



PROPOSAL FOR MULTI-INSTITUTIONAL RETROSPECTIVE ANALYSIS OF INTRAVASCULAR LYMPHOMATOSIS

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Intravascular lymphomatosis (IL) or “Angiotropic lymphoma” (formerly known as ‘malignant angioendotheliomatosis’) is a rare entity characterized by exclusive or predominant growth of neoplastic cells within blood vessel lumina. Most cases are B-cell in lineage, but rare cases of IL with a T-cell lineage do exist. Most common symptoms of presentation involve central nervous system (CNS) or skin; however, the large number of case reports concerning IL literature’s data bears witness to proteiform signs and symptoms of presentation. IL is characterized more by questions than answers. The aim of reaching significant advances in its understanding are often hampered by the rarity of this disease, that is quite exclusively reported in the literature in form of case reports, while the occasional studies analyzing IL usually do not exceed 10-15 patients. A large retrospective clinico-pathological review could allow us to better understand several aspects of these malignancies. Among others:

- 1) Clinical presentation and course. The heterogeneity of clinical symptoms may explain why about half of IL are diagnosed only after autopsy and most of the ante-mortem diagnoses are made on skin biopsy specimens or incidentally in biopsies performed for different reasons. The course of IL is generally fatal except for those cases limited to the skin. However, a fraction of patients achieving complete remission after varying chemotherapy regimens and rare cases off therapy with a relatively prolonged survival have been also reported.
- 2) Morphologic aspect: neoplastic cell population involves virtually any organ and is composed by large non-cleaved elements. Although ‘malignant histiocytosis – like’ (mainly in Asian countries) and an ‘anaplastic large cell’ types of IL are described, it seems that histologic variants of IL do not carry different prognostic impact.
- 3) Histopathologic characterization: many topics are still matter of investigation: they regard the studies on the phenotypic and molecular characteristics of the neoplastic cells, and the description of the possible normal counterpart.
- 4) Adhesion and dissemination properties and the possible relationships with the eventual concomitantly associated lymphomas: the basic defect of IL may be related to multiple impairments of adhesion molecules, most of which are still unknown. This statement can be confirmed by our and other observations of preferential involvement by IL cells of pre- existing haemangiomas or in the context of neovascularization of solid tumors: in both situations, reactive or neoplastic endothelia may act as selective attraction for neoplastic lymphocytes. For such reason, IL may be a good candidate for evaluation of lymphocytic migration and traffic and invasiveness of lymphoma cells. The striking tendency to intravascular localization of neoplastic cells regards mainly small vessels and the presence of mitotic figures in the context of neoplastic population, in addition to the lack of a significant extravascular neoplastic mass, led to the hypothesis that vascular lumen does not just represent a vehicle but instead it may be the site of active replication. On the other hand, IL may be associated to other forms of lymphomas; in a reviewing paper, 33 out of 103 IL cases were associated with extravascular lymphomatous mass.
- 5) Definition of an appropriate therapeutic approach.