptoms at the time of BNS diagnosis were cognitive impairment (35%), motor or sensitive defect (31% and 19% respectively), pain (19%), cranial nerves impairment (27%), headache (19%), poor performance status (23%) and cauda equina syndrome (23%). The CSF examination showed a lymphocytic meningitis in 89% of cases with a median of 46 cells/mm3 (range 8-3900), and elevated protein level in 95% (1,88 g/L in median, range 0,52-7,23). A monoclonal B-cell population was identified in 77% of cases. In one case the diagnosis required a brain biopsy. Magnetic resonance imaging (MRI) showed abnormalities in 81% of cases. Meningeal enhancement was present in 64% of cases with conus medullaris infiltration in half of these patients. Cerebral enhancement was present in 40 % of cases and a normal pressure hydrocephalus in 3 cases. In 16% of cases, MRI was normal. First-line treatment comprised systemic chemotherapy in 88% (23/26) of cases. Treatment of CNS involvement was based on high-dose chemotherapy in 12 cases (methotrexate or aracytine in 10 and 2 cases respectively) or intra-thecal chemotherapy in 8 patients. Rituximab was used in 65% of cases. Autologous stem-cell transplantation (ASCT) in first-line was performed in 3 cases. Two patients were treated up-front by whole-brain radiotherapy (in combination with systemic chemotherapy by fludarabine, cyclophosphamide and rituximab in 1 case). 22 patients were assessable for first-line treatment response: overall response rate (ORR) was 69% (n=13/22) including 4 complete remissions; 6 patients had a progressive disease. Six patients died and median follow-up
of alive patients was 27 months. Median overall survival was 70 months. Conclusion: Up to now, this is the most important retrospective cohort of patients presenting with Bing-Neel syndrome. Systemic chemotherapy and/or intra-thecal chemotherapy were the most widely used treatment strategies but CR rate remained poor. In order to define the best treatment strategies, collection of additional cases is currently ongoing.