

ÇOCUK HASTALARDA HENOCH SCHÖNLEIN PURPURASINDA BAŞLANGIÇ KLİNİK BULGULARI İLE BÖBREK TUTULUMU ARASINDAKİ İLİŞKİ

THE RELATIONSHIP BETWEEN INITIAL CLINICAL FINDINGS AND RENAL INVOLVEMENT OF HENOCH SCHÖNLEIN PURPURA IN PEDIATRIC PATIENTS

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ÖZET

AMAÇ: Henoch-Schönlein purpurası (HSP) non-trombositopenik palpabil purpura, karın ağrısı ve artritten oluşan üç önemli klinik bulgu ile karakterize IgA ilişkili sistemik bir vaskülitir. Böbrek tutulumu genellikle prognozu belirlemektedir. Bu çalışmada HSP tanısı ile izlenen çocukların klinik özelliklerini; cilt, gastrointestinal sistem (GİS), eklem ve böbrek tutulumunun şiddeti arasındaki ilişkinin belirlenmesi amaçlandı.

GEREÇ VE YÖNTEM: İleriye yönelik kesitsel olarak düzenlenen bu çalışmaya Ocak 2011 - Ocak 2012 tarihleri arasında izlenen 74 çocuk hasta öykü, fizik muayene, laboratuvar ölçümleri, izlemde aldıkları tedavi ve tedaviye alınan cevapla değerlendirildi. Hastaların sistem tutulumları deri, böbrek, GİS ve eklem tutulumu olarak sınıflandırıldı.

BULGULAR: Olguların %45,9'u kız, %54,1'i erkek olarak saptandı. İlk bir ayda artrit şiddeti ve böbrek tutulumu arasında anlamlı bir ilişki bulundu ($p<0,05$). Başvuru anında karın ağrısı şiddeti ile böbrek tutulumu arasında ve ayrıca altıncı ayda karın ağrısı şiddeti ve böbrek tutulumu şiddeti arasında anlamlı bir korelasyon saptandı ($p<0,05$). İlk bir ayda karın ağrısının ağrı kesiciye yanıtı ile böbrek tutulumu arasında anlamlı bir ilişki bulundu ($p<0,05$).

SONUÇ: Hastalığın başlangıcında ağır eklem ve GİS tutulumu ile başlangıçta GİS tutulumunun ağır olması 1. ve 6. ayda ağır böbrek tutulumu ile ilişkili bulundu. Başlangıçta şiddetli karın ağrısı olan bu nedenle hiç hareket edemeyen, oyundan geri kalan, sürekli yatmayı tercih eden olan ve/veya melena saptanan olgular böbrek tutulumu açısından daha dikkatli değerlendirilmelidir.

ANAHTAR KELİMELER: Vaskülit, Böbrek, Çocuk.

ABSTRACT

OBJECTIVE: Henoch-Schönlein purpura (HSP) is an IgA-associated systemic vasculitis characterized by three important clinical signs of non-thrombocytopenic palpable purpura, abdominal pain, and arthritis. Renal involvement generally determines the prognosis. In this study, it was aimed to determine the relationship between skin, gastrointestinal system (GIS), the severity of joint and renal involvement on the clinical features of children who were followed up with the diagnosis of HSP.

MATERIAL AND METHODS: In this prospective cross-sectional study, 74 pediatric patients followed up between January 2011 and January 2012 were evaluated with their history, physical examination, laboratory measurements, treatment received during follow-up, and response to treatment. System involvement of the patients was classified as skin, renal, GIS, and joint involvement.

RESULTS: It was determined that 45.9% of the cases were female and 54.1% were male. A significant correlation was found between the severity of arthritis and renal involvement in the first month ($p<0.05$). There was a significant correlation between the severity of abdominal pain and renal involvement at the time of admission, and also the severity of abdominal pain and severity of renal involvement at the sixth month ($p<0.05$). A significant correlation was found between the response of abdominal pain to painkillers and renal involvement in the first month ($p<0.05$).

