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Peripheral Lymphadenopathies in Childhood: Experience at a Pediatric Oncology Department in Turkey

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Abstract

Palpable lymph nodes are very common physical examination findings in childhood, and sometimes it can be challenging to say if it is benign or malignant.This retrospective study evaluated 157 children admitted to an oncology department because of lymphadenopathy and aimed to determine the clinical, laboratory, and epidemiologic data valuable for differential diagnosis.One hundred fifty-two cases were analyzed, which were defined as either malignant or benign by the etiology. The benign cases were also defined to three groups as ‘viral lymphadenopathy’, ‘bacterial lymphadenopathy’, and ‘other reactive lymphadenopathy’.A specific cause for lymphadenopathy was documented in 61 (40,1%) cases. Of 152 cases, benign causes were detected in 133 (87,5%), and malignant causes were detected in 19 (12,5%) cases. The most frequent cause in the benign group was reactive hyperplasia (59,8%) and in the malignant group was lymphoma (7,3%). A biopsy was performed from 19 of the cases for diagnosis. Malign causes were detected in 12 (58%), and benign causes were detected in the remaining 7 (42%). In terms of differential diagnosis, some symptoms, physical findings, and laboratory tests showed meaningful differences between the case groupsThe following findings were determined as being important to alert physicians about the probability of a malignant disorder: location of lymphadenopathy, number of associated systemic symptoms, size of lymph node, abnormal laboratory findings, abnormal chest X-ray.

Keywords: Childhood, etiology, lymph node, lymphoma, peripheral lymphadenopathy

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Introduction

Peripheral lymphadenopathy (LAP) is a frequently encountered physical finding in childhood. A palpable lymph node on physical examination poses a distressing situation for both the parents and the physician following the child. This study aims to determine the epidemiologic properties, clinical and laboratory findings, and etiologic distribution of patients with peripheral lymphadenopathy. These findings are featured in different case groups.

Highlight

- Lymphadenopathy in children is common and in the majority of cases are benign.
- It should be a sign of a serious disease.
- An appropriate history and examination, careful observation and appropriate investigations should help to decide which children require a biopsy or further treatment.

Materials and Methods

Informed consent information was obtained from all parents of participating childen in the study and the research protocols were approved by the Ethics Committee at Ankara University (Approval date/number: 08 June 2015/10-419-15). The cases that applied to the departments of pediatric oncology of the Medical Faculty of Ankara University between January 2013 and January 2015 were evaluated. The epidemiologic properties, clinical and laboratory findings of the cases were assessed retrospectively. The cases were defined as either malignant or benign by the etiology. The benign cases were also defined to three groups as 'viral lymphadenopathy', 'bacterial lymphadenopathy' and 'other reactive lymphadenopathiy'. Patients who had upper respiratory tract infection findings and had no antibiotic response or had a viral infection diagnose with serological tests were included in the viral lymphadenopathy case group. Patients who had an antibiotic response had group A β-hemolytic streptococcus (GAS) infection and had lymphadenitis according to the biopsy results in the bacterial lymphadenopathy case group. Patients with no systemic symptoms except for lymphadenopathy and had no antibiotic response were diagnosed with biopsy as reactive hyperplasias. They were included in the other reactive lymphadenopathy case group.

Lymph node enlargements were classified according to the size, extension, and duration of the LAP according to the following criteria:

- Size of lymp node: <1 cm, 1-3 cm, >3 cm
- Extention of the lymph nodes: localized LAP (a single or multiple but adjacent lymph node involvement) and generalized LAP (two or more lymph node involvement without neighborliness)
- Duration of lymph node enlargement: acute (<4 weeks) and chronic (≥4 weeks)

Patients who had a lymph node biopsy were also classified into the early biopsy group (went to biopsy within the first two weeks after its presentation) and late biopsy group (after the first two weeks of presentation). LAP features like size, location, extension, duration, mobility were evaluated. Other physical examinations and laboratory findings, radiological tests, and biopsy results were compared between the case groups. The data were analyzed by using the Statistical Package fort he Social Sciences Software Package (SPSS) (version 11.5). Comparisons between groups were made using appropriate statistical methods (Pearson chi-square and Student's T-test). A p-value of less than 0,05 was considered significant.

