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Original scientific paper

The Accuracy of Fine Needle Aspiration Cytology and Flow Cytometry in Evaluation of Nodal and Extranodal Sites in Patients with Suspicion of Lymphoma

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A B S T R A C T

Today lymphomas are defined according to a combination of morphology, immunophenotype, genetic features and clinical presentation, so beside the pure cytomorphologic analysis in diagnosis of lymphoma ancillary techniques such as cytochemistry, immunocytochemistry, molecular diagnosis and flow cytometry (FC) are often used. Our goal was to determinate how is information given by fine-needle aspiration cytology (FNAC) and FC correlated with pathohistologic diagnosis and to evaluate ability to diagnose and subclassify malignant lymphomas by FNAC and FC. This study is a retrospective chart review of patients with suspicion of lymphoma processed at University Hospital Dubrava in Zagreb. After analysis 50 patients fulfilled inclusion criteria for this study (FNAC diagnosis with or without FC and consecutive confirmatory pathohistological diagnosis). When analyzing accuracy of FNAC according to suspicion of lymphoma or NHL and differential diagnosis lymphoma sensitivity was 97.7%, specificity 85.7% and the diagnostic accuracy was 96%. When analyzing accuracy of FNAC according to the subclassification of lymphoma, sensitivity was 74.4%, specificity 85.7% and the diagnostic accuracy 76%. Combined FNAC and FC improved sensitivity, positive predictive value, negative predictive value and diagnostic accuracy. Sensitivity was 79.1% and the diagnostic accuracy 80%. We have shown that these methods can distinguish benign lymphadenopaties from lymphomas and also subclassify lymphomas and quickly provide clinicians with that information.

Key words: *lymphoma, fine-needle biopsy, cytology, flow cytometry*

Introduction

Nowadays fine-needle aspiration cytology (FNAC) is very often used as the first morphologic diagnostic procedure for the diagnosis of malignant lymphoma[1–3]. Today lymphomas are defined according to a combination of morphology, immunophenotype, genetic features and clinical presentation, so besides the cytomorphologic analysis ancillary techniques such as cytochemistry, immunocytochemistry, molecular tests (Southern blotting, the polymerase chain reaction /PCR/, fluorescent in situ hybridization /FISH/) and flow cytometry (FC) are often used[4]. The role of the FNAC in diagnosis of Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL) was often stated as controversial[5–7]. At first FNAC was mainly used to diagnose recurrent disease or for staging purposes[8]. The main controversy about the FNAC was its value in the primary diagnosis of lymphoma[9,10]. A

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large amount of published articles has shown the value of FNAC in the diagnosis and classification of lymphomas especially when FNAC was combined with other diagnostic techniques such as flow cytometry or other immunophenotypic procedures[1,6,9,11–15].

The FNAC and FC are complementary diagnostic procedures which play crucial role in the initial lymphoma diagnosing triage. University Hospital Dubrava is rare case in Croatia where FNAC and FC are situated at the same department (Department of Clinical Cytology and Cytometry). Both FNAC and FC are used for triaging benign from malignant lymphadenopathies but FC is not preformed in all cases. Considering clinical presentation and cytological findings a cytologist indicates FC analysis. FC analysis is used as an ancillary technique with purpose of distinguishing malignant from benign lymphadenopaties and classification of non Hodgkin's lymphomas. With this kind of organization the use of monoclonal antibodies used in FC is being rationalized. In this retrospective review we have analyzed the role of FNAC and FC in comparison to pathohistologic analysis. Our goal was to determinate how is the information given by FNAC and FC correlated with the pathohistologic diagnosis, to evaluate ability to diagnose and subclassify malignant lymphomas by FNAC and FC and to discover possible advantages or limitations of these procedures.

Patients and Methods

This study is a retrospective chart review of patients with suspicion of lymphoma processed at University Hospital Dubrava in Zagreb. We reviewed patient's charts at the Department of Clinical and Experimental Pathology and the Department of Clinical Cytology and Cytometry within two years and two months (from March 2007 to May 2009). In this study only patients with suspicion of lymphoma who underwent procedure of FNAC (with or without FC) and at the same time had consecutive confirmatory pathohistological diagnosis were included.

