Multiparametric Flow Cytometric Analysis of Fine Needle Aspirate of Enlarged Lymph Nodes: Validation with Histopathology

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Abstract: Objectives: The section of Hematopathology at King Fahd Specialist Hospital-Dammam (KFSHD) has expertise in diagnostic evaluation of patients with hematologic malignancy, interpretation of morphology of blood, bone marrow, and lymph node and other hematologic specimens as well as the application of ancillary techniques, especially flow cytometry (FCM). Using the four-color multiparameteric analysis, we are able to detect and immunophenotype malignant hematopoietic cells in lymph node aspirates allowing appropriate classification. We designed the current study to evaluate the validity of multiparameteric FCM as a diagnostic test for hematologic diseases in fine needle aspirated samples from patients with lymphadenopathies. **Methods***:* We evaluated the validity of multiparametric FCM in diagnosing oncohematologic disease in89 consecutive lymph node fine needle aspirate (FNA) specimens from patients with lymphadenopathy. All cases had excisional lymph node biopsy where histopathological evaluation and FCM when possible was performed for confirmation. **Results:** Flow cytometric diagnosis of non-Hodgkin's lymphomas on FNA specimens showed 100% correlation with the final histopathological interpretation. In addition, FCM enabled NHL sub-classification in all cases. The FCM interpretation was faster than histopathological examination, allowing quicker therapeutic decisions. FCM could not establish the diagnosis of our Hodgkin lymphoma cases since all these cases revealed unremarkable FCM features. **Conclusion:** Utilizing FCM is reliable and an accurate in the evaluation of lymphadenopathy in FNA material. We were able to validate our FCM technique in our laboratory for the evaluation of lymphoid malignancies.
[Heba N. Raslan and Arwa Al-Saber. **Multiparametric Flow Cytometric Analysis of Fine Needle Aspirate of Enlarged Lymph Nodes: Validation with Histopathology.** *J Am Sci* 2013;9(10):202-213]. (ISSN: 1545-1003). http://www.jofamericanscience.org. 26

Key words: multiparametric flow cytometry, fine needle aspiration, lymphoma, lymphadenopathy

1. Introduction:

Traditionally, the technique of choice for the diagnosis of lymph node pathology was based on histopathological studies of paraffin-embedded formalin-fixed biopsy specimens, where excisional biopsy of enlarged lymph nodes was considered the gold standard for the evaluation of lymphoproliferative disorders (1, 2). Currently, the addition of immunohistochemistry for the detection of cell-specific antigens is essential in the classification of hematological lymphoid diseases (3). In the context of lymphoma diagnosis, immunohistochemistry (IHC) has the advantage over FCM that the cells of interest are identified morphologically and that these studies can be applied retrospectively on archived fixed tissue specimen (4).

However, immunophenotyping by immunohistochemical techniques has few limitations, which include subjectivity, limited reproducibility, prolonged turnaround time and the lack of consensus in quantifying antigen expression and defining positive and negative results (5, 6). Moreover, fixation might lead to loss of some cells and/or the cellular antigenicity, and there is reported difficulty in demonstrating cytoplasmic immunoglobulin light chain expression (4,6). Because of these aforementioned limitations, immunophenotyping of lymphoid malignancies by FCM has become an essential diagnostic tool in the accurate classification of lymphoproliferative disorders. FCM offers many advantages. It is fast, qualitative as well as quantitative method in the evaluation of determining different cell antigens simultaneously using the current multiparametric analysis (7). Meanwhile, FCM suffers few limitations such as variability in antigen signature of expression and cellular fragility during processing (8). In the current era of cost containment, fine needle aspiration (FNA) became a valid initial diagnostic tool for the evaluation of different masses including lymphadenopathy particularly when conventional biopsy is not feasible (9).

It is well-established that FNA as a diagnostic approach is reliable, associated with fewer complications, and more cost effective than excisional biopsy, especially when deeply seated lymph nodes are involved (10, 11). FNA became an extremely helpful technique to help distinguish lymphoma and metastatic malignancies from benign lymphoid

proliferations (10-12). This option especially became very attractive when dealing with patients who are very sick or unstable enough to undergo surgical excisional biopsy procedures requiring general anesthesia (12).

However, there are few limitations for FNA as an initial diagnostic approach. These shortcomings are mostly related to sample adequacy and inability to evaluate architectural morphological features. Additional problems and complications with FNA are very rare and they may include bleeding, infections, and rarely pneumothorax (13). Nevertheless, the adequacy and complication of FNA procedures is operator dependent and improvements are achieved when they are performed by well-trained clinicians (14).

Currently, many centers utilize the combined approach where the morphological cytopathological features in conjunction with the FCM findings to establish an accurate diagnosis on enlarged lymph nodes (2). While limited markers are routinely used on tissue sections with relative subjectivity, FCM allows a more precise definition of individual cell types. This is achieved, since cells of interest are identified by a combination of physical characteristics and the use of multiple antibodies directly conjugated with fluorochromes (15). It also has the ability to assess monoclonality through detection of immunoglobulin light chain expression with an attractive speed (16).

2. Material and Methods:

After obtaining an approval from the Internal Review Board, prospective analysis of FCM performed on 89 patients with lymphadenopathy was carried out. The aspiration was performed by a pathologist or a radiologist when localization by image guidance was needed. The gauge of the needles used ranges between 21-23 and the number of passes varied from 2-4. Immediate adequacy evaluation of these aspirates was performed on all cases utilizing Diff Quick stain by pathologists on all cases. Material for FCM was collected into Roswell Park Memorial Institute (RPMI) medium for cell preservation and transfer to the hematology &flowcytometry laboratory. All samples were transported immediately at room temperature and stored at refrigerator (2-8°C) where testing was performed within 48 hours. They were transferred to a 5 ml tube and centrifuged for 2 minutes at approximately 400Xg. The supernatant was discarded and the cells were lysed in 2ml ammonium chloride solution then washed with 2 ml PBS-BSA. The cells were gently vortexed, incubated at room temperature for 10 minutes and then centrifuged again for 2 minutes. Leukocytes were resuspended in 1ml PBS and a basic panel of directly conjugated monoclonal antibodies was employed after capping with normal mouse IgG(Invitrogen Corporation, USA) and further extended according to the number of cells available (Table 1).The initial morphology of the preliminary slide is examined and patient's previous diagnosis if any. Samples were analyzed using the BD FACS-Canto II machine (Becton & Dickenson).

Table **1: List of the antibodies used in FCM panel.**

FITC	clone	PE	clone	PerCp	clone	APC	clone
IgG	X40	IgG	X40	CD45	2D1	IgG	X40
CD19	4G7	CD23	EBVCS-5	CD45	2D1	CD5	L17F12
CD7	M-T701	CD2	S5.2	CD45	2D1	CD5	L17F12
CD103	BER-ACT8	CD11c	S-HCL	CD45	2D1	CD25	2A3
CD34	8G12	CD33	P67.6	CD3		CD45	2D2
TdT	HT1,HT4,HT8,HT9	CD10	HI10a	CD45	2D1	CD34	8G12
Lambda	1-155-2	KAPPA	T28-2	CD45	2D1	CD19	SJ25C1
CD3	SK7	CD8	SK1	CD45	2D1	CD4	SK3

All specimens were tested for viability; samples with less than 60% viability were excluded and those with less than 85% viability were examined with *caution*. After examination of the forward and side scatter, cells within the lymphocyte gate were examined, excluding granulocytes and monocytes. All the cases concomitantly underwent detailed morphological cytological evaluation using Hematoxylin and Eosin stain on cell blocks. Standard cell block preparation was done using fixation in 10% neutral buffered formalin and embedding the tissue in paraffin. Routine IHC stains on cell block were done according to the morphology, also utilized for correlation with the flowcytometry.

Results:

A total of 89 consecutive Fine Needle Aspiration (FNA)/ lymph node (LN) samples from 53 males and 36 females were collected with male to female ratio of 1.5:1. Their ages ranged from 4 to 76 years with a median of 30 and a mean of 34. All 89 FNA/LN samples were deemed adequate for FCM analysis and interpretation and all patients had a follow up excisional biopsy of the same lymph node within 1 month.