CONCLUSIONS: Severe joint and GIS involvement at the beginning of the disease and severe GIS involvement at the beginning were found to be associated with severe renal involvement in the first and sixth months. Patients who initially had severe abdominal pain, and therefore could not move at all, fall behind from the game, prefer to lie down continuously, and/or those with melena should be evaluated more carefully in terms of renal involvement.

KEYWORDS: Vasculitis, Kidney, Child.

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INTRODUCTION

Henoch-Schönlein purpura (HSP) is known to be the most common vasculitis of childhood with an unknown etiology and involving joints, gastrointestinal system, kidneys, and less frequently other organs, especially the skin (1, 2). It frequently occurs with nonthrombocytopenic purpura, arthritis, arthralgia, abdominal pain, and variable renal involvement (3 - 7). The main factors determining the prognosis are the degree of renal involvement at the beginning, complications in the gastrointestinal system (GIS), and central nervous system (8, 9). One of the difficulties in making decisions about the treatment of children with renal involvement is that the severity of renal involvement cannot be determined and it varies. It typically occurs a month to a few months after the onset of systemic symptoms but is however it is not thought to be related to the severity of the extrarenal involvement.

The aim of this study was to evaluate the clinical characteristics of pediatric patients diagnosed with HSP and to determine the relationship between skin, GIS, the severity of joint involvement, and renal involvement.

MATERIALS AND METHODS

In this prospective cross-sectional study, 74 pediatric patients were observed from 2011 to 2012. The history, physical examination, laboratory measurements, treatment received during the follow-up, and responses to treatment were examined and evaluated. System involvement of the patients was classified as skin, kidney, GIS, and joint involvement. The following classification was used for the severity of the patients' system involvement. The severity of skin involvement; mild: limbs only, and/or gluteal area, severe: defined as a severe necrotizing rash and/or involving the extremities, gluteal area, and chest area. The severity of renal involvement; mild: Isolated hematuria (microscopic \pm macroscopic) and/or proteinuria not causing nephrotic syndrome, severe: defined as an acute nephritic syndrome and/or nephrotic syndrome and/or acute renal injury. The severity of GIS involvement; mild: mild abdominal pain (the child can move freely and does not fall behind from playing) and/or fecal

occult blood (FOB) (\pm), severe: defined as severe abdominal pain (unable to move, play, prefer to lie down all the time), and/or melena (\pm). The severity of joint involvement; mild: mild (can move easily or does not fall behind from playing) joint pain, severe: it was defined as severe joint pain (unable to move, play, prefer to lie down all the time). Evaluation of severe abdominal and joint pains after nonsteroidal antiinflammatory drugs (NSAID) treatment was evaluated as a response to pain relief therapy. The relationship between extrarenal involvement and severity of findings at the time of diagnosis and the presence and severity of renal involvement in the zeroth, first, sixth and twelfth months were investigated. The treatment received by the subjects participating in the study during their follow-up was recorded.

Ethical Committee

This study was approved by the local ethical committee (Tepecik Training and Research Hospital, date: 16.01.2013 number: 44/13).

Statistical Analysis

In statistical evaluation, comparisons were made with the chi-square test, correlations were made with Pearson's correlation test and significant risk factors were made with multivariate regression analysis. A value of $p < 0.05$ was considered significant.

RESULTS

The study group consisted of 34 (45.9%) female patients and 40 (50.1%) male patients. The median age was 8 years, and the mean duration of hospitalization was 11.17 ± 7.60 days (median 9 days). Renal involvement was detected in 37 (50%) cases, hematuria in 27 (36.5%) cases, hematuria \pm proteinuria in 7 (9.4%) cases, and acute nephritic nephrotic syndrome in 3 (4.1%) cases. 3 (4.1%) cases were evaluated as hypertensive. GIS involvement was detected in 48 (64.8%) patients, abdominal pain was observed in 40 (60.8%) patients, and GIS bleeding was observed in 34 (45.9%) patients. Melena was detected in only 2 (2.7%) of the cases with GIS bleeding. Joint involvement was detected in 67 (90.5%) cases, while arthritis was seen in 7 (9.5%) cases. 43 (58.1%) cases were treated with non-steroid-

idal anti-inflammatory drugs, 28 (37.8%) cases were treated by oral prednisone. 3 (4.1%) cases were observed without medication (**Table 1**).