Results

Epidemiologic and clinical data of 157 cases were evaluated. Lymphadenopathy-like mass was detected in 5 cases after the examination, and they were excluded from the study, which was a dermoid cyst, cystic hygroma, inguinal hernia, focal fat necrosis, and fibroma. The data of the remaining 152 cases were analyzed. The cases were defined as either malignant or benign by the etiology. The benign cases were also defined to three groups as 'viral lymphadenopathy', 'bacterial lymphadenopathy', and 'other reactive lymphadenopathy'. The classification of the case groups according to the definitive diagnosis is shown in **Table 1**.

Table 1.
The classification of the case groups according to the definitive diagnosis

Biopsy results	n	%
Granulamatous infection	2	10.5
Chronic lymphadenitis	1	5.2
Kikuchi disease	1	5.2
Reaktive hyperplasia	2	10.5
Florid follicular hyperplasia	1	5.2
Salivary gland	1	5.3
Hodgkin lympoma	8	42.3
Non Hodgkin lymphoma	3	15.7
Total	19	100.0

Of 152 cases, when 5 cases admitted with a lymphadenopathy-like mass were excluded, 133 cases (87.5%) were diagnosed with lymphadenopathy due to benign etiology. Malignant causes were detected in 19 cases (12.5%). No specific etiology was found in 91 patients (59.8%), and specific etiology was found in 61 (40.1%). Of all groups, 58 (38,2%) children were female, and 94 (62,8%) children were male. The male gender was dominant in both malignant and benign subgroups. The average age of the patients was 6,48±4,39 years; it was 8,85±5,89 years in the malignant group and 6,13±4,05 years in the benign group. The benign subgroups' average ages were similar to each other. There is no malignant lymphadenopathy between 0-2 years old, and for four groups, most cases were between 2-12 years old. 12-18 years old cases dominated malignant lymphadenopathies. Detailed information is given in **Table 2**.

Table 2.
Gender and age range of case groups

Physical examination/ laboratory findings	Viral	Bacterial	Other	Benign	Malignant	Total	p*	p**
	n (54) %	n(40) %	n (39) %	n (133) %	n (19) %	n (152) %		
Dispnea	1 1.9	0 0.0	0 0.0	1 0.8	4 21.1	5 3.3	<0.01	<0.01
Hepatomegaly	8 14.8	5 12.5	1 2.6	14 10.5	10 52.6	24 15.8	<0.01	<0.01
Splenomegaly	7 13.0	2 5.0	0 0.0	9 6.8	9 47.4	18 11.8	<0.01	<0.01
Anemia	2 3.7	3 7.5	2 5.1	7 5.3	13 68.4	20 13.2	<0.01	<0.01
Leukopenia	3 5.6	2 5.0	2 5.1	7 5.3	3 15.8	10 6.6	<0.01	0.003
Leukositosis	6 11.1	1 2.5	1 2.6	8 6.0	6 31.6	14 9.2	<0.01	0.003
Trombositopenia	0 0.0	1 2.5	0 0.0	1 0.8	6 31.6	7 4.6	<0.01	<0.01
Trombositosis	2 3.7	3 7.5	1 2.6	6 4.5	3 15.8	9 5.9	<0.01	<0.01
Atipic +virocit + downey	6 11.1	5 12.5	6 15.3	17 12.7	0 0.0	17 11.1	<0.01	<0.01
Blast	0 0.0	0 0.0	0 0.0	0 0.0	9 47.4	9 5.9	<0.01	<0.01
ESR> 20 mm/sa	19 35.2	14 35.0	9 23.1	42 31.6	16 84.2	58 38.2	<0.01	<0.01
CRP> 3 mg/L	15 27.8	10 25.0	7 18.4	32 24.2	14 73.7	46 30.5	<0.01	<0.01
ALT >41 IU/L	6 11.1	2 5.1	2 5.1	10 7.6	0 0.0	10 6.6	0.214	0.336
AST >45 IU/L	9 16.7	4 10.0	5 12.8	18 13.5	4 21.1	22 14.5	0.384	0.658
LDH> 200 IU/L	39 72.2	21 52.5	17 43.6	77 57.9	16 84.2	93 61.2	0.028	0.004

p*: Evaluation of benign-malignant lymphadenopathies
p**: Evaluation of viral-bacterial-other reactive hyperplasia-malign lymphadenopathies