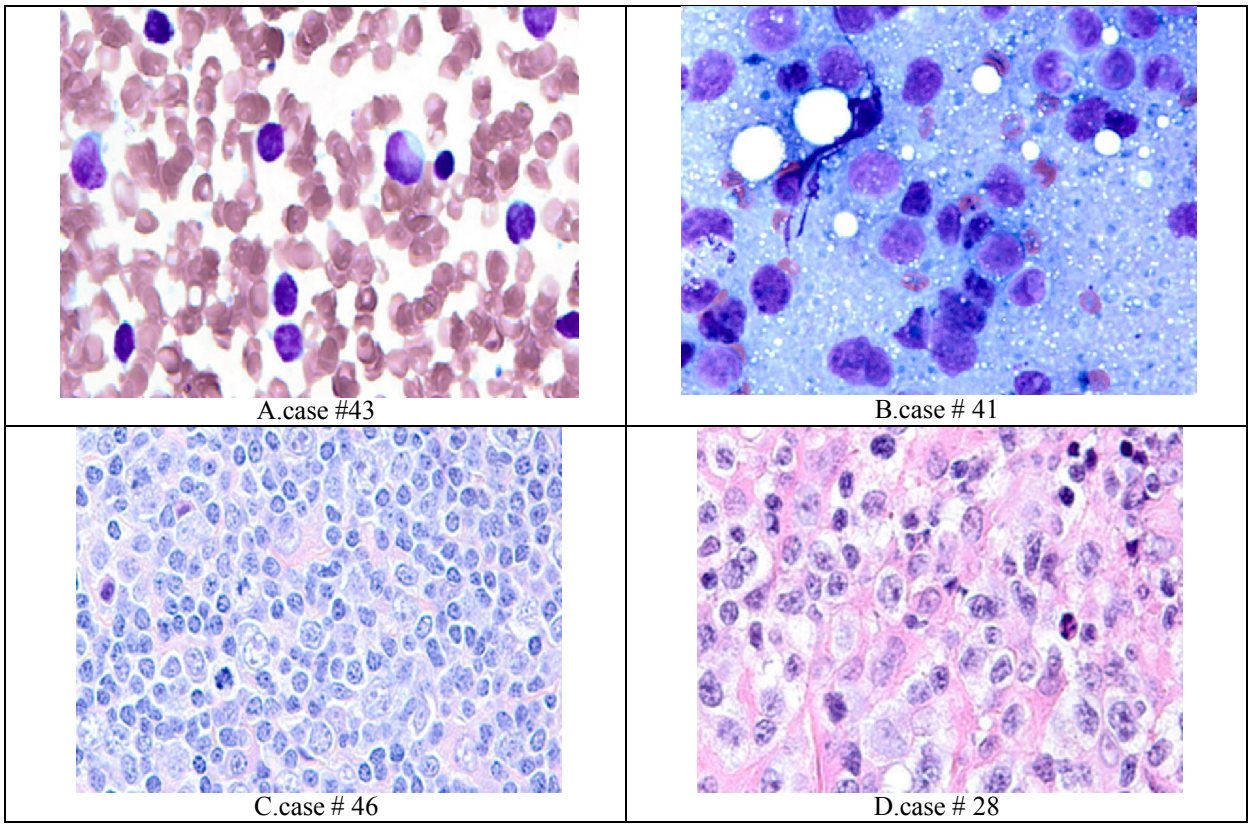


Figure 1: A: B-Non-Hodgkin'sLymphoma .B: Large B cell lymphoma with monoclonal lambda light chain restriction. C: Normal Lymph Node. D: Diffuse Large B-cell Lymphoma with Lambda light chain restriction

Table 2: List of reagents used & Clones used in histopathology

Antibody	Clone	Company
CD45	RP2/18	Ventana, Tucson, USA
	2B11 + PD7/26	Dako, Glostrup, Denmark
CD3	2GV6	Ventana, Tucson, USA
	Poly	Dako, Glostrup, Denmark
CD4	--	Ventana, Tucson, USA
	4B12	Dako, Glostrup, Denmark
CD2	MRQ-11	Ventana, Tucson, USA
	AB75	Dako, Glostrup, Denmark
CD1a	EP3622	Ventana, Tucson, USA
	--	Dako, Glostrup, Denmark
CD7	SP94	Ventana, Tucson, USA
	CBC.37	Dako, Glostrup, Denmark
CD8	--	Ventana, Tucson, USA
	C8/144B	Dako, Glostrup, Denmark
CD19	--	Ventana, Tucson, USA
	LE-CD19	Dako, Glostrup, Denmark
CD20	L26	Ventana, Tucson, USA
	L26	Dako, Glostrup, Denmark
CD79a	SP18	Ventana, Tucson, USA
	JCB117	Dako, Glostrup, Denmark
CD43	L60	Ventana, Tucson, USA
	DF-T1	Dako, Glostrup, Denmark
CD23	SP23	Ventana, Tucson, USA
	--	Dako, Glostrup, Denmark
CD15	MMA	Ventana, Tucson, USA
	Carb-3	Dako, Glostrup, Denmark
CD30	Ber-H2	Ventana, Tucson, USA
	Ber-H2	Dako, Glostrup, Denmark
Fascin	55k-2	Ventana, Tucson, USA
	--	Dako, Glostrup, Denmark

Antibody	Clone	Company
Pax5	SP34	Ventana, Tucson, USA
	--	Dako, Glostrup, Denmark
Ki-67	30-Sep	Ventana, Tucson, USA
	MIB-1	Dako, Glostrup, Denmark
CD138	B-A38	Ventana, Tucson, USA
	MI15	Dako, Glostrup, Denmark
Kappa	Poly	Ventana, Tucson, USA
	Poly	Dako, Glostrup, Denmark
Lambda	Poly	Ventana, Tucson, USA
	Poly	Dako, Glostrup, Denmark
Cyclin D1	SP4-R	Ventana, Tucson, USA
	--	Dako, Glostrup, Denmark
Alk1	ALK01	Ventana, Tucson, USA
	--	Dako, Glostrup, Denmark
Bcl-2	124	Ventana, Tucson, USA
	124	Dako, Glostrup, Denmark
Bcl-6	GI191E/A8	Ventana, Tucson, USA
	PG-B6p	Dako, Glostrup, Denmark
Cytokeratin	AE1/AE3 & PCK26	Ventana, Tucson, USA
	AE1/AE3	Dako, Glostrup, Denmark
Cytokeratin	Cam 5.2	Ventana, Tucson, USA
	--	Dako, Glostrup, Denmark
CD68	KP-1	Ventana, Tucson, USA
	KP-1	Dako, Glostrup, Denmark
CD68	--	Ventana, Tucson, USA
	PG-M1	Dako, Glostrup, Denmark
Epithelial Membrane Antigen	E29	Ventana, Tucson, USA
	E29	Dako, Glostrup, Denmark

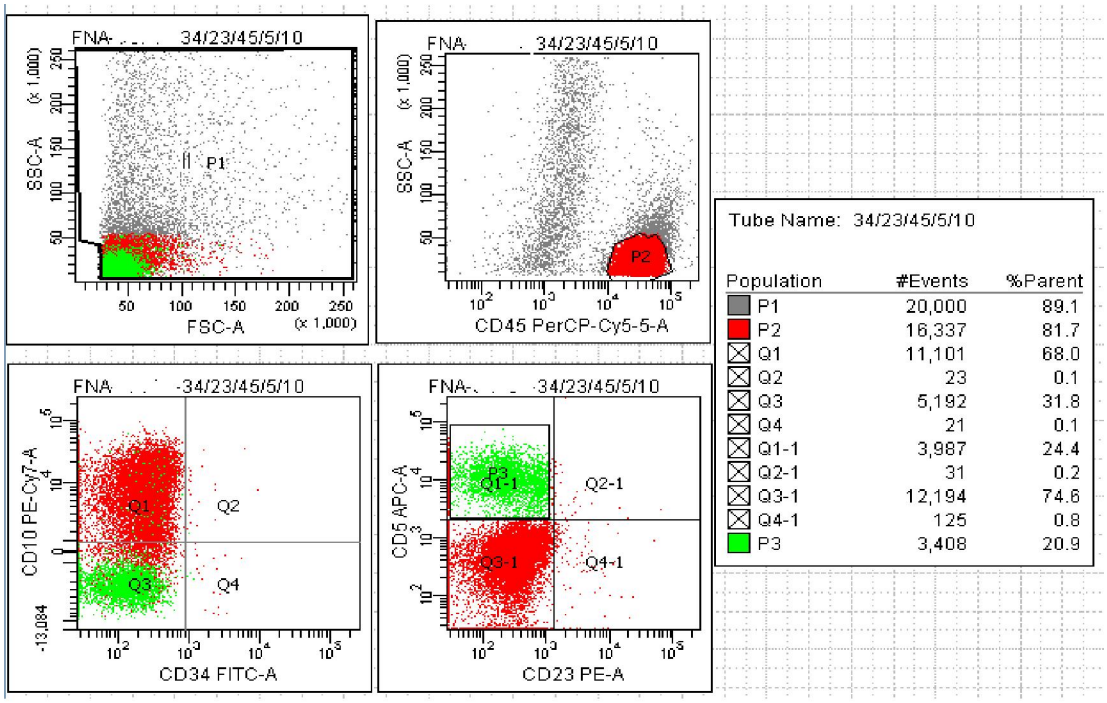


Figure2: (Case 43)B-lymphoproliferative Disorder co-expressing CD19 (not shown) & CD10. These cells where negative for both kappa (not shown) & lambda (not shown)

