Langerhans Cell Histiocytosis (LCH) is a proliferative disorder of activated Langerhans cells with highly variable biological behavior and clinical severity. The treatment of LCH over the years has reflected the changing concepts of the disease process. Studies have shown that although many organs can harbor proliferating Langerhans cells, only if organ function were disrupted is such involvement of prognostic significance. Patients are thus stratified into different risk categories based on the extent of their disease and the degree of organ dysfunction. Patients with single-system disease confined to a single site usually require only local therapy or observation. For patients with more extensive disease (multiple bone lesions or multiple lymph nodes) the treatment recommended by the Histiocyte Society includes a 6-week induction with prednisone and vinblastine, followed by continuation treatment with pulses of the same agents every 3 weeks. The prognosis for this group of patients is usually excellent, although approximately 30% of the patients will experience disease reactivations that continue to respond to treatment. The Histiocyte Society trials LCH-I, LCH-II, and LCH-III addressed treatment for patients with multi-system disease. These risk-adapted protocols were based in different combinations of prednisone, vinblastine, etoposide, methotrexate and 6-mercaptopurine. In all those studies, survival rates for patients with multi-system disease without involvement of risk organs were in excess of 90%, and the current recommended management for this group of patients is a 12-month regimen with prednisone and vinblastine. Involvement of the risk organs carried the worse prognosis; with mortality rates of approximately 40%. The addition of etoposide in LCH-II or methotrexate in LCH-III to the prednisone-vinblastine backbone did not improve outcome. The results of those trials provide the rationale for the LCH-IV protocol, which objectives are: 1) To improve survival for patients with risk-organ involvement by early switching to intensive nucleoside-analogue based therapy; 2) To investigate whether further prolongation of therapy will decrease reactivation rates; and 3) To investigate the incidence, pathogenesis and treatment of LCH-induced neurodegeneration.

References