Some systemic symptoms, pathologic physical examination findings, and characteristics of lymphadenopathies are given in **Table 3**. Most of the patients (82.8%) have to swell in the neck. The acute process was typical in viral cases; bacterial cases and other reactive groups were mostly chronic. No significant difference was detected in terms of duration between malignant and benign cases. Seventy-five (49.3%) patients had upper respiratory tract infection, and it was the most common examination finding for all groups, followed by fever. Fever ($p<0.01$), weight loss ($p<0,05$), skin eruption ($p<0.01$), leg pain ($p<0.01$), abdominal swelling ($p<0.01$) were statistically significant findings as well as in comparing the four groups and the comparison of the benign-malignant groups. The presence of systemic symptoms ($p<0.01$), upper respiratory tract infection ($p<0.01$) were significant findings only in benign and malignant comparison. Also, the malign cases had an increasing number of symptoms.

Of 152 cases, 47 (%30.9) of them had recurrent infection stories, 34 (22.4%) of them had a chronic disease, and 3 (2%) patients had a vaccination story. Chronic diseases included asthma (9), adenoid hypertrophy (12), hypochondroplasia (1), Kawasaki disease (1), Hashimoto thyroiditis (4), familial mediterranean fever (1), psoriasis (1), chronic kidney failure (1), ataxia-telangiectasia (1), and allergic rhinitis (2). Bilateral cervical lymphadenopathy (59,5%) was the most frequent generalized lymphadenopathy type. Cervical+inguinale (20.6%) and cervical+axillar+inguinale (7.6%) followed that. 101 (66.4%) patients had cervical lymphadenopathy. This was the most common area for all case groups. Of 5 supraclavicular nodes, 4 of them were malignant. The mean diameter of the malign lymph nodes was 3.29±2.18 cm (cervical: 3.3±2.2 cm, axillar: 2.2±2.1 cm, inguinal: 0.6±0.3). In the benign group, the mean diameter of the lymph nodes was 1.63±1.07 cm (cervical: 1.6±1.02 cm, axillar: 1.1±1.1 cm, inguinal: 0.5±0.3 cm). Malign lymph nodes were bigger than benign lymph nodes. 47.4% of the malignant lymph nodes were fixed, and 95.5% of the benign lymph nodes were mobile and this was statistically significant ($p<0.01$).