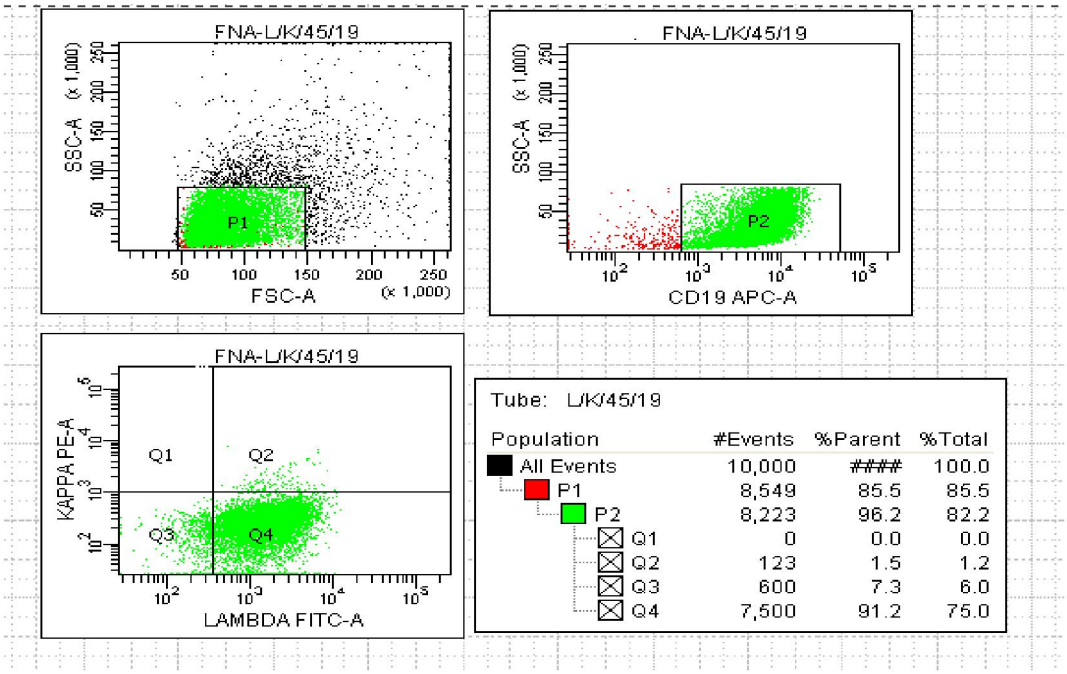


Figure 3: (Case 41) Large B cell Lymphoma Expressing CD19 & Lambda light chain restriction

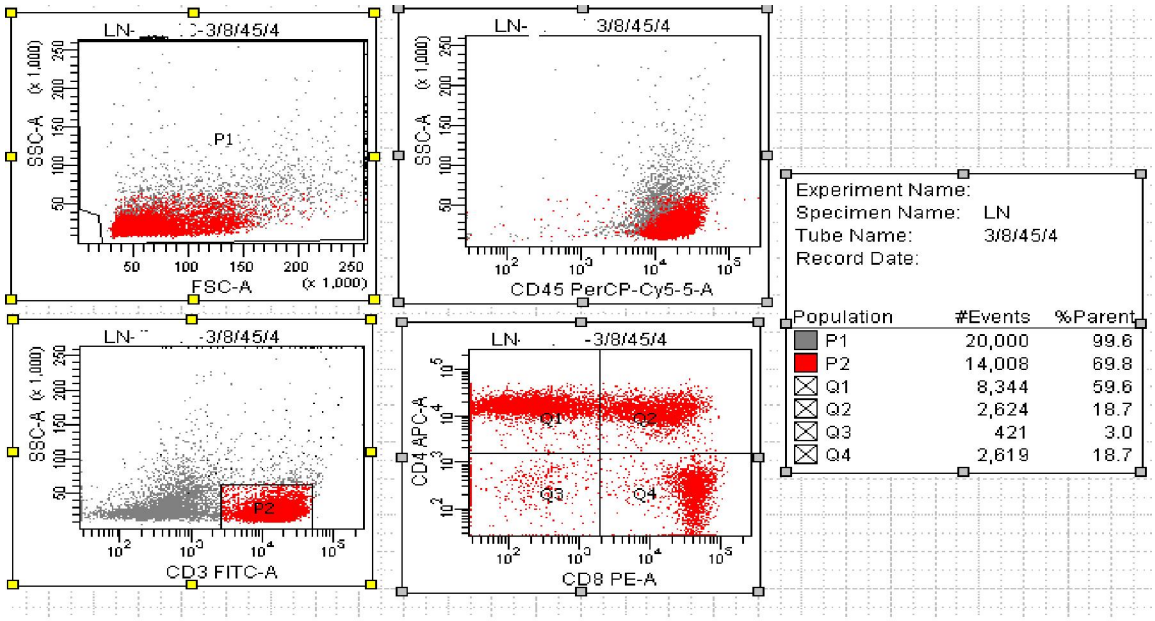


Figure 4: (Case 46) 16% of the population co-expressing CD4& CD8 suggesting normal peripheral cells.

