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Healthcare professionals who did not get COVID-19 vaccine, but why?

COVID-19 aşısı yaptırmayan sağlıkçılar, ama neden?

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SUMMARY

Aim: In this study, it was aimed to determine the percentage of not being vaccinated and the reasons for not being vaccinated among 112 Emergency Health Services employees.

Material and Methods: 197 healthcare workers' files were scanned backwards. The effects of various sociodemographic and other variables (age, gender, marital status, cases of tetanus, measles, rubella, mumps vaccinations) were investigated retrospectively by scanning the files. Calculations were made by applying chi-square test and logistic regression using windows SPSS Version 21.0 (SPSS, Inc., Chicago, IL, USA). The study was conducted on 06.2021 as a retrospective file review.

Results: Of the 197 employees participating in the study, 128(65%) healthcare workers accepted the vaccine, 69 healthcare workers refused the vaccine (35%). Of the 69 people who did not receive the vaccine, 37 (53.6%) were women, 49 were between the ages of 20-30 (71%), 44 were married (63.8%), and 64 were non-physician health personnel.(92, 8%). Being married increased the rejection of vaccines 2.3 times (p = 0.017). Being previously infected with COVID-19 increased vaccine rejection 2.2 times (p = 0.033).

Conclusion: Even if the number of unvaccinated people in the study was not in the majority, the finding of this number among health workers is disappointing for epidemic disease management. In order to quickly get rid of this pandemic, the public should be informed about COVID-19 vaccines by reliable scientists and their fear, anxiety and reservations should be eliminated. The higher the number that cannot be persuaded, the less useful the vaccines will be..

Keywords: COVID-19 vaccines, healthcare professionals, vaccine hesitancy, safety, efficacy

ÖZET

Amaç: Bu çalışmada 112 Acil Sağlık Hizmetleri çalışanları arasında aşı yaptırmama yüzdesini ve aşı yaptırmama nedenlerini belirlemek amaçlanmıştır

Materyal ve Metodlar: 197 sağlık çalışanının dosyası geriye doğru tarandı. Dosyalar taranarak çeşitli sosyodemografik ve diğer değişkenlerin (yaş, cinsiyet, medeni durum, tetanoz, kızamık, kızamıkçık, kabakulak aşısı vakaları) etkileri geriye dönük olarak araştırıldı.Hesaplamalar Windows SPSS Sürüm 21.0 (SPSS, Inc., Chicago, IL, ABD) programı kullanılarak ki-kare testi ve lojistik regresyon uygulanarak yapılmıştır. Çalışma 06.2021 tarihinde retrospektif dosya taraması şeklinde yapılmıştır.

Bulgular: Araştırmaya katılan 197 çalışandan 128'i (%65) aşıyı kabul ederken, 69'u aşıyı (%35) reddetti. Aşılanmayan 69 kişiden 37'si (%53,6) kadın, 49'u 20-30 yaşları arasında (%71), 44'ü evli (%63,8) ve 64'ü hekim dışı sağlık personeliydi. (92, %8). Evli olmak aşı reddini 2,3 kat artırmıştır (p = 0,017). Daha önce COVID-19 ile enfekte olmak aşı reddini 2,2 kat artırmıştır (p = 0.033).

Sonuç: Çalışmada aşılanmamış kişi sayısı çoğunlukta olmasa da sağlık çalışanları arasında bu sayının bulunması salgın hastalık yönetimi için hayal kırıklığı yaratıyor. Bu pandemiden hızlı bir şekilde kurtulmak için halkın güvenilir bilim adamları tarafından COVID-19 aşıları hakkında bilgilendirilmesi, korku, endişe ve çekincelerinin giderilmesi gerekmektedir. İkna edilemeyen sayı ne kadar yüksek olursa, aşılar o kadar az faydalı olacaktır.

Anahtar kelimeler: COVID-19 aşıları, sağlık çalışanları, aşı tereddütü, güvenlik, etkinlik

INTRODUCTION

COVID-19 is a disease that was investigated and announced to the world with the increase of common respiratory symptoms and probably started in a fish market in Wuhan, China on December 31, 2020. As a result of research by China and WHO (World Health Organization), it is a disease called COVID-19, whose factor is Sars cov-2(Severe acute respiratory syndrome coronavirus-2), which was declared an epidemic on March 11, 2020 [1] During the peak periods, primary care, hospital and 112 emergency health care workers spend too much time and come into contact with COVID-19 patients. The way to be protected is explained as mask, distance and hygiene. The way to be protected much more precisely is vaccination. With the first emergence of the epidemic, scientists quickly started vaccine studies, and many vaccines that could be applied in a short time could be produced with the support of a known virus family, rapid genetic sequencing, new vaccine technologies and financial opportunities. As of January 2021, vaccination studies have started in the world and in Turkey, primarily risk groups. There are many COVID-19 vaccines produced by various countries and companies around the world. Coronavac vaccine produced by Sinovac company of Chinese origin and German-American vaccine produced by Biontech-Pfizer company are used in Turkey. Sinovac is a type of vaccine produced by the inactive virus method. Biontech- Pfizer vaccine is a vaccine produced with mRNA technology. As in all over the world, there is distrust, prejudice and opposition to COVID-19 vaccines in Turkey.[2] Vaccination percentages are not at the desired level in Turkey, where almost all adult population should be vaccinated in order to achieve social immunity.There are also health workers among those who refuse to be vaccinated. The opposition of those who will persuade the public to be vaccinated raises concerns about the course of the epidemic.[3] There are not many publications on vaccine rejection in healthcare professionals. Existing publications generally reflect the situation regarding influenza vaccines. According to the publications, they do not have influenza vaccines due to lack of time, because they think they are not at risk or because of insecurity against the vaccine.[4] In a study conducted in Turkey, only 6.7% of healthcare workers regularly get influenza vaccine. 55% of them have never had an influenza vaccine so far. [5] If there are low vaccination percentages in healthcare workers against a well-known disease such as influenza, it is possible that such a vaccine rejection exists against COVID-19, a very new disease. It is important to investigate this situation in a critical group such as healthcare professionals.

There are many factors that can lead to vaccine rejection; Insecurity in the production of vaccines, in their efficacy, in production technologies, in their content, in their rapid availability, sociocultural factors, religious factors, social beliefs, political factors, the media, press, and social media, which are caused by negative publications, and caused by conspiracy theories, factors such as avoidance of side effects, inability to grasp the severity of the disease, and the inability of knowledgeable and reliable scientists to provide adequate explanations can increase vaccine rejection at an alarming rate.[6-8]

In this study, it was aimed to investigate the vaccination rates among Emergency Health Services employees, the rate of COVID-19, and the factors affecting those who were not vaccinated.

MATERIAL AND METHODS

Study Design

Emergency Health Services employees, who were periodically examined in the Occupational Health and Safety Unit of the Kayseri Provincial Health Directorate on March 1-April 15, 2021, were asked about their COVID-19 vaccine, their status of COVID-19 vaccine during the examinations, and if they did not, the reasons were recorded in their files. 197 healthcare workers' files were scanned backwards. The effects of various sociodemographic and other variables (age, gender, marital status, cases of tetanus, measles, rubella, mumps vaccinations) were investigated retrospectively by scanning the files. To explain the terms used in the study; the presence of contraindications; pregnancy, chronic immune disorders, groups with chronic diseases for which the physician did not recommend vaccination, not trusting the vaccine; On the other hand, reasons such as not trusting the content, refraining due to its side effects, distrust due to social media, and not believing that the vaccines produced will protect from the disease are meant by the term not believing in its protection. The last 6 months were taken as the duration of previous covid-19 disease.

Statistical Analyses

Kolmogorov-Smirnov test was used for normality distribution and it was found that the data were not normally distributed. Descriptive statistics, chi-square test, regression test were applied using SPSS-21 program. (IBM SPSS Corp.; Armonk, NY, USA) Institutional permit from Kayseri Provincial Directorate of Health, work permit from Ministry of Health and ethical permission from Sivas Cumhuriyet University Non-Invasive Research Ethics Committee.(Decision date:26.05.2021, Decision No: 2021-05/02) $p < 0.05$ was considered statistically significant.

RESULTS

The distribution of sociodemographic and some other characteristics of healthcare workers according to their status of being vaccinated against COVID-19 is shown in Table 1. Of the 197 employees participating in the study, 128(65%) healthcare workers accepted the vaccine, 69 healthcare workers refused the vaccine (35%). Of the 69 people who did not receive the vaccine, 37 (53.6%) were women, 49 were between the ages of 20-30 (71%), 44

were married (63.8%), and 64 were non-physician health personnel.(92, 8%). Of the 197 employees participating in the study 26 were doctors (13.2%), 171 (86.8%) were nurses, health officers, emergency medical technicians, paramedics, and other healthcare professionals. 106 of them were female (53.8%), 91 (46.2%) were male. 132 people were between 20-30 years old (67.0%) 55 people were 31-50 years old (27.9%) 10 people (5.1%) were between 51-65 years old. 110(55.8%) of them were married, 87 were single (44.2%) or separated. There was no difference between the categories related to healthcare workers' socio-demographic characteristics and their COVID-19 vaccination status. There was also no difference between getting infected with COVID-19 before and COVID-19 vaccination. And also there was no significant difference between getting other vaccines and getting the COVID-19 vaccine.

Table 2 presents the distribution of socio-demographic and some characteristics of healthcare workers who did not have the COVID-19 vaccine by the reasons for not having the vaccine. There was no significant difference between categories related to socio-demographic characteristics, getting infected with COVID-19 before or other vaccines status and reasons for COVID-19 vaccine rejection.

Table 3 shows the logistic regression model predicting COVID-19 vaccine rejection. Being between the ages of 20-30 increased vaccine rejection 2.1 times (p= 0.047). Being married increased the vaccine rejection 2.3 times (p= 0.017). Getting infected with COVID-19 before, increased the vaccine rejection 2.2 times (p= 0.033)

Table 1. Distribution of socio-demographic and some other characteristics of the healthcare workers according to their status of being COVID-19 vaccine

	COVID-19 Vaccine Status			
	Yes (n,%)	No (n,%)	Total (n,%)	*p*
Gender				
Female	69(53.9)	37(53.6)	106(53.8)	x^2=0.001
Male	59(46.1)	32(46.4)	91(46.2)	p=0.970
Age group				
20-30 years	83(64.8)	49(71.0)	132(67.0)	x^2=0.518
31-65 years	45(35.2)	20(29.0)	65(33.0)	p=0.472
Marital status				
Single+Widow	62(48.4)	25(36.2)	87(44.2)	x^2=2.709
Married	66(51.6)	44(63.8)	110(55.8)	p=0.100
Occupation				
Physcian	21(16.4)	5(7.2)	26(13.2)	x^2=2.533
Other healthcare workers	107(83.6)	64(92.8)	171(86.8)	p=0.112
Getting infected with COVID-19 before				
No	99(77.3)	45(65.2)	144(73.1)	x^2=2.764
Yes	29(22.7)	24(34.8)	53(26.9)	p=0.096
Td* vaccine status				
No	95(74.2)	52(75.4)	147(74.6)	x^2=0.031
Yes	33(25.8)	17(24.6)	50(25.4)	p=0.860
Other vaccines status**				
No	92(71.9)	50(72.5)	142(72.1)	x^2=0.115
Yes	11(8.6)	5(7.2)	16(8.1)	p=0.944
Getting infected before	25(19.5)	14(20.3)	39(19.8)	
All participants	128(65.0)	69(35.0)	197(100.0)	

* Tetanus diphtheria, ** Measles, rubella, mumps, chickenpox vaccines

Table 2. Distribution of socio-demographic and some characteristics of healthcare workers who did not have the COVID-19 vaccine by the reasons for not having the vaccine.

	Reason for not getting the COVID-19 vaccine				
	Presence of contraindication (n,%)	Distrust (n,%)	Not believing its protects (n,%)	Total (n,%)	*p*
Gender					
Female	10(76.9)	19(44.2)	8(61.5)	37(53.6)	x^2=0.001
Male	3(23.1)	24(55.8)	5(38.5)	32(46.4)	p=0.970
Age group					
20-30 years	8(61.5)	32(74.4)	9(69.2)	49(71.0)	x^2=0.518
31-65 years	5(38.5)	11(25.6)	4(30.8)	20(29.0)	p=0.472
Marital status					
Single+Widow	3(23.1)	20(46.5)	2(15.4)	25(36.2)	x^2=2.709
Married	10(76.9)	23 (53.5)	11(84.6)	44(63.8)	p=0.100
Occupation					
Physcian	1(7.7)	3(7.0)	8(61.5)	5(7.2)	x^2=2.533
Other healthcare workers	12(92.3)	40(93.0)	5(38.5)	64(92.8)	p=0.112
Getting infected with COVID-19 before					
No	6(46.2)	6(46.2)	11(84.6)	45(65.2)	x^2=2.764
Yes	7(53.8)	7(53.8)	2(15.4)	24(34.8)	p=0.096
Td* vaccine status					
No	10(76.9)	33(76.7)	9(69.2)	52(75.4)	x^2=0.031
Yes	3(23.1)	10(23.3)	4(30.8)	17(24.6)	p=0.860
Other vaccines status**					
No	11(84.6)	32(74.4)	7(53.8)	50(72.5)	x^2=0.115
Yes	1(7.7)	4(9.3)	0(0.0)	5(7.2)	p=0.944
Getting infected before	1(7.7)	7(16.3)	6(46.2)	14(20.3)	
All participants	69(100.0)	13(18.8)		43(62.3)	

* Tetanus diphtheria, ** Measles, rubella, mumps, chickenpox vaccines

Table 3. Logistic regression model predicting COVID-19 vaccine rejection1 (n= 197)

Category	OR (95% CI)	*p*
Gender		
Female	1.00	
Male	1.26(0.67-2.36)	0.473
Age group		
31-65 years	1.00	
20-30 years	2.09(1.01-4.33)	**0.047**
Marital status		
Single+Widow	1.00	
Married	2.31(1.16-4.61)	**0.017**
Occupation		
Other healthcare workers	1.00	
Physician	0.34 (0.12-1.01)	0.050
Getting infected with COVID-19 before		
No	1.00	
Yes	2.18(1.07-4.47)	**0.033**
Td* vaccine status		
No	1.00	
Yes	0.88(0.31-2.48)	0.811
Other vaccines status**		
No	1.00	
Yes	0.84(0.19-3.77)	0.821
Getting infected before	1.12(0.43-2.89)	0.818

OR Odds ratio, CI Confidence interval, Reference category; 1= COVID-19 vaccine yes, * Tetanus diphtheria, ** Measles, rubella, mumps, chickenpox vaccines

DISCUSSION

As of January 2021, Sinovac vaccine of Chinese origin has been started to be administered primarily to healthcare workers in Turkey. Later, it continued with other risk groups and the Pfizer-Biontech vaccine was introduced as the second vaccine. As of May-June, the Russian origin Sputnik V vaccine will be available. As in all over the world, there is a suspicion and even opposing views against vaccines in Turkey. The vaccine hesitancy has been explained by the World Health Organization (WHO) as follows; "Vaccination indecision is defined as delay or rejection in accepting vaccination despite the availability of vaccine services. Vaccine hesitancy is a complex phenomenon; may vary depending on time, place and experience. It can be affected by factors such as indifference, relevance and trust. [9,10] There is distrust and even opposition in healthcare professionals, who are occupational groups that will apply and explain vaccines to the public, and convince the public, as in the whole world, in Turkey. Vaccination hesitancy in healthcare professionals, is a serious obstacle to achieving community immunity. Because the community will be persuaded to get vaccinated through health officials. They rely the most on information disclosed by healthcare professionals. First of all, health professionals must be highly persuaded and thus able to persuade people.[11] People may say that they will be vaccinated until they have the opportunity to get vaccinated, but they can give up when vaccination is possible. People who say that I will be vaccinated when the vaccine is found in the surveys conducted in the whole society do not get vaccinated when the vaccines are started. This is also the case with healthcare professionals. Having the thought of being vaccinated does not mean that you will be vaccinated.[11] For this reason, we must first strongly convince the health professionals and the public through them.

In this study, it was determined that there were those who did not get vaccinated in emergency health services employees who were in intensive contact with positive COVID-19 patients. 69 (35%) of 197 participants did not get vaccinated. In a review article, the vaccine acceptance rates of countries were found as follows; the highest COVID-19 vaccine acceptance rates were found in Ecuador (97.0%), Malaysia (94.3%), Indonesia (93.3%) and China (91.3%), the lowest COVID-19 vaccine acceptance rates were found in Kuwait (23.6%), Jordan (28.4%), Italy (53.7), Russia (54.9%), Poland (56.3%), US (56.9%), and France (58.9%). When the results of the work done to healthcare professionals are evaluated; only eight surveys among healthcare workers (doctors and nurses) were found, with vaccine acceptance rates ranging from 27.7% in the Democratic Republic of the Congo to 78.1% in Israel.8 In a study of vaccine rejection rates in Ireland and the United Kingdom, the vaccine rejection rate was found to be 35% in Ireland and 31% in the United Kingdom.[12] In a study conducted in Spain, 164 (22.43%) out of 731 participants stated that they would not be vaccinated. 20-24% of them were non-healthcare workers or unemployed, 17.5% were doctors, 31.5% were other health workers and 35.2% were nurses.