Table 3.
Some systemic symptoms and characteristics of lymphadenopaties

		Viral	Bacterial	Other	Benign	Malignant	Total	p*	p**
		n (54) %	n (40) %	n (39) %	n (133) %	n (19) %	n (152) %		
Duration	Acute	32 59.3	15 37.5	16 41	63 47.3	9 47.4	72 47.4	0.158	0.154
	Chronic	22 40.7	25 62.5	23 59.0	70 52.7	10 52.6	80 52.6		
Systemic symptoms	Have a symptom	42 77.8	28 70.0	7 17.9	77 57.9	15 78.9	92 60.5	0.079	<0.01
	Fever	12 22.2	10 25.0	1 2.6	23 17.3	10 52.6	33 21.7	<0.01	<0.01
	Weight loss	2 3.7	4 10.0	2 5.1	8 6	5 26.3	13 8.6	0.003	0.019
	Night sweat	1 1.9	4 10.0	3 7.7	8 6.0	4 21.1	12 7.9	0.023	0.058
	Flu symptoms	40 74.0	23 57.5	1 2.5	64 48.1	11 57.9	75 49.3	0.425	<0.01
	Itching	3 5.6	0 0.0	3 7.7	6 4.5	0 0.0	6 3.9	0.345	0.237
	Skin eruption	3 5.6	0 0.0	0 0.0	3 2.3	6 31.6	9 5.9	<0.01	<0.01
	Tooth decay	8 14.8	8 20.0	5 12.8	21 15.8	1 5.3	22 14.5	0.223	0.497
	Leg pain	0 0.0	0 0.0	0 0.0	0 0.0	2 10.5	2 1.3	<0.01	0.003
	Abdominal swelling	0 0.0	0 0.0	0 0.0	0 0.0	2 10.5	2 1.3	<0.01	0.003
Number of symptoms	No symptom	12 22.2	12 30.0	32 82.1	56 42.1	4 21.1	60 39.5	<0.01	<0.01
	+1 symptom	28 51.9	19 47.5	4 10.3	51 38.3	5 26.3	56 36.8		
	+2 symptom	11 20.4	7 17.5	1 2.6	19 14.3	0 0.0	19 12.5		
	+3 symptom	3 5.6	0 0.0	2 5.1	5 3.8	5 26.3	10 6.6		
	>3 symptom	0 0.0	2 5.0	0 0.0	5 3.8	5 26.3	10 6.6		
Extension	Localizated	6 11.1	4 10	8 20.5	17 12.8	4 21.1	22 14.4	0.584	0.354
	Generalizated	48 88.9	36 90.0	31 79.5	115 86.5	15 78.9	130 85.5		
Localization	Preairucular	0 0.0	0 0.0	1 2.6	1 0.8	0 0.0	1 0.7	0.705	0.405
	Postairicular	0 0.0	0 0.0	3 7.7	3 2.3	1 5.3	4 2.6	0.444	0.073
	Submental	1 1.9	0 0.0	1 2.6	2 1.5	0 0.0	2 1.3	0.591	0.712
	Submandibular	34 63.0	27 67.5	15 38.5	76 57.1	4 21.1	80 52.6	0.030	0.010
	Cervical	39 72.2	25 62.5	23 59.0	87 65.4	14 73.7	101 66.4	0.475	0.473
	Supraclavicular	0 0.0	0 0.0	1 2.6	1 0.8	4 21.1	5 3.3	<0.01	<0.01
	Axillar	9 16.7	3 7.5	7 17.9	19 14.3	6 31.6	25 16.4	0.057	0.135
	İnguinal	14 25.9	8 20.0	14 35.9	36 27.1	7 36.8	43 28.3	0.376	0.347
Size	<1 cm	9 16.7	3 7.5	12 30.8	24 18	6 31.6	30 19.7	<0.01	<0.01
	1-3 cm	41 75.9	35 87.5	26 66.7	102 76.7	2 10.5	104 68.4		
	>3 cm	4 7.4	2 5.0	1 2.6	7 5.3	11 57.9	18 11.8		
Mobility	Fixed	1 1.9	3 7.7	2 5.1	6 4.5	9 47.4	15 9.9	<0.01	<0.01
	Mobile	53 98.1	37 92.5	37 94.9	127 95.5	10 52.6	137 90.1		

p*: Evaluation of benign-malignant lymphadenopathies
p**: Evaluation of viral-bacterial-other reactive hyperplasia-malign lymphadenopathies

