Introduction

Performing an excisional biopsy of an enlarged lymph node has been considered standard practice for the evaluation of lymphadenopathy, especially in-patients without prior history of lymphoma [1]. An excised lymph node provides sufficient histologic material to assess cytologic and architectural details. In many centers including ours, it is now becoming more common to forego excisional biopsy and instead perform fine-needle aspiration (FNA) as the initial work-up for lymphadenopathy [2-5]. In addition to being a safe and rapid procedure, FNAs are effective because current lymphoma classification systems place more emphasis on immunophenotype and genotype [6]. Sufficient material can be aspirated for cytomorphology, flow cytometry (FCM), and molecular studies. Even though FNAs have been shown to be effective in the evaluation of lymphomas, especially when used in conjunction with FCM, certain disorders may be difficult to diagnose.

Diagnosis of Hodgkin lymphoma by FNA biopsy is difficult [7-9]. It requires the presence of diagnostic Reed-Sternberg (R-S) cells or their variants (classic, lacunar, popcorn (lymphocytic histiocytic, L&H) and mummified) in a mixed cellular background composed of small lymphocytes, eosinophils, plasma cells, and neutrophils. The difficulty arises from the fact that the number of diagnostic cells may be limited to a few R-S cells or variants. Also, R-S cells may not be seen because the aspirated lymph node is only partially involved by the neoplastic process, which decreases the chance of obtaining the diagnostic cells, or because the neoplastic cells are hidden by fibrosis, granulomas or necrosis, which also changes the cellular background composition, and further complicates the diagnosis. Furthermore, cases were neutrophils are prominent may be mistaken for suppurative lymphadenitis [10]. In addition, this characteristic mixed cellular background is absent in cases of nodular lymphocyte predominant Hodgkin lymphoma and lymphocyte rich classical Hodgkin lymphoma, which in these conditions makes the diagnosis dependent on detection of L&H or R-S cells. On the other hand, in classical HL while the background mixed infiltrate is almost always seen, it is non-specific and may be seen in a variety of other reactive conditions.

Earlier studies examined the lymphocytic component of the background mixed infiltrates to help in diagnosing Hodgkin lymphoma and understanding the biology of this disease. Using immunohistochemical techniques the majority of lymphocytes in the background were shown to be T cells with an increase in helper/suppressor (CD4/CD8) ratio [11,12]. More recent studies showed that the mixed cellular infiltrate characteristic of HL contains an abundant amount of CD4 positiveTh2-lymphocytes [13]. Several cytokines are released by R-S cells leading to stimulation of the influx of CD4+ lymphocytes. Poppema et al. have demonstrated that CC chemokines TARC and MDC attract CD4+ T lymphocytes by binding to a CC-chemokine receptor (CCR4) found specifically on Th2 cells [14]. Fibroblasts in HL have also been shown to produce a CC-chemokine, eotaxin, which has been shown to increase the influx of Th2 lymphocytes and eosinophils [15]. This Th2 milieu generates a comfortable environment for the neoplastic R-S cells to survive and expand.

Table 1: Summary of patient's characteristics and clinical history

Patients	No.
Total no. of FNA	85
No. of patients	85
Gender (M:F)	29:56 (1/1.9)
Age (yr.)	19–87
Site of FNA	
Cervical	43
Axillary	15
Inguinal	14
Submental	5
Epitrochlear	2
Subauricular	2
Inta-parotid	2
Occipital	1
Mediastinal	1

In this study we investigated the value of an increased CD4/CD8 ratio (≥4), in otherwise non-diagnostic flow cytometry findings, as a diagnostic marker for Hodgkin lymphoma in FNA biopsies. In 85 cases with increased CD4/CD8 T-cell ratio, only 7 cases were proven, using tissue sections, to be Hodgkin lymphoma with one additional case called by cytology (9%). 6 cases were proven to be non-Hodgkin lymphoma (7%). The CD4/CD8 T-cell ratio was not significantly different in these populations 5.27–13 vs. 4.2–14 with average of 7.7 vs. 7.3.

Materials and methods

A review of the cytology records at New York University Medical Center and Bellevue Hospital revealed that between 1996 and 2002, 837 lymph node FNAs were performed in which material was submitted for FCM. In 119 cases (14%), the material submitted was insufficient for flow cytometric evaluation. Our sole selection criterion for including cases in our study was an elevated CD4/CD8 ratio by flow cytometry, defined as greater than or equal to 4. 85/718 (12%) cases fit our criteria. In all the cases, the B lymphocyte component was polyclonal and the T cells showed no aberrant immunophenotype.