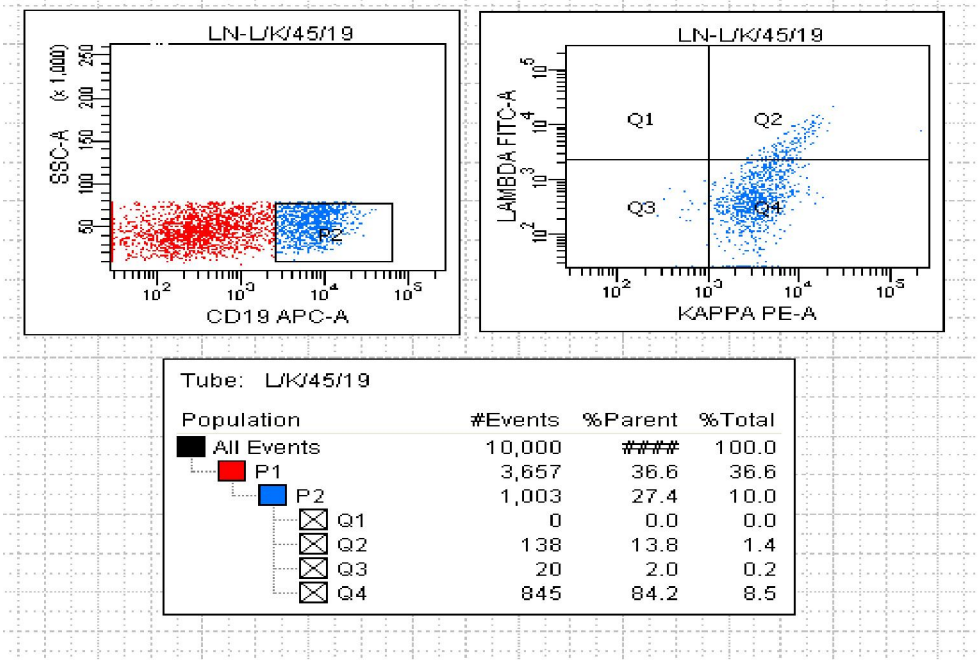
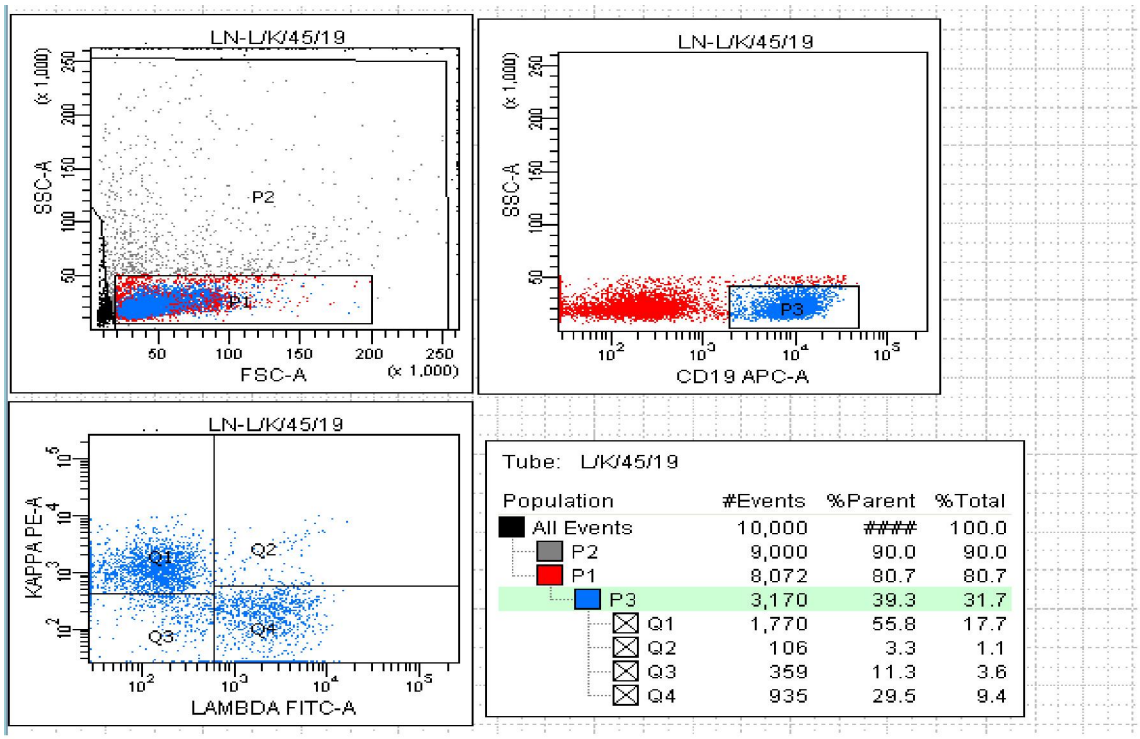


Figure 5: (Case 28) Diffuse Large B cell Lymphoma expressing CD19 & Kappa light chain restriction



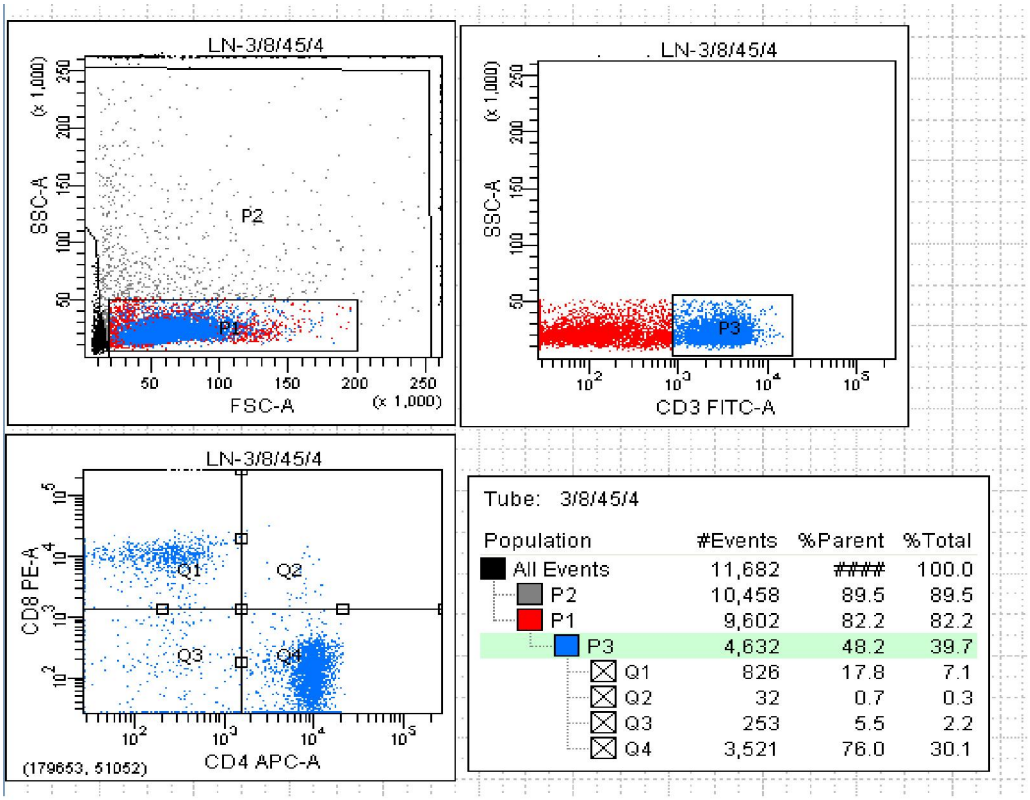


Figure 6: Normal Lymph node.

4, Discussion:

The results of this study confirm the reliability and validity of utilizing FNA/LN as an initial diagnostic tool where combining morphology and FCM analysis aids in reaching an adequate diagnosis (17). In all our cases, the technique provided an accurate diagnosis of non Hodgkin lymphomas (NHL) and the ability to differentiate benign from malignant lymphoid diseases. Similar to previous reports the accuracy of this approach provides an alternative diagnostic approach and saves patients unnecessary more invasive surgical biopsy intervention (17).

In the present study, combined FNA and FCM allowed an unequivocal distinction between non lymphomatouslymph node pathology(57/89) and NHL in all cases (32/89). FCM was thus 100% reliable in the diagnosis of reactive hyperplasia (Figures 1C, 4 & 6) and the exclusion of non-lymphomatous lymph node pathology such as necrotizing granulomatous inflammation, dermatopathic lymphadenopathy and Castleman's disease. In one case, the FCM on the FNA material was more accurate than the FCM that was performed on the fresh lymphoid tissue. In this case and as shown in the representative figures, the T-cell anaplastic large cell lymphoma involved certain areas of the lymph node where the aspirated material were more representative and most likely was not affected by the dilutional effect of the normal surrounding lymphoid cells.

Light chain restriction allowed an unequivocal diagnosis of B cell lymphoma to be made in most studied cases (12/14 of B-celllymphoproliferative disorders) (Figures 1B, 1D, 3 & 5). Two cases diagnosed as follicular lymphoma and diffuse large B-cell Lymphoma, were both positive for CD10 however not showing K/L chain restriction.Those two cases werediagnosed by morphology, supported by the presence of CD10; a marker which shouldn't have been present normally. Negativity of kappa and lambda thus doesn't exclude malignancy; however monoclonality proves its presence. Dunphy et al reported a concordance rate of 94.1% between FCM and histopathology while Mandacova et al. reported a concordance of 89% between the two techniques in cases suspected to be lymphoma (4,18). However, their number of cases was much higher than ours and Mandacova included bone marrow samples in their cases.

As it is well-known and was heavily investigated in the literature and simply because the number of malignant cells in Hodgkin lymphoma (HL) is very low compared to the surrounding benign lymphoid cells, all our cases of HL showed no monoclonality in FCM. The supportive element to the presence of Hodgkins Lymphoma is the disturbed ratio between CD4 & CD8. Although our FCM lymphoma panel lacks CD 30 and CD 15, we do FCM in HL suspected cases to exclude B cell lymphoproliferative disorders such as T cell rich B cell lymphoma.

