CLINICAL STUDY

THE ROLE OF NEUTROPHIL / LYMPHOCYTE AND PLATELET / LYMPHOCYTE RATES IN CHILDREN WITH CERVICAL REACTIVE LYMPHADENOPATHY

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SUMMARY

Objective: We aimed to evaluate whether Neutrophil/Lymphocyte Ratio (NLR) and Platelet/Lymphocyte Ratio (NLR) values can be used in the follow-up of children with cervical reactive lymphadenaopathy.

Methods: Patients were divided into two subgroups according to the reduction of lymphadenaopathy ; regressive and non-regressive groups. Then hemogram parameters, NLR and PLR were compared between study subgroups and control group.

Results: There was no significant difference between the patient and the control groups in terms of NLR values, but we found a statistically significant difference between the no-regressive group and regressive, control groups. There was no significant difference in PLR and other hemogram values between the both patient subgroups and the control group.

Conclusion: NLR value of a pediatric patient with reactive lap on the neck may give an idea to the clinician about the patient's close follow-up or possible viral etiology. The NLR value may also be useful for the treatment of this patients by guiding the disease to be resistant.

Keywords: Child, neck, reactive lympadenopathy

SERVİKAL REAKTİF LENFADENOPATİLİ ÇOCUKLARDA NÖTROFİL/LENFOSİT VE PLATELET/LENFOSİT ORANLARININ ROLÜ

ÖZET

Amaç: Servikal reaktif lenfadenopati tanılı çocukların izleminde Nötrofil / Lenfosit Oranı (NLR) ve Trombosit / Lenfosit Oranı (NLR) değerlerinin kullanılıp kullanılamayacağını değerlendirmeyi amaçladık.

Yöntem: Hastalar kontrol ve çalışma grubu olmak üzere ikiye ayrıldı. Çalışma grubu ise lenfadenopati boyutlarındaki azalmaya göre iki alt gruba ayrıldı; gerileme olan ve gerileme olmayanlar. Daha sonra hemogram parametreleri, NLR ve PLR açısından çalışma alt grupları ve kontrol grubu karşılaştırıldı.

Bulgular: NLR değerleri açısından çalışma grubu ile kontrol grubu arasında anlamlı fark yok iken gerileme olmayan grup ile gerileme olan ve kontrol grupları arasında istatistiksel olarak anlamlı bir fark bulundu. Her iki hasta grubu ile kontrol grubu arasında PLR ve diğer hemogram değerleri arasında anlamlı fark yoktu.

Sonuç: Boyunda reaktif lap olan pediatrik bir hastaya ait NLR değeri klinisyene hastanın yakın takibi veya muhtemel viral etyoloji hakkında fikir verebilir. NLR değeri, bu hastalığın tedaviye dirençli olup olmadığı açısından da faydalı olabilir.

Anahtar Sözcükler: Çocuk, boyun, reaktif lenfadenopati

INTRODUCTION

Cervical lymphadenopathy (lap) is a common pathology of childhood and often causes parents to be anxiously admittance to clinicians. Although congenital lesions are the most common cause of neck masses, some authors argue that reactive laps which develop after viral and bacterial infections are the most common cause.[1,2] Lymphadenomegaly is a palpation examination of an enlarged lymph node while the term lymphadenopathy is often used as a synonym for disease-induced lymph node enlargement.[3,4] Lymph nodes, usually more common in children, undergo hyperplasia when encountered with a new antigen. Laps are usually caused by infectious diseases, but malignancies, autoimmune diseases, metabolic disorders and chronic inflammatory processes may also be the cause. In children, usually self-limiting acute

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upper respiratory viral infections cause laps and they spontaneously regress.[3,4]

It is very important to correct diagnosis and closely follow up of children with cervical laps. This patient group can usually be diagnosed with anamnesis and physical examination findings without the need for additional examinations, but hemogram test that is usually found in many clinics with no additional charge can be useful in the differential diagnosis. Neutrophil / Lymphocyte Ratio (NLR) and Platelet / Lymphocyte Ratio (PLR) values are also available markers from the hemogram parameters. In this study, we aimed to evaluate whether NLR and PLR values can be used in the follow-up of children with cervical reactive LAP in our clinic.