The most common reasons for not being vaccinated in the study were found to be insecurity, not believing that it is protective, and side effects.[13] 53 (26.9%) of the participants in the study had COVID-19 disease. 69 people did not get vaccinated. In this study, the acceptance rate was found to be higher than the studies conducted with healthcare professionals and the society. Nevertheless, it requires immediate action. When the reasons for these were examined, 13 people stated that they were not vaccinated due to contraindications such as pregnancy, breastfeeding, medical conditions that would cause contraindications, or they had recently had COVID-19. In some studies, vaccine instability or opposition was stated to be common in groups with contraindications.[14-16] 43 (21.8%) did not trust the vaccine, and 13 (6.6%) did not think that the vaccine was protective. 2058 people participated in a study conducted in China and 1879 people stated that they will be vaccinated whenever vaccine is available. (91.3%) Those who agreed that the vaccine would be vaccinated when it was available was 52.2% of the group, and 47.8% of the group stated that they would postpone it until its reliability is proven and then have it done later. It was found that not reliance on the vaccine affected the vaccination 0.69 times. In other words, insecurity reduces vaccine acceptance.[17] In a study examining anti-vaccination websites, it was found that 76-88% of the opposition cited emotional reasons such as the violation of civil liberties by vaccines, the dangers of side effects of vaccines, and 20-50% of these groups underestimate the disease prevention effect of vaccines. In this study, reliance on vaccines and doubts about the vaccine's protection came to the fore.[18,19]

When examining the status of having additional vaccinations consisting of measles, mumps, rubella (MMR), chickenpox, vaccines among the examined personnel, 142 people (72.1%) did not have these vaccines. 39 people (19.8%) stated that they had these diseases as children. 16 people (8.1%) had these vaccinations. When tetanus (Td) vaccination status was examined, 50 people (25.4%) stated that they had the vaccine, while 147 (74.6%) did not. Due to rumors that MMR and Hepatitis B vaccines cause autism and multiple sclerosis, cause aluminum poisoning, and are used to insert microchips, resistance and opposition to these vaccines have also occurred.[20-22] This resistance can be broken with public statements by reliable scientists. However, it is seen in this study that healthcare workers are still not vaccinated with these vaccines. This should be evaluated together with the reasons for not being vaccinated with COVID-19.

When the COVID-19 vaccination status was examined according to the professions, 5 (19.2%) of 26 physicians did not have the vaccine. In the study in Spain, this rate

was found to be 17.5%. [13] In a study on vaccine anti-vaccination in Ireland and the United Kingdom. İt was found that rejections were higher for the female sex and mostly at younger ages.[12] In a study conducted in China, it was found that male gender increased the acceptance of COVID-19 vaccine by 1.25 times and being married 1.70 times.[17] The results in this study were determined as follows; among those not vaccinated, 37 were female (53.6%), 32 were male (46.4%). Of the unvaccinated, 49 were in the 20-30 age range (71%), 20 were in the 31-65 age range (29%). Of those who were not vaccinated, 25 were single or widowed (36.2%), 44 were married (63.8%). The results in this study were similar to other publications.

The biggest reason for not being vaccinated was the distrust towards vaccines (62.3%). When the reasons for vaccination rejection were examined by professions, 5 of those who were not vaccinated were doctors (7.2%), 64 (92.8%) of them were other healthcare professionals 3 of those who did not trust the vaccine were doctors (7%), 40 of them were other healthcare workers (93%). Thirty-two (74.4%) of the group that did not trust the vaccine were in the 20-30 age group, 11 (25.4%) were in the 31-65 age group. Of those who did not trust the vaccine, 23 were married (53.5%) and 20 were single (46.5%). When the getting infected with COVID-19 status was examined, in the group that did not trust the vaccine, 28 did not get infected with COVID-19 (65.1%), 15 got infected with COVID-19 (34.9%).In a study conducted with Egyptian medical students, 43.6% got infected with COVID-19. There was no significant difference in vaccine acceptance between the getting infected with COVID-19 group and the group that did not. A significant difference was found in vaccine acceptance among those who got infected with COVID-19 in their immediate vicinity compared to those who did not. [23]

In the study conducted in China, it was found that getting the influenza vaccine last season increased the COVID-19 vaccine acceptance 1.46 times.[17] In a study conducted with healthcare professionals in Izmir, it was found that having a flu vaccine beforehand significantly increased the rate of acceptance of COVID-19 vaccines.[24] In this study, it was determined that 33 (25.8%) of those who had the COVID-19 vaccine also vaccinated with the tetanus vaccine, and 11 (8.6%) of those with the COVID-19 vaccine also vaccinated with other additional vaccines (measles, rubella, mumps). It was found that those who had additional vaccines and tetanus vaccines had more covid-19 vaccines. (Tetanus 66%, other vaccines 68.7%) It is seen from these results that vaccine resistance continues for all vaccines. With the evidence of reliable scientists and people that the society will trust, it is thought that it will be effective in all vaccines in terms of breaking this resistance.

In the model created in the study in China, being married and male gender were found to be significant and positive in vaccine acceptance. In a study conducted in Spain, a significant difference was found between nurses (OR=1.146 %95CI (Confidence İnterval)(1.052–1.249) P=0.002) and other healthworkers(OR=1.119 %95CI (1.012–1.238) P=0.028) in modeling vaccine acceptance. [13-17] In a study conducted in healthcare personnel in İzmir, it was found that the COVID-19 vaccine acceptance was significantly different between doctors, midwives, nurses and others, men and women, student midwives and nurses, young age group and other age groups. [24] In this study, being between the ages of 20-30 increased vaccine rejection 2.1 times (p = 0.047). Being married increased the rejection of vaccines 2.3 times (p = 0.017). Being previously infected with COVID-19 increased vaccine rejection 2.2 times (p = 0.033).

Limitations

-The study was carried out on a certain part of the emergency health services workers. More studies, including primary care and hospitals, are needed to determine vaccine rejection rates in healthcare workers.

-The study could be done retrospectively. Opportunities did not allow for a face-to-face study.

-Data distributions were not normal, so non-parametric tests were used.

CONCLUSION

The presence of this opposition and reservations in the section that can convince the society such as the health personnel shows that there is a much higher percentage in the society. Even if the number of unvaccinated people in the study was not in the majority, the finding of this number among health workers is disappointing for epidemic disease management. In order to quickly get rid of this pandemic, the public should be informed about COVID-19 vaccines by reliable scientists and their fear, anxiety and reservations should be eliminated. The higher the number that cannot be persuaded, the less useful the vaccines will be. In the study, it was found that being married, being in the 20-30 age group, and having had Covid-19 before, increased covid-19 vaccine rejection. In the light of this information, it would be useful to conduct more persuasion studies on these groups.

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REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. New England Journal of Medicine [Internet]. 2020 Feb 20;382(8):727–33. Access Date:08.03.2022
2. Prüβ BM. Current State of the First COVID-19 Vaccines. Vaccines 2021 Jan 8;9(1):30. Access Date:08.03.2022
3. Kwok KO, Li K-K, WEI WI, Tang A, Wong SYS, Lee SS. Influenza vaccine uptake, COVID-19 vaccination intention and vaccine hesitancy among nurses: A survey. International Journal of Nursing Studies 2021 Feb;114:103854. Access Date:08.03.2022
4. Thoon KC, Chong CY. Survey of healthcare workers' attitudes, beliefs and willingness to receive the 2009 pandemic influenza A (H1N1) vaccine and the impact of educational campaigns. Annals of the Academy of Medicine, Singapore 2010 Apr;39(4):307–6. Access Date:08.03.2022
5. Korkmaz N, Nazik S, Gümüştakım RŞ, Uzar H, Kul G, Tosun S, et al. Influenza vaccination rates, knowledge, attitudes and behaviours of healthcare workers in Turkey: A multicentre study. International Journal of Clinical Practice 2021 Jan;75(1). Access Date:08.03.2022
6. Reiter PL, Pennell ML, Katz ML. Acceptability of a COVID-19 vaccine among adults in the United States: How many people would get vaccinated? Vaccine 2020 Sep;38(42):6500–7. Access Date:08.03.2022
7. World Health Organization Behavioral Considerations for Acceptance and Uptake of Covid-19 Vaccines:Who Technical Advisory Group on Behavioral İnsights and Sciences for Health;meeting report,15 October 2020. Geneva: World Health Organization;2020.https://ww. Access Date:08.03.2022
8. Sallam M. COVID-19 Vaccine Hesitancy Worldwide: A Concise Systematic Review of Vaccine Acceptance Rates. Vaccines 2021 Feb 16;9(2):160. Access Date:08.03.2022
9. MacDonald NE. Vaccine hesitancy: Definition, scope and determinants. Vaccine 2015 Aug;33(34):4161–4. Access Date:08.03.2022
10. Sage report of the sage working group on vaccine hesitancy 2014. Access Date:08.03.2022
11. Malik AA, McFadden SM, Elharake J, Omer SB. Determinants of COVID-19 vaccine acceptance in the US. EClinicalMedicine 2020 Sep;26:100495. Access Date:08.03.2022
12. Murphy J, Vallières F, Bentall RP, Shevlin M, McBride O, Hartman TK, et al. Psychological characteristics associated with COVID-19 vaccine hesitancy and resistance in Ireland and the United Kingdom. Nature Communications 2021 Dec 4;12(1):29. Access Date:08.03.2022
13. Eguia H, Vinciarelli F, Bosque-Prous M, Kristensen T, Saigí-Rubió F. Spain's Hesitation at the Gates of a COVID-19 Vaccine. Vaccines 2021 Feb 18;9(2):170. Access Date:08.03.2022
14. England PHH protection report. Pertussis Vaccination Programme for Pregnant Women: vaccine coverage estimates in England, September to December 2014. 2015. Access Date:08.03.2022
15. Centres for Disease Control & Prevention. Vaccines and Preventable Diseases: Who Should NOT Get Vaccinated with these Vaccines? [Internet]. Available from: https://www.cdc.gov/vaccines/vpd/should-not-vacc.html Access Date:08.03.2022
16. Gall SA, Poland GA. A maternal immunization program (MIP): Developing a schedule and platform for routine immunization during pregnancy. Vaccine 2011 Nov;29(51):9411–3. Access Date:08.03.2022
17. Wang J, Jing R, Lai X, Zhang H, Lyu Y, Knoll MD, et al. Acceptance of COVID-19 Vaccination during the COVID-19 Pandemic in China. Vaccines 2020 Aug 27;8(3):482. Access Date:08.03.2022
18. Bean SJ. Emerging and continuing trends in vaccine opposition website content. Vaccine 2011 Feb 24;29(10):1874–80. Access Date:08.03.2022
19. Kata A. A postmodern Pandora's box: Anti-vaccination misinformation on the Internet. Vaccine 2010 Feb;28(7):1709–16. Access Date:08.03.2022
20. DeStefano F, Shimabukuro TT. The MMR Vaccine and Autism. Annual Review of Virology 2019 Sep 29;6(1):585–600. Access Date:08.03.2022
21. Mouchet J, Salvo F, Raschi E, Poluzzi E, Antonazzo IC, De Ponti F, et al. Hepatitis B vaccination and the putative risk of central demyelinating diseases – A systematic review and meta-analysis. Vaccine 2018 Mar;36(12):1548–55. Access Date:08.03.2022
22. Goullé J-P, Grangeot-Keros L. Aluminum and vaccines: Current state of knowledge. Médecine et Maladies Infectieuses 2020 Feb;50(1):16–21. Access Date:08.03.2022
23. Saied SM, Saied EM, Kabbash IA, Abdo SAE. Vaccine hesitancy: Beliefs and barriers associated with COVID-19 vaccination among Egyptian medical students. Journal of Medical Virology 2021 Mar 25;jmv.26910. Access Date:08.03.2022
24. Kose S, Mandiracioglu A, Sahin S, Kaynar T, Karbus O, Ozbel Y. Vaccine hesitancy of the COVID-19 by health care personnel. International Journal of Clinical Practice 2021 May 19;75(5). Access Date:08.03.2022

KLİNİK ARAŞTIRMA
ORIGINAL ARTICLE

Çocukluk çağı hodgkin lenfomalarında CD163 ekspresyonunun prognostik önemi

The prognostic impact of CD163 expression in childhood hodgkin lypmhomas

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ÖZET

Amaç: Bu çalışmanın amacı, pediatrik Hodgkin lenfoma olgularında CD163 ekspresyonunun prognozla ilişkisini incelemektir.

Materyal ve Metodlar: Bu çalışmaya retrospektif olarak; Ocak 2014- Aralık 2020 tarihleri arasında Sağlık Bilimleri Üniversitesi Prof. Dr. Cemil Taşcıoğlu Şehir Hastanesi Pediatrik Onkoloji ve Hematoloji Klinikleri'nde Hodgkin Lenfoma (HL) tanısı ile tedavi ve takipleri yapılan 0-18 yaş aralığındaki, 21 pediatrik hasta dahil edildi. Olguların ilk tanı biyopsilerine CD163 immünhistokimyası uygulandı. CD163 ekspresyonlarına göre; <%5, %5-25, >%25 olmak üzere 3 gruba ayrıldı.

Bulgular: Olguların yaşları 6 ile 17 arasında değişmekte olup %4,8'i (n=1) Evre 1, %28,6'sı (n=6) Evre 2, %33,3'ü (n=7) Evre 3, %33,3'ü (n=7) Evre 4 olarak tanı almıştır. Olguların %42,9'unda (n=9) B semptomu, %15'inde (n=3) progresyon, %38'inde (n=8) dalak tutulumu mevcuttur. Histolojik subtip dağılımları; %4,8 (n=1) lenfositten fakir tip, %33,3 (n=7) mikst selüler tip, %4,8 (n=1) nodüler lenfosit predominant HL, %57,1 (n=12) nodüler sklerozan tip şeklindedir. CD 163 ekspresyon değerleri incelendiğinde, olguların %38,1'inin (n=8) %5'in altında, %33,3'ünün (n=7) %5-25 aralığında, %28,6'sının (n=6) >%25 olduğu görülmektedir. CD163 ekspresyon gruplarına göre olguların cinsiyetleri, yaşları evreleri, B semptomu varlığı, progresyon durumu, histolojik subtipler ve dalak tutulumu açısından istatistiksel olarak anlamlı farklılık göstermemektedir (p>0,05).

Sonuç: CD163 ekspresyonun pediatrik HL olgularında prognostik öneminin anlaşılması için daha kapsamlı araştırmalar gerekmektedir.

Anahtar kelimeler: CD163, pediatrik hodgkin lenfoma, tümör ilişkili makrofaj

SUMMARY

Aim: The aim of this studay is to examine the relationship betwen CD163 expression and prognosis in pediatrik Hodgkin lymphoma cases.

Material and Methods: In this study retrospectively; twenty-one pediatric patients were included who were treated and followed-up with the diagnosis of Hodgkin Lymphoma (HL) in the Pediatric Oncology and Hematology Clinics of Prof. Dr. Cemil Taşcıoğlu City Hospital, between January 2014 and December 2020. CD163 immunohistochemistry was applied to the initial diagnostic biopsies of the cases.

Results: The ages of the cases ranged from 6 to 17, with 4.8 % (n=1) Stage 1, 28.6 % (n=6) Stage 2, 33.3 % (n=7) Stage 3, 33.3 % (n=7) were diagnosed as Stage 4. B symptoms were present in 42.9 % (n=9) of the cases, progression in 15 % (n=3), and spleen involvement in 38 % (n=8). Histological subtype distributions; 4.8 % (n=1) lymphocyte-poor type, 33.3 % (n=7) mixed cellular type, 4.8 % (n=1) nodular lymphocyte predominant HL, 57.1% (n=12) nodular sclerosing type. When CD 163 expression values were examined, 38.1% (n=8) of the cases were below 5 %, 33.3 % (n=7) were between 5-25 %, 28.6 % (n=6) were >25% appears to be. According to CD163 expression groups, there was no statistically significant difference in terms of gender, age, stage, presence of B symptoms, progression status, histological subtypes and spleen involvement (p>0.05).

Conclusion: More extensive studies are required to understand the prognostic significance of CD163 expression in pediatric HL cases.

Keywords: CD163, childhood hodgkin lymphoma, tumor-associated macrophage

GİRİŞ

Hodgkin lenfoma (HL) tüm çocukluk çağı kanserlerinin yaklaşık %5 ila %6'sını oluşturmakta olup sosyoekonomik düzey ve coğrafi alanlara göre karakteristik epidemiyolojik, klinik ve patolojik özellikler sergilemektedir. Modern tıbba her geçen gün eklenen yeni araştırmalar ile tedavide daha az yan etkili komplikasyonsuz yöntemler araştırılmaktadır (1,2). Son yıllarda, enflamatuar hastalıklar ve malignensilerde farmakolojik tedavinin bir parçası olarak makrofaj aktivitesinin etkisinin gösterilmesi, klinik çalışmalardan geçen birden fazla ilaç adayının gelişmesine ve araştarılmasına yol açmış, klinik onayla tedavide kullanılmışlardır. Genel olarak makrofaj yönlendirilmiş tedavide, makrofaj reseptörleri veya makrofajlar tarafından salgılanan sitokinler hedeflenir (3-5).