The diagnostic tests and abnormal physical examination findings are given in **Table 4**, comparing data between the case groups. Dyspnea, hepatomegaly, splenomegaly, anemia, leukopenia, leukocytosis, thrombocytopenia, thrombosis, atypical lymphocytes, virocytes, Downey cells or blasts in peripheric blood smear, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were significant findings as well as in comparing the four groups and the comparison of the benign-malignant groups. Anemia (13.2%) was the most common abnormal CBC result. Not only anemia but also other pathological CBC results and elevated ESR, CRP, LDH levels were significant in malignant cases. Elevated LDH levels were also significant in viral LAPs. Also, elevated lactate dehydrogenase (LDH) enzyme level was significant at the benign and malignant comparison. Elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels have seen mostly malignant and viral lymphadenopathies. We performed an excisional biopsy to 19 (12.5%) patients; 15 (78.9%) of them were early biopsy. Nine (81.8%) cases who underwent early biopsy had been diagnosed as having a malignant disorder. Histopathologic examination showed 11 lymph nodes were lymphoma, 2 of them granulomatous infection, one chronic lymphadenitis, 1 Kikuchi disease, two nonspecific reactive hyperplasias florid follicular hyperplasia, one salivary gland. Bone marrow aspiration was performed in 28 cases, and 35.7% of them was diagnosed as a malignant disorder. All cases had a chest X-ray; 6 (3.9%) patients had mediastinal adenopathy, and 5 of those patients were diagnosed with malignancy. 58 (39.2%) had abdominal ultrasonography (USG); it resulted as normal (51.7%), splenomegaly (10.3%), hepatomegaly (8.6%), hepatosplenomegaly (8.6%), mesenteric lymphadenitis (13.8%), hypoechoic lesion in spleen (3.4%), hypoechoic lesion in liver (1.7%). Three patients who had a hypoechoic lesion in the spleen or liver received the diagnosis of malignant. Superficial USG was performed in 101 (71.1%) patients; it resulted as reactive lymphadenopathy (92%), suspicious for malignancy (4%), granulomatous infection (1%), lymphadenitis (2%), solid mass (1%). Of 4 suspicious for malignancy cases according to USG, 2 of them were Hodgkin lymphoma, one patient had reactive hyperplasia, and one patient had a GAS infection. Ectopic sinüs was found in two patients, and a colloid cyst of the thyroid was found in two patients in addition to lymphadenopathy.

Table 4.
Physical examination and laboratory findings

		Diagnosis	n	%
Malignant		ALL	7	4.6
		Hodgkin lymphoma	8	5.3
		nonHodgkin lymphoma	3	2.0
		AML	1	0.7
		Group total	**19**	**12.5**
Benign	Viral lymphadenopaties	Viral reactive hyperplasia	30	19.7
		EBV	18	11.8
		CMV	6	3.9
		Group total	**54**	**35.5**
	Bacterial lymphadenopaties	Bacterial reactive hyperplasia	25	16.4
		GAS	6	3.9
		Acute lymphadenitis	6	3.9
		Chronic lymphadenitis	1	0.7
		Granulomatous lymphadenitis	2	1.3
		Group total	**40**	**26.2**
	Other reactive lymphadenopaties	Nonspesific reactive hyperplasia	35	23.0
		Florid follicular hyperplasia	1	0.7
		Kikuchi disease	1	0.7
		Toxoplasma infection	1	0.7
		Scabies	1	0.7
		Group total	39	25.8
		Total	**152**	**100**

Table 5.
Biopsy results

		Viral	Bacterial	Other	Benign	Malignant	Total	p*	p**
		n (54) %	n (40) %	n (39) %	n (133) %	n (19) %	n (152) %		
Gender	Male	16 39.6	15 37.5	19 48.7	50 37.6	8 42.1	58 38.2	0.444	0.303
	Female	38 70.4	25 62.5	20 51.5	83 62.4	11 57.9	94 61.8		
Age	0-2 years	6 11.1	5 12.5	9 23.1	20 15	0 0	50 32.9	0.010	0.040
	2-12 years	44 81.4	30 75	26 66.7	100 75.2	13 68.4	64 42.1		
	12-18 years	4 7.4	5 12.5	4 10.3	13 9.8	6 31.6	38 25.0		

p*:Evaluation of benign-malignant lymphadenopaties
p**: Evaluation of viral-bacterial-other reactive hyperplasia-malign lymphadenopaties

Discussion

Palpable lymph nodes are common physical examination findings in childhood. That usually causes anxiety for parents. Finding and understanding the cause of the lymphadenopathy is also important for clinicians. A good anamnesis and physical examination occur the basis of the diagnosis. The laboratory tests and radiological imaging methods can be used if necessary.