The histological examination combined with immunohistochemistry confirmed the diagnosis of HL. It is worthwhile noting that our FCM lymphoma panel lacks CD 30 and CD 15, while they are available in our immunohistochemistry antibody panel to characterize HL diagnosis.

The present study demonstrates that the application of ancillary methods to cytological specimens such as IHC and FCM leads to precise sub-classification of lymphomas in the majority of cases. In most cases typing of non-Hodgkin lymphoma was according to the WHO classification and it agrees in this contest with the results of other investigators (19-22).

Correct selection of cases submitted for FCM is crucial and enhances diagnostic accuracy of the cytomorphological interpretation. As recommended by many researchers, combining cytomorphology with immunophenotyping by FCM in the context of the appropriate clinical data is very helpful to reach a specific diagnosis on lymphadenopathy thru FNA.

In conclusion, the combination of FCM analysis and cytomorphology on FNA material for lymphadenopathy samples is a valuable technique for providing rapid, precise and minimally invasive tool for diagnostic evaluation of lymphoid cell population. In large centers FCM should be incorporated as a routine diagnostic method for lymphadenopathy. Similar to other centers, we were able to validate this diagnostic approach in our laboratory.

Conflict of interest:

We declare there is no conflict of interests which may bias our study; and no financial fund has been given from any company. The usage of different reagents was upon, the experience of our pathologists or, the availability in the market.

Acknowledgement:

We acknowledge all the financial support to King Fahad Specialist Hospital –Dammam; which is a tertiary hospital and cancer center, a governmental non profitable organization. This work is part of our work to ensure a better quality, faster and accurate service to the cancer patients.

LYMPH NODE VALIDATION FLOW CYTOMETRY vs HISTOPATHOLOGY

	name	MRN	sample	date diagnosed		Gender	Age		Flowctometry	Histopathology	Comment
1	Mariam Al-Najrani	45205	LN	diagnosed with lymphadenitis on 17-10-2009	1	F	37y	Positive	CD19, 20,23,K,L,45,2,3,4,5,7,8	No IHC	Histopathology report was depending on morphology
								Negative	CD10,25, 103, 11c, TdT	No IHC	
								Diagnosis	No Malignancy/monoclonality detected	Castleman's Diseas,plasma cell variant,Negative for malignancy	
2	Ahmed Al_Samti	29886	LN	sly diagnosed with dermatopathic lymphader in 25-09-2011	2	M	27y	Positive	CD3,4,partial5,8,19,20,K,L,34,TdT	No IHC	
								Negative	CD23,103, 11C	No IHC	
								Diagnosis	No Malignancy/monoclonality detected	LymphadenopathyNegative for malignancy	
3	Ahlam Al-Khoufi	53586	LN	previously diagnosed with HL in 4-9-2012	3	F	46y	Positive	CD2,3,4,5,7,8,19,K,L	CD30 & fascin	No availibility of CD30 by FCM
								Negative	CD10,34,20	CD3, 20,15	
								Diagnosis	detected	variant	
4	Ahmed Goma	53940	LN	previously established micronodular cirrhosis on 26-1-2012	4	M	54y	Positive	CD2,3,4,5,7,8,19,22,45	No IHC	Histopathology report was depending on morphology
								Negative	CD10,20,23,25,sIgM,103,IgG,K,L,11c, 34,TdT	No IHC	
								Diagnosis	detected	Inflamation	
5	Sattam Yousef	60978	LN	newly diagnosed as Burkitts lymphoma on 20-9-2011	5	M	33y	Positive	CD19,20,22,sIgM,K, 45	CD20,Mum-1,Bcl-6, Faint CD10	
								Negative	CD2,3,4,5,7,8,10,23,25,L,11c,34,HLA-DR	CD3,Bcl-2,CyclinD1, TdT	
								Diagnosis	Burkitt Lymphoma	Burkitts lymphoma	
6	Saleha Harobi	50236	LN	previously diagnosed with DLBCL 10/03/2010	6	M	44y	Positive	CD2,3,4,5,7,8,19,20,23,45	No IHC	Histopathology report was depending on morphology
								Negative	CD10,103,K,L,11c,34,TdT	No IHC	
								Diagnosis	No Malignancy/monoclonality detected	inflamationpredominently non-necrotizing	
7	Abdulla Al-Nasser	60598	LN	previously diagnosed with b-cell lymphoma on 19-09-2011	7	M	24y	Positive	CD2,3,4,5,7,8,25,19,20,K,L	No IHC	Histopathology report was depending on morphology
								Negative	TdT, CD34,23	No IHC	
								Diagnosis	No Malignancy/monoclonality detected	histocytosisNo Malignancy/monoclonality detected	
8	Rabab Al-Ema	60930	ovary	newly diagnosed 6-9-2011	8	F	24y	Positive	CD3,4,8,19,20,K,L	faintCD117, PLAP,CK	
								Negative	CD10,CD117	CD30, AFP, HCG	
								Diagnosis	detected	lymph node Negative for metastasis	
9	Naif Al-Otaibi	60554	FNA	newly diagnosed on 23-08-2011	9	M	30y	Positive	CD3,4,5,7,	CD3,5,7,4,30	
								Negative	CD2,8,10,19,20,25,103,K,L,11c,34, TdT	CD2,Alk-2, CD10 & Bcell markers,	
								Diagnosis	detected	cell lymphoma	
10	Naif Al-Otaibi	60554	LN	newly diagnosed on 23-08-2011	10	M	30y	Positive	CD2,3,4,5,7,8,19,K,L	CD30,3,7,4	sample was diluted with many normal cells& apparently the normal part of the LN was sent to
								Negative	CD10,25,103,11c,34,TdT,30	Alk-1,CD2,5,15,8,20	
								Diagnosis	No Malignancy/monoclonality detected	Alk-Negative T-cell anaplastic Large cell lymphoma	
11	yousef AL-Bohasan	58075	LN	lously diagnosed with lymphoepithelial sialade on 24-04-2012	11	M	71y	Positive	CD2,3,4,5,7,8,19,20,23,K,L	No IHC	
								Negative	CD103,11c,34,TdT	No IHC	
								Diagnosis	detected	detected	
12	Ali Al-Saheemi	54533	LN	diagnosed with DLBCL on 4-12-2010	12	M	49y	Positive	CD19,20,23,K, 11c,HLA-DR	Mum-1	
								Negative	CD2,3,4,5,7,8,10,25,103,L,34,45,TdT, 14	CD3, 10	
								Diagnosis	B-Cell Lymphoma	Diffuse Large B-cell Lymphoma	
13	Ahmed Al-Moher	61249	LN	newly diagnosed on 10-10-2011	13	M	61y	Positive	DR,sIgM,L	67	
								Negative	CD3,4,5,8,38,103,11c,30,K	CD3,5,21,23	
								Diagnosis	B-Cell Lymphoma	IIIa	?????
14	Fawzya Al-Abad	61681	LN	newly diagnosed on 24-10-2011	14	F	48y	Positive	CD2,3,4,5,7,8,19,20,23,K,L	No IHC	
								Negative	CD25, 103,11c,TdT	No IHC	
								Diagnosis	detected	Atypical Large Lymphoid Cells	
15	Zahra Al-Muslem	61262	neck	newly diagnosed on 18-10-2011	15	F	18y	Positive	CD2,3,4,5,7,8,19,20,23,25,K,L	CD15,30,few CD20	No availibility of CD30 by FCM
								Negative	CD10,103,11c,34,TdT	CD3	
								Diagnosis	detected	Classical Hodgkin's Lymphoma	
16	Abdulrahman Naqi	60928	LN	newly diagnosed on 10-10-2011	16	M	22y	Positive	CD3,4,5,8,19,20,22,45,56,79b,HLA-DR	No IHC	
								Negative	CD23,10,25,sIgM,38,103,K,L,11c,34, TdT,14,FMC7	No IHC	
								Diagnosis	detected	benign Reactive lymph node	
17	Nawal Al-Timani	56946	LN	newly diagnosed on 18-10-2011	17	F	56y	Positive	CD2,3,4,5,7,8,19,20,K,L	occasional CD20, weak CD15 & CD30	No availibility of CD30 by FCM
								Negative	CD10,23,25,103,11c,34,TdT	CD3, CD45	
								Diagnosis	detected	Classic Hodgkins Lymphoma	
18	Masoma Al-Awjami	915	Thyroid	viously diagnosied with focal thyroid inflamati in 16-2-2012	18	F	55y	Positive	CD2,3,4,5,7,8,19,20,23,K,L	No IHC	report was depending on morphology
								Negative	CD10,25,103,11c,34	No IHC	
								Diagnosis	detected	Hashimoto's Thyroditis	
19	Saadon Al-Sadoon	42813	LN	diagnosed with ostiosarcoma in 22-9-2009	19	M	18y	Positive		No IHC	
								Negative	CD10,25,103,11c,34,TdT,30	No IHC	
								Diagnosis	Normal T & B cells, No monoclonality	reactive lymphoid hyperplaia	
20	Rami Al-Harbi	12695	opharyn biopsy	diagnosed in 26-10-2011	20	M	23y	Positive	CD2,3,4,5,7,8,19,20,23,K,L	No IHC	
								Negative	CD10,25,103,11c,34,TdT	No IHC	
								Diagnosis	detected	Reactive Follicular hyperplasia	
21	Fatima al-Marzooq	51134	LN	diagnosed in 29-11-2011	21	F	76y	Positive	CD10,19,20,23,L	CD20,23,10,Bcl-2, faint Bcl-6	
								Negative	CD2,3,4,5,7,8,25,K,103,11c,34,TdT	CD3,5,Cyclin D	
								Diagnosis	Follicular Lymphoma	grade	
22	Safa Alawad	53440	LN	usly diagnosed with classical Hodgkins Lymph in 16-8-2010	22	F	11y	Positive	CD2, 3, 4, 5, 7, 8, 19,20, 11c, K ,L, partial 23	CD3, CD20	
								Negative	CD10,25,103,34,TdT	CD30, CD15	
								Diagnosis	No Malignancy/monoclonality detected	hyperplaia, no evedience of recurrent Hodgkins Lymphoma	
23	Mujtaba Alalwan	55820	LN	usly diagnosed with classical Hodgkins Lymph lymphocytes rich in 23-3-2011	23	M	10y	Positive	CD2,3,4,5,7,8,19,K,L	CD30	toNebraska medical center: No evidence of
								Negative	CD10,23,25,33,11c,34,TdT	CD15	
								Diagnosis	detected	Atypical Lymphoproliferative lesion	
24	Mohammed Al-Jaber	64325	LN	iagnosed with classical Hodgkins Lymphoma in 19-2-2012	24	M	17y	Positive	CD2,3,4,5,7,8,19,K,L,11c	CD15,30,focal CD20	No availibility of CD30 by FCM
								Negative	CD10,23,25,33,34,TdT	CD45,3	
								Diagnosis	detected	Classic Hodgkins Lymphoma	
25	Muayad Al-Darweesh	56677	LN	iagnosed with classical Hodgkins Lymphoma in 28-3-2011	25	M	20y	Positive	CD3,4,5,8,19,45,20,22,23,79b,K,L, HLA-DR	CD30	
								Negative	CD10,34,	CD15	
								Diagnosis	detected	hyperplasia	