MATERIAL and METHODS

Between June 2016 and June 2017, the files of pediatric patients who were admitted to our clinic with the diagnosis of reactive cervical lymphadenopathy as a result of physical examination and diagnostic ultrasonography, were reviewed. Fifty-six patients who were diagnosed with cervical reactive lap and underwent physical examination at least 2 times during the follow-up period, were included in this study. In addition to physical examination, hemogram and neck ultrasonography examinations were performed at the first application. Physical examination and ultrasonography were repeated in the follow-up examinations. The patients were divided into two groups according to the changes in the size of the lymph nodes at the ultrasonography. Patients who had 50 % or more decrease in their lap size were defined as regressive group and those with no or less than 50% reduction in size were defined as a non-regressive group. The results of hemogram from pediatric patients who presented to our clinic without any disease were included in the study as a control group. Patients with diabetes mellitus, auto immune disease or chronic infection, heart failure, acute chronic infection, other known malignancies, myeloproliferative disorders, hepatorenal disorders, epilepsy, and patients taking anticoagulation medication and patients with lympadenitis or other neck masses except for reactive lymphadenopathy and reactive laps bigger than 20 mm were excluded from the study.

The NLR value was calculated by dividing the neutrophil count to the lymphocyte count, and the PLR by dividing the platelet count to the lymphocyte count. The groups were compared in terms of hemogram parameters such as hemoglobin (Hb) white blood cell (WBC), platelet (PLT), neutrophil count, lymphocyte count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), NLR and PLR.

The hematologic values were measured in our laboratory with in the first 20 minutes after venous puncture (bloodskeep in potassium EDTA tubes) and then analysed using Sysmex XP-300 (Sysmex Corporation, Japan).

All ultrasonographic examinations were performed by the same person. Ultrasonography was performed to the patients in the supine position. All neck areas such as submandibular, submental, postauricular ve preauricular, anterior and posterior cervical triangles were screened. Long axis/short axis ratio of lymph node, echogenicity of hilum and vascular pattern were checked.

STATISTICAL ANALYSIS

Normally distributed continuous variables (Shapiro-Wilk test) were age, Hb, PLT, PLR, MPV and PDW in the patient group and those were Hb, WBC, neutrophil and PDW in the control group. In the patient group; WBC, neutrophil, lymphocyte, NLR and PCT were not normally distributed but age, PLT, lymphocyte, NLR, PLR, MPV and PCT did not have normal distribution in the control group. When the patient group was divided into two; age, Hb, PLR, PDW, PCT values were normal distributed in the both groups, WBC was normal in the non-regressive group and PLT, lymphocyte in the regressive group. Student t test was used for the pairwise comparisons of normal and continuous variables, while one way variance analysis (Oneway ANOVA) was used for more than two comparisons in the both groups. Mann - Whitney U test was used for the pairwise comparison of continuous variables which is not normally

distributed and Kruskal Wallis test was used for comparison of more than two groups. Fisher"s Exact test was used in the 2x2 tables between the patient and the control groups and between the remissive and non-remissive groups in terms of discrete variables, gender and initial lap size. P value of <0.05 was considered statistically significant. SPSS 15.0 for Windows was used in statistical analysis.

RESULTS

A total of 100 children were included in this study, 51 were in the study group and 49 were in the control group. The 51 patients who formed the study group consisted of 32 males and 19 females with a mean age of 8,9±3,9 (1-16 age), the 49 patients who formed the control group consisted of 29 males and 20 males with mean age of 10,3±3,9 (1-16 age) (Table 1). No statistically significant difference was present between the study and the control groups in terms of age and gender (p>0.05). While 14 patients had unilateral lap in the neck, 37 patients had bilateral in the study group. The distribution of laps according to the neck regions was level 1 10 patients, level 2-4 13 patients and level 1-5 28 patients. At the time of first visit, 30 of the 51 patients in the study group had a lap size of 1-10 mm and 21 had 11-20 mm laps. During follow-up period, 25 of these 51 patients were found to have reduction of more than 50% in the lap size (11 of 1-10 mm, 14 of 11-20 mm). The remaining 26 patients had no change or less than 50% reduction in the lap size (19 of 1-10mm, 7 of 11-20mm) (p=0,048 Fisher"sExact Test) (Table 1). When the study group compared with the control group; age, Hb, WBC, neutrophil, lymphocyte, PLT, NLR, PLR, MPV, PDW, PCT values were not statistically significant (p >0,05) (Student t test for Hb and PDW, Mann - Whitney U test for others) (Table 2).