Patients were first identified by searching the archive of the Department of Clinical and Experimental Pathology for Lymphoid Lesions. Patients with diagnosis of HL, NHL and benign lymphadenopathy were included in the study. Patients with diagnosis of carcinoma, melanoma and other solid tumors were excluded from analysis as well as the patients with previously diagnosis of lymphoma. Tissue samples were lymph nodes and extranodal sites. After identifying 88 patients with pathohistological diagnosis we analyzed the archive of the Department of Clinical Cytology and Cytometry to identify which of those patients underwent procedure of FNAC and on which of those samples was FC also preformed. We found 50 patients that underwent the procedure of FNAC with or without FC, so 38 patients were excluded from the study. Results were compared for all patients who underwent procedure of FNAC (with or without FC) and at the same time had consecutive confirmatory pathohistological diagnosis.

Pathohistological diagnoses were made by two pathologists from the Department of Clinical and Experimental Pathology and the cytological diagnoses were made by three cytologists from the Department of Clinical Cytology and Cytometry. FC was preformed by a biologist from the Department of Clinical Cytology and Cytometry.

All the calculations in this study, including sensitivity, specificity, positive predictive value, negative predictive value and the diagnostic accuracy were manually computed. None specific statistical computer software was used.

Results

After analyzing the archive of Department of Pathology we found 88 patients with lymphoma and benign

TABLE 1
SUMMARY OF PATIENT'S CHARACTERISTICS

Variable	Number (N)
Patients	50
Gender	
Male	27
Female	23
Age	
Minimum	25
Maximum	83
Median	53.5
Biopsy sites	
Lymph node	42
Liver	1
Spleen	1
Soft tissue	4
Brest	1
Submandibular salivatory gland	1
Confirmatory pathohistological diagnoses	
B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma	2
Splenic marginal zone zone B-cell lymphoma	1
Follicular lymphoma	6
Grade I	1
Grade I/II	2
Grade II	1
Grade III	1
No grade	1
Mantle cell lymphoma	5
Diffuse large B-cell lymphoma	16
T-lymphoblastic lymphoma/leukemia	1
Anaplastic large cell lymphoma	3
High grade non-Hodgkin's lymphoma	1
Hodgkin's lymphoma	8
Benign lympadenopathy	7

TABLE 2
THE ACURACCY OF DIAGNOSTIC PROCEDURES

Criteria	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %	Diagnostic accuracy %
Diagnosis of Lymphoma (FNAC)	97.7	85.7	97.7	85.7	96
Subclasiffication of lymphoma (FNAC)	74.4	85.7	97	35.3	76
Subclassification of lymphoma (FNAC + FC)	79.1	85.7	97.1	40	80

FNAC – fine needle aspiration cytology, FC – Flow cytometry

lymphadenopathies. Samples were taken from nodal and extranodal sites. After analysis and comparison with the archive of the Department of Clinical Cytology and Cytometry, 50 patients fulfilled inclusion criteria for this study (FNAC diagnosis with or without FC and consecutive confirmatory pathohistological diagnosis). All of 50 patients were analyzed for the fist time for suspicion of lymphoma so all of the lymphoma diagnoses were primary. Recurrent patients were excluded from the analysis. Age of the patients ranged from 25 to 83 years, with the median of 53.5 years. There were 27 (54%) male and 23 (46%) female patients. The most frequent samples for the analysis were lymph nodes (42 out of 50, 84%) and the biopsy of soft tissue (4 out of 50, 8%). Pathohistological diagnoses were made according to WHO classification of lymphomas[4]. The most frequent diagnosis was diffuse large B-cell lymphoma (DLBCL) (16 out of 50, 32%) followed by HL (8 out of 50, 16%), follicular lymphoma (FCL) (6 out of 50, 12%) and mantle cell lymphoma (MCL) (5 out of 50, 10%). One sample was classified as high grade non-Hodgkin's lymphoma. Seven specimens (14%) were pathohistologically diagnosed as benign. Table 1 summarizes our patients' characteristics.

TABLE 3
COMPARISON OF FINE-NEEDLE ASPIRATION CYTOLOGY (FNAC) AND PATHOHISTOLOGIC DIAGNOSIS

	Pathohistological diagnosis										
FNAC diagnosis	CLL/SLL	SMZL	FCL	MCL	DLBCL	T-LBL	ALCL	Hg NHL	HL	Benign	Total
CLL /SLL	1										1
FCL			4		1						5
MCL				1							1
SMZL		1									1
Large B-cell NHL				1*	11						12
LBL						1					1
ALCL							2		1		3
High grade NHL					1						1
Low grade NHL				1				1			2
Small cell NHL				1*	1						2
NHL			1	1	1						3
Chronic lymphoproliferative disease	1		1								2
Suspicious NHL										1	1
Suspicious lymphoma									1		1
Malignant tumor, differential diagnosis lymphoma							1				1
HL									6		6
Malignant tumor					1						1
Benign										6	6
Total	2	1	6	5	16	1	3	1	8	7	50