Biz de bu çalışmamızda tümör ilişkili makrofalajlar üzerinde CD163 protein ekspresyonunu, immünohistokimya (IHC) kullanarak inceleyip, çocukluk çağı HL hastalarında risk sınıflandırmasında ve prognozda etkisini araştırmak istedik.

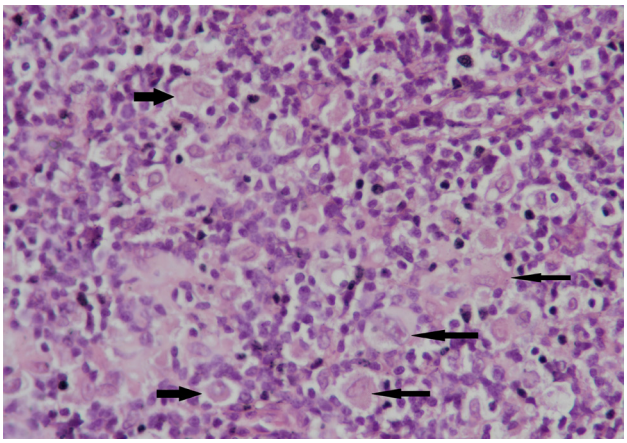
MATERYAL VE METOTLAR

Bu çalışmaya retrospektif olarak; Ocak 2014- Aralık 2020 tarihleri arasında Sağlık Bilimleri Üniversitesi Prof. Dr. Cemil Taşcıoğlu Şehir Hastanesi Pediatrik Onkoloji ve Hematoloji Klinikleri'nde HL tanısı ile tedavi ve takipleri yapılan 0-18 yaş aralığındaki, ilk tanı biyopsilerine ulaşılabilen, tanı sonrası en az 12 ay takibi olan 21 pediatrik hasta dahil edildi. Olgulara ait demografik veriler, tanı anındaki evreleri, HL alt tipi, B semptomu varlığı (gece terlemesi, kilo kaybı, ateş), progresyon durumu, dalak tutulumu gibi veriler hastane bilgi işletim sistemi, hasta takip dosyaları, patoloji raporları ve hastalarla/hasta yakınlarıyla telefonla görüşülerek elde edildi.

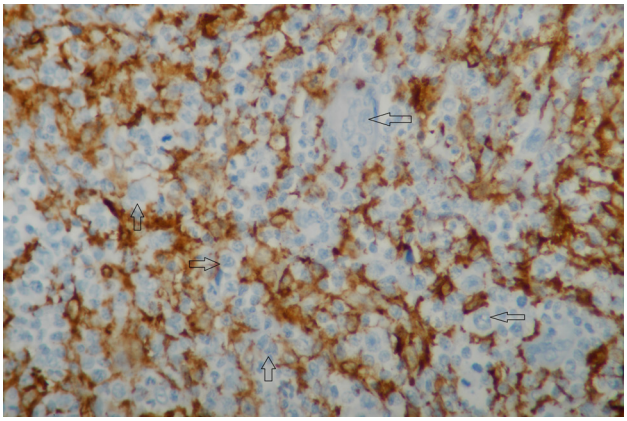
Her olgunun ilk tanı materyalinden, Reed-Sternberg hücreleri içeren tümörün tamamını temsil edebilen, %10'luk tamponlu formalin ile fikse, parafine gömülü bir blok seçildi. Bu bloklardan pozitif yüklü lamlara 2 µm kalınlığında kesitler alındı. CD163 (klon EP324, Epitomics, dilüsyon 1/150) antikoru Ventana Benchmark Ultra otomatik boyama cihazında uygulandı.

Hazırlanan immünhistokimya boyalı preparatlar ışık mikroskobunda olguların klinikopatolojik verileri ve sağkalım durumlarını bilmeyen iki patolog tarafından değerlendirildi. Membranöz ve/veya sitoplazmik boyanma gösteren makrofajlar CD163 pozitif olarak kabul edildi. Değerlendirmeler Reed-Sternberg hücrelerinden zengin alanda yapıldı (Şekil 1a, 1b). İmmünreaktivite toplam selüleriteye göre skorlanarak; <%5, %5-25, >%25 olmak üzere 3 gruba ayrıldı (6).

İstatistiksel analizler için NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) programı kullanıldı. Çalışma verileri değerlendirilirken tanımlayıcı istatistiksel metodlar (ortalama, standart sapma, medyan, frekans, yüzde, minimum, maksimum) kullanıldı. Nicel verilerin normal dağılıma uygunlukları Shapiro-Wilk testi ve grafiksel incelemeler ile sınanmıştır. Normal dağılım göstermeyen nicel değişkenlerin iki grup arası karşılaştırmalarında Mann-Whitney U test kullanıldı. Nitel verilerin karşılaştırılmasında Fisher-Freeman-Halton exact test kullanıldı. İstatistiksel anlamlılık $p<0.05$ olarak kabul edildi.



Şekil 1a: Neoplastik Reed-Sternberg hücreleri (H&E, x400)



Şekil 1b: Neoplastik hücreler çevresindeki CD163+ tümör ilişkili makrofajlar (x400)

BULGULAR

Olguların yaşları 6 ile 17 arasında değişmekte olup, ortalama yaş 13,05±3,22 olarak belirlenmiştir. Tanı anındaki evreler incelendiğinde, olguların %4,8'inin (n=1) Evre 1, %28,6'sının (n=6) Evre 2, %33,3'ünün (n=7) Evre 3, %33,3'ünün (n=7) Evre 4 olduğu görülmektedir. Olguların %42,9'unda (n=9) B semptomu, %15'inde (n=3) progresyon, %38'inde (n=8) dalak tutulumu mevcuttur. Histolojik subtip dağılımları; %4,8 (n=1) lenfositten fakir tip, %33,3 (n=7) mikst selüler tip, %4,8 (n=1) nodüler lenfosit predominant HL, %57,1 (n=12) nodüler sklerozan tip şeklindedir (Tablo 1).

Tablo 1. Tanımlayıcı özelliklerin dağılımı

Özellikler		n (%)
Cinsiyet		
	Kız	6 (28,6)
	Erkek	15 (71,4)
Yaş		
	Ortalama ± ss	13,05 ± 3,22
	Medyan (Min-Maks)	14 (6-17)
Evre		
	Evre 1	1 (4,8)
	Evre 2	6 (28,6)
	Evre 3	7 (33,3)
	Evre 4	7 (33,3)
B Semptomu		
	Yok	12 (57,1)
	Var	9 (42,9)
Progresyon		
	Yok	17 (85,0)
	Var	3 (15,0)
Histolojik Tip		
	Lenfositten fakir tip	1 (4,8)
	Mikst selüler tip	7 (33,3)
	NL predominant	1 (4,8)
	Nodüler sklerozan tip	12 (57,1)
Dalak tutulumu		
	Yok	13 (61,9)
	Var	8 (38,1)
CD 163 ekspresyon yüzdesi		
	<%5	8 (38,1)
	%5-25	7 (33,3)
	>%25	6 (28,6)

CD 163 ekspresyon değerleri incelendiğinde, olguların %38,1'i (n=8) %5'in altında, %33,3'ü (n=7) %5-25 aralığında, %28,6'sı (n=6) >%25 olduğu saptanmıştır.

CD163 ekspresyon gruplarına göre olguların cinsiyetleri ve yaşları istatistiksel olarak anlamlı farklılık göstermemektedir (p>0,05) (Tablo 2).

Tablo 2. Demografik özelliklerin CD 163 ekspresyon gruplarına göre değerlendirilmesi

		CD 163 ekspresyon yüzdeleri			*p*
		<%5	%5-25	>%25	
Cinsiyet					
	Kız	4 (50,0)	2 (28,6)	0 (0)	[a]*0,158*
	Erkek	4 (50,0)	5 (71,4)	6 (100)	
Yaş					
	Ort±Ss	14,63±2,20	12,43±2,70	11,67±4,37	[b]*0,200*
	Medyan (Min-Maks)	15 (11-17)	14 (9-16)	11 (6-17)	

[a]Fisher Freeman Halton Test

[b]Kruskal Wallis Test

CD163 ekspresyon gruplarına göre olguların evreleri, B semptomu varlığı, progresyon durumu, histolojik subttipler ve dalak tutulumu açısından istatistiksel olarak anlamlı farklılık göstermemektedir (p>0,05) (Tablo 3).

Tablo 3. CD 163 ekspresyon gruplarına göre değerlendirmeler

		CD 163 ekspresyon yüzdeleri			*P*
		<%5	%5-25	>%25	
Evre					
	Evre 1	0 (0)	1 (14,3)	0 (0)	[a]*0,810*
	Evre 2	3 (37,5)	2 (28,6)	1 (16,7)	
	Evre 3	3 (37,5)	1 (14,3)	3 (50,0)	
	Evre 4	2 (25,0)	3 (42,9)	2 (33,3)	
B Semptomu					
	Yok	4 (50,0)	5 (71,4)	3 (50,0)	[a]*0,738*
	Var	4 (50,0)	2 (28,6)	3 (50,0)	
Progresyon					
	Yok	5 (62,5)	7 (100)	5 (100)	[a]*0,088*
	Var	3 (37,5)	0 (0)	0 (0)	
Histolojik Tip					
	Lenfositten fakir	1 (12,5)	0 (0)	0 (0)	[a]*0,111*
	Mikst	0 (0)	4 (57,1)	3 (50,0)	
	Nlpredominant	1 (12,5)	0 (0)	0 (0)	
	Nodüler sklerozan	6 (75)	3 (42,9)	3 (50,0)	
Dalak tutulumu					
	Yok	5 (62,5)	5 (71,4)	3 (50,0)	[a]*0,855*
	Var	3 (37,5)	2 (28,6)	3 (50,0)	

TARTIŞMA

Transmembran reseptörü CD163 sadece monositler (düşük ekspresyon) ve makrofajlarla (yüksek ekspresyon) ifade edilir (7). CD163 ekspresyonu ateroskleroz, miyokard enfarktüsü, lupus nefriti gibi birçok hastalıkta gösterilmiş olup reseptörün hastalıktaki patolojik rolü hakkındaki bilgiler henüz tam değildir (8-10).

CD163'ün olumsuz prognostik öneminin HL hastaları için öngörücü bir biyobelirteç olduğu çeşitli çalışmalarda doğrulanmıştır (11,12). Yoon ve arkadaşlarının yaptığı çalışmada yüksek bir CD163 immün boyama yoğunluğunun özellikle azalmış tam remisyon oranı ile ilişkili olduğu ve HL'de spesifik bir güvenilir prognostik gösterge olarak kabul edildiği sonucuna varılmıştır (13). Huda Al Sayed Ahmed ve arkadaşları yaptığı çalışmada CD163'ün tümör ilişkili makrofajlar için spesifik bir belirteç olduğu ve aşırı ekspresyonunun, nüks ve tedavi sonrası azalmış sağkalım ile önemli ölçüde ilişkili olduğu sonucuna varmışlardır (14). Sumit ve arkadaşlarının pediatrik grupta yaptığı çalışmada yetişkin HL'den farklı olarak, Reed Sternberg hücrelerinin daha yüksek bir yüzdesi kötü sonuçla ilişkilendirilirken, tümör ilişkili makrofajların yüksek düzeyi ile ilişki bulunmamıştır (15).

Çalışmamızda CD163 ekspresyon gruplarına göre olguların evreleri, B semptomu varlığı, progresyon durumu, histolojik tipler ve dalak tutulumu ile istatistiksel olarak anlamlı farklılık göstermemektedir (p>0,05). Benzer şekilde D.Azambuja ve arkadaşlarının yaptığı çalışmada CD68 veya CD163 ekspresyonları ile klinik özellikler ile arasında ilişki saptamamışlardır. Ayrıca CD68 veya CD163 ekspresyonunu progresyon ve survi ile ilişkilendirememişlerdir (16).

Sonuç olarak CD163 ekspresyonunu çocukluk çağı HL hastalarında prognostik sınıflandırması için kullanımı önerilmeden önce daha fazla çalışma gerekmektedir. Pediatrik olgularda tümör mikro ortamının erişkinlerden daha farklı olabileceği ve bu farklı bileşenlerinin sonuçla ilişkisini ileriye dönük olarak belirlemede daha kapsamlı, ayrıntılı çalışmalar gerekmektedir.

Yazar Katkıları: Çalışma Konsepti/Tasarımı: ÖY, DKA, Veri Toplama: ET, Yazı Taslağı: ÖY,ET, DKA, İçeriğin Eleştirel İncelemesi: ÖY,ET, DKA, Son Onay ve Sorumluluk: ÖY,ET
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KAYNAKLAR

1. Chang ET, Zheng T, Weir EG, Borowitz M, Mann RB, Spiegelman D et al. Childhood social environment and Hodgkin's lymphoma: new findings from a population-based case-control study. Cancer Epidemiol Biomarkers Prev. 2004;13(8):1361-1370.
2. Punnett A, Tsang RW, Hodgson DC. Review Hodgkin lymphoma across the age spectrum: epidemiology, therapy, and late effects. Semin Radiat Oncol. 2010;20(1):30-44.
3. Werner L, Dreyer J.H, Hartmann D, Barros M.H.M, Büttner-Herold M, Grittner U et al. Tumor-associated macrophages in classical Hodgkin lymphoma: Hormetic relationship to outcome. Sci. Rep. 2020;10: 1–11.
4. He W, Kapate N, Shields CW, Mitragotri S. Drug delivery to macrophages: A review of targeting drugs and drug carriers to macrophages for inflammatory diseases. Adv. Drug Deliv. Rev. 2019.
5. Cassetta L, Pollard JW. Targeting macrophages: Therapeutic approaches in cancer. Nat. Rev. Drug Discov. 2018; 17:887–904.
6. Harris JA, Jain S, Ren Q, Zarineh A, Liu C, Ibrahim S. CD163 versus CD68 in tumor asociated macrophages of classical hodgkin lymphoma. Diagnostic Pathology. 2012;7:12.
7. Kristiansen M, Graversen JH, Jacobsen, C, Sonne O, Hoffman HJ, Law SA. et al. Identification of the haemoglobin scavenger receptor. Nature. 2001;409:198–201.
8. Guo L, Akahori H, Harari E, Smith SL, Polavarapu R, Karmali V et al. CD163+ macrophages promote angiogenesis and vascular permeability accompanied by inflammation in atherosclerosis. J. Clin. Investig. 2018;128:1106–1124.
9. Li J, Liu CH, Xu DL,Gao B. Significance of CD163-Positive Macrophages in Proliferative Glomerulonephritis. Am. J. Med. Sci. 2015;350:387–392.
10. Olmes G, Buettner M, Ferrazzi F, Distel LV, Amann K, Daniel C. CD163+ M2c-like macrophages predominate in renal biopsies from patients with lupus nephritis. Arthritis Res. Ther. 2016;18:90.
11. Tan KL, Scott DW, Hong F, Kahl BS, Fisher RI, Bartlett NL et al. Tumor-associated macrophages predict inferior outcomes in classic Hodgkin lymphoma: A correlative study from the E2496 Intergroup trial. Blood. 2012;120:3280–3287.
12. Steidl C, Lee T, Shah SP, Farinha P, Han G, Nayar T et al. Tumor-associated macrophages and survival in classic Hodgkin's lymphoma. N Engl J Med. 2010;362:875–885.
13. Yoon DH, Koh YW, Kang HJ, Kim S, Park CS, Lee SW et al. CD68 and CD163 as prognostic factors for Korean patients with Hodgkin lymphoma. Eur J Haematol. 2012 ;88:292–305.
14. Al Sayed Ahmed H, Raslan WF, Deifalla AHS, Fathallah MD. CD163 is a predictive biomarker for prognosis of classical Hodgkin's lymphoma in Saudi patients Mol Clin Oncol. 2019;11(1): 67–76.
15. Gupta S, Yeh S, Chami R, Punnett A, Chung C. The prognostic impact of tumour-associated macrophages and Reed-Sternberg cells in paediatric Hodgkin lymphoma European Journal of Cancer. 2013;49(15):3255-3261.
16. Azambuja D, Natkunam Y, Biasoli I, Lossos IS, Anderson MW, Morais JC et al. Lack of association of tumor-associated macrophages with clinical outcome in patients with classical Hodgkin's lymphoma. Ann Oncol. 2012;23(3):736-742.

KLİNİK ARAŞTIRMA
ORIGINAL ARTICLE

Geçirilmiş sezaryen öyküsü olan hastalarda ikinci trimester tarama testi biyokimyasal belirteçlerinin kötü gebelik sonuçlarıyla ilişkisi

The relationship of second trimesters screening test biochemical markers and poor pregnancy outcomes in patients with a history of cesarean

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ÖZET

Amaç: Geçirilmiş sezaryen öyküsü olan hastalarda ikinci trimesterde bakılan maternal serum Alfa-fetoprotein (AFP), insan koryonik gonadotropin (HCG) ve serbest estriol (uE3) seviyeleri ile kötü gebelik sonuçları arasındaki ilişkiyi incelemek, kötü gebelik sonuçlarını öngörmede etkili olup olmadığını değerlendirmek ve geçirilmiş sezaryen öyküsü olan ve olmayan gebeleri bu belirteçler açısından kıyaslamak.

