

## Correlation of IgA Accumulation with Clinical Findings in Children with Henoch-Schoenlein Nephritis

### *Henoch-Schönlein Nefritli Çocuklarda IgA Birikiminin Klinik Bulgular ile Korelasyonu*

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#### Abstract

**Objective:** Henoch-Schoenlein purpura (HSN), an IgA-mediated disease is the most common form of systemic vasculitis seen in childhood and long-term prognosis depends on renal involvement. We aimed to investigate the influence of renal IgA accumulation on clinical and histopathological findings in children with HSN.

**Materials and Methods:** Seventeen patients who were diagnosed as HSN based on renal biopsy were included in the study. The clinical assessment at baseline and last visit were done according to a classification adapted from that of Goldstein et al and renal histopathological changes were graded according to the classification of International Study of Kidney Disease in Childhood. IgA accumulation was quantified as +1 to +4. Based on this, patients were divided into group 1 (+1 or +2 accumulation) and group 2 (+3 or +4 accumulation). All parameters were compared between the groups.

**Results:** There was no significant difference between the groups with respect to clinical findings and histopathological changes. The amount of IgA accumulation was not correlated with clinical or histopathological status.

**Conclusion:** The amount of renal IgA deposition is not associated with clinical or histological findings in our sample. These results need to be confirmed in larger samples.

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**Key words:** Henoch-Schoenlein nephritis, IgA accumulation

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#### Özet

**Amaç:** Henoch-Schoenlein purpura çocukluk çağında görülen en sık vaskülit olup uzun dönem prognozu renal tutulumla bağlıdır. Henoch-Schoenlein nefriti IgA aracılı bir hastalıktır ve bu çalışmada renal IgA birikiminin klinik ve histopatolojik bulgular üzerine etkilerinin araştırması planlanmıştır.

**Yöntem ve Gereçler:** HSP tanısı almış ve biyopsi yapılmış 17 hasta çalışmaya alındı. Tanı anında ve son vizitteki klinik bulgular Goldstein ve ark.'dan uyarlanan sınıflamaya göre değerlendirildi. Histopatolojik değişiklikler ise International Study of Kidney Disease in Childhood tarafından belirlenen sınıflamaya göre değerlendirildi. IgA birikimi semi-kantitatif olarak +1 ve +4 arasında evrelendi. IgA birikimine göre Grup 1 (+1 ve +2 IgA birikimi) ve Grup 2 (+3 ve +4 IgA birikimi) olmak üzere iki grup oluşturuldu. Bulgular iki grup arasında değerlendirildi.

**Bulgular:** Klinik bulgular ya da histopatolojik değişiklikler açısından iki grup arasında farka rastlanmadı. Ayrıca, IgA birikim miktarı da klinik ya da histopatolojik bulgular ile korelasyon göstermemekte idi.

**Sonuç:** Hasta sayımız kısıtlı olmakla beraber, HSN bulunan çocuk hastalarımızda IgA birikim miktarı ile klinik ya da histopatolojik bulgular arasında ilişki kurulamamıştır. Bulguların daha büyük örneklemede doğrulanmasına ihtiyaç vardır.

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**Anahtar sözcükler:** Henoch-Schoenlein nefriti, IgA birikimi

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#### Introduction

Henoch-Schoenlein purpura (HSP) is the most common form of systemic vasculitis in childhood. The International Consensus Conference on Nomenclature of Systemic

Vasculitides defined the disease as "a vasculitis with IgA dominant immune deposits affecting small vessels and typically involving skin, gut and glomeruli and associated with arthralgias or arthritis" (1). It is mostly self-limiting but long-term prognosis depends on renal involvement (2, 3).

Renal disease may occur in approximately 40% of children with HSP and presents as microscopic or macroscopic hematuria, proteinuria, hypertension or renal insufficiency (4). In renal pathologic examination with light microscopy, besides endocapillary and extracapillary inflammation and crescent formation of the glomeruli, mesangial proliferation and sclerosis are commonly observed. In immunofluorescence microscopy, mesangial IgA deposition and capillary wall staining for IgA are frequent findings for Henoch-Schoenlein nephritis (HSN) (5). IgA accumulation is classified as +1 to +4 according to the amount of visible fluorescence (6). The aim of the study was to evaluate the influence of the amount of IgA accumulation on clinical and histopathological findings in children with HSN.

### Materials and Methods

The data of 17 children with biopsy-proven HSN who had been treated in our clinics between 1995 and 2005 were evaluated retrospectively. The diagnosis was based on the presence of microscopic or gross hematuria and/or proteinuria along with characteristic purpuric rash, abdominal or joint pain.

Hematuria was defined as "gross" when it was visible with naked eye and "microscopic" if five or more red blood cell per high power field was observed in microscopic examination (4). "Hypertension" was defined as systolic or diastolic blood pressure >95th percentile for the specific age (7).

The clinical statuses at the time of the diagnosis and at the last visit were evaluated according to the classification adapted from Goldstein et al (8):

- A. Normal: Normal physical examination, urine and renal function.
- B. Minor urinary abnormalities: microscopic hematuria or proteinuria (<40mg/m<sup>2</sup>/h) but normal physical examination.
- C. Active renal disease: proteinuria of 40 mg/m<sup>2</sup>/h or more and serum creatinin <3mg/dL with or without hematuria and hypertension.
- D. Renal insufficiency: serum creatinine >3mg/dL, ESRD

The histopathological findings of percutaneous renal samples were graded according to the classification of International Study of Kidney Disease in Childhood (ISKDC) (9):

- Grade 1: Minor glomerular abnormalities.
- Grade 2: Pure mesangial proliferation.
- Grade 3: Minor glomerular abnormalities or mesangial proliferation with crescents/ segmental lesions (sclerosis, adhesions, thrombosis, necrosis) in less than 50% of glomeruli.
- Grade 4: As grade 3 but with crescents/segmental lesions in 50-75% of glomeruli.
- Grade 5: As grade 3 but with crescents/segmental lesions in more than 50% of glomeruli
- Grade 6: Membranoproliferative-like lesions

Direct immunofluorescence was used for staining and examination was performed with epi-fluorescence microscope. The grading used for the positivity of the fluorescence was as follows (6):

- (+1): visible fluorescence at x 400
- (+2): visible fluorescence at x 200
- (+3): visible fluorescence at x 40
- (+4): visible fluorescence at x 40 with presence of fluorescent throughout the glomeruli.