*immunophenotype suggested MCL characteristics, CLL/SLL – B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma, SMZL – Splenic marginal zone B-cell lymphoma, FCL – Follicular lymphoma, MCL – Mantle cell lymphoma, DLBCL – Diffuse large B-cell lymphoma, T-LBL – Precursor T-lymphoblastic lymphoma/leukemia, ALCL – Anaplastic large cell lymphoma, Hg NHL – High grade non-Hodgkin's lymphoma, HL – Hodgkin's lymphoma, NHL – non-Hodgkin's lymphoma, LBL – Lymphoblastic lymphoma, FNAC – fine needle aspiration cytology

Comparison of pathohistological and FNAC analysis

The most common diagnosis by the FNAC was a large B-cell non-Hodgkin's lymphoma (12 out of 50, 24%) followed by HL (6 out of 50, 12%), benign lymphadenopathy (6 out of 50, 12%) and FCL (5 out of 50, 10%). There was no case pathohistologically diagnosed as lymphoma that was diagnosed benign by the FNAC. Nevertheless, there was one case pathohistologically diagnosed as benign that was stated by the FNAC as suspicious of NHL. When analyzing accuracy of FNAC according to the suspicion of lymphoma or NHL and the differential diagnosis lymphoma, sensitivity was 97.7%, specificity 85.7% and the diagnostic accuracy was 96%. When analyzing accuracy of FNAC according to the subclassification of lymphoma, sensitivity was 74.4%, specificity 85.7% and the diagnostic accuracy 76% as shown in table 2. One case of B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) was stated by FNAC as CLL/SLL and one as chronic lymphoproliferative disease. There was only one case of splenic marginal zone B-cell lymphoma (SMZL) and it was stated as SMZL. Four out of six (66.7%) of the FCLs were diagnosed as the FCLs, one was stated as NHL and one was stated as chronic lymphoproliferaive disease. One out of five (20%) MCLs was classified as the MCL, other four were stated as large B-cell NHL, low grade NHL, small cell NHL and NHL (not specified). Eleven out of sixteen (68.7%) DLBCLs were classified as large B-cell lymphomas and in one case DLBCL was classified as FCL, high grade NHL, small cell NHL, NHL (not specified) and malignant tumor. One T-cell lymphoblastic lymphoma (T-LBL) was correctly diagnosed as the lymphoblastic lymphoma. Anaplastic large cell lymphoma (ALCL) was twice classified correctly (66.7%) and was once stated as a malignant tumor with differential diagnosis of lymphoma. One result pathologically diagnosed as high grade NHL was cytologically diagnosed as low grade NHL. Six out of eight cases (75%) of HLs were classified correctly, one was classified as ALCL and one was classified as suspicious of lymphoma. Six out of seven (85.7%) benign lymphadenopathies were cytologically classified as benign and one (14.3%) was stated as suspicious of NHL. Table 3 shows comparison of pathohistological and FNAC analysis.

Comparison of pathohistological and FC analysis

FC analysis was performed on 44 (88%) patients in our study. Table 4 shows the comparison of pathohistological and FC analysis. All of B-cell non Hodgkin's lymphomas were stated as monoclonal with the confirmation of B phenotype except of two inadequate samples. One case of ALCL was stated as polyclonal. One case of CLL/SLL was stated as B-cell NHL and one as CLL/SLL. SMZL was stated as a chronic lymphoproliferative disease. All of FCLs, MCLs and one high grade NHL were classified as B-cell NHL. Fourteen out of sixteen (87.5%) DLBCLs were classified as B-cell NHL. Two samples of DLBCLs (12.5%) were inadequate for analysis. T-LBL was classified as T-cell NHL and one ALCL was classified as polyclonal. Two out of five (40%) HLs were stated as polyclonal. In three (60%) samples of HL predominance of CD4 positive lymphocytes (CD4+ CD8-) was found. CD4+CD8- result is not able to distinguish malignant T-lymphocytes from benign reactive result (or in this cases lymphocyte background of HL). In the cases of homogenous nodal lymphocyte proliferation with decreased number of polyclonal B-lymphocytes, analysis of subpopulation of T-lymphocytes is also usually preformed with a purpose of finding a lymphocyte abnormalities. Six out of seven (85.7%) benign lymphadenopathies were diagnosed as polyclonal and one result suggested possibility of T-cell lymphoma.