Table 1: Characteristics and system involvement of the patients

Number of patients (n)	74
Age (year) (Median)	8
Gender [Male, n, (%)]	40 (54.1)
Duration of hospitalisation (days) (Median)	9
Treatment [n, (%)]	
✓ None	3 (4.1)
✓ NSAID	43 (58.1)
✓ Steroid	28 (37.8)
Skin involvement [n, (%)]	74 (100)
Renal involvement [n, (%)]	37 (50)
GIS involvement [n, (%)]	48 (64.8)
Joint involvement [n, (%)]	67 (90.5)
Edema of the scalp	11 (14.9)
Edema of the scrotum	8 (10.8)

GIS: Gastrointestinal system, NSAID: Nonsteroidal antiinflammatory drugs

In the follow-up of 37 patients with renal involvement, it was observed that only isolated hematuria persisted in 6 (8.1%) patients at 12 months (**Table 2**).

Table 2: Severity of the system involvement of the patients according to the follow-up period

System involvement	0. month	1. month	6. month	12. month
Severity of skin involvement [n, (%)]	74 (100)	0 (0)	0 (0)	0 (0)
✓ Mild	48 (64.8)			
✓ Severe	26 (35.2)			
Severity of renal involvement [n, (%)]	37 (50)	36 (48.6)	12 (16.2)	6 (8.1)
✓ Hematuria+proteinuria	34 (45.9)	33 (44.5)	12 (16.2)	6 (8.1)
✓ Syndrom (ANS±NS)	3 (4.1)	3 (4.1)	0 (0)	0 (0)
Severity of GIS involvement [n, (%)]	48 (64.8)	0 (0)	0 (0)	0 (0)
✓ Mild	46 (62.1)			
✓ Severe	2 (2.7)			
Severity of joint involvement [n, (%)]	67 (90.5)	0 (0)	0 (0)	0 (0)
✓ Mild	61 (82.4)			
✓ Severe	6 (8.1)			

ANS: Acute nephritic syndrome, NS: Nephrotic syndrome, GIS: Gastrointestinal system

Correlation analyzes were made between the renal involvement of the disease and the severity of this involvement and the severity of other system involvements, and only the significant ones were specified in **Table 3**.

Table 3: Correlation results with renal involvement and severity of involvement and other parameters at 0, 6, 12 months*

		0 month	1 month	6 month	12 month
		Renal involvement	Severity of renal involvement	Renal involvement	Severity of renal involvement
Severity of joint involvement	p	0.02	0.01		
	r	0.26	0.27		
Severity of GIS involvement	p	0.01		0.05	0.02
	r	0.27		0.3	0.25
Response of abdominal pain to pain relievers	p	0.03	0.02		
	r	0.27	0.27		

Correlation results with renal involvement and severity of involvement and other parameters at 0, 6, 12 months

There was a statistically significant positive correlation between the presence of renal involvement at the time of diagnosis and the severity of joint ($p=0.02$, $r=0.26$) and GIS involvement ($p=0.01$, $r=0.27$), however no significant correlation was found between severe renal involvement and other findings. There was a statistically significant positive correlation between renal involvement in the first month and the severity of joint involvement ($p=0.01$, $r=0.27$) and response to painkiller treatment for abdo-

minal pain ($p=0.02$, $r=0.27$). A statistically significant positive correlation was found between the severity of GIS involvement ($p=0.005$, $r=0.3$). While no significant correlation was found between renal involvement and other findings in the sixth month, a statistically significant positive correlation was found between severe renal involvement and only the severity of GIS involvement ($p=0.02$, $r=0.25$). There was no significant correlation between both renal involvement and severe renal involvement and other findings in the twelfth month.

