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**Case Report**

**Recurrent adult onset Henoch-Schonlein Purpura: a case report**

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**Abstract**

Henoch-Schonlein purpura is an immunoglobulin A (IgA)-immune complex mediated leukocytoclastic vasculitis that classically manifests with palpable purpura, abdominal pain, arthritis, and hematuria or proteinuria. The condition is much more predominant in children (90% of cases) and commonly follows an upper respiratory infection. We present a case of recurrent Henoch-Schonlein purpura (HSP) complicated by nephritis in an adult female initially categorized as IgA nephropathy (IgAN). We review the pathophysiologic basis of HSP nephritis as the variant of HSP accompanied by renal involvement and its pathogenetic commonality with IgA nephropathy.

**Key Words: Henoch-Schonlein purpura, IgA nephropathy, leukocytoclastic vasculitis**

**Introduction**

Henoch-Schonlein purpura is an IgA-immune complex mediated leukocytoclastic small vessel vasculitis that predominantly affects children. The rash begins as symmetric erythematous macules that evolve into purpuric papules and classically involve the buttocks and lower extremities [1, 2]. The most current classification criteria require the presence of palpable purpura with at least one of the following additional clinical and or pathological features: diffuse abdominal pain, arthritis or arthralgia, a biopsy showing IgA predominant deposition, and/ or renal involvement such as hematuria or proteinuria [3]. The most commonly

affected organs are the skin, kidneys, gastrointestinal tract, and joints while involvement of the lungs, genitourinary tract, and central nervous system is a rare occurrence [2].

The incidence of disease is estimated at 15 cases/100,000 children and 3.4 to 14.3 cases/1,000,000 adults per year [1, 4]. There are two broad categories of HSP namely HSP without kidney involvement and HSP nephritis. HSP nephritis ranges from asymptomatic hematuria to one of full blown nephrotic or nephritic syndrome. Abnormal O-glycosylation of serum IgA1 and its deposition into the renal mesangium is thought to be pathogenetically significant in both IGA nephropathy and HSP nephritis. Of note, HSP which does not involve the kidneys lacks this abnormal O-glycosylation. The severity of the initial renal presentation is a critical determinant in regards to long term prognosis whereby the risk of progression to chronic renal failure is less than 5% when initial signs at presentation are only those of hematuria and/or minimal proteinuria compared to 50% when both nephritic and nephrotic syndromes present [5]. We introduce a case of HSP nephritis in an adult in whom the initial diagnosis was made of IgA nephropathy.

## Case Synopsis

A 37-year old white female presented to the dermatologist with a 2-week history of pruritic, painful, violaceous purpura on her lower extremities with no associated symptoms. The dermatologist determined the lesions to be vasculitic in nature and prescribed a prednisone taper and referred her to nephrology. Laboratory studies revealed a 24-hour urine protein of 2.2 grams, a creatinine clearance of 135 milliliters per minute, microscopic hematuria, and C reactive protein of 2.3. The patient's antineutrophilic cytoplasmic antibody assay was negative. The skin lesions resolved and her nephritis persisted until her next appointment; at that point a renal biopsy was ordered. The biopsy showed a mesangiopathic glomerulonephritis associated with prominent mesangial deposits of IgA consistent with IgA nephropathy.

She was treated over the next 6 months with ramipril and valsartan. During that time, her proteinuria decreased from 2.2 g to 340 mg over 24 hours. She was feeling well until she developed pharyngitis and fever at which point there was a recurrence of the palpable purpura that had afflicted her 6 months earlier. Laboratory studies at this point revealed a peripheral blood leukocytosis (white blood cell count: 16.57k/uL) with a left shift, hemoglobin of 13.2 g/dL, hematocrit of 38.9%; platelet count of 214k/uL, blood urea nitrogen of 11 mg/dL and serum creatinine of 0.83 mg/dL. Her streptococcal rapid screen test was positive.