Comparison of FNAC and FC diagnoses

Comparison between FNAC and FC diagnoses is summarized in Table 5. In 26 patients diagnosed with some type of NHL by FNAC, FC showed B-cell phenotype. In one case stated as chronic lymphoproliferative disease by

TABLE 4
COMPARISON OF FLOW CYTOMETRY (FC) ANALYSIS AND PATHOHISTOLOGICAL DIAGNOSIS

	Pathohistological diagnosis										
FC diagnosis	CLL/SLL	SMZL	FCL	MCL	DLBCL	T –LBL	ALCL	Hg NHL	HL	Benign	Total
B-NHL	1		5	5	14			1			26
CLL/SLL	1										1
Chronic lymphoproliferative disease		1									1
T-NHL						1				1	2
CD4+CD8-									3		3
Polyclonal							1		2	6	9
Inadequate sample					2						2
Total	2	1	5	5	16	1	1	1	5	7	44

CLL/SLL – B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma, SMZL – Splenic marginal zone B-cell lymphoma, MALT – Marginal zone B-cell lymphoma of MALT type, FCL – Follicular lymphoma, MCL – Mantle cell lymphoma, DLBCL – Diffuse large B-cell lymphoma, T-LBL – Precursor T-lymphoblastic lymphoma/leukemia, ALCL – Anaplastic large cell lymphoma, Hg NHL – High grade non-Hodgkin's lymphoma, HL – Hodgkin's lymphoma, B-NHL – B-cell non Hodgkin's Lymphoma, T-NHL – T-cell non--Hodgkin's lymphoma, CD4+CD8- – predominance of CD4 positive lymphocytes, FC – flow cytometry

FNAC, FC correctly diagnosed it as CLL/SLL. In case of SMZL (also pathohistologically verified) FC diagnosis was chronic lymphoproliferative disease. Lymphoblastic lymphoma was correctly classified by FC as T-cell NHL (pathohistologically verified as T-LBL). In one case of suspicious NHL (pathohistologically verified as benign) FC suggested possibility of T-NHL. Predominance of CD4 positive lymphocyte by FC was to one patient diagnosed as ALCL by FNAC (pathohistologically HL), to the other patient suspicious of lymphoma by FNAC (pathohistologically HL) and to the third patient HL by FNAC (pathohistologically confirmed). In one patient cytological diagnosis of the malignant tumor and differential diagnosis of lymphoma was established by FNAC; and FC stated polyclonal result and pathohistological diagnosis was ALCL. Two patients diagnosed of HL by FNAC that were pathohistologically confirmed were polyclonal by FC. Benign lymphadenopathies diagnosed by FNAC were confirmed as polyclonal by FC. There were two inadequate samples for FC; FNAC's diagnoses were NHL and malignant tumor and pathohistologically both cases were diagnosed as DLBCL.

In one patient large B-cell NHL and in another small cell NHL were diagnosed by the FNAC and immunophenotype suggested MCL that was confirmed by the pathohistology as shown in Table 3. Combined, FNAC and FC improved sensitivity, positive predictive value, negative predictive value and diagnostic accuracy (sensitivity was 79.1%, specificity 85.7% and diagnostic accuracy 80%) as shown in Table 2.

Discussion and Conclusion

Our research showed that FNA and FC are complementary diagnostic procedures which play important role in the process of diagnosing malignant lymphomas. There was no case pathohistologically diagnosed as lymphoma that was diagnosed benign by the FNAC. Nevertheless, there was one case pathohistologically diagnosed as benign that was stated by the FNAC as suspicious of NHL. When analyzing accuracy of the FNAC according to the suspicion of lymphoma or NHL and the differential diagnosis lymphoma, sensitivity was 97.7%, specific-

TABLE 5
COMPARISON OF THE FINE-NEEDLE ASPIRATION CYTOLOGY (FNAC) AND FLOW CITOMETRY (FC) DIAGNOSIS

	FC diagnosis							
FNAC diagnosis	B-NHL	CLL/SLL	Chronic lymphoproliferative disease	T-NHL	CD4+CD8-	Polyclonal	Inadequate sample	Total
CLL /SLL	1							1
FCL	5							5
MCL	1							1
SMZL			1					1
Large B-cell NHL	12							12
LBL				1				1
ALCL					1			1
High grade NHL	1							1
Low grade NHL	2							2
Small cell NHL	2							2
NHL	2						1	3
Chronic lymphoproliferative disease		1						1
Suspicious NHL				1				1
Suspicious lymphoma					1			1
Malignant tumor, differential diagnosis lymphoma						1		1
HL					1	2		3
Malignant tumor							1	1
Benign						6		6
Total	26	1	1	2	3	9	2	44