Materyal ve Metodlar: Gebelik takipleri aynı klinikte yapılmış, geçirilmiş uterin cerrahisi olup sezaryen doğum yapan gebeler (n=87) ve normal spontan doğum yapan (n=105) gebelerin verileri retrospektif olarak değerlendirildi. Gebelerin yapılmış olan ikinci trimester taraması testinin kapsadığı biyokimyasal belirteçlerden AFP, HCG ve uE3 düzeyleri ve düzeltilmiş medyan katları (MoM-multiples of median) değerleri değerlendirilmeye alındı. Biyokimyasal belirteçlerin değerelerinin gruplar arasındaki farkı ve kötü maternal-fetal sonuçlarla ilişkisi değerlendirildi.

Bulgular: İkinci trimester tarama testi belirteçlerinden AFP, HCG ve uE3 seviyelerinde, gruplar arasında istatistiksel olarak anlamlı bir fark bulunmamıştır. Her iki grup birlikte değerlendirildiğinde neonatal ağırlık ile AFP düzeyi arasında negatif yönde, istatistiksel olarak anlamlı bir ilişki bulunmaktadır. Fetal komplikasyon varlığı ile ikinci trimester tarama testi biyokimyasal belirteçlerinden HCG ve E3 kıyaslandığında istatiksel olarak anlamlı bir fark izlenmemiştir. Fetal komplikasyon görülen olguların AFP düzeyleri, fetal komplikasyon görülmeyen olgulardan istatistiksel olarak anlamlı düzeyde yüksek bulunmuştur (p<0.01).

Sonuç: Yüksek AFP MoM değerleri fetal komplikasyon görülmesi açısından uyarıcı olabilirken ikinci trimester tarama testi belirteçlerinin maternal komplikasyonları öngörmede yetersiz olduğu izlenmiştir. Uterin cerrahi geçirilmiş olan ve olmayan gruplarda bu değerlerde fark izlenmemiştir. Bu çalışmanın daha büyük örneklem ile yapılması daha değerli bilgiler elde edilmesini sağlayacaktır.

Anahtar kelimeler: İkinci trimester tarama testi, alfa-fetoprotein, insan koryonik gonadotropin, kötü gebelik sonuçları

SUMMARY

Aim: The purpose of this study is to investigate the association between maternal serum levels of alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), unconjugatedestriol (uE3) and poor pregnancy outcomes, determine whether these markers are effective predictors of poor pregnancy outcomes and to compare their levels in women with prior cesarean section and no prior uterine surgery.

Material and Methods: Women with cesarean section due to a previous uterine surgery (n= 87) and women with no prior uterine surgery and performed vaginal delivery (n= 105) whose prenatal care was performed in the same clinic were included. Second trimester maternal serum levels of AFP, HCG and uE3, as well as multiples of the median (MoM) of these markers were evaluated. Differences in biochemical marker levels between groups and their relationship to poor maternal-fetal outcomes were assessed.

Results: AFP, HCG, and uE3 levels of second trimester screening test markers, no statistically significant difference was found between the groups. When both groups are evaluated together, there is a negative, statistically significant association between neonatal weight and AFP level. When comparing the presence of fetal complications and the biochemical markers of the second trimester screening test HCG and E3, no statistically significant difference was observed. It was found that AFP levels of cases with fetal complications were statistically significantly higher than those of cases without fetal complications (p<0.01).

Conclusion: While high AFP-MoM levels may be a warning of fetal complications, second trimester screening test markers were found to be insufficient to predict maternal complications. The levels of these markers was not different between women with prior cesarean section or no prior uterine surgery. Conducting this study with a larger sample could provide further valuable information.

Keywords: Second trimester screening test, alpha-fetoprotein, humanchorionicgonadotropin, poor pregnancy outcomes

GİRİŞ

Anomaliler açısından yüksek risk barındıran gebelerin belirlenmesi için yapılan tarama testlerinin kullanımı oldukça yaygındır. Son 20 yıl içinde sonografide gerek teknik özellik, gerekse hekimlerin sistematik yaklaşımları sayesinde yaşanan ilerlemeler pek çok anomalinin erken dönemde tanınmasını mümkün kılmıştır. İntrauterin gelişme geriliği (IUGG), preeklampsi, dekolman plasenta gibi gebelikle ilişkili pek çok komplikasyonun, erken gebelik haftalarında uygulanabilecek güvenli, birtakım testlerle belirlenebilmesi, bu komplikasyonların neden olduğu mortalite ve morbiditenin azaltılması açısından son derece önemlidir. Biyokimyasal belirteçler 1980 ve 90'lı yıllarda fetüsteki genetik hastalıkların araştırılması için kullanılmaya başlanmıştır. Başlangıçta sadece nöral tüp defektleri açısından risk altındaki gebeleri araştırmak için kullanılmaya başlanan bu testler daha sonraları diğer anatomik anomaliler, anöploidiler ve üçüncü trimester komplikasyonlarının da araştırılması için kullanılmaya başlanmıştır (1).

16.-20. gebelik haftasında normal fetüse sahip annelerin serumundaki AFP, uE3, HCG düzeylerinin medyan değerinin, trizomi 21'li fetüs taşıyan gebelerdeki medyan değerinden farklı olduğu anlaşılmış, bu belirteçlerin riskli grubu taramada kullanılabileceği düşünülerek 'üçlü test' olarak kullanılması önerilmiştir. Ayrıca test sonuçları trizomiler için riskli bölgede olmasa da yüksek AFP ve/veya yüksek HCG düzeyleri, açık nöral tüp defekti, abdominal duvar defekti ve plasental anomaliler gibi bazı yapısal fetal anomalilerle birlikte olduğu görülmüştür.

Yapılan son çalışmalar birinci ve ikinci trimesterde bakılan serum belirteçlerinin, anne serum seviyelerinin anöploidi ya da nöral tüp defekti yokluğunda kötü obstetrik sonuçlar ile ilişkili bulunduğunu göstermektedir (2).

Bu çalışmanın amacı ikinci trimester biyokimyasal belirteçlerin geçirilmiş uterin cerrahisi bulunan gebeler ile geçirilmiş uterin cerrahisi bulunmayan gebeler arasındaki doğum sonrası maternal ve fetal komplikasyonlar ile ilişkisini değerlendirmektir.

MATERYAL VE METOTLAR

Çalışma Tasarımı

Çalışma Ocak 2011 – Aralık 2012 tarihleri arasında Göztepe Eğitim ve Araştırma Hastanesi Kadın Doğum Kliniğine başvuran uterin cerrahisi olup sezaryen doğum yapmış olan gebeler ve vajinal doğum yapmış olan gebeler dahil edilerek retrospektif olarak planlandı. Tüm olguların hastanemizde yapılmış olan ikinci trimester tarama testlerine biyokimya veri tabanı kullanılarak ulaşıldı. Testin kapsadığı biyokimyasal belirteçlerden serum AFP, HCG ve uE3 düzeyleri ve düzeltilmiş MoM değerleri kayıt edildi.

Çalışmaya Dahil Edilme Kriterleri

1) Kadın hastalıkları ve doğum kliniğinde tek canlı doğum yapan 18 yaş üstü gebeler
2) Aynı klinikte ikinci trimester üçlü tarama testi yaptırmış olan gebeler.

Çalışma Dışı Bırakılma Kriterleri

1) Maternal diyabet, ilk trimesterde yoğun kanama, çoğul gebelikler
2) 2. trimester tarama testinde anöploidi riskinin yüksek olması, fetal nöral tüp defekti, gastroşizis, gastrointestinal atreziler, konjenital hidronefroz, hipospadias gibi AFP düzeylerinin yükselmesine neden olabilen fetal anomaliler.

Kayıtları taranan 155 sezaryen doğumun 87'si bu kriterlere uygun bulunarak çalışmaya dahil edildi. 173 normal doğum yapan olgunun, randomizasyonla belirlenmiş olan 105'i normal doğum grubu olarak belirlendi.

Veriler

Olguların demografik verilerinin sorgulanması amacı ile yaş, gebelik sayısı, doğum sayısı gibi veriler kaydedildi. Geçirilmiş uterin cerrahisi olan hastaların, geçirilmiş olan uterin cerrahi sayısı ve en son uterin cerrahi operasyonunu kaç yıl önce geçirdiği sorgulandı ve kaydedildi.

İkinci trimester taramasında; gebelik haftası, anne yaşı, örnek alınma tarihi ve AFP, HCG, uE3 değerleri kullanılarak MoM değerleri hesaplandı.

Gebeliğin maternal sonuçlarını değerlendirmek için obstetrik nedenli doğum sonu kanama, kan transfüzyonu ihtiyacı, uterin rüptür, histerektomi operasyonu gibi veriler bilgisayar ve dosya kayıtlarından sorgulandı ve kaydedildi.

Düşük doğum ağırılığı doğumdaki gebelik haftasına göre doğum tartısının 10. persentilin altında olması olarak tanımlandı. Neonatal ölüm 22. gebelik haftasında veya daha sonrasında doğan yeni doğanların ilk 29 gün içinde ölümü olarak tanımlandı.

Kötü fetal sonuçlar; neonatal yoğun bakım ünitesinde bakım ihtiyacı, neonatal ölüm, düşük doğum ağırlığı olarak belirlendi ve değerlendirmeye alındı.

İstatiksel İnceleme

Çalışmada elde edilen bulgular değerlendirilirken, istatistiksel analizler için IBM SPSS 22 (IBM SPSS, Türkiye) programı kullanıldı. Çalışma verileri değerlendirilirken tanımlayıcı istatistiksel metotların (Ortalama, Standart sapma, frekans) yanı sıra parametrelerin gruplar arası karşılaştırmalarında Kruskal Wallis testi kullanıldı. Parametrelerin iki grup arası karşılaştırmalarında Mann Whitney U test kullanıldı. Parametreler arasındaki ilişkilerin incelenmesinde Spearman's rho korelasyon analizi kullanıldı. Anlamlılık $p<0.05$ düzeyinde değerlendirildi.

Etik Kurul

Helsinki deklarasyonu ile uyumlu olarak, çalışma Medeniyet Üniversitesi Göztepe Eğitim ve Araştırma Hastanesi Etik Kurulundan 26.08.2014 tarihli karar ile onay alındı.

BULGULAR

Çalışma yaşları 19 ile 43 arasında değişmekte olan toplam 192 kadın ile yapılmıştır. Olguların ortalama yaşları 30.77±4.56 yıldır. Olguların gravida sayıları 1 ile 10 arasında değişmekte olup, ortalaması 2.81±1.23'dır. Olguların parite sayıları 0 ile 7 arasında değişmekte olup, ortalaması 1.40±0.79'dur. Doğum haftası 28 hafta ile 41 hafta arasında değişmekte olup, ortalaması 38.72±1.33 haftadır.

Olguların 87'si (%45.3) sezaryen doğum yaparken, 105'i (%54.7) normal spontan doğum yapmıştır. Sezaryen doğum yapan olguların geçirdikleri uterin cerrahi sayısı 1 ile 3 arasında değişmekte olup, ortalaması 1.15±0.39'dur. Cerrahiyi geçirme süreleri 1 yıl ile 14 yıl arasında değişmekte olup, ortalaması 4.60±2.78'dir.

Olgular uterin cerrahi sonrası sezaryen doğum yapan hasta ve normal spontan doğum yapan hasta grubu olarak değerlendirildiğinde, yaş ortalamaları arasında anlamlı bir farklılık bulunmamaktadır (p>0.05). Normal spontan doğum yapan olguların gravida ve parite sayıları, sezaryen doğum yapan olgulardan anlamlı şekilde yüksektir (Tablo 1).

Tablo 1. Doğum şekli ile yaş, gravida ve parite değerlendirilmesi

	Doğum Şekli		
	Sezaryen Doğum Ort±SS (medyan)	Normal Spontan Doğum Ort±SS (medyan)	*p*
Yaş	30,91±4,13	30,66±4,91	**0,706**[1]
Gravida	2,57±1,07 (2)	3,00±1,32 (3)	**0,002**[2]**
Parite	1,24±0,61 (1)	1,53±0,90 (1)	**0,004**[2]**

Olguların obstetrik ve neonatal sonuçlarına bakıldığında sadece 5 (%2.6) olguda transfüzyon gerektirecek kanama görülmüştür. Bu olguların 5'ine (%2.6) eritrosit transfüzyonu gerekirken sadece 1 (%0.5) olguya TDP transfüzyonu yapılmıştır. Dahil edilen tüm hasta popülasyonunda sadece 3 (%1.6) hastada yoğun bakım ünitesi ihtiyacı duyulmuştur. Yoğun bakım ünitesi ihtiyacı olan hastaların 2'si daha önce uterin cerrahi geçirmiş bu gebeliğinde de sezaryen ile doğum yapmıştır. Normal doğum yapan hastaların sadece 1 tanesinin yoğun bakım ünitesi ihtiyacı olmuştur. Bebeklerin neonatal ağırlıkları 1980 gr ile 5500 gr arasında değişmekte olup, ortalaması 3398.38±477.93 gr'dır. Bebeklerin 6'sı (%3.1) düşük doğum ağırlıklı, 172'si (%89.6) normal doğum ağırlıklı, 14'ü (%7.3) yüksek doğum ağırlıklıdır. Fetal komplikasyon görülen bebek sayısı 5 (%2.6) tir (Tablo 2).

Uterin cerrahi sonrasında sezaryen doğum yapan grup ile normal spontan doğum yapan grubun ikinci trimester maternal serum AFP, HCG ve uE3 MoM düzeyleri arasında istatistiksel olarak anlamlı farklılık bulunmamaktadır (p>0.05) (Tablo 3). Geçirilmiş sezaryen öyküsü olan olguların 3'ün de (%3.4) AFP 2.0 MoM üzerinde izlenirken normal spontan doğum grubunda sadece 1 hastada (%0.95) AFP 2.00 MoM üzerindedir.

Tablo 2. Obstetrik ve neonatal sonuçlar

		n	%
Doğum Şekli	**Sezaryen**	87	45,3
	NSD	105	54,7
Doğum Kilosu	**Düşük**	6	3,1
	Normal	172	89,6
	Yüksek	14	7,3
Maternal Komplikasyon	**Var**	3	1,6
	Yok	189	98,4
Eritrosit Transfüzyonu	**Var**	5	2,6
	Yok	187	97,4
TDP Transfüzyonu	**Var**	1	0,5
	Yok	191	99,5
Fetal Komplikasyon	**Var**	5	2,6
	Yok	187	97,4

Tablo 3. Gruplar arasında HCG, E3 ve AFP MoM değerlerinin kıyaslanması

	Doğum Şekli		
	Uterin cerrahi sonrası sezaryen doğum Ort±SS (medyan)	Normal spontan doğum Ort±SS (medyan)	*p*
HCG (MoM)	1,09±0,59 (0,96)	1,07±0,51 (0,99)	0,827
E3 (MoM)	0,99±0,39 (0,93)	0,93±0,39 (0,84)	0,138
AFP (MoM)	1,01±0,49 (0,89)	0,97±0,34 (0,91)	0,979

Mann Whitney U Test

Her iki grup birlikte değerlendirildiğinde neonatal ağırlık ile AFP düzeyi arasında negatif yönde, %16.3 (çok zayıf) düzeyde ancak istatistiksel olarak anlamlı bir ilişki bulunmaktadır (p:0.024; p<0.05). Neonatal ağırlık ile E3 ve HCG düzeyleri arasında anlamlı bir ilişki bulunmamaktadır (p>0.05) (Tablo 4).

Maternal komplikasyon varlığına göre olguların maternal serum AFP, HCG ve uE3 düzeyleri arasında istatistiksel olarak anlamlı farklılık bulunmazken (p>0.05), fetal komplikasyon görülen olguların maternal serum AFP düzeyleri, fetal komplikasyon görülmeyen olgulardan istatistiksel olarak anlamlı düzeyde yüksek bulunmuştur (p:0.004; p<0.01) (Tablo 5).

Tablo 4. Neonatal ağırlık ile HCG, E3 ve AFP MoM değerleri korelasyonu

	Neonatal Ağırlık	
	r	p
HCG	-0,026	0,723
E3	-0,007	0,924
AFP	-0,163	0,024*

Spearman's rho korelasyon *p<0.05

Tablo 5. Fetal komplikasyona göre HCG, E3 ve AFP MoM seviyelerinin değerlendirilmesi

	Fetal Komplikasyon		
	Var Ort±SS (medyan)	Yok Ort±SS (medyan)	*p*
HCG	1,34±0,77 (0,88)	1,07±0,54 (0,97)	0,498
E3	0,93±0,4 (0,84)	0,95±0,39 (0,88)	0,804
AFP	1,76±0,89 (1,46)	0,97±0,38 (0,88)	0,004**

Mann Whitney U Test **p<0.01

TARTIŞMA

Çalışmamızda anormal maternal serum belirteç seviyeleri ile kötü obstetrik sonuçlar arasındaki ilişki değerlendirildiğinde sadece fetal komplikasyon görülmesi ile yüksek AFP MoM değerleri arasında anlamlı ilişki gözlenmiştir. Geçirilmiş uterin cerrahi sonrasında sezaryen ile doğum yapan grup ile normal spontan doğum yapan grup arasında ikinci trimester maternal serum belirteçleri arasında fark izlenmemiştir.

