

## EDITORIAL

## LABORATORY DIAGNOSIS OF HODGKIN'S DISEASE: WHAT ARE THE CHALLENGES?

Hodgkin's lymphoma (HD) comprises 15% of malignant lymphomas, 85% being NonHodgkin's lymphomas (NHL)(1). Historically, sub-classification of HD was considered very important, but the clinical relevance of sub-typing HD has diminished with modern therapy(2). Age is now considered the single most important prognostic factor. HD has an overall three-year survival rate of over 80%; treated patients are now living long enough to develop secondary malignancies (induced by the powerful therapeutic agents) which are an added challenge to the pathologist(3). HD, one of the commonest malignancies in young adults (half the patients are aged 20-40 years, may present with systemic symptoms. Clinical and morphologic similarities to infectious mononucleosis make it prudent to perform a *Monospot* test before diagnosing HD in a young patient(4).

The classic Reed-Sternberg(RS) cell is variable in size, average 40 to 70 (range 10-300) microns in diameter with bi-lobed nuclei or multinucleated(5). A wide variety of benign and malignant cells mimic RS cells, and are sometimes almost indistinguishable from them(6), which is why RS cells are considered necessary but insufficient for the diagnosis of HD. Binucleate immunoblasts, smaller, and only rarely binucleate, are commonly mistaken for RS cells(2), but a continuum of morphology in the lymphoid cells in either benign or malignant lesions is the norm whereas Hodgkin's disease shows discontinuity between the neoplastic and reactive cells(7). Markers may be helpful: RS cells tend to be LCA and pan-B cell negative, and CD 15 positive, while the RS-like immunoblasts may be LCA and Pan-B cell positive and CD 15 negative, but these findings are not absolutely specific. Other RS cell variants may all present difficulties. One cell type may predominate and the presence of any of the RS cell variant is sufficient to suspect HD. Familiarity with the histologic patterns of HD is helpful in distinguishing it from benign and malignant disorders that mimic HD(2). LP HD grows in a diffuse or vaguely nodular pattern. The latter frequently transforms into large B-cell non-Hodgkin's lymphoma (Hodgkin's disease, nodular lymphocyte-predominant type, with co-existent large cell lymphoma)(8). Because malignant cells are rare and the dominant cells are small, mature and activated T lymphocytes, a diagnosis of HD may not be apparent. The differential diagnosis includes small lymphocytic lymphoma (WDLL); small cleaved lymphocytic lymphoma (PDLL) and reactive hyperplasia. Mixed cellularity Hodgkin's disease, histologically has a diffuse growth pattern. RS cells and variants are easy to find, and lymphocytes are fewer than in LP HD. Reactive lymphocytes, plasma cells, eosinophils, and epithelioid cells are variable, but often prominent(9). The differential

diagnosis includes reactive immunoblastic proliferation, especially viral, granulomatous inflammation, and mixed NHL, especially T cell, and where there is diffuse fibrosis, nodular sclerosing RD. Lymphocyte depleted Hodgkin's disease (LD HD) may represent the final common pathway of Hodgkin's disease. This anaplastic malignancy should be identified as HD since therapy may result in cure. Pleomorphic RS cells are abundant and non-neoplastic lymphoid cells are sparse(5). Of the two types of LD HD: reticular and diffuse fibrosis, necrosis is a more common feature in the reticular variant. Not uncommonly large cell non-Hodgkin's lymphoma may be mistaken for a LD HD and vice versa, a differential that may be difficult or impossible by morphology alone. In immunologic studies, LD HD is usually (90%) CD 15 positive, but so are some T-cell lymphomas, However, LD HD does not show lymphoid cell markers and must be distinguished from pleomorphic carcinomas, sarcomas, and melanoma for proper therapy. Nodular Sclerosing HD (NS HD), the most common type of HD(8) has a varied background cellularity and can be lymphocyte predominant, mixed cellularity or lymphocyte depleted. NS HD, even when focal, takes precedence in diagnosis over other sub-categories of HD(2). Two features distinguish the NS HD variant: collagen bands (sclerosis) extending from the capsule, dividing it into nodules; and the presence of lacunar cells. Some argue that NS HD can be diagnosed in the proper setting, by the presence of characteristic lacunar cells, even in the face of minimal or absent sclerosis (cellular phase of NS HD)(8). The mere presence of fibrosis is non-specific, and some degree of fibrosis can be seen in other subtypes of HD particularly after therapy(10).

Other mimickers of HD include such benign conditions as virally infected cells (CMV, mononucleosis, herpes), megakaryocytes, drug-induced immunoblastic proliferation; malignant lesions such as anaplastic carcinoma, melanoma, pleomorphic sarcomas, NHLs, mycosis fungoides, anaplastic myeloma and malignant megakaryocytic proliferation. Taken together, the cytologic features are characteristic enough, in the proper setting to render a high degree of diagnostic accuracy, over 70% with routine stains alone(11). Selective use of immunohistochemical markers in low resource settings should be reserved for the doubtful or difficult cases and in those cases where the clinical and initial histological diagnoses are discordant.

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## REFERENCES

1. Wingo, P.A., Tong, T. and Bolden, S. Cancer Statistics. *CA Cancer T. Clin.* 1995; **45**:8-30.
2. Dorfman, R.F. and Colby, T.V. The Pathologist's Role in the Management of Patients with Hodgkin's Disease. *Cancer Treat Rep.* 1982; **66**:675-680.
3. Prostnitz, L.R., Farber, L.R., Kapp, D.S. *et al.* Combined Modality Therapy for Advanced Hodgkin's Disease: Long-Term Follow-up data. *Cancer Treat Rep.* 1982; **66**:871-879.
4. Loachim, H.L. Lymph Node Pathology, Second Edition. JB Lippicott Co, Philadelphia. 1994: 47-53
5. Das, D.K., Gupta, S.K., Datta, B.N. *et al.* Fine Needle Aspiration Cytodiagnosis of Hodgkin's Disease and Its Subtypes: I. Scope and Limitations. *Acta. Cytol.* 1990; **34**:329-336.
6. Kline, T.S. Karman, V. and Kline, I.K. Lymphadenopathy and aspiration Biopsy Cytology. Review of 376 Superficial Nodes. *Cancer.* 1984; **54**:1076-1081.
7. Banks, P.M. The Pathology of Hodgkin's Disease. *Semin Oncol.* 1990; **17**:693-695.
8. DeMay, R.M. The Art and Science of Cytopathology. Y.2 Aspiration Cytology. *ASCP Press Chapter.* 1996; **18**:816-821.
9. Colby, T.V., Hoppe, Z.T. and Warnke, R.A. Hodgkin's Disease: A Clinicopathologic Study of 659 Cases. *Cancer.* 1981; **49**:1848-1858.
10. Moriarty, A.T, Banks, E.R. and Bloch, T. Cytologic Criteria for Subclassification of Hodgkin's Disease Using Fine Needle Aspiration. *Diagn. Cytopathol.* 1989; **5**:122-125.
11. Tumwine, L.K., Wabinga, H. and Odoida, M. Haematoxylin and Eosin staining in the diagnosis of Hodgkin's disease in Uganda. *East Afr. Med. J.* 2003; **80**:119-123.