The patients were divided into two groups according to the intensity of IgA accumulation in renal specimens as group I (+1 and +2 IgA accumulation) and group II (3+ and +4 IgA accumulation).

The correlation between the clinical status and histopathological grades and between both of two and intensity of IgA accumulation was evaluated with Spearman correlation test.

### Results

The rate of female patients was 53% (M/F: 8/9). The mean age at onset of HSV was 9.3±3.13 years. The interval between the time of the biopsy and the time when the first symptoms appeared was 5.1±6.9 months (10 days-24 months). The mean duration of the follow-up was 39.7±26.8 months (4-94 months). The clinical status at the time of diagnosis was class A in 1 patient (6%), class B in 10 patients (59%), and class C in 6 patients (35%). Renal histopathological classification of patients were grade 1 in 1 patient (6%), grade 2 in 11 patients (65%) and grade 3 in 5 patients (29%). None of the patients experienced deterioration in renal functions and in 65% of them the clinical status drew back to a better class in the follow-up. All these findings were summarized in Table 1.

The clinical status was not correlated with histopathological classification of ISKDC. Detailed biopsy reports of two patients could not be reached. The immunofluorescent IgA accumulation of the rest of the patients were classified into two groups as mild (+1, +2) and severe (+3, +4). There was no significant difference in age, gender, frequency of hematuria/proteinuria attacks, modified Goldstein classification of clinical outcome, accumulation of C3, IgG, IgM, fibrinogen, albumin or C1q between the two groups. In addition, the intensity of IgA accumulation was positively correlated with C3, fibrinogen and albumin accumulation.

### Discussion

HSP is most frequently a self-limiting form of vasculitis in childhood and the long-term prognosis depends on renal involvement (2, 3). A rapidly progressive form of glomerulonephritis may extend to renal impairment or even end-stage renal disease 20 years after the diagnosis in up to 5 or 20 % of children in different series (8, 10). None of our patients experienced impaired renal functions at the initial status. Since the risk of renal impairment is mostly related to the initial clinical presentation (8), none

**Table 1.** Clinical and histopathological findings of children

No	Sex	Age (years)	ICS	LCS	ISKDC	IgA	Follow-up (months)
1	F	9	B	A	G2	+2	64
2	M	6	B	A	G2	+3	94
3	F	12	C	B	G3	+2	73
4	F	8	A	A	G1	+2	26
5	F	7	B	B	G2	+4	78
6	M	14	B	B	G2	+1	23
7	M	9 <sup>3/12</sup>	B	B	G2	+4	40
8	M	8	C	A	G3	-	45
9	M	4 <sup>8/12</sup>	B	B	G3	+3	22
10	F	9	C	B	G2	-	4
11	M	10	B	B	G3	+1	41
12	F	8	C	B	G2	+3	7
13	F	2 <sup>10/12</sup>	C	A	G2	+3	27
14	M	11 <sup>10/12</sup>	B	A	G2	+1	14
15	F	14	C	B	G3	+4	29
16	F	12 <sup>10/12</sup>	B	A	G2	+4	19
17	M	10 <sup>9/12</sup>	B	A	G2	+4	69

ICS: initial clinical status, LCS: last clinical status (according to modified Goldstein classification) ISKDC: International Study of Kidney Disease in Childhood

had deteriorating renal functions in the follow-up and 65% of them progressed to a better clinical stage. The correlation between the clinical and histopathological findings in patients with HSN is controversial in the current literature. Renal biopsy findings were not correlated with the risk of poor outcome in some cases while they correlated well in some other studies (4, 8, 11). The clinical status according to modified Goldstein classification was not correlated with ISKDC classification of histopathological findings in our patients.

Predominant mesangial IgA deposits is a frequent finding in HSN, but this may be absent in some rare cases (12, 13, 14). Sometimes capillary wall-staining for IgA may predominate on mesangial IgA deposition (5). Glomerular deposits of IgG, IgM, C3 and alternative complement pathway components may also be found in HSP nephritis (5, 12, 15). However, clear-cut correlations between the severity of the intensity of glomerular deposition of immunoglobulin and complement fractions and histological or clinical findings are still lacking and there are few studies investigating that correlation in the literature (16). In a recent study on patients with mesangioproliferative glomerulonephritis, presence of IgA deposition has been demonstrated to be associated with a worse clinical and histopathological status, but cumulative renal survival has not been significantly effected in those patients (17). In another study, a case with deteriorating renal histopathological findings on repeated biopsies had significant IgA deposition at a degree of (2+) to (3+) (4). In our study, no correlation was determined between the glomerular IgA

deposition and clinical findings or ISKDC classification. In addition, demographic, clinical and histological findings were not different in patients with mild or severe IgA accumulation.

In this study, we conclude that intensity of IgA deposition has no clinical or histological importance in HSN in childhood. Besides, considering the limited number of our patients, we believe that more studies on larger series are needed to make an accurate decision.

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