Birinci ve ikinci trimester tarama testleri fetal anöploidi taraması amacıyla yapılmaktadır. Günümüzde birinci trimester tarama testi öncelikli olarak tercih edilmektedir. Ultrason teknolojilerinin günden güne gelişmesiyle birlikte ikinci trimesterde maternal serum HCG ve maternal serum AFP taramasına olan gereksinim giderek azalmaktadır (3). Yapılan son çalışmalar birinci ve ikinci trimester tarama testi biyokimyasal belirteçlerinin anne serum seviyelerinin anöploidi ya da nöral tüp defekti yokluğunda kötü obstetrik sonuçlar ile ilişkili bulunduğunu göstermektedir (2).

J.-L. Hu ve arkadaşlarının yaptığı çalışmada artmış maternal serum AFP düzeyleri kötü gebelik sonuçları ile ilişkili bulunmuştur. Nöral tüp defekti yokluğunda maternal serum AFP yüksekliğinin en sık sebepleri spontan abort, ölü doğum ve erken başlangıçlı preeklamsi olarak gösterilmiştir (4).

Yapılan başka bir çalışmada açıklanamayan ikinci trimester maternal serum AFP yüksekliğinin kötü maternal /fetal sonuçlar ile anlamlı ilişkili olduğu saptanmıştır. Bu çalışmada maternal serum AFP (>2.50 MOM) olan grupta preterm doğum, preterm erken membran rüptürü (PPROM), IUGG riskinin belirgin olarak arttığı görülürken preeklamsi riskinde anlamlı bir fark bulunamamıştır (5).

Açıklanamayan maternal serum belirteçleri yüksekliğinde artmış olan kötü obstetrik sonuçların patofizyolojik mekanizmasının plasental fonksiyon bozukluğuyla ilişkili olduğu düşünülmektedir. Tespit edilen maternal serum AFP yüksekliğinin, plasental feto-maternal yüzey alanı hasarına bağlı olarak, AFP'nin maternal dolaşıma artmış geçişine bağlanmıştır. (6)

Hsieh ve arkadaşları da çalışmalarında uteroplasental dolaşımın bozulduğu gebelerde maternal serum serbest HCG seviyesinin belirgin olarak yüksek olduğunu saptamışlardır. Özellikle plasentanın uterus duvarına yapışma anomalilerinde serbest HCG'nin yüksek bulunduğunu belirtmektedirler (7).

Literatürde anomali olmayan fetüste artmış maternal serum AFP'nin plasenta akreata ile ilişkili olduğunu gösteren çalışmalar vardır (8). Benzer şekilde Dj. Lyell ve arkadaşları da artmış ikinci trimester maternal serum AFP seviyelerini uterusa ileri derecede yapışmış plasenta ile ilişkili bulmuştur (9).

E.Öztaş ve arkadaşları yaptıkları çalışmada ikinci trimesterde yükselmiş maternal serum AFP'nin plasenta previa totalis olan hastalarda histerektomi, gerektiren ileri derecede yapışmış plasentayı öngörebileceğini öne sürmüşlerdir (10).

Daha önceden uterin cerrahi geçirmenin plasentanın myometriuma invazyonu olsun ya da olmasın sadece myometrial bütünlüğün bozulmasının plasental yüzeyden maternal dolaşıma fetal serum belirteçlerinin geçişine neden olabileceğini düşünerek önceki doğumunu sezaryenle yapıp myometrial bütünlüğü bozulmuş hastaların maternal kandaki 2. trimester biyokimyasal belirteçlerinin düzeylerini uterin cerrahi geçirmemiş hastalarla kıyasladık. Çalışmamızda bir önceki doğum şekline göre AFP, HCG, E3 düzeyleri ortalamaları karşılaştırıldığında istatistiksel olarak anlamlı fark bulunamamıştır.

Krause ve arkadaşları yaptığı çalışmada AFP'nin 0.25 MoM altında olmasını spontan abort, preterm doğum (<37 gebelik haftası), ve ölü doğum ile ilişkili bulmuştur. Aynı zamanda AFP seviyesi 0.25 MoM altında olduğunda 90. persentil üzerinde doğum ağırlığı insidansının arttığını bildirmişlerdir (11). Bizim çalışmamızda AFP 0.25 MoM düzeyi altında hasta bulunmamaktadır, fakat benzer şekilde bizim çalışmamızda da neonatal ağırlık ile AFP düzeyi arasında negatif yönde, %16,3 (çok zayıf) düzeyde ancak istatistiksel olarak anlamlı bir ilişki bulunmaktadır (p:0,024). Neonatal ağırlık ile HCG ve E3 düzeyleri arasında anlamlı bir ilişki bulunamamıştır.

Gebelik boyunca veya doğum sonrası dönemde yaşamı tehdit edici olaylar ve yoğun bakım gereksinimi olabilir (12). Çalışmamıza dahil edilen tüm hasta popülasyonunda yoğun bakım ünitesi ihtiyacı sadece 3 (%1.6) hastada duyulmuştur. Sezaryen doğum ile meydana gelen postoperatif komplikasyonlar, normal vajinal doğumla olanlardan daha yüksek olmaya devam etmektedir (13). Anneye ait komplikasyonlar sezaryen ile doğumda, vajinal doğuma göre daha fazladır (14). Bizim çalışmamızda da yoğun bakım ünitesi ihtiyacı olan hastalarda 2'si daha önce geçirilmiş sezaryen öyküsü bulunup bu gebeliğinde de sezaryen ile doğum yapmıştır. Normal doğum yapan hastaların sadece 1 tanesinin yoğun bakım ünitesi ihtiyacı olmuştur. Çalışmamızdaki olgu sayısının azlığı bu konuda net bir kanaat oluşumunu engellemektedir.

Heinonen ve arkadaşları 2.0 MoM üzerindeki HCG değerlerinin gebelik komplikasyonları ve kötü sonuçlarından preeklampsi gelişme oranı, IUGG gelişimi, valematöz umblikal kord insersiyonu risklerinin arttığı ancak preterm doğum, fetal distress, fetal-perinatal ölüm ve yeni doğan yoğun bakım ünitesi kabul oranlarında kontrol grubuna göre istatistiki anlamlı fark olmadığı sonucuna varmışlardır (15). Bizim çalışmamızda da artmış HCG değerleri ile fetal komplikasyon olarak değerlendirilen yeni doğan yoğun bakım ünitesi ihtiyacı arasında istatistiksel olarak anlamlı fark bulunmamıştır. Bunun yanında fetal komplikasyon

görülen olguların AFP düzeyleri, fetal komplikasyon görülmeyen olgulardan istatistiksel olarak anlamlı düzeyde yüksek bulunmuştur (p:0.004; p<0.01). Literatürde gebelik komplikasyonlarıyla ilgili çelişkili sonuçlar olmakla birlikte genel kanı AFP yüksekliği ile IUGG, preterm eylem ve intrauterin fetal ölümün arttığıdır (2,4,5).

Yapılan çalışmaların aksine biz çalışmamızda ikinci trimester tarama testleri serum belirteçlerinin gebelik komplikasyonlarını öngörmede yetersiz olduğunu gördük. Çalışmanın görece az sayıda olgu ile yapılmış olması sonuçların yorumlanmasında kısıtlılık oluşturmaktadır.

Sonuç olarak gebelikte bakılan ikinci trimester biyokimyasal belirteçlerin, kötü gebelik sonuçlarını öngörebilirliği tartışmalı bir konu olmaya devam etmektedir. Anormal maternal serum belirteç seviyeleri ile kötü obstetrik sonuçlar için uyarıcı olmasına rağmen klinik tarama testi olarak kullanılmak için sensitiviteleri ve pozitif prediktif değerleri düşüktür. Kötü perinatal sonuçların öngörülebilmesi için daha fazla çalışmaya ihtiyaç vardır. Uterin cerrahi geçirmiş olan ve olmayan gruplarda bu değerlerde fark izlenmemiştir. Bu çalışmanın daha büyük örneklem ile yapılması daha değerli bilgiler elde edilmesini sağlayacaktır.

Yazar Katkıları: Çalışma Konsepti/Tasarımı: HKY, HB, AG, Veri Toplama: HKY, Veri Analizi/Yorumlama: HKY, ADEC, ZEUK Yazı Taslağı: HKY, HB, ADEC, İçeriğin Eleştirel İncelemesi: HB, ADEC, ZEUK, AG Son Onay ve Sorumluluk: HKY, Malzeme ve teknik destek: HKY, ZEUG, Süpervizyon: HB, ADEC
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KAYNAKLAR

1. Sayın N, Canda M, Ahmet N, Arda S, Süt N, Varol F The association of triple-marker test results with adverse pregnancy outcomes in low-risk pregnancies with healthy newborns. Arch of Gynecol&Obstet. 2008;277(1):47-53
2. Dugoff L. First and second-trimestermaternal serum markers for aneuploidy and adverse obstetric outcomes. Obstet Gyne¬col.2010;115(5):1052-61
3. Gagnon A, Wilson RD, Audibert F, Allen VM, Blight C, Brock JA. Obstetrical complications associated with abnormal maternal serum markers analytes. J Obstet Gynaecol Can. 2008;30(10):918–32
4. Hu JL, Zhang YJ, Zhang JM et al Pregnancy outcomes of women with elevated second-trimester maternal serum alpha-fetoprotein. Taiwan J Obstet Gynecol. 2020;59(1):73-78
5. Başbuğ D, Başbuğ A, Gülerman C Is unexplained elevated maternal serum alpha-fetoprotein still important predictor for adverse pregnancy outcome? Ginekol Pol. 2017;88(6):325-330
6. Morssink LP, Wolf BT, Kornman LH, Beekhuis JR. The relation between serum markers in the second trimester and plasental pathology. Br J Obstet Gynaecol.1996;103(8):779-83
7. Hsieh TT, Hung TH, Hsu JJ, et al. Prediction of adverse perinatal outcome by maternal serum screening for Down syndrome in an Asian population. Obstet Gynecol. 1997;89(6):937-40
8. Hung TH,Shau WY,Hsieh CC, et. Al.Risk factors for placenta accreta. Obstet Gynecol.1999;93(4):545-50
9. Lyell DJ, Faucett AM, Baer RJ 3, et. al. Maternal serum markers, characteristics and morbidly adherent placenta in women with previa. J Perinatol. 2015;35(8):570-4.
10. Oztas E, Ozler S, Caglar AT, Yucel A Analysis of first and second trimester maternal serum analytes for the prediction of morbidly adherent placenta requiring hysterectomy. Kaohsiung J MedSci. 2016;32(11):579-85.
11. Krause TG, Christens P, Wohlfahrt J, Lei U, et al. Second-trimester maternal serum alpha-fetoprotein and risk of adverse pregnancy outcome. Obstet Gyneacol. 2001;97(2):277-82
12. Demirkiran O, Dikmen Y, Utku T, Urkmez S. Critically ill obstetric patients in the intensive care unit. Int J Obstet Anesth. 2003;12(4):266-70.
13. Ott W: Primary caesarean section; factors related to postpartum infection. Obstet Gynecol. 1981;57(2):171–78
14. Çiçek N, Akyürek C,Çelik Ç, Haberal A. İkinci Trimester Fetal Anomali Tarama Testleri Ch.35 Kadın Hastalıkları ve Doğum Bilgisi II. Baskı Ankara: Güneş Kitabevi,2006;399-410
15. Heinonen S, Ryynanen M, Kirkinen P, Saarikoski S. Elevated mid-trimester maternal serum HCG in chromosomally normal pregnancies is associated with preeklampsia and velamentous umblical cord insertion. Am J Perinatol 1996; 13(7): 437-41

ORIGINAL ARTICLE
KLİNİK ARAŞTIRMA

Portabl pulse oxymetry and contrast echocardiography in hepatopulmonary syndrome diagnosis

Hepatopulmoner sendrom tanısında portabl pulse oksimetre ve kontrast ekokardiyografi

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SUMMARY

Aim: The aim of this study is investigating hepatopulmonary syndrome's (HPS) diagnosis in cirrhosis patients with ortodeoxy symptom by portabl pulse oxymetry and transthoracic echocardiography with contrast enhancement.

Material and Methods: Ninety five (95) patients (67/28 M/F) with the diagnosis of cirrhosis were included into the study. Mean age of the patients was 52,28±12,0. Measurements of portabl pulse oximetry were obtained in a supin position and in a seated position breathing room air. The suitable patients' response to oxygen therapy with nasal cannula was evaluated. The patients with hypoxaemia (Sa,02<%94) in seated position were investigated HPS by transthoracic echocardiography with contrast enhancement.

Results: Eight (8) patients defined HPS had hypoxaemia in seated position with pulse oxymetry and positive contrast echocardiography. Four patients (4) had type I HPS and four patients (4) had type II HPS.

Conclusion: In conclusion, eight of 95(%8,4) patients had HPS. Patients with HPS were old age and were in Child B and C class. In cirrhosis patients with hypoxaemia in seated position, further studies are needed to investigate HPS.

Keywords: Hepatopulmonary syndrome, hypoxaemia, pulse oxymetry, transthoracic contrast echocardiography

ÖZET

Amaç: Bu çalışmanın amacı, ortodeoksi semptomu olan siroz hastalarında hepatopulmoner sendrom (HPS) tanısının portabl pulse oksimetri ve kontrastlı transtorasik ekokardiyografi ile araştırılmasıdır.

Materyal ve Metodlar: Çalışmaya siroz tanılı doksan beş (95) hasta (67/28 E/K) dahil edildi. Hastaların yaş ortalaması 52,28±12,0 idi. Portabl nabız oksimetresi ölçümleri, supin pozisyonunda ve oturma pozisyonunda oda havasını soluyarak elde edildi. Uygun hastaların nazal kanül ile oksijen tedavisine yanıtları değerlendirildi. Oturur pozisyonda hipoksemisi (Sa,02<%94) olan hastalarda kontrastlı transtorasik ekokardiyografi ile HPS incelendi.

Bulgular: HPS olarak tanımlanan sekiz (8) hastada nabız oksimetrisi ve pozitif kontrastlı ekokardiyografi ile oturur pozisyonda hipoksemi vardı. Dört hastada (4) tip I HPS ve dört hastada (4) tip II HPS vardı.

Sonuç: Sonuç olarak 95 (%8,4) hastanın sekizinde HPS vardı. HPS'li hastalar ileri yaştaydı ve Child B ve C sınıfındaydılar. Oturur pozisyonda hipoksemisi olan siroz hastalarında HPS'yi araştırmak için daha ileri çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Hepatopulmoner sendrom, hipoksemi, nabız oksimetrisi, transtorasik kontrast ekokardiyografi

INTRODUCTION

One of the pulmonary complications of cirrhosis, which is related to portal hypertension and important for liver transplantation, is hepatopulmonary syndrome (HPS). Hepatopulmonary syndrome with arterial hypoxemia, intrapulmonary vascular dilatation or shunts is very important especially in the process of identifying transplant candidates and evaluating the efficiency of transplantation (1,2). Intrapulmonary vascular dilatation or shunt is indicated by positive transthoracic contrast echocardiography, especially in patients with hypoxemia in the seated position (Pa,02<80 mmHg and Pa,02<70 mmHg with arterial blood gas or Sa,02 <92% with pulse oximetry). In these patients, the demonstration of extrapulmonary involvement by lung scintigraphy with macroaggreated albumin labeled with technetium 99m and the demonstration of dilated vessels or arteriovenous connections by pulmonary angiography support the diagnosis of HPS. Many studies have investigated the frequency of HPS in cirrhotic patients with hypoxemia, especially with pulse oxymetry sampling. Contrast echocardiography is the gold standard for HPS screening in patients with hypoxemia (3-6).
We aimed to diagnose hepatopulmonary syndrome by pulse oxymetry and transthoracic contrast echocardiography in patients with cirrhosis with orthodeoxy symptom.

MATERIAL AND METHODS

In accordance with the Ethics Committee of Çukurova University Faculty of Medicine (13092006/8) and in accordance with the Principles of the Declaration of Helsinki, 95 patients with cirrhosis who were followed up in Çukurova University Faculty of Medicine Gastroenterology Department were included in this single center cohort study. HCC, lung cancer diagnosis. history of upper and lower GI bleeding, history of COPD, history of right heart failure and previous transplantation were considered exclusion criteria.

Diagnostic Criteria of HPS

Chronic Liver Disease,Late positive contrast echocardiography (left atrial microbubble opacification after 3 heart beats after right atrial opacification) Abnormal oxygenation (pulse oximetry) when transitioning from supine to seated position were considered HPS diagnosis.
Cirrhosis was classified according to functional, etiological and clinical stages.

Severity of liver disease was evaluated by Child-Pugh scoring method (Table-1).

Table 1. Modified child-pugh-turcott scoring system

Parameter	Numerical score		
	1	2	3
Ascites	None	Slight	Moderate to severe
Encephalopathy	None	Slight to moderate	Moderate to severe
Bilirubin (mg/dL)	< 2.0	2-3	> 3.0
Albumin (g/dL)	> 3.5	2.8-3.5	< 2.8
Prothrombin time (prolonged in seconds)	1-3 s	4-6 s	> 6.0

Child's Pugh Class A = 5-6 points; Child's Pugh Class B = 7-9 points; Child's Pugh Class C = 10-15 points.