At the time she developed her second episode of palpable purpura, she was referred to a different dermatologist. The patient's symptoms continued to progress with the new onset of arthralgias, abdominal pain, and hematemesis.



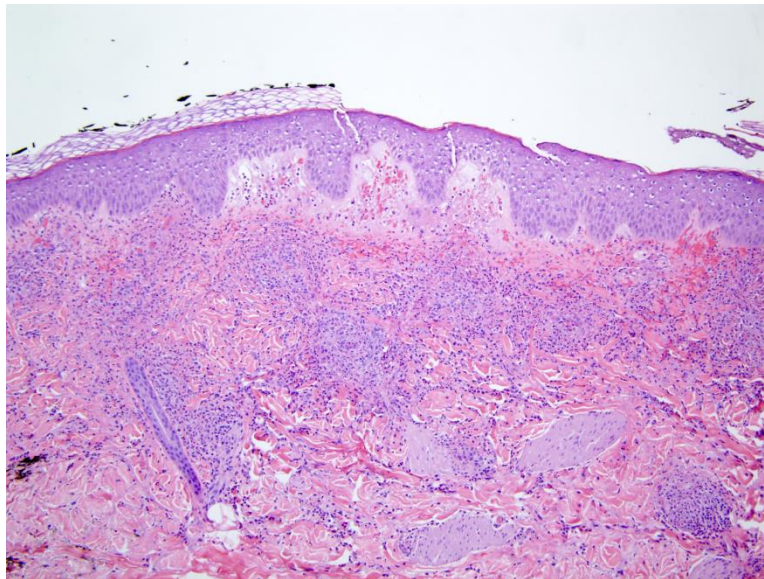
**Figure 1.** The patient exhibited striking symmetrical purpura distribution.

At this point her lesions of palpable purpura were much more extensive, exhibiting striking symmetry with involvement of lower extremities, buttocks, torso and upper arms. It was remarkably symmetrical.



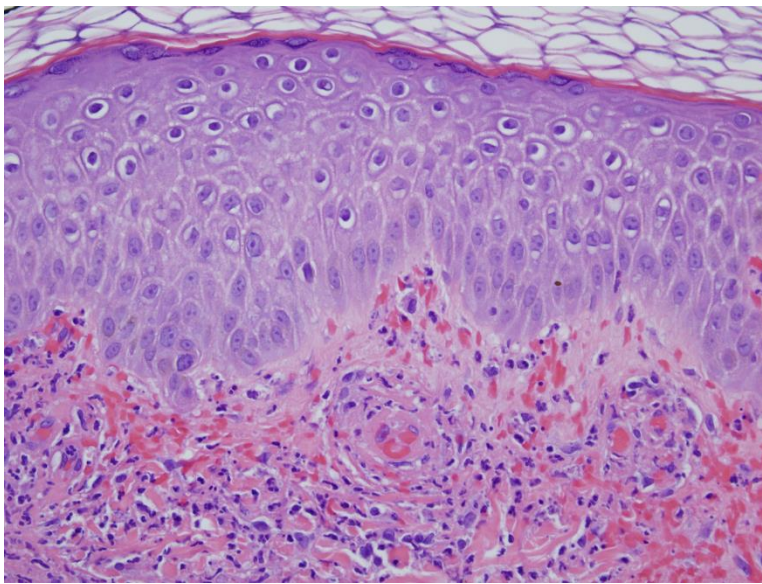
**Figure 2.** Some lesions had a bullous slate grey appearance on a hemorrhagic purpuric base.

A few of the purpuric lesions had a raised grey bullous quality, a distinct clinical manifestation reflective of the extent of extravascular neutrophilia. This distinctive clinical morphology reflects the combination of marked superficial extravascular neutrophilia with subepidermal bulla formation in concert with severe small vessel vascular compromise. There was accompanying fever and malaise.