DISCUSSION

Renal involvement is the complication that poses the greatest potential danger and leaves the most serious sequelae in HSP (10). Hematuria is usually the earliest and most common sign of renal involvement. However, symptoms of renal involvement in HSP may show a wide range. A wide variety of clinical pictures can be seen, ranging from microscopic and/or macroscopic hematuria, proteinuria, less frequently nephrotic syndrome, acute nephritic syndrome, hypertension, and acute renal injury (11). Although renal involvement was detected in 50% of the patients (37 cases) in our study, Kendirli et al. (12) observed 73 patients diagnosed with HSP for 31 months and reported a total of 25 (35%) patients had renal involvement. Candemir et al. (13) found the rate of renal involvement as 11.1%. Renal involvement rates in our study can be interpreted as one of the examples to be given for variable renal involvement, as in other data in the literature. We think that the most important reason for this difference is the different definitions made for the definition of renal involvement. (14).

The frequency of detecting renal involvement is gradually increasing with close follow-up of patients after the diagnosis of HSP. It has been reported that renal involvement can generally be seen within three months after the onset of the rash, and it occurs in 80% of the patients in the first 4 weeks, and in the remaining 20% in the second and third months (15). Moreover, renal involvement, which is typically seen one month to a few months after the onset of systemic symptoms, is not considered to be related

to the severity of the extrarenal systemic involvement. Nevertheless, there is no consensus on this issue in the literature. In a prospective study of 223 children under the age of 16, it was found that abdominal pain without melena or joint complaints significantly increased the risk of nephritis (2.1, 95% CI 1.1-3.7) (16).

Although a clear marker could not be found for predicting children with renal involvement at the onset HSP and determining the severity of renal involvement from clinical features (17), some studies suggest that faecal calprotectin may be a reliable marker for HSP, exclusively for determining GIS and renal involvement as well as disease severity (18, 19). Therefore, the relationship between GIS and renal involvement in HSP is revealed in the last study. Additionally, we propose the correlation between GIS, joint and renal involvement in our study. When the gastrointestinal system findings are examined, it is reported that it was observed in 60-70% of the patients. The most common intermittent colic type abdominal pain is seen and found in more than 80% of the cases with GIS involvement. It is thought that the pain caused by the GIS is caused by submucosal and serosal bleeding due to vasculitis, as well as the bowel wall edema. Although 25-50% of the patients have occult or significant bleeding in the stool, it has been reported that severe, life-threatening bleeding may occur in only 5% of the patients, and blood transfusion may be required (20). In our study, a statistically significant positive correlation was found between the presence of renal involvement and severity of GIS involvement, response of abdominal pain to painkillers at the time of the diagnosis. The significant relationship was continued between renal involvement and response of abdominal pain to painkillers at the first month. Moreover, it was determined that the significant positive correlation between severity of renal and GIS involvement at the first and sixth month. Ekinci et. al pointed that severe GIS involvement associated with renal outcome in their study (21). Similarly, it was indicated that severe GIS involvement was one of the risk factors associated with renal involvement in HSP in a meta-analysis including 13 studies(22).

Arthritis or arthralgia is the second most common clinical findings of HSP and is seen in 60-84% of the cases. It doesn't caused permanent damage and is reported as an important feature (2, 23). In the study of Peru et al. (24), joint involvement was found in 42 (55%) of 76 patients with renal involvement. Kaku et al. (25) stated that severe joint involvement with arthritis affects renal involvement and prognosis. In the study conducted by Akça et al., renal involvement was found in 51% of the patients with severe joint involvement (26). In our study, mild joint involvement was observed in 61 cases (82.4%) at the onset of the disease, and severe joint involvement was observed in six cases (8.1%). A statistically significant positive correlation was found between the presence of renal involvement and the severity of joint involvement at the time of diagnosis and first month. Ozturk et. al. reported that arthralgia and arthritis were significantly higher in patients with renal involvement in HSP (27). Additionally, Chan et. al. supported that arthritis/arthralgia was also associated with renal involvement in their meta-analysis (22).

The present study has some limitations. First, given the nature of this prospective cross-sectional study determined classifications of system involvements according to clinical symptoms, physical examinations, and laboratory findings. Second, this study consisted of small-sized group.

As a result, scoring the severity of system involvement including particularly joint and GIS at the beginning and follow up HSP may be beneficial for predicting morbidity and its long-term results.

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