At the end of the scoring, those with 5-6 points were considered as Child-Pugh A, those with 7-9 points as Child-Pugh B and those with 10-15 points as Child-Pugh C (Severe liver disease).

Echocardiographic Criterion

Trans-thoracic contrast-enhanced echocardiography was performed in patients with cirrhosis who could be compatible with HPS. After 10 ml of %3 saline solution was administered from the upper extremity peripheral vein, patients with positive contrast echocardiography were described as having intrapulmonary vascular dilatation. Positive contrast echocardiography was performed 3 heartbeats without right atrial opacification following administration of saline solution. It was considered as the opacification of microbubbles in the left atrium after post-operative period (7). These findings supported the dilated precapillary or capillary or direct arteriovenous connections of microbubbles in intrapulmonary passage. Intra atrial right-to-left shunt supported by opacification in the left atrium in less than 3 cardiac cycles was not observed in any patient.

Abnormal Oxygenation Criterion

Oxygen saturation measurement with portable pulse oximetry was applied to evaluate the oxygenation of the patients in the lying (after 10 minutes) and seated (at the end of 15 minutes) positions.

Working Design

95 cirrhosis patients followed in Çukurova University Faculty of Medicine Gastroenterology Department were included in the study. The functional, clinical stages and etiological classifications of chronic liver diseases of the patients were performed. The oxygenation status of the patients was measured by pulse oximetry. Oxygenation was evaluated with pulse oximetry in 95 patients. SaO2 <94% in sitting position with pulse oximetry (3.4) was considered significant for HPS. Response to oxygen therapy with pulse oximetry in sitting position was evaluated by giving 02 through nasal cannula for 15 minutes in the seated position to patients who were compatible with HPS. Sa02 >97% after 15 minutes of nasal cannula 02 was evaluated as response to treatment. The patient group responding to oxygen was classified as HPS type I. The patient group that did not respond to oxygen was classified as HPS type II.

Augmented transthoracic contrast echocardiography was performed in patients who were hypoxemic in the seated position. In patients with positive contrast echocardiography results, technetium 99m-labeled macroaggregated albumin lung scintigraphy was used to evaluate HPS severity and intrapulmonary shunt, lung HRCT to exclude comorbid disease, and arteriovenous focal arteriovenous connections, spider varicose or diffuse arteries. Pulmonary angiography was performed to show vascular abnormalities. Intracardiac right-to-left shunt was excluded with contrast echocardiography. The dyspnea-orthopnea status of the patients compatible with HPS was evaluated by physical examination, and the acid status by ultrasonography.

Statistical Analysis

Data were analyzed with SPSS (Statistical Packages of Social Sciences, SPSS for Windows Version 25.0, Chicago, IC, USA) package program. Age values were summarized as mean, SD, median, min and max values, and discrete variables such as gender and etiology were summarized as numbers and percentages. Chi-square test was used to compare discrete variables, and Mann-Whitney U test was used to compare continuous variables.

RESULTS

Findings

95 patients with cirrhosis were included in the study. 67 (70.5%) of the patients were male. The mean age of the patients was 52.28±12.0.

The chronic liver disease etiologies of the patients included in the study were examined. (Table 2)

Table 2. Etiology of cirrhosis

Etiology	Number	Percent
Unknownn	18	18,9
HBV	44	46,3
HCV	18	18,9
Alcohol	9	9,5
Autoimmune	2	2,1
Others (Metabolic..)	4	4,2
Total	95	100,0

The distribution of patients included in the study according to Child-Pugh scoring was analyzed (Table 3)

Table 3. Distribution of patients according to Child-Pugh scoring

Child-Pugh scoring	Number (n)	Percent (%)
Child A	14	14,7
Child B	41	43,2
Child C	40	42,1
Total	95	100,0

In 95 cirrhosis patients included in the study, hypoxemia in the seated position and 8 (8.42%) patients were diagnosed with HPS according to the results of positive contrast echocardiography (Table 4,5). 4 of 8 HPS patients were considered as HPS type I responding (50%) to oxygen therapy and 4 as HPS type II unresponsive to oxygen therapy (50%).

Table 4. Frequency of HPS

HPS	Number (n)	Percent (%)
HPS not detected	87	91,6
Type 1 HPS	4	4,2
Type 2 HPS	4	4,2
Total	95	100,0

Table 5. Evaluation of patients with orthodeoxia by contrast echocardiography

Positive contrast echocardiography	Number (n)	Percent (%)	Valid Percentage (%)	Cumulative Percentage (%)
negative	11	11,6	57,9	57,9
grade 1	4	4,2	21,1	78,9
grade 2	1	1,1	5,3	84,2
grade 3	3	3,2	15,8	100,0
Total	19	20,0	100,0	
Others	76	80,0		
Total	95	100,0		

The etiology of the underlying cirrhosis was HCV in 3 of 8 patients diagnosed with HPS (37.5%), HBV (25%) in 2, and the etiology of the underlying cirrhosis in 3 (37.5%). 3 of the patients were female (27.5%) and 5 were male (62.5%). 6 of 8 patients who were diagnosed with HPS had a Child score of C (75%) and 2 had a Child score of B (Ascites was present in 7) (87.5%) of 8 HPS patients and no acid was detected in 1 HPS patient (12.5%). We detected HPS in 8 patients with pulse oximetry (Sa 02 as ≤94%). In patients diagnosed with HPS, lung HRCT was performed to exclude comorbidities and no comorbidity was detected in the patients. MAA lung scintigraphy and pulmonary angiography were performed in 3 patients to show intrapulmonary vascular dilatation or shunt, but no significant results were obtained.

The mean age of HPS patients with cirrhosis (58.75±11.63) and Child Pugh score were significantly higher than the mean age of the other 87 patients with cirrhosis (51.68±11.9) and Child Pugh score (with 99% confidence interval)($P < 0.001$).

DISCUSSION

Hepatopulmonary Syndrome is a pulmonary complication of cirrhosis and its frequency is 4-29% in patients with cirrhosis (7-9). The average incidence is 15% (10,11). The causes of HPS are not fully known, but are considered to

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result from an imbalance between vasoconstrictors and vasodilators and/or hepatic factors that stimulate and inhibit vascular cell growth (5-7). It is defined as an arterial oxygenation defect caused by intrapulmonary vascular dilatations (IPVD) associated with liver disease (4-6). Its vascular component typically includes diffuse or localized dilated pulmonary capillaries, and less commonly pleural and pulmonary arteriovenous connections. Shortly, HPS is defined a clinical triad that includes arterial deoxygenation ,IPVD and liver disorder.

In our study, of 8 patients who were diagnosed with HPS in 95 cirrhosis patients, 6 were Child C and 2 were Child score B class. Similar findings were shown in a study which was conducted with 98 cirrhosis patients, 9 of 33 HPS patients were in Child B and 24 in Child C, and 66% of 98 cirrhosis patients included in the study were male and 34% were female (12). Likewise, in a study by Amir Houshang Muhammed Alizadeh friends, age and Child C classification were significantly associated with HPS (13). With portable pulse oximetry, we detected 8 patients (8.42%) with a Sa02 <94 in 95 cirrhosis patients in seated position and positive results with contrast echocardiography. Peter Deibert et al. found the frequency of HPS to be 5.4% with contrast echocardiography in patients with Sa02≤93 in the seated position (13). As a result of the same study, they recommend pulse oximetry and HPS examination with portable pulse oximetry in patients with severe hypoxemia. HPS was investigated by transthoracic contrast echocardiography in patients with hypoxemia in the seated position. Positive contrast echocardiography results were obtained in 8 (42%) of 19 eligible hypoxemic patients. Similar results were obtained with a positive contrast echo of 47% in 53 hypoxemic cirrhosis patients performed by Hopkins et al.(14).

CONCLUSION

In our study, the frequency of hepatopulmonary syndrome was found to be 8.4% in patients with cirrhosis. HPS has been investigated to identify candidates suitable for liver transplantation and to predict post-transplant survival and mortality. Oxygenation status was investigated with an easy-to-use noninvasive pulse oximeter, and HPS was diagnosed by transthoracic contrast echocardiography, a noninvasive method, in suitable patients. Larger case studies are needed for HPS screening in patients with cirrhosis.

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REFERENCES

1. Peter Schenk,Maximilian Schöniger-Hekele,Valentin Fuhrmann,Christian Madl, Gerd Silberhumer,Christian Müller. Prognostic significance of the hepatopulmonary syndrome in patients with cirrhosis. Gastroenterology 2003;125:1042–1052.
2. Offer J, Green L, Houghton AR, Campbell J. A case of hepatopulmonary syndrome. Echo Res Pract. 2015;2(2):K25-K27.
3. Lenci I, Alvior A, Manzia TM, Toti L, Neuberger J, Steeds R. Saline contrast echocardiography in patients with hepatopulmonary syndrome awaiting liver transplantation. J Am Soc Echocardiogr. 2009;22(1):89-94.
4. Lucas SoutoNacif,Erica Karen DextreTorres,Paola Sofia etal. Hepatopulmonary syndrome in waiting list and liver transplant. Transplantation Reports. 2020; Volume 5, Issue 3.
5. Piltcher-da-Silva R, Chedid MF, Grezzana Filho TJM, et al. Severe hepatopulmonary syndrome with hypoxemia refractory to liver transplant: Recovery after 67 days of ECMO support. The International Journal of Artificial Organs. 2022;45(1):121-123.
6. Abrams GA et al. Diagnostic utility of contrast echocardiography and lung perfusion scan in patients with hepatopulmonary syndrome. Gastroenterology. 1995;109:1283–1288.
7. María J. Rollán, Ana C. Muñoz, Teresa Pérez, José L. Bratos, Value of contrast echocardiography for the diagnosis of hepatopulmonary syndrome, European Journal of Echocardiography. 2007;8(5):408–410.
8. Whyte MK et al.Analysis of intrapulmonary right to left shunt in the hepatopulmonary syndrome. J Hepatol. 1998;29:85–93.
9. Jensen DM, Pothamsetty S, Ganger D, et al. Clinical manifestations ofcirrhotic patients with intrapulmonary shunts. Gastroenterology 1994;106.
10. Aller R et al. Diagnosis of hepatopulmonary syndrome with contrast transesophageal echocardiography: advantages over contrast transthoracic echocardiography. Dig Dis Sci. 1999;44:1243–1248.
11. Schenk P et al. Hepatopulmonary syndrome: prevalence and predictive value of various cut offs for arterial oxygenation and their clinical consequences. Gut. 2002;51:853–859.
12. Amir Houshang Mohammad Alizadeh et al. Clinical features of hepatopulmonary syndrome in cirrhotic patients. World J Gastroenterol. 2006;28:1954-1956.
13. Deibert P et al.Hepatopulmonary syndrome in patients with chronic liver disease : role of pulseoximetry. BMC Gastroenterology. 2006;6:15.
14. Hopkins WE, Waggoner AD, Barzilai B. Frequency and significance of intrapulmonary right-to- left shunting in endstage hepatic disease. Am J Cardiol. 1992;70:516–519.

CASE REPORT
OLGU SUNUMU

Reverse palmaris longus: A benign cause of swelling on the forearm

Ters palmaris longus: Ön kolda benign bir şişlik nedenifi

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SUMMARY

As a normal anatomic structure, the palmaris longus muscle originates from the medial epicondyle of the humerus and descends obliquely through the wrist. It has a flattened tendon distally and, after passing over the flexor retinaculum, inserts to the palmar aponeurosis superficially. As the exact opposite of this normal anatomy of palmaris longus muscle, reversed palmaris longus (RPL) has a tendinous part proximally and a muscular portion distally. RPL is a rare muscular abnormality. On MRI, RPL muscle belly is typically evident at the volar aspect of forearm, medial to the flexor carpi radialis tendon, which is of muscle signal on all sequences. Familiarity with the variant, ultrasound and MRI appearance of RPL and accurately describing relevant imaging findings is essential for guiding effective management decisions and optimizing treatment outcomes.

Keywords: Palmaris longus, muscle, reversed, ultrasound, magnetic resonans imaging

ÖZET

Normal bir anatomik yapı olarak palmaris longus kası, humerusun medial epikondilinden köken alır ve ön kol boyunca ilerleyerek distalde fleksör retinakulumu geçtikten sonra yüzeyel bir tendon olarak palmar aponevroza yapışır. Bu normal palmaris longus kas anatomisinin tam tersi olarak, ters palmaris longus proksimalde tendinöz bir kısma ve distalde kaslı bir kısma sahiptir. Ters palmaris longus nadir görülen bir kas anomalisidir. MRG'de, ters palmaris longus kasına ait kas öbeği fleksör karpi radialis tendonunun medialinde, ön kol volar yönünde tüm sekanslarda kas ile eş sinyalli olarak karşımıza çıkmaktadır. Bu anatomik varyantın ultrason ve MR görünümüne aşina olmak ve görüntüleme bulgularını doğru bir şekilde tanımlamak, tedavi kararlarına rehberlik etmek ve tedavi sonuçlarını optimize etmek için esastır.

Anahtar kelimeler: Palmaris longus, kas, ters, ultrason, manyetik rezonans görüntüleme

INTRODUCTION

Reversed palmaris longus (RPL) is a rare muscular abnormality. As a normal anatomic structure, the palmaris longus muscle (PLM) originates from the medial epicondyle of the humerus and descends obliquely through the wrist. It has a flattened tendon distally and, after passing over the flexor retinaculum, inserts to the palmar aponeurosis superficially. As the exact opposite of this normal anatomy of PLM, RPL has a tendinous part proximally and a muscular portion distally. The muscle shows significant anatomical variance such as agenesis, hypertrophy, duplication, bifid, and variations in its origin and insertion (1). These variations of PLM can be symptomatic in some cases involving peripheral nerve compression and effort-related compartment syndrome (2).

Even ultrasound (US) and magnetic resonance imaging (MRI) are frequently used in the workup, little has been previously described in the literature regarding ultrasound and MRI findings of RPL. In this case report, we present a patient with the complaint of forearm swelling and pain who was ultimately diagnosed with RPL.

CASE REPORT

A 38-year-old woman presented with a history of persistent swelling on her right forearm since her childhood. She had no health complaints other than the disorder involving her arm. She is the first of three children born to non-consanguineous healthy parents. Her sibling and parents do not have any skeletal disorders. The patient reported effort-related pain on the swelling side. On physical examination, Mishra's test was applied to the patient. While the fingers are hyperextended, the patient was asked to flex the wrist (3). The test demonstrated palmaris longus muscle (PLM) tendon on the distal forearm which is the normal anatomical location. On the other hand, her right wrist has shown no superficial tendinous structure, but a palpable lump was visible on her forearm measured approximately 8 cm long and 2 cm in diameter (Figure 1). The patient reported having undergone the US and MRI scans three years ago and received conflicting reports such as muscle herniation or lipoma.

Figure 1 (a). Examination of the patient's left wrist and forearm revealed PLM's tendon which has a superficial lying. This is the normal anatomic extension of the tendon (black arrow). **(b)** Examination of the patient's right wrist and forearm showed absence of PLM's tendon. There's a swelling which represent reverse muscle belly instead of the tendon of PLM.

Antero-posterior and lateral radiograph of right forearm revealed no pathology. For further evaluation, the patient underwent to ultrasound and MRI. Antebrachial fossa ultrasound demonstrated a muscle belly located superficially on the flexor compartment of the wrist (Figure 2). A wrist MRI revealed an extra muscle belly located anterolaterally of the flexor retinaculum as well as adjacent to the median nerve (Figure 3).

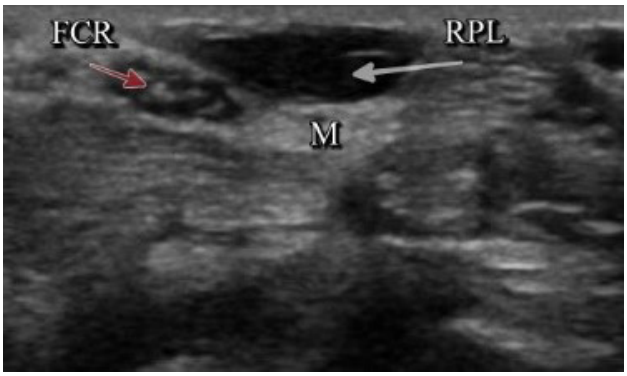

Figure 2. Transverse US images of the right wrist showing the flexor tendons (FT) and median nerve (M). On the volar surface of the forearm show the distal belly of the reversed palmaris longus (RPL) lying in a superficial position, adjacent to the flexor carpi radialis (FCR) tendon. The median nerve is deeper than the RPL.