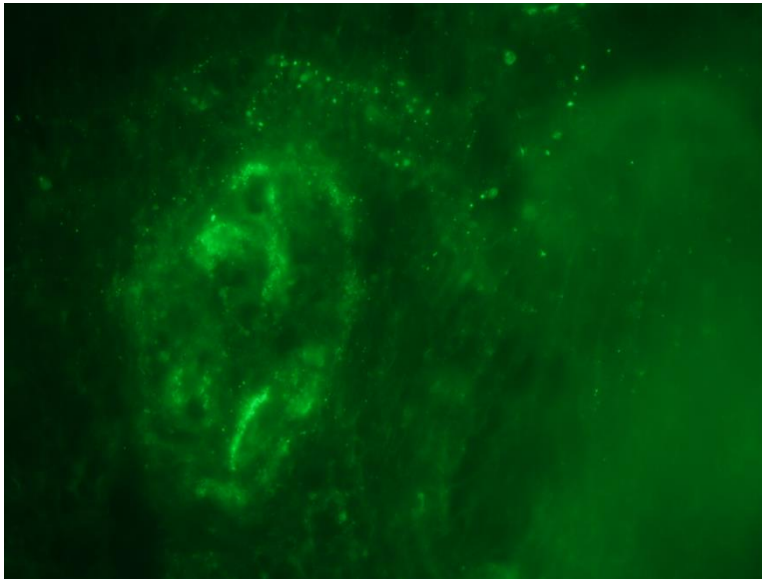
**Figure 3.** Punch biopsy showing a vascular reaction of the superficial dermis and papillary dermal edema.

A punch biopsy was performed and showed a striking vascular reaction affecting capillaries and venules of the superficial half of the dermis with accompanying marked papillary dermal edema.



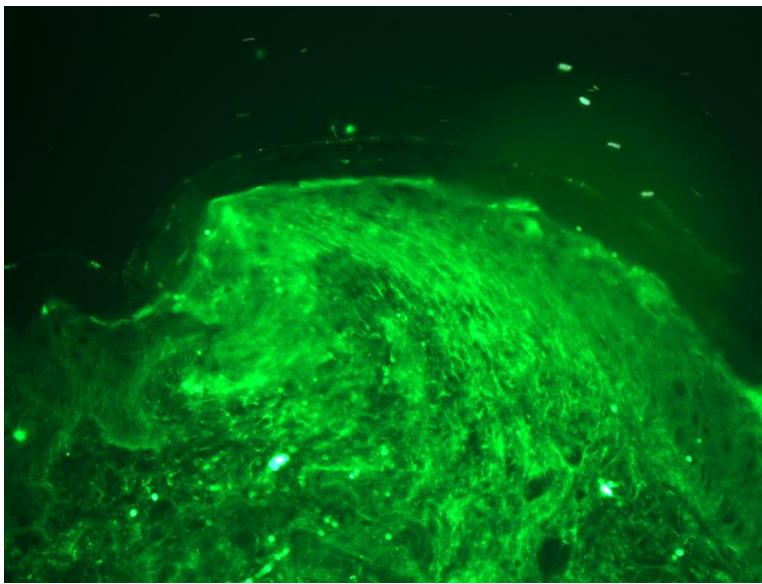
**Figure 4.** Neutrophilia around vessels and accompanying leukocytoclasia, along with prominent mural fibrin deposition.

The vessels were surrounded and permeated by a mixed inflammatory cell infiltrate comprising lymphocytes, monocytes and neutrophils. There was extensive leukocytoclasia. Very prominent luminal and mural fibrin deposition was noted. Dermal papillae microabscesses were conspicuous in the biopsy. In addition, the pustular component extended to involve a hair follicle. A characteristic feature of IgA vasculitis is one of extravascular neutrophilia including accumulations of neutrophils within the dermal papillae as noted here