In our study, lymphadenopathy like mass was detected 5 cases after the examination; these were dermoid cyst, cystic hygroma, inguinal hernia, focal fat necrosis, and fibroma, and there is no dominancy between the masses. Yarıs *et al.* studied 126 lymphadenopathy cases, and 28 (22%) of them were lymphadenopathy like mass, and lymphangioma was the most common one(21.4%).[1] Taiseer evaluated 2063 children with neck masses, and 252 (12%) of them were congenital neck masses, which were mostly thyroglossal cysts (53%).[2] Finally, the data of the remaining 152 cases were analyzed. 87.5% were benign, and 12.5% were malignant LAPs. In 61 patients (40.1%), we found a specific etiology, 19 cases were malignant disorder, 41 cases had infectious causes, and one patient was Kikuchi disease. The most frequently seen malignant disease was Hodgkin lymphoma (5.3%). If there is no inflammation story, negative laboratory tests, progressive minimalization in 6 months period, it is nonspecific reactive hyperplasia.[3] Peripheral lymph nodes were palpable 44% of healthy children and 64% of sick children.[4] In Kumral's study[5] only 46.5% of cases had a specific etiology, which was 39% in Oguz's study[6] Empiric antibiotic therapy and limited viral tests may be causing that situation; moreover, clinicopathologic supplementation does not need for the diagnosis.[7]

All malignant cases referenced or consulted; none of them applied itself. In the literature, the malignancy rates are significantly low in family practice, the first step.[8,9] In oncology clinics, malignancy rates are higher. In Kumral's study, 30% of the cases had malign disorder.[5] In Lake's study[10] which was a biopsy serial, 17% of cases were malignant. In this study, 12.5% of cases were malignant.

In this study, the average age was higher in the malign group, and these findings were similar to the other studies.[1,6,11,12] 0-2 years, the other reactive lymphadenopathies (23.1%) was the most common case group, while malignant LAPs were never seen in this age range.

The duration of the LAP was similar to benign and malignant cases. The acute process was typical in viral cases; bacterial and other reactive groups were chronic mostly. According to most studies, malignant LAPs were chronic,[5,6] although Karaman found malignant LAPs were acute and benign LAPs were chronic mostly.[11]

Generalized LAP was more frequently encountered in all case groups. Extension of lymph nodes did not help us evaluating whether it was benign or malignant LAP. Evaluating the localization of lymph nodes, cervical nodes (66.4%) were the most frequently involved localization for malignant and benign subgroups. Axillar LAP was more common in malignant nodes (31.6%) than benign nodes (14.3%). 80% of the supraclavicular nodes were malignant in our study. According to the literature, epitrochlear, supraclavicular, and popliteal lymph node palpation is not common in any age, and supraclavicular nodes are abnormal.[13] Supraclavicular localization of the lymph node is always warranted for physicians.[14] Furthermore, the posterior cervical triangle[15] and postauricular area in older ages[4] are important for malignancy.

The size of the node was not diagnostic when it was between 1 and 3 cm. Nodes that were smaller than 1 cm were common in other reactive LAPs, which was a benign subgroup (30.8%) and malignant LAPs (31.6%). 57.9% of the malignant LAPs were bigger than 3 cm. These findings were compatible with relevant studies.[1,5,6] Most of the benign LAPs were mobile (95.5%), and most of the malignant LAPs were fixed (47.4%); this was similar to other studies.

Upper respiratory tract infection symptoms (49.3%) were more frequently encountered in all case groups. Although upper respiratory tract infection was more significant in viral LAPs, fever and B symptoms were common in malignant LAPs. Malignancy was getting significant when the number of symptoms increased. According to the studies, fever is the most detected symptom accompanying the LAP.[5,6,16] In Oguz's study[6] night sweats and weight loss were seen mostly in malignant LAP and fever in benign LAP. However, in Kumral's study[5] weight loss was seen mostly in malignant LAP; fever and night sweat in benign LAP.

Dyspnea, hepatomegaly, splenomegaly were significant examination findings in terms of malignancy. Hepatomegaly and splenomegaly are also significant in viral LAP. Abnormalities in chest X-ray and abdominal ultrasonography were suggestive of a malignant disorder. In Knight's study[14] which lymphadenopathies researched, 56% of patients with hepatomegaly and 77.7% of them with an abnormal chest X-ray had a malign disorder. According to Saltztein[17] big mediastinal LAPs are often caused by malignancy or granulomatous diseases. In Jing Fu Wang's study[18] 13 of the 168 patients with LAP (7,7%) had an abnormal chest X-ray.