26	Thaidan Al-Eid	44091	LN	diagnosis 19-5-2012	26	M	24	Positive	CD3,4,5,8,19,K,L,11c,20,22,23,79b, HLA-DR	CD3,20,21,5,10	
								Negative	CD10,23,25,33,34,TdT,38,103,sIgM,F		
								Diagnosis	detected	Reactive Follicular hyperplasia	
27	Hager Al-Abdulaziz	46624	LN	previously diagnosed as Ewing sarcoma in 28-9-2009	27	F	12y	Positive	CD3,4,8,19, partial sIgM,K,L	No IHC	
								Negative	CD10	No IHC	
								Diagnosis	detected	Reactive Lymphoid hyperplasia	
28	moneera Al-Zuabi	65308	LN	previously diagnosed follicular lymphoma in 28-3-2012	28	F	48y	Positive	CD 19,K	CD20	
								Negative	L, sIgM, CD3,4,8,10,	CD3, 10	
								Diagnosis	B-Cell Lymphoma	Diffuse Large B-cell Lymphoma	
29	Ali Al-Ashwan	58583	LN	previously diagnosed as HL on 4-5-2011	29	M	14y	Positive	CD3,4,8,19,K,L,45	No IHC	
								Negative	CD10,103, sIgM	No IHC	
								Diagnosis	detected	Reactive Follicular hyperplasia	
30	fayez Al-Essa	18377	LN	18/08/2012	30	M	38	Positive	CD19,20,K,L	scattered CD30	
								Negative	CD10,4,8,3	CD15, 20	
								Diagnosis	detected	follow up	
31	Ahmad Hosny	17783	LN	18/08/2012	31	M	9y	Positive	CD19,20, K,L	No IHC	
								Negative	CD3,4,5,8,10	No IHC	
								Diagnosis	detected	Reactive Follicular hyperplasia	
32	Ibrahim Bo-Howaid	68612	LN	diagnosed on 19-8-2012	32	M	49y	Positive	CD3,4,5,8,19,20,sIgM,K,L,45	CD30,15,20	No availibility of CD30 by FCM
								Negative	CD10,23,103,34	CD45,3	
								Diagnosis	detected	Classic Hodgkins Lymphoma	
33	Areej Al-Gobaise	68983	LN	diagnosed on 25-8-2012	33	F	16y	Positive	CD3,4,5,8,19,20,23,sIgM,K,L,45	CD30,15	No availibility of CD30 by FCM
								Negative	CD10,103,34,TdT		
								Diagnosis	detected	Classic Hodgkins Lymphoma	
34	Fatemah Al-Owiss	48560	FNA	diagnosed on 14-3-2010 as DLBCL germinal center type	34	F	44y	Positive	CD19, Kappa	No IHC	
								Negative	CD10, sIgM, Lambda	No IHC	
								Diagnosis	B-Cell Lymphoma	Few atypical large lymphoid cels highly suspesious for lymphoma	
35	Alyaa Al-Shameri	24042	LN	diagnose as DLBCL on 19-9-2009	35	F	64y	Positive	CD19, CD23	CD20, BCL-2, BCL-6 Ki 67	
								Negative	& lambda	CD10	
								Diagnosis	B-Cell Lymphoma	Follicular B-cell Lymphoma	
36	Mujtaba Al-Alwan	55820	LN	diagnosed as EBV related lymphadenitis on 23-1-2011	36	M	10Y	Positive	CD3,4,8	CD68, 3	
								Negative	CD10,19,sIgM, 34	CD20	
								Diagnosis	detected	Lymphadenitis	
37	Mohammed Al-Hilal	68842	LN	diagnosed 12-9-2012	37	M	15y	Positive	CD3,4,8,19,45, kappa, lambda	CD30,15, PaX-5	No availibility of CD30 by FCM
								Negative	CD10	CD20,45,3	
								Diagnosis	detected	Sclerosis	
38	Hattan Al-Mutairi	58049	LN	diagnosed 4-5-2011	38	M	4y	Positive	CD3,4,8,19,45, kappa, lambda	CD15,CD30,Fascin,PAX5	No availibility of CD30 by FCM
								Negative	CD10	CD45,3,20	
								Diagnosis	detected	Classic Hodgkins Lymphoma	
39	fatima Baaqeel	69105	FNA	diagnosed 14/10/2012	39	F	44y	Positive	CD2,3,4,5,7,8,TCRab,19,k,l,	No IHC	
								Negative	TCRgd, CD1a, CD34	No IHC	
								Diagnosis	3% of T-cells coexpress CD4&8 which can be found in T-cell malignancies or autoimmune disease.	lymphocytes. CD3 & CD20 show mixed population of T & B cells. Diagnosis favor reactive intra-parotid LN, However, it is clinically suspecious for lymphoma an	
40	Jaber Sahloli	36747	LN	diagnosed 10-3-2009	40	M	46y	Positive	19,20,23,38,79B,11c,45	CD20,BCL6,Mum,Ki index 70%	
								Negative	CD2,3,4,5,7,8,10,103,138,sIgM,k,l,FMC7,CD14,34,56,HLA-DR	CD3,5,10	
								Diagnosis	B-Cell Lymphoma	monomorphic post transplantation lymphoproliferative diorder.(DLBCL)	
41	Ajlan Altaleedi	65838	FNA	Known case diagnose 18-4-2012	41	M	71y	Positive	CD19,20,22,L,45	No IHC	
								Negative	CD3,4,5,8,38,10,23,103,sIgM,K,11c,34	No IHC	
								Diagnosis	B-Cell Lymphoma	known case Larg B-cell Lymphoma	
42	Faisal Al-Mutairi	61207	LN	busly diagnosedf Hodgkins lymphoma in 27-9-	42	M	4 y	Positive	CD3,4,8,19,22,K,L	CD38, 20 show reactive cells	
								Negative	CD10	CD30& 15	
								Diagnosis	No Malignancy/monoclonality detected	detected	
43	Fakra Al-Hemaidan	69628	FNA	newly diagnosed in 27-10-2012	43	F	56y	Positive	CD10,19	No IHC	No availibility of CD30 by FCM
								Negative	CD3,4,5,8,23,K,L,34	No IHC	
								Diagnosis	B-Cell Lymphoma	Hodgkins lymphoma	
44	Abderahman Al-rabiaah	32792	FNA	newly diagnosed in 12-11-2012	44	M	51y	Positive	CD3,4,5,8,19,K,L	No IHC	No availibility of CD30 by FCM
								Negative	CD10,23,34	No IHC	
								Diagnosis	detected	mixed cellularity classical HL	
45	Muna AlZahrani	57471	LN	patient with history of obstructive jaundice No history of malignancy tested on 5-11-2012	45	F	26Y	Positive	CD45,11c,	population	
								Negative	CD2,3,4,5,7,8,10,19,23,25,103,k,l,33,34,TdT		
								Diagnosis	detected	detected	
46	Hashem Al-Hshem	70609	LN	newly tesed on 11-11-2012	46	M	14y	Positive	CD2,3,4,5,7,8,19,23,K,L,45	No IHC	
								Negative	CD10,25,103,33,11c,34	No IHC	
								Diagnosis	There is 16% population coexpressing CD4& CD8 suggesting normal peripheral cells	follicular hyperplasia, inspect the patient for viral infection	
47	Mareem alkhaldi	69182	LN	07/01/2013		F	37y	Positive	CD3,CD4,CD5,CD8,CD19, KAPPA, LAMBDA	No IHC	
								Negative	CD10, CD34, TdT	No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	Negative for granuloma or malignancy	
48	Abdulla Al-Shehri	72023	LN	08/01/2013		M	11y	Positive	CD3,CD4,CD7,CD8,CD19, KAPPA, LAMBDA	No IHC	
								Negative		No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	Negative for primary lymphoma, metastatic malignancy or granulomatous inflamation	
49	Hussain Al-Shoman	63995	LN	13/01/2013		M	61y	Positive	CD19	CD79a, CD20, (CD3 & 5 positive on the t-cells)	
								Negative	CD3,CD4,CD8,CD20	CD10, CD30,	
								Diagnosis	inconclusive kappa & lambda. QNS sample was processed show 10% population of large B-cells. But clonality couldn't be proven	Diffuse Large B-cell Lymphoma with plasmablastic features, non G.C.B type	
50	Fahad Al-Harbi	70828	LN	13/01/2013		M	73y	Positive	CD3, CD4, CD8, CD19	No IHC	
								Negative	CD20, kappa, Lambda	No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	Negative for metastatic tumer, polymorphic population of lymphocytes	