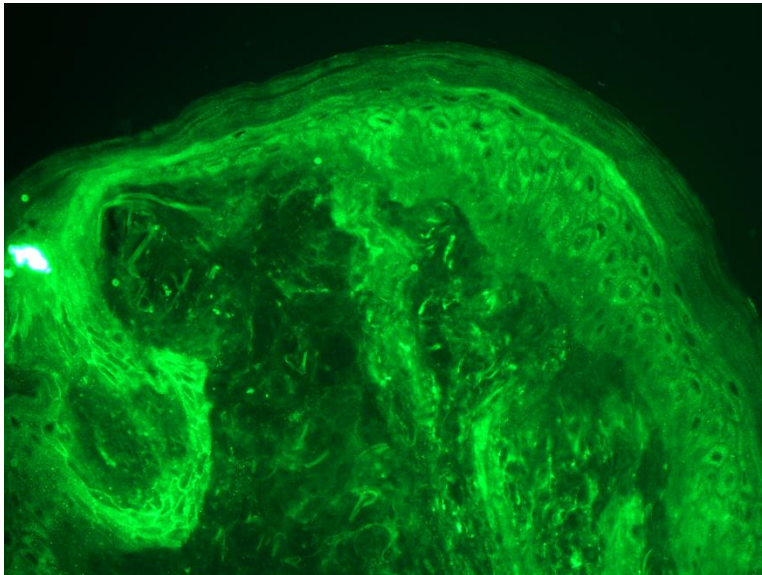
**Figure 5.** Direct immunofluorescence for IgA deposition.

Direct immunofluorescence of the specimen demonstrated extensive granular deposits of IgA within the cutaneous vasculature.



**Figure 6.** Direct immunofluorescence of the specimen does not show evidence of vascular IgM deposition.

A similar deposition pattern was not observed for either IgM or IgG.



**Figure 7.** Absence of staining for C1q and C4d did not support a role for classic complement activation. Illustrated is C1q.

The lack of staining for C1q and C4d did not support a role for classic complement activation. At this point a diagnosis was made of nephritic recurrent HSP.

## Discussion

Henoch-Schönlein purpura is a distinct multiorgan small vessel vasculitic syndrome that was first described in the early part of the 19<sup>th</sup> century by Heberden. Schönlein identified the arthropathy component of the syndrome, designating the clinical complex as peliosis rheumatica. The full designation as *Henoch Schönlein purpura* acknowledges the contributions made by Henoch in the later part of the 19<sup>th</sup> century when he described gastrointestinal symptoms, skin lesions, arthralgias and kidney involvement in some patients. The two broad categories of HSP are based on the presence or absence of renal involvement independent of severity and symptoms. The designation of HSP nephritis is used when there is renal involvement, and recognizes a spectrum of disease clinically and pathologically affecting the kidney. The most severe would be true nephritic HSP whereby the patient has nephritic syndrome. Perhaps the most famous patient to die from nephritic HSP was Wolfgang Amadeus Mozart. Unfortunately, at the time of his untimely and premature demise, neither HSP nor its effective treatment was known [6, 7].

We have presented a case of classic recurrent HSP precipitated by an exogenous trigger, namely Streptococcal pharyngitis. Given the extent of renal involvement with diminished renal function and hematuria, the patient's syndromic complex fulfilled criteria to warrant categorization as HSP nephritis. While her initial episode had been mislabeled as IgA nephropathy, a common pathogenetic mechanism related to a genetically aberrant IgA1 underlies both HSP nephritis and IgA nephropathy. IgA nephropathy and HSP nephritis have many overlapping features clearly indicative of a clinical and pathologic continuum but are sufficiently distinctive to warrant their categorization as separate nosologic entities. The similar and contrasting clinical, serologic and pathologic features of IgA nephropathy and HSP are presented in Table 1.