HL – Hodgkin's lymphoma, B-NHL – B-cell non Hodgkin's Lymphoma, T-NHL – T-cell non-Hodgkin's lymphoma, CD4+CD8- – predominance of CD4 positive lymphocytes, CLL/SLL – B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma, FCL – Follicular lymphoma, MCL – Mantle cell lymphoma, ALL – acute lymphoblastic leukemia, LBL – lymphoblastic lymphoma, ALCL – Anaplastic large cell lymphoma, NHL – non-Hodgkin's lymphoma, FNAC – fine needle aspiration cytology, FC – flow cytometry, SMZL – Splenic marginal zone B-cell lymphoma

ity 85.7% and the diagnostic accuracy was 96%. When analyzing accuracy of the FNAC according to the subclassification of lymphoma, sensitivity was 74.4%, specificity 85.7% and the diagnostic accuracy 76%. Combined, FNAC and FC improved sensitivity, positive predictive value, negative predictive value and the diagnostic accuracy. Sensitivity was 79.1% and diagnostic accuracy 80% what is shown in Table 2.

In the case of FCL diagnosed as chronic lymphoproliferative disease, pathohistological was graded I/II. In the case of the DLBCL that the FNAC diagnosed as FCL it was stated that it was FCL grade II/III. In one case the diagnose of the DLBCL was not specified and in one case it was incorrectly diagnosed as small cell NHL. Pathohistologically diagnosed high grade lymphoma which was stated by the FNAC as low grade, was interesting case because bone marrow biopsy (pathohistologically examined) showed infiltration with low grade lymphoma, suggesting that it was a case of disease transformation. In this case FNA failed to aspirate from the place of transformation. Two similar cases described Nicol et al. in their research[14]. Immunohystochemistry is an essential procedure for separating ALCL from metastatic carcinoma, melanoma and Hodgkin's disease[8]. In the case of HL diagnosed as ALCL by the FNAC, immunocytochemistry failed and it was not diagnostic, so mistake was highly possible. HL was correctly diagnosed by the FNAC in 6 out of 8 (75%). Our result is lower than Jiménez-Heffernan et al.[16]. Their research was focused on the value of the FNAC in the initial diagnosis of HL. Sensitivity of their series was 82.4% (86.1% excluding non representative cases). In the research of Chhieng et al. 60.7% biopsy-proven HLs were correctly diagnosed or strongly suspected based on the cytological findings[17]. Their study included 67.4% cases from primary tumors and 32.6% were recurrent lesions. The only benign case which was stated as suspicious of lymphoma was at first pathohistologically diagnosed as possible B-cell lymphoma of MALT type, but that diagnosis was excluded by further analysis (immunohistochemistry and PCR). Sensitivity of the FNAC in the diagnosis of lymphoma (including suspicion of lymphoma or NHL and differential diagnosis lymphoma), was 97.7%. The result is similar to one of Stewart et al. whose study showed sensitivity of 91%[18]. However in their study 27% of the patients with recurrent lymphoma were accounted.

In the comparison of the pathohistological and FC diagnoses we found 2 out of 44 samples (4.5%) inadequate for analysis. Inadequate and suspicious case rates in the literature range from 4% to 30%[6,7,14,15,19,20]. Therefore our findings are closer to lower part of the range. Both of the inadequate samples were those pathohistologically diagnosed as DLBCLs (FNAC diagnoses were NHL and malignant tumor). The large neoplastic cells are often disrupted during FNA and processing for flow cytometry and then are usually markedly reduced or absent, in comparison with their frequency on cytologic preparations[21]. In the one case of ALCL (diagnosed as malignant tumor, differential diagnosis lymphoma) FC detected polyclonal population of B lymphocytes in that sample. Regarding to only one case of FC performed on ALCL samples, it is not possible to conclude about its usefulness for those cases. Five out of eight samples diagnosed as HL by the pathohistology were analyzed by the FC. FC is not adequate method for diagnosing Hodgkin's lymphoma because of the relative lack of neoplastic cells in relation to background cells[8]. In our case, in three out of five samples background cells showed predominance of CD4+ lymphocytes and two samples presented polyclonal population of B lymphocytes. As stated earlier, FC is not adequate method for diagnosing Hodgkin's lymphoma. However, when lack of monoclonal B lymphocytes is found by FC in samples stated as suspicious of lymphoma by FNAC, HL should be considered as differential diagnosis along with benign result. In one case of the benign result (stated as suspicious of NHL) FC found predominance of T lymphocytes and suggested possibility of T-cell lymphoma. Pathohistological analysis found diffuse proliferation of small T lymphocytes (also suggested possibility of B-cell lymphoma of MALT type) in that sample but by further analysis the diagnosis of lymphoma was excluded.