51	Najla Al-Abdulqader	71219	LN	13/01/2013		F	33y	Positive	CD19, CD20 Lambda	No IHC	
								Negative	CD3, CD4, CD8,kappa	No IHC	
								Diagnosis	QNS sample sugest B-cell lymphoproliferative clone	Atypical large lymphoid cells with rare formed non-necrotizing granulomas. Refer to flow result.	
52	Ariam Al-Shammari	64001	LN	15/01/2013		F	7Y	Positive	CD2,CD3,CD4,CD5,CD7,CD19,CD20,CD22,CD23, Kappa, Lambda		
								Negative	CD103, CD10		
								Diagnosis	No Malignancy/ monoclonality detected	CD3, CD20, CD30, CD15 fail to elict viable RS cells. No evidence of residual hodgkins lymphoma	
53	Mohammed Al-Shamma	72017	LN	20/01/2013		M	18y	Positive	CD2,CD3,CD4,CD5,CD7,CD19,CD23 dim, Kappa, Lambda	CD45,CD20,EMA,Fascin, BCL6, PAX5	
								Negative	CD10,CD5,CD103,CD11c, CD34	CD30,CD15,CD23	
								Diagnosis	No Malignancy/ monoclonality detected	Nodular Lymphocyte predominant hodgkin lymphoma (NLPHL)	
54	Nawal Al-Timani	56946	LN	27/01/2013		F	57y	Positive	CD3,CD4,CD8,CD19Kappa, Lambda	No IHC	
								Negative		No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	few large atypical cells, Hodgkins lymphoma cannot be totally excluded	
55	Khalifah Al-Hamad	72276	LN	28/01/2013		F	33y	Positive	CD2,CD4,CD5dim,CD7dim,CD8, CD38,TdT dim & partial	TdT, CD3	
								Negative	CD1a,CD3,CD10,CD19,CD20,CD23, CD25, CD103,Kappa,Lambda,FMC7, CD11c,CD34	CD20	
								Diagnosis	Tcell Lymphoma/Leukemia	T-cell Lymphoblastic Lymphoma	
56	Rayan Al-Eniz	72217	LN	29/01/2013		F	8y	Positive	CD3,CD4,CD8,	No IHC	
								Negative	CD19, Kappa,Lambda	No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	Tuberculous Granulomatous Inflamation	
57	Mutib Al-Harthi	2179	LN	02/02/2013		M	49y	Positive	CD3,CD4,CD8,CD19, Kappa,Lambda	No IHC	
								Negative		No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node, negative for malignancy	
58	Noura Al-Arfaj	12643	LN	05/02/2013		F	77y	Positive	Normal T cells 26 %, & are positive for CD3,CD2,CD4,CD5,CD7,CD8, &CD38; Normal B cells 5 %, &are positive for CD19,CD20,kappa &lambda.	CD15, CD30	
								Negative		CD3, CD20, CD10	No availibility of CD30 by FCM
								Diagnosis	The sample is infiltrated with CD45 negative cells 60%, are seen in the scatter;the population is negative to CD3, CD10, CD5, CD19CD15; morphology and flowcytometry suggestive of Hodgkin Lymphoma.	Hodgkin Lymphoma.	
59	Nawal Al-Timani	56946	LN	09/02/2013		F	57y	Positive	CD3, CD4, CD8,CD19,kappa,lambda	No IHC	
								Negative		No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node, negative for malignancy	
60	Ahmed Mahalawi	72112	LN	12/02/2013		M	48y	Positive	CD3,cCD3, CD4, CD8, CD19, CD79a, kappa, lambda, MPO	No IHC	
								Negative		No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	negative for malignancy	
61	Nowal Al-Timani	56946	LN	23/02/2013		F	55y	Positive	CD3,CD4, CD5, CD7, CD8, CD19, CD20, CD79a, kappa, lambda, CD45		
								Negative	CD10, CD23, CD25, CD103, CD33, CD117, MPO, FMC7, CD11c, CD34, CD64, Tdt		
								Diagnosis	No Malignancy/ monoclonality detected	negative for malignancy	
62	Modi Al-Abdulla	73283	LN	26/02/2013		F	19y	Positive	CD3, CD4, CD8		
								Negative	CD19, kappa, lambda		
								Diagnosis	No Malignancy/ monoclonality detected	atypical lymphoproliferation	
63	Khatebah Al-Meshal	71826	LN	10/03/2013		F	34y	Positive	CD3, CD4, CD5, CD8, CD19, CD20, kappa, lambda	No IHC	
								Negative	CD10,	No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node, negative for malignancy	
64	Zafer Al-Shhrani	73544	LN	10/03/2013		M	75y	Positive	CD4, CD5, CD3, CD8, CD19, kappa, lambda	CD15, CD30,	
								Negative		CD3, CD20, CD23, CD10	No availibility of CD30 by FCM
								Diagnosis	No Malignancy/ monoclonality detected	Classical Hodgkin's Lymphoma	
65	Modi Al-Abdulla	73283	LN	11/03/2013		F	19y	Positive	CD3, CD4, CD5, CD8, CD19, CD20, kappa, lambda		
								Negative	CD10,		
								Diagnosis	No Malignancy/ monoclonality detected	No Malignancy / kikuchi Fujimoto diseas	
66	Ali Al-Mohsen	67822	LN	13/03/2013		M	62y	Positive	CD19, CD5, CD20, CD23, kappa, partial FMC7, CD45	CD20 , CD5, Zap70	
								Negative	CD3, CD4, CD7, CD8, CD10, CD25, CD103, CD38, Lambda, CD34	CD3	
								Diagnosis	CLL/SLL	SLL	
67	Murtadah Al-Salem	72695	LN	26/03/2013		M	24y	Positive	CD3, CD20, kappa, lambda	No IHC	
								Negative		No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node, negative for malignancy	
68	Moneera Al-Zuabi	65308	LN	27/03/2013		F	49y	Positive	CD19, CD25, CD45, kappa	CD20 , CD79a,	
								Negative	CD5, CD10, CD23, CD103, lambda FMC7, CD11c	CD3, CD10, CD43	
								Diagnosis	relapsed B-cell Lymphoma	Marginal zone Lymphoma in transformation to large b-cell lymphoma	
69	Hitham Al-Dokhi	74265	LN	06/04/2013		M	24y	Positive	CD3, CD4, CD5, CD7, CD8, CD19, CD20 , CD38, CD45, kappa, lambda	CD15 , CD30,	
								Negative	CD10, CD23, CD25, CD11c	CD10 , CD20, CD3, CD45	No availibility of CD30 by FCM
								Diagnosis	T-cell population show inapropriate ratio between CD4/CD8 with increased CD4, to correlate with clinical findings.	Classical Hodgkin's Lymphoma, mixed cellularity type.	
70	Ajab Al-Qahtani	74397	LN	15/04/2013		M	73y	Positive	CD19, CD20, kappa	CD20 ,	
								Negative	lambda, CD5, CD10, CD23, CD25, CD38, CD103, FMC7, CD34	CD5, CD10, CD34, CD3	
								Diagnosis	B-cell lymphoproliferative disorder	Diffuse large B-cell lymphoma, non-germinal center type	
71	Mohamed Al-Hagri	74556	LN	22/04/2013		M	2y	Positive	CD3, CD4, CD5, CD8, CD19, CD20, kappa, lambda	No IHC	
								Negative	CD10, CD23, CD25, FMC7, CD11c, CD34,	No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node, negative for malignancy	
72	Saleh Alkhofi	74115	LN	22/04/2013		M	30y	Positive	CD3, CD4, CD8, CD19, kappa, lambda	CD15 , CD30	
								Negative			No availibility of CD30 by FCM
								Diagnosis	No Malignancy/ monoclonality detected	Classical Hodgkins Lymphoma	
73	Lolwah Al-Rasheed	74721	LN	06/05/2013		F	54y	Positive	CD3, CD4, CD8, CD19, kappa, lambda	No IHC	
								Negative		No IHC	
								Diagnosis	No Malignancy/ monoclonality detected	polymorphic population of lymphocytes & rare follicular cells consistent with chronic lymphocytic thyroditis	
74	Mutlaq Al-Amohsen	24064	LN	19/05/2013		M	69y	Positive	CD3, CD4, CD5, CD7, CD8, CD19, CD20, CD23, kappa, lambda	CD3, CD5, CD10, CD30,	
								Negative	CD10, CD25, CD103, fmc7, CD11c, CD38	CD8, TdT	
								Diagnosis	No Malignancy/ monoclonality detected	portion of the Lymph Node partially infiltrated with peripheral T-cell lymphoma	
75	Abdulmalek Al-hamed	75500	LN	20/05/2013		M	13y	Positive	CD3, CD4, CD8, CD19, kappa, lambda	CD3, CD10, TdT	
								Negative		CD20, CD5, Zap70	
								Diagnosis	No Malignancy/ monoclonality detected	T-cell Lymphoblastic Leukemia/Lymphoma	