When control group, regressive and non-regressive groups were compared as the three groups in itself; there were no statistically significant difference in terms of Hb, PDW, age, WBC, PLT, lymphocyte, neutrophil, PLR, MPV, PDW and PCT values, there was a significant difference at NLR values between three groups (p=0,009 (Kruskal Wallis Test) (Table 3). The non-regressive group had a lower NLR value than control and regressive groups. When regressive and non-regressive were compared with each other ; there was no statistically significant difference in terms of age, Hb, PLR, PDW, PCT (Student t test), WBC,PLT, lymphocyte and MPV values between two groups (Mann-Whitney U test). There was a statistically significant difference in terms of lap size (p = 0.031), neutrophil count (p = 0.019) and NLR (p = 0.010) between the two groups (Mann - Whitney U test).

Table 1. Lap size distributions according to the subgroups of the study group

LAP Size (mm)	Study Group (Regressive) n=25	Study Group (Non-Regressive) n=26	*P* value
1 – 10	11	19	0,048
11 - 20	14	7	

Table 2. Demographic data of the study and control groups and hemogram parameter results

Parameter	Control Group n= 49	Study Group n=51	*P* value
Gender F/M	20/29	19/32	0,838
Age	10,2±3,91	8,9±3,89	0,066*
min-max	1-16	1-16	
Hb (g/dL)	13,7±1,31	13,4±1,21	0,139
WBC ($10^3/mm^3$)	8.04±2.11	8.39±2.24	0,521*
PLT ($10^3/mm^3$)	309±77,6	312±80,1	0,381*
Neutrophil ($10^3/mm^3$)	4.21±1.44	4.29±1.96	0,705*
Lymphocyte ($10^3/mm^3$)	2,80±1,11	3,14±0,98	0,062*
MPV (fL)	9,38±0,66	9.,6±0,86	0,433*
PDW (fL)	10,5±1.16	10,5±1,02	0,939
PCT (%)	0.31±0.05	0,30±0,06	0,719*
NLR	1,73±0,89	1,49±0.95	0,096*
PLR	124,3±49,4	106,4±27,7	0,154*

Table 3. Comparison of hemogram parameters between control, regressive and non-regressive groups

	Control Group n= 49	Study Group (Regressive) n=25	Study Group (Non-Regressive) n=26	*P* value Three group	*P* value Study group
Gender F/M	20/29				
Age	10,2±3,91	8,56±3,58	9,27±4,21	0,146**	0,521
Hb (g/dL)	13,7±1,31	13,24±1,29	13,55±1,14	0,229	0,362
WBC (10^3/mm^3)	8.04±2.11	8,78±2,32	8,03±2,14	0,389**	0,178*
PLT (10^3/mm^3)	309±77,6	309,04±93,7	316,27±66,23	0,657**	0,843*
Neutrophil (10^3/mm^3)	4.21±1.44	4,84±2,24	3,76±1,51	0,071**	**0,019***
Lymphocyte (10^3/mm^3)	2,80±1,11	2,94±0,84	3,33±1,07	0,094**	0,221*
MPV (fL)	9,38±0,66	9,27±0,70	9,65±0,97	0,305**	0,143*
PDW (fL)	10,5±1.16	10,4±0,96	10.68±1.09	0,757	0,432
PCT (%)	0.31±0.05	0.29±0.076	0.32±0.049	0,730**	0,171
NLR	1,73±0,89	1,80±1,14	1,20±0,61	**0,009****	**0,010***
PLR	124,3±49,4	112,68±28,87	100,43±25,65	0,164**	0,115
LAP Size		11,64±3,68	9,77±3,01		**0,031***

DISCUSSION

The definitive diagnosis of pediatric cervical lymphadenopathies may still be a problem for clinicians despite advanced diagnostic methods. Differential diagnosis is very important in order to make a proper and timely diagnosis. Most of the cases are benign, self-limiting and regress within a certain period of time without any sequelae.[5] On the other hand, it is one of the biggest dilemmas to distinguish benign and malignant lymphadenopathies, especially in pediatric patients. Therefore, when a child is brought with lymphadenopathy in the neck, the clinician should be able to exclude malignancy but should avoid as much as possible in unnecessary research and procedures. When we encounter a case like this in our own clinic, we perform a routine head and neck examination and then perform neck ultrasonography and complete blood count tests in the required patients especially at first visits. Then we follow whether the lesion is decreasing or not at regular intervals with neck ultrasonography. Ultrasonography provides a better feasibility compared to other imaging modalities due to high resolution, low cost, good recognition at soft tissue and easy accessibility. Ultrasonography, not only in the diagnosis of lymphadenopathy, also has an essential role in predicting whether the lesion is benign or malignant.[6]

Palpable lymph nodes are usually detected between 3 and 5 years of age[7]. Normal lymph nodes are typically detected in cervical and axillary areas up to 1 cm and 1,5 cm in the inguinal region.[8] Lymph nodes reach the maximum size around 8 and 12 years of age and begin atrophy begins after puberty.[9,10] The palpable lymph node in the neck can be found in

children aged between 4 and 8 years with a rate higher than 90%.[11] In this study, the age of the patients ranged from 1 to 16 years, and the mean age was 8,9 years.

