Haematological malignancies

**PAX-5 downregulation is pivotal for transformation of non-Hodgkin’s lymphoma into histiocytic sarcoma: a meta-analysis**

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**Aim/Background:** Histiocytic sarcoma (HS) is a rare malignancy with an aggressive clinical course and no well-established treatment protocols. Sporadic cases of HS, having synchronous or metachronous occurrence with various malignancies, most often non-Hodgkin’s lymphoma (NHL) have been described previously. Molecular analysis in certain instances has suggested a clonal relationship between HS and the primary lymphoma. It has been postulated that downregulation of PAX-5, a transcription factor that plays a decisive role in maintaining B-cell identity, may contribute to lineage switching and trans-differentiation of the primary B-Cell lymphoma. Our aim was to assess the association of PAX-5 in cases of B-cell NHL transforming into HS.

**Methods:** A literature review was conducted in PubMed/Medline to identify cases of synchronous or metachronous HS associated with mature B-cell NHL, reported between the years 2000-2015. Only cases with presence of cytogenetic or gene rearrangement assay data were included. Seventeen such cases of HS with NHL sharing a common clonal origin were thus identified.

**Results:** Median age of diagnosis of HS was 61 (range 30-85), 64.7% (11/17) were males. Most cases of HS cases were diagnosed in lymph nodes (52.9%), followed by skin (17.6%), 70.6% (12/17) had follicular lymphoma (FL) associated HS. Median interval between diagnosis of NHL and evolution into HS was 24 ± 11.83 months. Grading of FL did not impact time to diagnosis of HS (P = 0.13). All cases that had PAX-5 done (15/17), showed its downregulation. CEBP and PU-1 upregulation was seen in 7 and 9 patients respectively and this observation did not seem restricted to cases of FL only. All patients with reported survival time (4/17), died within 1 year of diagnosis of HS.

**Conclusions:** PAX-5 downregulation is consistently found in patients with HS arising out of NHL. Lack of somatic hyper-mutation as seen previously, strongly suggests other factors including perhaps, alterations in critical epigenetic switches may contribute to PAX-5 downregulation. Further studies to elucidate the underlying processes including the contribution of epigenetic mechanisms in regulating lineage switching, are needed to understand the evolution of secondary HS.

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