**Table 1.** Similarities and differences between IgA nephropathy and HSP nephritis

Features	IgA Nephropathy	HSP Nephritis
Peak age, years/Sex predominance	15-30/male	<10 /male
Association with exogenous trigger	No	Yes
Extra renal disease	Absent	Present
Renal disease - Hematuria - Nephrotic/Nephritic syndrome - Chronic renal insufficiency	- Present - Not always present - Commonly seen	- Present - Not always present - Variable clinical course, few cases developing chronic renal insufficiency
Serum IgE levels/ Eosinophil cationic protein	Normal	IgE levels are elevated; increased eosinophil cationic protein with higher levels in HSP nephritis compared to HSP without nephritis
Serum IgA	Increased	Increased
Abnormal IgA1 glycosylation	Abnormal	Abnormal
Serum Kappa/Lambda IgA1 ratio	Decreased	Normal
Small vessel vasculitis	Absent	Present
Renal biopsy	- Mesangial hypercellularity more common - Occasional crescentic glomerulonephritis	- Crescentic glomerulonephritis more common - Mesangial hypercellularity

Several studies have elucidated the role of galactose-deficient IgA1 in the pathogenicity of IgAN and nephritic HSP. IgA1 is produced predominantly in the bone marrow and mucosal tissues. Reduced activity of  $\beta$ 1,3-galactosyltransferase in the peripheral B cells of patients with IgAN and nephritic HSP has been correlated with reduced glycosylation of IgA1 O-glycans [8]. Bacterial IgA-specific proteases have been utilized with lectin western blotting and mass spectrometry to suggest that Gal-deficient O-glycans occur at T228/S230 and S232 in the hinge region of IgA1. When there is a concurrent infection that triggers the production of the abnormal IgA1, the immune complex comprising bacterial antigen and the galactose deficient IgA serves as an antigen for IgG. It is this IgA1-IgG immune complex that stimulates the proliferation of cultured human mesangial cells [9]. It is hypothesized that the binding of these immune complexes to mesangial cells leads to enhanced mesangial proliferation and augments the production of extra-cellular matrix [8,9]. They also evoke an effective Arthus type III immune complex reaction that manifests as a small vessel vasculitis in the skin, gut, and synovium. The recurrent nature of HSP nephritis relates to the episodic nature of exogenous antigens that trigger the production of the genetically abnormal IgA1. The IgA1 unaffixed to exogenous antigen rarely evokes an autoantibody response.

Also implicated in the pathogenesis of HSPN and IgAN are the N-Acetylgalactosamine (GalNAc) residues which are exposed on the hinge regions of IgA1 due to lack of terminal  $\beta$ 1 galactosylation. Impaired resistance to antigen penetration at mucosal levels in HSPN may play a role in the accumulation of large amounts of GalNAc-IgA1 that cannot be cleared by the asialoglycoprotein receptor of hepatocytes [5,8, 10]. This accumulation of GalNAc-IgA1 in the blood favors formation of large IgA1-containing complexes that deposit in different tissues and induce inflammation. CD71 was implicated as the receptor in the binding of GalNAc-IgA1 immune complexes to mesangial cells. However, this process requires further study [8].

Additional components of the immune system besides galactose deficient-IgA1 have been implicated in the pathogenesis of IgAN and HSP nephritis. Activation of the mannose binding lectin pathway has been associated with more severe proteinuria and hematuria in the setting of HSP nephritis [8]. Mannose-binding lectin forms complexes with MBL-associated serine protease-1 (MASP-1), MASP-2, and MASP-3 [10]. These complement complexes are routinely found in the glomeruli of patients with HSPN suggesting a pathophysiological role of the lectin pathway in the disease process [8,10].