76	Mohammed Al-taibi	51769	LN	20/05/2013		M	5y	Positive	CD3, CD4, CD8, CD19, kappa, lambda	No IHC		
								Negative		No IHC		
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node, negative for malignancy		
77	Abdullah Al-Harbi	62491	LN	03/06/2013		M	29y	Positive	CD2, CD5, CD7CD3, CD4, CD8, CD19, kappa, lambda	No IHC		
								Negative		No IHC		
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node (HIV related benign lymphadenopathy), negative for malignancy		
78	Hussain Al-Mussaly	68137	LN	10/06/2013		M	16y	Positive	CD3, CD4, CD8, CD19, kappa, lambda	No IHC		
								Negative		No IHC		
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node, negative for malignancy		
79	Ali Al-Ghamdi	62394	LN	17/06/2013		M	48y	Positive	CD19, CD20, lambda	CD10, CD20,		
								Negative	CD3, CD5, CD10, sIgM, kappa	CD5, CD3, TdT		
								Diagnosis	Monoclonal B-cell population. To be correlated with histopathology	low grade follicular lymphoma		
80	Lolwah al-Bin ali	69825	LN	22/06/2013		F	56y	Positive	CD19, kappa	CD45, CD20		
								Negative	CD3, CD4, CD5, CD8 lambda	CD10, CD30,		
								Diagnosis	Large cells show B-cell monoclonality , correlate with histopathology	Diffuse Large B-cell Lymphoma, non-germinal center b-cell		
81	Huda Al-Turki	37997	LN	23/06/2013		F	45y	Positive	CD10, CD19, Lambda	CD20, CD10		
								Negative	CD3, kappa	CD5		
								Diagnosis	Follicular Lymphoma	Follicular Lymphoma		
82	Hasna Al-Shammary	74184	LN	07/07/2013		f	36y	Positive	CD3, CD4, CD8, CD7			
								Negative				
								Diagnosis	No dim CD4 seen, correlate with histopathology	No difinite evidence of lymphoma seen		
83	Anas Al-Abdulatif	66055	LN	09/07/2013		M	21y	Positive	CD4, CD8	CD30, CD15		
								Negative		CD45, CD20, CD3		No availibility of CD30 by FCM
								Diagnosis	no monoclonality proven, correlate with histopathology	Recurrent Classical Hodgkins Lymphoma		
84	Ali Al-Bouri	75352	LN	10/07/2013		M	7y	Positive	CD4, CD8	CD68		
								Negative				
								Diagnosis	No Malignancy/ monoclonality detected	Reactive Hyperplasia		
85	Rami Al-Harbi	12695	LN	15/07/2013		M	22y	Positive	CD3, CD4, CD8, CD19, kappa, lambda			
								Negative				
								Diagnosis	No Malignancy/ monoclonality detected	reactive lymphe node, negative for malignancy		
86	Dalilah Al-Haisoni	75562	LN	25/07/2013		F	53y	Positive	CD3, CD4, CD8, CD19, kappa, lambda			
								Negative				
								Diagnosis	necrotic sample correlate with histopathology	Necrotizing Granulomatous Inflamation. Negative for malignancy		
87	Roqayah Al-Mahdi	65728	LN	31/07/2013		M	41y	Positive	CD5,CD7,CD3, CD4, CD8,CD19, CD20, kappa, lambda	CD30, CD15		
								Negative	FMC7,CD10	CD45, CD3, CD20		No availibility of CD30 by FCM
								Diagnosis	No Malignancy/ monoclonality detected	Classical Hodgkins Lymphoma		
88	Safa Al-Awad	53440	LN	31/07/2013		F	12y	Positive	CD3, CD4, CD5, CD8, CD19, CD20, kappa, lambda	CD30, CD15		
								Negative	CD10, FMC7	CD45, CD3, CD20		No availibility of CD30 by FCM
								Diagnosis	No Malignancy/ monoclonality detected	Classical Hodgkins Lymphoma		
89	Khalil Al-Ateyah	76804	LN	31/07/2013		M	26y	Positive	CD3, CD4, CD5, CD8, CD19, CD20, kappa, lambda	CD30, CD20		
								Negative	CD10, FMC7	CD45, CD3, CD15		No availibility of CD30 by FCM
								Diagnosis	No Malignancy/ monoclonality detected	Classical Hodgkins Lymphoma		

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9/10/2013