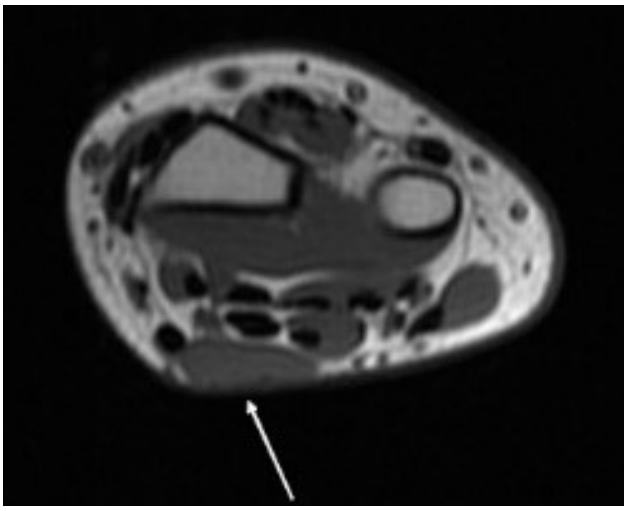

Figure 3. Axial T1-weighted image at the level of flexor tendons shows reverse palmaris longus muscle belly isointense to the adjacent muscles (white arrow).

DISCUSSION

RPL is a rare muscular abnormality and was first described as an anatomic variant through the dissection in 1868 at King's College London (4). Subsequently, in 1993, Giunta et al. first described a symptomatic case of a 21-year-old male who had suffered from median nerve compression

that was treated with surgical excision (5). It is generally known that palmaris longus is the most variable muscle in human anatomy (6). PLM agenesis has been described as the most common anatomical variation observed in about 2% to 25% of the population. All other anatomical variants are found in about 9% of the population, which includes duplicated PLM, triple-headed PLM, accessory PLM, and RPL (7,8). Approximately 70% of RPL cases present in the right forearm, while near 30% were found in the left and no significant correlation was reported between gender and RPL (6).

For the initial diagnosis, the history of the patient and a careful physical examination are helpful. Swelling on the forearm has been present for a long time in patients with RPL. The clinical presentation of RPL widely ranges from asymptomatic swelling to pressure on the ulnar nerve, ulnar artery, and median nerve proximal to the carpal tunnel (9). The pathophysiology of symptomatology is thought to be due to the compression of nerves beneath the reversed muscle. The case presented here occurred effort-related land unlike the findings of other reported cases of RPL (1,7,10) our patients did not complain of paresthesia. We believe that hypertrophy of the RPL muscle belly within the unyielding ante-brachial fascia resulted in an effort-related compartment syndrome (2).

Radiographs are the first-line imaging modality for patients with forearm complaints in these cases are almost always nondiagnostic. Ultrasound combines the excellent ability for deep penetration into soft tissues with good spatial resolution and can be helpful in the diagnosis. Nevertheless, cross-sectional imaging is generally needed to confirm the diagnosis. On MRI, RPL muscle belly is typically evident at the volar aspect of forearm, medial to the flexor carpi radialis tendon, which is of muscle signal on all sequences (1). Even, ultrasound and MRI are frequently used in the workup of wrist and forearm complaints, little has been previously described in the literature with regard to ultrasound and MRI findings of RPL (10,11). Ultrasound and MRI are not also particularly useful incorrect diagnosis but also very accurate in highlighting the etiology of the pain by detecting arterial or neural pathologies such as edema or pressure in the adjacent soft tissues.

Recommended treatment for symptomatic RPL is surgery and generally involves excision of the muscle. Prompt and accurate diagnosis of RPL is crucial as delayed treatment can lead to progressive muscle atrophy and nerve impingements with disability (12). Surgical outcomes are excellent with reduction in symptoms and no residual physical limitations (13). It is important that the hand surgeon is aware of the RPL to prevent intraoperative confusion and allow appropriate intervention in the case of clinical symptomatic. It should be noted that RPL may be symptomatic and that a high index of clinical suspicion should be used in conjunction with ultrasound and MRI.

CONCLUSIONS

RPL is rare based on a limited number of published case reports, but the prevalence may be higher than originally thought when more cases are recognized by advanced imaging methods. Definitive diagnosis is made almost exclusively by ultrasound and cross-sectional imaging and radiologists play a key role in initial diagnoses. Familiarity with the variant, US, and MRI appearance of RPL and accurately describing relevant imaging findings, including peripheral nerve abnormalities and flexor retinacular structures is essential for guiding effective management decisions and optimizing treatment outcomes.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Author Contributions: Working Concept/Design: TA, AT, CEB, Data Collection: TA, Data Analysis/Interpretation: TA, Text Draft: TA, AT, CEB, Critical Review of Content: TA, AT, CEB, Final Approval and Responsibility: TA, AT, CEB.
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REFERENCES

1. Twoon M, Jones CD, Foley J, Davidson D. Reversed palmaris longus muscle: a report of two cases. Case Reports Plast Surg Hand Surg. 2017 Jul 24;4(1):73-76. doi: 10.1080/23320885.2017.1353424. eCollection 2017. PubMed PMID: 28804743; PubMed Central PMCID: PMC5532760.
2. Martens MA, Moeyersoons JP.. Acute and recurrent effort-related compartment syndrome in sports. Sports Med. 1990;9:62–68. [PubMed] [Google Scholar]
3. Mishra S. Alternative tests in demonstrating the presence of the palmaris longus. Indian J Plast Surg. 2001;34:12–14. [Google Scholar]
4. Wood J IV. Variations in human myology observed during the winter session of 1866-67 at King's college, London (1867). Proc R Soc Lond 15:518–546
5. Giunta R, Brunner U, Wilhelm K Bilateral reversed palmaris longus muscle—a rare cause of peripheral median nerve compression syndrome. Case report. (1993) Unfallchirurg 96:538–540.
6. Longhurst G, Stone D, Mahony N. Bilateral reversed palmaris longus muscle: a case report and systematic literature review. Surg Radiol Anat. 2019 Nov 12. doi:10.1007/s00276-019-02363-z. [Epub ahead of print] Review. PubMed PMID: 31720753.
7. Park MJ, Namdari S, Yao J. Anatomic variations of the

palmaris longus muscle. Am J Orthop (Belle Mead NJ) 2010; 39:89-94
8. Murabit A, Gnarra M, Mohamed A. Reversed palmaris longus muscle: Anatomical variant- case report and literature review. Can J Plast Surg. 2013. Spring;21(1):55-6. PubMed PMID: 24431941; PubMed Central PMCID: PMC3891100
9. Kopkin R, Gimenez C, Rudman E. A teenager presenting with a forearm mass. Reversed palmaris longus. Skeletal Radiol. 2017 Oct;46(10):1397-1398, 1459-60. doi: 10.1007/s00256-017-2717-3. PubMed PMID: 28733829.
10. Schuurman AH, van Gils AP. Reversed palmaris longus muscle on MRI: report of four cases. Eur Radiol. 2000;10(8):1242-4. PubMed PMID: 10939482.
11. Kikano, R., Charbel, C., Assi, C. et al. Prevalence, variants, and morphometrics of Palmaris Longus tendon: a magnetic resonance imaging study. Surg Radiol Anat 43, 749–753 (2021). https://doi.org/10.1007/s00276-020-02608-2
12. Linda D, Harish S, Stewart B, Finlay K, Parasu N, Rebello R. Multimodality imaging of peripheral neuropathies of the upper limb and brachial plexus. Radiographics. 2010; 30:1373–400.
13. Getzmann, J. M., & Schweizer, A. (2018). Surgical Resection of a Reversed Palmaris Longus Muscle Causing Chronic Exertional Compartment Syndrome in a Competitive Swimmer: A Case Report. Orthopaedic journal of sports medicine, 6(5), 2325967118769615. doi:10.1177/2325967118769615

OLGU SUNUMU
CASE REPORT

Tenesmusun nadir bir nedeni: Perirektal lipom

A rare cause of tenesmus: Perirectal lipoma

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ÖZET

Lipom vücudun herhangi bölgesinde ortaya çıkabilen, yağ dokusunun kapsüllü ve iyi huylu tümörüdür. Genelde asemptomatik, yumuşak, hareketli kitleler olarak tanımlanırlar. Perineal lipom nadir görülen bir lipom bölgesi olup; hastanın oturmasında zorluğa ve rahatsızlık hissine neden olabilmektedir. Lipom boyutu büyük ise etraf sinirlerde bası etkisi oluşturarak, zamanla deformasyon oluşturarak veya sürekli sinir uyarılması nedeni ile tenesmusa neden olabilmektedir. Çalışmamızda perianal bölgede ele gelen ve sürekli dışkılama isteği şikâyeti ile polikliniğe başvuran, muayenede perirektal alanda dev lipom tanısı konulup, lipom eksizyonu yapılan olgunun sunumu amaçlanmaktadır.

Anahtar kelimeler: Tenesmus, perirektal lipom, rektal tuşe

SUMMARY

Lipoma is an encapsulated and benign tumor of adipose tissue that can occur in any part of the body. They are generally defined as asymptomatic, soft, mobile masses. Perineal lipoma is a rare lipoma region, it can cause difficulty and discomfort for the patient to sit. If the size of the lipoma is large, it may cause tenesmus by creating a pressure effect on the surrounding nerves, creating deformation over time or due to continuous nerve stimulation. In our study, it is aimed to present the case of a patient who applied to the clinic with the complaint of persistent desire to defecate in the perianal region and was diagnosed with a giant lipoma in the perirectal area and underwent lipoma excision.

Keywords: Tenesmus, perirectal lipoma, digital examination

GİRİŞ

Lipom vücudun herhangi bölgesinde ortaya çıkabilen, yağ dokusunun kapsüllü ve iyi huylu tümörüdür. En sık görülen benign yumuşak doku tümörü olup; tüm yaş gruplarında görülebilmektedir (1). Nedeni belirsiz olmakla birlikte; aile öyküsü, obezite, sedanter yaşam ve Gardner Sendromu gibi bazı genetik hastalıklarda lipom görülme sıklığı artmıştır.

Lipomlar, yavaş büyüyen kitleler olmasına rağmen zamanla dev boyutlara kadar ulaşabilirler. Genelde asemptomatik, yumuşak, hareketli kitleler olarak tanımlanırlar. Ancak rejyonel sinirlerde deformasyon oluşturmaları nedeniyle ağrıya sebep olabilirler. Derinin hemen altında oluşabilecekleri gibi abdominal organlar, ağız boşluğu, toraks, kolon veya perirektal alan gibi daha derin yerleşimli de olabilirler (2). Yerleşim yeri ve boyutuna bağlı olarak; tenesmus, disparoni, ani dışkılama isteği, solunum yetmezliği veya yutma güçlüğü gibi bulgular da gözlenebilirler (1-3). Lipom tanısı fizik muayene ile konulmakla beraber; şüpheli durumlarda ultrasonografi (USG) veya manyetik rezonans görüntüleme (MRG) tanıda yardımcıdır. Genelde tedaviye gerek olmayıp; semptomatik olgularda ve 5 cm'in üzerindeki lipomlarda kozmetik nedenlerden dolayı cerrahi tedavi önerilmektedir. Kesin tedavisi ise kapsül ile total eksizyondur.

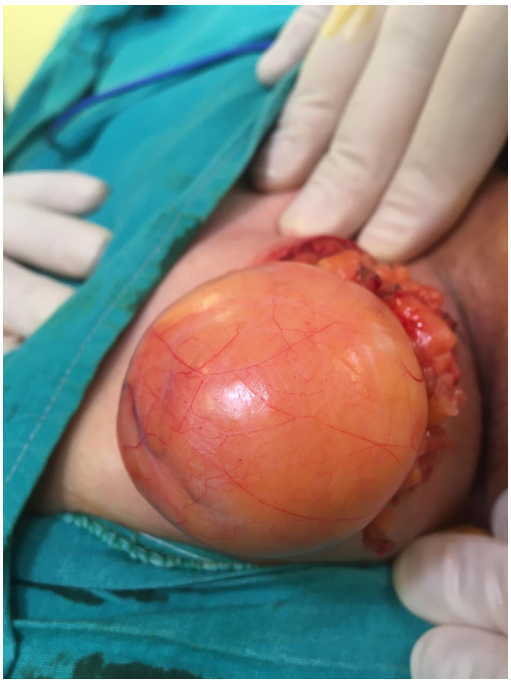
Çalışmamızda perianal bölgede ele gelen ve sürekli dışkılama isteği şikâyeti ile polikliniğe başvuran, muayenede perirektal alanda dev lipom tanısı konulup, lipom eksizyonu yapılan olgunun sunumu amaçlanmaktadır.

OLGU

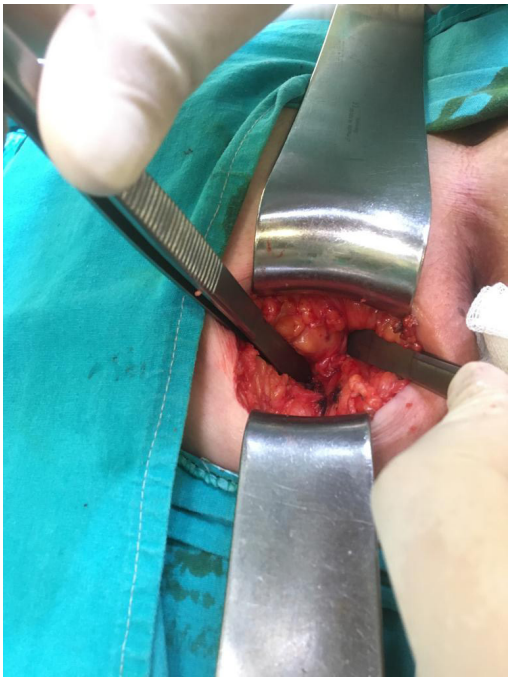
44 yaşında kadın hasta, sürekli dışkılama isteği ve perianal bölgede ele gelen kitle şikayetleri ile Erzurum Bölge Eğitim ve Araştırma Hastanesi Genel Cerrahi Kliniği'ne başvurdu. Ek hastalığı ve ameliyat öyküsü olmayan hastanın anamnezinde kitlenin yaklaşık bir yıldır mevcut olduğu, otururken rahatsızlık hissi verdiği öğrenildi. Ayrıca son 3 ayda mevcut şikayetlerine tenesmusun da eklendiği ve zamanla tenesmus sıklığının arttığı (günde 15 defa dışkılama isteği) öğrenildi.

Başvuru anında hastanın vital bulguları sırası ile şöyle idi: Arteriyel tansiyon 125/75 mm Hg, nabız: 82 atım/dk., solunum sayısı:16/dk., oksijen saturasyonu: %92 (oda havasında), vücut ısısı: 36.7oC idi. Fizik muayenede batın muayenesi doğaldı. Perianal alanda anüs sol lateralinde palpasyonla ele gelen yumuşak ve hareketli kitle mevcuttu. Rektal tuşede anal girim dördüncü santimetrede, rektuma sol lateralden bası yapan ancak lümen tıkanıklığa yol açmayan hareketli bir kitle mevcuttu. Kitlenin muayene özellikleri benign natürde olduğundan ek görüntülemeye ihtiyaç duyulmadan hastaya elektif cerrahi planlandı.

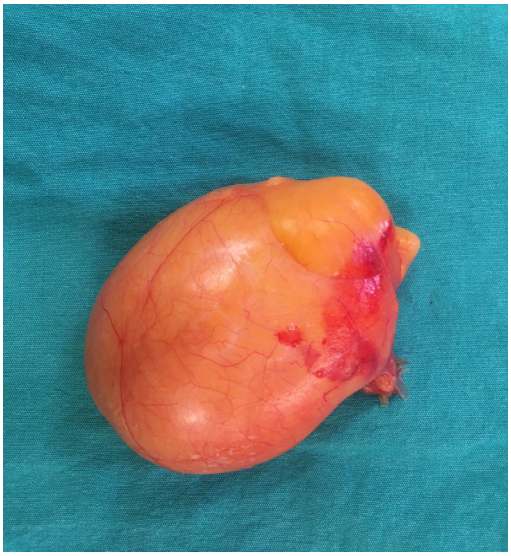
Gerekli preoperatif hazırlıklar yapıldıktan sonra spinal anestezi altında, yüzükoyun pozisyonunda sol perianal bölgeye yapılan lineer insizyon ile kitleye ulaşıldı. Yaklaşık 80x60 mm boyutlarında, rektum duvarına dıştan basına yapan ancak duvar invazyonu göstermeyen, iyi sınırlı lipomatöz kitle kapsülü ile en blok eksize edildi **(Resim 1,2 ve 3)**. Ameliyat sonrası serviste takibi yapılan hastanın postoperatif 6. saatte oral beslenmesi başlandı. Takiplerinde komplikasyon görülmeyen hasta postoperatif 2. günde taburcu edildi. Operasyon materyalinin patolojik incelemesi, lipomatöz doku ile uyumluydu.



Resim 1.



Resim 2.



Resim 3.

TARTIŞMA

Lipom, yağ dokusunun iyi huylu ve kapsüllü tümörüdür. Cinsiyetler arasında belirgin farklılık olmaksızın beşinci ve altıncı dekatlarda sık görülmektedir (4). Yumuşak doku lipomları günlük pratikte yaygın olarak görülür ve popülasyonun yaklaşık %2'sinde bulunur (5). Hiperkolesterolemi, obezite, diyabet ve travma gibi durumlar subkutan lipomların gelişimi için risk faktörleri olarak kabul edilir. Lipomun patogenezi henüz tam olarak anlaşılamamakla beraber hem sporadik hem de kalıtsal vakalar görülebilmektedir. Lipomlar yetişkin yağ hücrelerinden değil, mezenkimal primordial yağ dokusu hücrelerinden köken aldığında inanılmaktadır (6). Lipom tespit edilen olgumuz 4. dekatta olup altta yatan bir predispozan faktör veya kalıtsal faktör mevcut değildi.