Other potential cofactors contributing to the development of HSP nephritis include increased IgE levels, higher levels of serum eosinophil cationic protein compared to controls, enhanced TGF- $\beta$  production and the presence of anti-cardiolipin antibodies [9]. The role of IgE in the pathogenesis of HSP is certainly noteworthy and was first recognized in 1994 when it was established by a group of researchers that the serum IgE was higher in patients with HSP nephritis as opposed to IgA nephropathy. In addition, there was a higher incidence of an atopic diathesis in HSP nephritis patients compared to patients with IgA nephropathy. Significant deposits of IgE could be identified on Langerhans cells and mast cells in skin biopsies of patients with HSP nephritis leading the authors to hypothesize that an allergen results in mast cell degranulation, potentially facilitating capillary permeability and the deposition of perivascular deposits of IgA in select organs where this allergen-mast cell interaction could occur, namely the gastrointestinal tract, lung and skin [11]. The eosinophil cationic protein is a secretory ribonuclease released from eosinophils and has a number of deleterious effects of which the most important are neurotoxicity, endothelial cell injury promoting thrombosis, and fibrogenic properties. It has been established that abnormally elevated serum levels above 15ug/L are seen in 50% of HSP patients without kidney disease compared to controls while all patients with kidney disease have elevated eosinophil cationic protein, indicative of its role in the pathogenesis of HSP with and without renal involvement. One might speculate that endothelial cell injury could facilitate the entrapment of IgA containing immune complexes within the microvasculature while the inherent fibrogenic properties of the protein could promote mesangial matrix synthesis [12]. It has been demonstrated that IgA anticardiolipin antibodies are pathogenic antibodies and when present in the setting of autoimmune disease, most specifically lupus erythematosus, are associated with thrombotic events, fetal demise, and thrombocytopenia. Children in the acute phase of HSP have elevated IgA anticardiolipin antibodies whereby the levels are significantly higher compared to children in convalescence and in controls. Certain infections such as *Mycoplasma*, *Streptococcus* and select viruses including parvovirus B19 are a critical trigger to the development of HSP. It is possible that there is molecular mimicry between microbial pathogens and cardiolipin, leading to the development of anticardiolipin antibodies. In addition, the organisms trigger a Th3 cell immune response which in turn results in the elaboration of TGF- $\alpha$ , a critical impetus to the clonal class switching in B cells to IgA. The actual immune complex evoking the vasculitic reaction through activation of the alternate complement pathway could be one containing anti-cardiolipin antibodies of IgA isotype [13]. Pentraxin 3 is a specific biomarker of inflammatory vascular disease similar to C reactive protein. It would appear that patients with HSP who develop renal involvement (i.e. HSP nephritis) have significantly higher levels of pentraxin 3 and therefore this biomarker does have prognostic value and should likely be assessed in all patients developing HSP.

The current management of HSP includes oral prednisone, topical and intravenous corticosteroids, dapsone, and cyclophosphamide. When renal involvement occurs, such as in the case of HSPN, angiotensin converting enzyme inhibitors, cyclosporine A, azathioprine, mycophenolate mofetil, intravenous immunoglobulin, and plasma exchange can be incorporated into the treatment plan. The efficacy of the previously mentioned treatments is still uncertain due to lack of a controlled study [1, 2, 9].

Rituximab has been used with some success in child and adult corticosteroid dependent patients with HSP. The authors propose that the elimination of B lymphocytes may reduce IgA1 and therefore IgG anti-glycan antibodies, removing one of the inciting agents in the disease process [14].

Anakinra, the interleukin-1 receptor antagonist, was used with partial response in a child with severe systemic HSP. The patient failed treatment with methylprednisolone, mycophenolate mofetil, and IVIG therapy. Anakinra was implemented under the rationale that the IL-1 blockade could improve the massive inflammatory assault on the patient's end organs. The patient improved with anakinra therapy but ultimately died of renal failure [15].

## Conclusion

Henoch-Schonlein purpura is a distinct syndromic complex where many of the manifestations are attributable to a leukocytoclastic vasculitis such as palpable purpura, arthritis, and gastrointestinal and pulmonary hemorrhage. The renal involvement reflects both



the mesangial proliferative effects of abnormal IgA containing immune complexes as well as small vessel injury, the latter manifesting as crescentic glomerulonephritis. HSP with renal involvement is pathogenetically distinct and is associated with a genetic abnormality in IgA, with the potential for progression to chronic renal disease. Such patients must be carefully monitored since common exogenous triggers especially related to infection serve as an impetus to abnormal IgA1 production.