Ultrasonography is a beneficial method for screening palpable peripheral lymph nodes. It is easily accessible, cheap, has no radiation, needs no sedation, and does not use contrast. It gives many ideas about solid-cystic separation and size, nature, replacement of the lymph node. Also, doppler USG gives us information about the vascularization of the nodes.[19] Niedzielska evaluated 87 patients with LAP and diagnosed reactive hyperplasia 57.5% of them with USG.[16] Ingolfsdottir evaluated 18 of 43 lymphadenopathies by USG, and five suspected malignancy; however, 4 of these patients gave false-positive results. Besides, USG gave false results in 2 of 3 patients who were diagnosed as malignant histologically. This study argues that ultrasonography is not a reliable method in the benign-malignant differentiation of lymphadenopathy.[20] In Fu's study[21] USG was a lodestar method distinction between malignant and benign LAPs. Lymph node structure, central hiler vascularity, absence of the hilum, peripheral vascularization were significant

markers for malign LAPs. In the literature, we can conclude that ultrasonography, in general, is a useful method that helps to get an idea about the structure of lymphadenopathy, is frequently used by physicians and can be used in diagnosis and follow-up; however, it should be kept in mind that it can give false positive and negative results in distinguishing malignancy. In our study, the vast majority of patients who underwent USG were reported as reactive hyperplasia, which was higher than the literature. The agreement between ultrasonographic diagnosis and histopathological diagnosis was similar to the general literature.

Excisional biopsy is the gold standard in lymphadenopathies with suspected malignancy. The biopsy results show that a good history, physical examination, and laboratory tests, and if necessary, to decide on a biopsy after giving antibiotics seems to be the best decision. In Koçak's study[22] 18 (24%) of 74 patients with lymphadenopathy had lymph node biopsy; 11 (61%) of these cases were diagnosed as malignant, and 7 (39%) were benign. The most common malignant cause was non-Hodgkin's lymphoma, and the most common benign cause was reactive lymphoid hyperplasia. In Knight's study,[14] 239 children with peripheral lymphadenopathy were biopsied; Reactive lymph node hyperplasia in 52% of cases, a granulomatous disease in 32%, malignant disease in 13%, chronic lymphadenitis in 3%. We found a malignant disease in more than half of our patients, whom we followed within the framework of a similar algorithm and made a biopsy decision. However, reactive hyperplasia, which could not be specifically diagnosed after biopsy, was present in our study and the literature.[10,15,18,24] Our study was compatible with the literature to detect the most benign causes in etiology and the most common reactive lymph node hyperplasia among these benign causes.[1,5,6,24,25]

Immune suppression and immune deficiencies are communicated with malignancy in some conditions. Especially EBV is a human virus that is a known relationship between malignancy.[26] One patient was ataxia-telangiectasia, and the other had an EBV infection, which was diagnosed as non-Hodgkin lymphoma later.

In cases presenting with peripheral lymphadenopathy, after a history and physical examination, it should be considered whether lymphadenopathy is a symptom of severe disease. To determine the etiology, firstly, non-invasive tests should be selected after a good history and physical examination, complete blood count and peripheral blood smear should be the tests that should be performed in the first plan. If the patient is considered a nonspecific infection, the patient should be treated with 7-10 days of empirical antibiotic therapy. If a specific infection is considered first, chest radiography, serological tests, or specific diagnostic methods of the disease should be used in addition to the above tests. If this diagnosis and post-treatment do not make a specific diagnosis, if the size of lymphadenopathy does not decrease or shrink or grow, lymph node biopsy should be performed to make a definitive diagnosis without wasting time.

Ethics Committee Approval: The Ethical Committee of Ankara University, approved this study (date: 08.06.2015, number: 10-419-15).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Conflict of Interest: The authors have no conflict of interest to declare.

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