Lipomlar histopatolojik özelliklerine göre birçok alt tipe ayrılmaktadır: Konvansiyonel lipom, anjiyolipom, fibrolipom, fusiform hücreli lipom, miyelolipom ve pleomorfik lipom (7). Abdominal bölge, ekstremiteler, mediastinal bölge ve pelvik bölge dahil olmak üzere vücudun yağ içeren herhangi bir bölümünde lipomatöz lezyonlar ile karşılaşılabilmektedir. Ancak perine gibi daha az yağ dokusu içeren bölgelerde nadiren tespit edilmektedir.

Pelvik yerleşimli bir lipom, siyatik foramen, obturator foramen veya pelvik taban yoluyla kasık veya perineal bölgelere uzanabilir. Bu yumuşak ve hareketli kitleler tipik olarak asemptomatiktir ve yavaş büyürler; ancak zamanla pelvik lipomlar önemli boyutlara ulaşabilir ve semptomatik hale gelebilirler (8). Pelvik ağrı, dizüri, poliüri, hematüri (daha az sıklıkla), idrara sıkışma, idrar retansiyonu ve inkontinans, kabızlık, tenesmus, diyare, venöz obstrüksiyon, lenfödem, tromboflebit, siyatalji gibi çeşitli semptomlar ortaya çıkabilirler (9). Olgumuzun perianal bölgede palpe edilen bir yumuşak doku kitlesi mevcut olup; bu kitle tenesmusa neden olmaktaydı.

Perineal lipom nadir görülen bir lipom bölgesi olup; hastanın oturmasında zorluğa ve rahatsızlık hissine neden olabilmektedir. Ayrıca, şişlik nedeniyle rektal obstrüksiyon oluşturup defekasyonu engelleyebilmektedir. Lipom boyutu büyük ise etraf sinirlerde bası etkisi oluşturarak, zamanla deformasyon oluşturarak veya sürekli sinir uyarılması nedeni ile tenesmusa neden olabilmektedir. Tenesmus sürekli dışkılama hissine rağmen, dışkıyı tam olarak yapamama, boşaltamama durumudur. Hastalar dışkısının geldiğinin düşünerek tuvalete giderler ancak uzun süre beklemelerine rağmen dışkılayamazlar. Bu durumun gün içerisinde sürekli tekrarlaması hastanın hayat konforunu olumsuz etkilemektedir. Tenesmus genellikle; inflamatuvar barsak hastalıkları, irritable barsak hastalığı, rektal kanserler, anal bölge selim hastalıkları gibi barsakla ilişkili hastalıklarda görülen bir durumdur. Nadiren de imperfore himen, idrar yolu enfeksiyonu, vajinal kist ve rektum duvarına bası yapan lipom benzeri kitlelere bağlı olarak ortaya çıkmaktadır (10-12). Bizim olgumuzda hastada oturmakla rahatsızlık hissi veren kitle ilk şikâyet olup; bunu takiben zaman içerisinde tenesmus hissi de semptomatolojiye eklenmiştir.

Lipomların tanısı fizik muayene ile konulmakta ve genellikle ek görüntülemeye ihtiyaç duyulmamaktadır. Perianal bölgedeki yumuşak tümörler için ilk görüntüleme yöntemi olarak ultrasonografi tercih edilmektedir. USG'de lipomlar düzgün kenarları olan, oval ve hiperekoik kitleler şeklinde görülürler. İçerlerinde ince fibröz septalar saptanabilmektedir. Renkli dopler USG'de lezyon içi veya perilezyonel damarlanma eksikliği görülmektedir (8). USG'nin bulguları tek başına kesin tanı koymak için yetersiz kaldığında, bilgisayarlı tomografi (BT) veya manyetik rezonans görüntüleme (MRG) taraması şeklinde daha ileri görüntülemelere ihtiyaç vardır. BT taraması yağlı bir tümörü teşhis etmek için kullanılabilmekle beraber; MRG daha iyi yumuşak doku kontrast çözünürlüğü verdiğinden daha üstündür. MRG'nin BT taramasına göre bir başka avantajı da, cerrahi hazırlıklar için çok önemli bir adım olan kitlenin anatomik boyutunun ayrıntılı bir şekilde tanımlanmasına izin vermesi, çevre planlar ile kitle ilişkisini daha sağlıklı göstermesi yeteneğidir (13). Tenesmus gibi gastrointestinal bulgular veren perirektal lipomlarda malignite ekartasyonu için rektoskopik inceleme önerilebilmektedir.

Semptom vermeyen lipomlarda cerrahi tedavi gereksiz olup; cerrahi tedavi semptomatik ve kozmetik sorunlar yaşayan hastalarda endikedir. Olgumuzda kitlenin perianal bölgeden palpasyon ile yumuşak ve mobil karakterde palpe edilmesi ve rektal tuşe ile benign natürel lezyon olarak değerlendirmesi nedeniyle ek görüntülemeye ihtiyaç duyulmamıştır. Aktif tenesmus şikâyeti ve otururken rahatsızlık hissi vermesi ve yaklaşık boyutunun 80 mm olması nedeniyle cerrahi olarak lipom eksizyonu yapılmıştır. Sonuç olarak; perianal lipomlar nadir görülen bir durum

olup; hasta için sürekli rahatsızlık hissi veren hayat konforunu önemli derecede etkileyen ve tenesmus gibi sorunları mevcut olan hastalarda perirektal lipom tanısı akılda bulundurulmalı ve hasta konforunu sağlamak için cerrahi eksizyon uygulanmalıdır.

Yazar Katkıları: Çalışma Konsepti/Tasarımı: TK, MK, Veri Toplama: TK, MK, Veri Analizi/Yorumlama: TK, MK, Yazı Taslağı: TK, MK İçeriğin Eleştirel İncelemesi: OB, ŞY, HK, NG TK, MK Son Onay ve Sorumluluk: TK, MK, Malzeme ve teknik destek: TK
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KAYNAKLAR

1. Del Rey IAG, Marcano AJL, Velasco AAM, de la Plaza Llamas R, Ramia JM. Giant ischiorectal lipoma as a cause of anal pain, fecal incontinence and dyspareunia. An exceptional association. Revista Argentina de Cirugía. 2021;113(3):384-7.
2. Salam GA. Lipoma excision. Am Fam Physician. 2002;65(5):901-4.
3. Johnson CN, Ha AS, Chen E, Davidson D. Lipomatous Soft-tissue Tumors. J Am Acad Orthop Surg. 2018;26(22):779-88.
4. Dhouha B, Maroua W, Seifeddine B, Ghofrane T, Lassaad G, Rached B, et al. [Giant pelvic lipoma mimicking a liposarcoma]. Pan Afr Med J. 2019;33:20.
5. Rahman GA, Abdulkadir AY, Yusuf I. Lipomatous lesions around the shoulder: Recent experience in a Nigerian hospital. International Journal of Shoulder Surgery. 2009;3(1):13.
6. Chander B, Krishna M, Thakur S, Mahajan N, Vij A, Diwakaran J. Extremely rare giant retroperitoneal fibrolipoma: a case report. J Cancer Res Ther. 2012;8(2):314-6.
7. Martinez CA, Palma RT, Waisberg J. Giant retroperitoneal lipoma: a case report. Arq Gastroenterol. 2003;40(4):251-5.
8. van der Byl G, Cerica A, Sala MG. Retroperitoneal lipomas: A case report. J Ultrasound. 2012;15(4):257-9.
9. Weniger M, D'Haese JG, Kunz W, Pratschke S, Guba M, Werner J, et al. En-bloc resection of a giant retroperitoneal lipoma: a case report and review of the literature. BMC Res Notes. 2015;8:75.
10. Cauvin A, Sullivan M, Harvey M, Thompson H. Vaginal cysts causing tenesmus in a bitch. Journal of Small Animal Practice. 1995;36(7):321-4.
11. Mwenda AS. Imperforate Hymen-a rare cause of acute abdominal pain and tenesmus: case report and review of the literature. Pan African Medical Journal. 2013;15(1).
12. Jergens AE. Dyschezia and tenesmus. BSAVA Manual of Canine and Feline Gastroenterology: BSAVA Library; 2005. p. 94-6.
13. Dozois EJ, Malireddy KK, Sim FH, Wenger DE. Surgical approach to a large dumbbell-shaped pelvic lipoma extending through the obturator foramen. Tech Coloproctol. 2007;11(3):271-4.

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A brief overview of the application of triage systems in the emergency department during pandemic period

Pandemi döneminde acil serviste triyaj sistemlerinin uygulanmasına kısa bir bakış

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Dear Editor;

Emergency services are units of health institutions that provide uninterrupted service 24 hours a day, 7 days a week, and are an important door of the health system. It has an important place in people's access to health services. This situation causes the emergency services to be easily accessible and overcrowded with unnecessary use. One of the reasons for the crowds is that it is the first place where patients apply in disasters and epidemics (1).

Triage systems have been developed over time in order to avoid this crowd in the emergency services and to use the emergency services in the most efficient way. Routine circulation is the most important part of patient evaluation in the emergency department. Routine triage aims to evaluate the patient in the fastest way at the time of admission in the emergency services, to determine the treatment priorities of the patients, and thus to use the emergency department capacity in the most efficient way, starting with the most urgent patient (2). Architectural arrangements have been made, such as separating ambulance and outpatient entrances, in order to obtain maximum data in large and modern hospitals (2). According to the policies of health planners, there are also applications where surgical emergencies, pediatric emergencies and internal emergencies have separate entrance doors.

The word triage comes from the French word “trier” meaning to choose, to separate. It is thought that triage practices started during the wars in the Napoleonic era. It was first applied in the medical field by Baron Dominique Jean-Larrey, in the 18th century during the Napoleonic era, to help the seriously injured soldiers return to the battlefields by intervening in the untreated and less injured ones (3). Priority is given to more recoverable patients due to insufficient health resources. Patients are often divided into three groups:

1. Non-urgent: The patient may wait for a long time until he sees a doctor, or he may be referred to primary health care services (green).

2. Urgent: Diagnosis and treatment of the patient in the emergency room is necessary. It should be checked at regular intervals until the diagnosis and treatment is made (yellow).

3. Emergency: The patient should be treated as soon as possible without waiting. Illness or injury to the patient may result in disability or death (red).

The use of triage in emergency services coincides with the end of the 1950s. In the early 1960s, triage systems began to be developed in response to the rapidly increasing emergency services patient population in the USA (1). With the increase in the number of emergency visits, especially in patients with low urgency, triage practices were started in order to give priority care to emergency patients, and they took their place in routine use over time (3).

COVID-19 first reported from Wuhan and it was defined as a pandemic on March 11 due to the incidence of cases in 113 countries, the spread and severity of the virus. On the same date, the first case was reported from our country. During the COVID-19 pandemic, emergency services were the first health unit that patients applied to, and the entrance door of pandemic clinics was emergency services (4). However, there have been unexpected changes in the behavior of societies, and non-pandemic emergency service applications have decreased considerably. Despite this, pre-hospital emergency health services and emergency services have remained inadequate almost all over the world due to COVID-19.

The increasing burden of the pandemic has increased the importance of triage practices in emergency services and pandemic clinics. Researchers have done research on triage

systems (4,5). They showed that these systems, which are based on vital parameters (body temperature, pulse, heart rate, respiration rate, and arterial blood pressure) and can be applied by non-doctor health personnel, can be applied. On the other hand, service treatment protocols and intensive care hospitalization indications were changed due to the fact that the intensive care beds were full, and the number of intensive care beds was limited. Studies were carried out on triage systems within the priority of intensive care (5).

As a result, triage applications that emerged to determine the priority in war surgery are applied in crowded emergency services today. Efforts to use resources effectively during the pandemic period have led to an increase in the importance of triage systems.

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REFERENCES

1. Gilboy N, Travers D, Wuerz R. Re-evaluating triage in the new millennium: A comprehensive look at the need for standardization and quality. J Emerg Nurs. 1999 Dec;25(6):468-73. doi: 10.1016/s0099-1767(99)70007-3.
2. Gunaydin YK, Çağlar A, Kokulu K, Yıldız CG, Dündar ZD, Akıllı NB, et al. Triage using the Emergency Severity Index (ESI) and seven versus three vital signs. Notfall Rettungsmed 19, 209–216 (2016). doi:10.1007/s10049-015-0119-4
3. Nakao H, Ukai I, Kotani J. A review of the history of the origin of triage from a disaster medicine perspective. Acute Med Surg. 2017;4(4):379-384. doi:10.1002/ams2.293
4. Özdemir S, Akça HŞ, Algın A, Altunok İ, Eroğlu SE. Effectiveness of the rapid emergency medicine score and the rapid acute physiology score in prognosticating mortality in patients presenting to the emergency department with COVID-19 symptoms. Am J Emerg Med. 2021;49:259-264. doi:10.1016/j.ajem.2021.06.020
5. Akça HŞ, Algın A, Özdemir S, Sevimli H, Kokulu K, Eroğlu SE. Comparison of the efficacy of PSI, CURB-65, CALL and BCRSS in predicting prognosis and mortality in COVID-19 patients. J Exp Clin Med. 2021; 38(4): 434-439.

LETTER TO THE EDITOR
EDİTÖRE MEKTUP

Prognosticating critical illness and an early warning score: ANDC

Kritik hastalıkların öngörüsü ve erken uyarı skoru: ANDC

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Dear editor,

We have read the article titled "Mild/moderate and severe COVID-19 pneumonia: Can the clinical course be predicted?" prepared by Hamidi et al. with great interest (1). We thank the authors and the editorial board for publishing this informative and successful manuscript. We also would like to mention a few important points about predictors used in COVID-19.

Since the COVID-19 pandemic was declared in March 2020, more than 350 million people have been infected with SARS-CoV-2, and more than five and a half million people have died from COVID-19. During the peak periods of the pandemic, health resources were insufficient all over the world. To use scarce resources effectively and to prioritize patients, researchers studied parameters that would predict death and severe illness (1-6). The authors suggested that early warning scores could be used in early emergency departments and pandemic clinics. Rapid acute physiology score and rapid emergency medicine score are two of the most studied early warning scores (2). Some researchers studied on scoring systems such as PSI, CURB-65 and CURB, which were used in pneumonia before (3). On the other hand, laboratory parameters, especially those that are inexpensive and easily accessible, were studied more (1,4). Moreover, the ratios of these parameters such as neutrophil-to-lymphocyte ratio, C-reactive protein-to-albumin ratio were studied to find the ideal predictor (5).

Weng et al, like Hamidi et al, studied laboratory parameters in the early period of the pandemic. In their study in Wuhan, similar to Hamidi et al., they found neutrophil-to-lymphocyte ratio, D-dimer and C-reactive protein as independent predictors of laboratory parameters (6). By adding age to these laboratory parameters, they developed a scoring system named ADNC. When developing ADNC, they multiplied each variable with coefficients according to their importance. They calculated ADNC by using the following formula: Total points = 1.14 × (age – 20) (years) + 1.63 × neutrophil-to-lymphocyte ratio + 5.00 × D – dimer (mg/L) + 0.14 × C-reactive protein (mg/L). They recommended ADNC as the ideal predictor with good calibration and discrimination (the area under the curve of 0.975 and 0.921 for the validation and derivation) (6).

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REFERENCES

1. Hamidi AA, Ulu Y. Mild/moderate and severe COVID-19 pneumonia: Can the clinical course be predicted? Maltepe Medical Journal. 2021;13(3):92-6. Doi:10.35514/mtd.2021.55.
2. Özdemir S, Akça HŞ, Algın A, Altunok İ, Eroğlu SE. Effectiveness of the rapid emergency medicine score and the rapid acute physiology score in prognosticating mortality in patients presenting to the emergency department with COVID-19 symptoms. Am J Emerg Med. 2021;49:259-64. Doi: 10.1016/j.ajem.2021.06.020.
3. Akça HŞ, Algın A, Özdemir S, Sevimli H, Kokulu K, Eroğlu SE. Comparison of the efficacy of PSI, CURB-65, CALL and BCRSS in predicting prognosis and mortality in COVID-19 patients. J Exp Clin Med. 2021;38(4):434-9.
4. Özdemir S, Eroğlu SE, Algın A, Akca HS, Ozkan A, Pala E, et al. Analysis of laboratory parameters in patients with COVID-19: Experiences from a pandemic hospital. Ann Clin Anal Med. 2021;12 (Supp 4):518-23. Doi: 10.4328/

ACAM.20678.
5. S Özdemir, A Algin. Evaluation of the ability of the C-reactive protein-to-albumin ratio to predict short-term mortality in patients with COVID-19. J Clin Med Kaz. 2021;18(6):35-9. Doi: 10.23950/jcmk/11324.
6. Weng Z, Chen Q, Li S, Li H, Zhang Q, Lu S, et al. ANDC: an early warning score to predict mortality risk for patients with Coronavirus Disease 2019. J Transl Med. 2020;18:328. Doi:10.1186/s12967-020-02505-7.