Dong et al. evaluated a series of 139 confirmed lymphomas diagnosed using the FNAC with and without the FC immunophenotyping analysis, including 60% cases in which the primary diagnosis was represented. They evaluated the ability to positively diagnose lymphoma and the frequency of cases that were accurately subclassified[7]. Cytomorphology coupled with FCM provided a definitive diagnosis of lymphoma in 77% of the cases (82% of NHL). In their study the accuracy rate was 67% without FC suggesting great importance of FC in subclassification of lymphomas. In the study of Meda et al. a definitive diagnosis of NHL was made in 76.7% (158/206) of the patients with lymphoma on the basis of combined FNA and FC, including 72.3 (86/119) of primary lymphomas and 83% (72/87) of the previously diagnosed or recurrent lymphomas[6]. Young et al. reported their experience with the FNAC and the FC[13]. In their study definitive diagnosis of NHL was made in 80% of their lymphoma cases on the basis of the FNA and FC, including 62% of primary lymphomas and 89% of previously diagnosed or recurrent lymphomas (with no need for histological sampling).

University Hospital Dubrava is rare case in Croatia where FNAC and FC are situated at the same department (Department of Clinical Cytology and Cytometry). Considering clinical presentation and cytological findings a cytologist indicates FC analysis with the purpose of rationalizing use of monoclonal antibodies. It is important to state FNAC and FC diagnoses are independent. There is no influence of cytologist at FC diagnosis and also biologist performing FC at FNAC result. This kind of organization results with faster and more efficient sample management what is important for fast and accurate diagnosis. In that way clinicians are quickly provided with the required information.

To summarize, in this study we have shown that the FNAC and the FC are complementary methods which play an important role in the process of diagnosing lymphoma. We have shown that these techniques can distinguish benign lymphadenopaties from lymphomas and also subclassify lymphomas and quickly provide clinicians with that information.

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TOČNOST ASPIRACIJSKE CITOLOGIJE I PROTOČNE CITOMETRIJE U PROCJENI NODALNIH I EKSTRANODALIH SIJELA KOD PACIJENATA SA SUMNJOM NA LIMFOM

SAŽETAK

Limfomi se danas dijagnosticiraju kombinacijom morfologije, imunofenotipa, genetskih značajki i kliničke slike, tako da se uz samu citomorfološku analizu u procesu dijagnosticiranja koriste i pomoćne tehnike kao što su citokemija, imunocitokemija, molekularna dijagnostika i protočna citometrija. Cilj našeg istraživanja bio je utvrditi dijagnostičku povezanost aspiracijske citologije i protočne citometrije te procijeniti mogućnost tih metoda u dijagnosticiranju i subklasifikaciji limfoma, pri čemu je patohistologija služila kao zlatni standard. Ova studija je retrospektivni pregled nalaza pacijenata obrađenih u Kliničkoj bolnici Dubrava zbog sumnje na limfom. Nakon analize, 50 pacijenata je zadovoljilo kriterije uključivanja u ovu studiju (dijagnoza postavljena na temelju aspiracijske citologije s ili bez protočne citometrije te patohistološka dijagnoza). Kod određivanja točnosti citologije u odnosu na postavljenu dijagnozu limfoma, non Hodgkinovog limfoma ili sumnje na limfom, osjetljivost je bila 97,7%, specifičnost 85,7% i dijagnostička točnost 96%. Kod određivanja točnosti citologije s obzirom na subklasifikaciju limfoma osjetljivost je bila 74,4%, specifičnost 85,7% i dijagnostička točnost 76%. Kombinacija citologije s protočnom citometrijom povisila je senzitivnost, pozitivnu prediktivnu vrijednost, negativnu prediktivnu vrijednost i dijagnostičku točnost. Senzitivnost je tada iznosila 79,1%, a dijagnostička točnost 80%. Našim istraživanjem pokazali smo da ove metode dobro razlikuju benigne limfadenopatije od limfoma, a isto tako mogu i subklasificirati limfome te relativno brzo pružiti potrebnu informaciju kliničaru.