Researches point out that bilateral cervical lymphadenopathies are more likely to be reactive than unilateral lymphadenopathies.[12] However, Gryznya et al.[12] Reported that 70% of patients with reactive nodal changes had unilateral lymphadenopathy. In our study group, 73% of the patients were bilateral while 27% were unilateral. In a study of 153 enlarged lymph nodes in 98 patients, Yaris[13] reported the most commonly affected sites as submandibular (36.7%) and upper cervical region (33,6%). Because of the small number of patient groups, we classified three main regions instead of subdividing the lap into sub-regions and identified 10 patients at level 1, 13 patients at level 2-4, and 28 patients at level 1-5. It was detected that most of the laps were located in the anterior cervical and submandibular regions. When we subdivided the study group, we found that there was no statistical difference in the size and localization of the laps at the time of admission between the regressive and non-regressive groups. In other words, our study subgroups had similar features in terms of lap characteristics.

Neutrophils, lymphocytes and platelets are blood cells that have function in the inflammatory process. Platelets secrete and express a large number of substances, which are important mediators of coagulation, inflammation, thrombosis and atherosclerosis. NLR is an easily calculated and highly cost-effective test with a simple ratio of absolute neutrophil count to absolute lymphocyte count and PLR with platelet count to lymphocyte count. NLR is a marker used to evaluate systemic inflammation and is superior to other WBC subtype counts (eg., Neutrophil, lymphocyte, and total leukocyte counts).[14,15] Inflammatory and immune response to stress can also be effectively demonstrated by NLR.[16] In the practice of ear nose and throat diseases, studies on the relationship between NLR and vestibular neuritis, facial nerve paralysis, sudden hearing loss and severe tinnitus have been performed previously.[15] In our study, there was no significant difference between the patient and the study groups in terms of NLR values, but we found a statistically significant difference between the no-regressive group and regressive, control groups. When we examined the causes of this result, we found that there was no statistically significant difference between three groups in terms of both neutrophil and lymphocyte values. However, the number of lymphocytes in the non-regressive group was higher than the other two groups and the number of neutrophils was lower. This finding led us to believe that the lap in these patients may have developed due to a recent upper respiratory tract infection. Therefore, children with cervical reactive lap and low NLR can be investigated for possible viral etiology. In addition, unnecessary antibiotic use can be prevented by taking NLR into consideration.

The size and functional efficacy of circulating platelets may vary. Large platelets usually produce a younger, more reactive and thrombogenic factor. Mean platelet volume, an indicator of platelet activation, can be an important prophylactic and diagnostic tool in thrombotic and prothrombotic cases.[14] MPV also increases as an inflammatory marker in the initial stage of infections.[16] PLR is easily detectable like NLR and a marker that evaluates inflammation. PLR was found to be increased at vascular disease, coronary artery disease, chronic renal failure and head and neck cancers and also associated with poor prognosis.[14,17] In this study, there was no significant difference in PLR and MPV values between the both patient subgroups and the control group.

The primary limitation of this study is that it has a retrospective screening, if the study was planned prospectively and the hemogram parameters could be determined at the time of follow-up, not only the NLR and PLR rates at the time of admission, it would probably be a more valuable study. Therefore, the relationship between the change in hemogram parameters and the change in lap dimensions could be revealed. Another issue in this study is that we have diagnosed patients by physical examination and ultrasound findings, not by pathological

methods. The reason for this is that we want to diagnose the children by using minimally invasive methods.

CONCLUSION

In this study, there was no significant difference between the control and patient groups in terms of NLR, PLR and MPV, but in NLR, there was a significant difference between the non-remissive group and the control group and remissive group. Therefore, the NLR value of a pediatric patient with reactive lap on the neck may give an idea to the clinician about the patient's close follow-up or possible viral etiology. The NLR value may also be useful for the treatment of this patients by guiding the disease to be resistant.

Conflict of Interest : None

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