## References

1. Jithpratuck W, Elshenawy Y, Saleh H, Youngberg G, Chi D, Krishnaswamy G. The clinical implications of adult-onset henoch-schonlein purpura. *Clinical and Molecular Allergy*. 2011;9(1):9. [PMID: 21619657]
2. Sohagia AB, Gunturu SG, Tong TR, Hertan HI. Henoch-Schonlein Purpura; A Case Report and Review of the Literature. *Gastroenterology Research and Practice*. 2010; 2010:597648. [PMID: 20508739]
3. Ozen S, Ruperto N, Dillon MJ, et al. EULAR/PReS endorsed consensus criteria for the classification of childhood vasculitides. *Annals of the Rheumatic Diseases*. July 1, 2006 2006;65(7):936-941. [PMID: 16322081]
4. Pillebout E, Thervet E, Hill G, Alberti C, Vanhille P, Nochy D. Henoch-Schönlein Purpura in Adults: Outcome and Prognostic Factors. *Journal of the American Society of Nephrology*. May 1, 2002 2002;13(5):1271-1278. [PMID: 11961015]
5. Davin J-C, Ten Berge IJ, Weening JJ. What is the difference between IgA nephropathy and Henoch-Schonlein purpura nephritis? *Kidney Int*. 2001;59(3):823-834. [PMID: 11231337]
6. Matteson EL. Notes on the history of eponymic idiopathic vasculitis: the diseases of Henoch and Schönlein, Wegener, Churg and Strauss, Horton, Takayasu, Behçet, and Kawasaki. *Arthritis Care Res*. 2000 Aug;13(4):237-45. [PMID: 14635278]
7. Zegers RH, Weigl A, Steptoe A. The death of Wolfgang Amadeus Mozart: an epidemiologic perspective. *Ann Intern Med*. 2009 Aug 18;151(4):274-8, W96-7. [PMID: 19687494]
8. Allen AC, Willis FR, Beattie TJ, Feehally J. Abnormal IgA glycosylation in Henoch-Schönlein purpura restricted to patients with clinical nephritis. *Nephrology Dialysis Transplantation*. 1998;13(4):930-934. [PMID: 9568852]
9. Lau K, Suzuki H, Novak J, Wyatt R. Pathogenesis of Henoch-Schönlein purpura nephritis. *Pediatr Nephrol*. 2010/01/01 2010;25(1):19-26. [PMID: 19526254]
10. Davin J-C. Henoch-Schönlein Purpura Nephritis: Pathophysiology, Treatment, and Future Strategy. *Clinical Journal of the American Society of Nephrology*. March 1, 2011 2011;6(3):679-689. [PMID: 21393485]
11. Davin JC, Pierard G, Dechenne C, Grossman D, Nagy J, Quacoe M, Malaise M, Hall M, Jansen F, Chantraine JM, et al. Possible pathogenic role of IgE in Henoch-Schönlein purpura. *Pediatric Nephrol*. 1994 Apr; 8(2):169-71. [PMID: 8018493]
12. Luca CM, Laicini EA, Fossali EF. Eosinophil cationic protein in Henoch-Schönlein purpura. *World J Pediatr*. 2014 Feb;10(1):90-1. [PMID: 24464674]
13. Yang YH, Huang MT, Lin SC, Lin YT, Tsai MJ, Chiang BL. Increased transforming growth factor-beta (TGF-beta)-secreting T cells and IgA anti-cardiolipin antibody levels during acute stage of childhood Henoch-Schönlein purpura. *Clin Exp Immunol*. 2000 Nov;122(2):285-90. [PMID: 11091287]
14. Pindi Sala T, Michot J-M, Snanoudj R, et al. Successful Outcome of a Corticoid-dependent Henoch-Schonlein Purpura Adult with Rituximab. *Case Reports in Medicine*. 2014;2014:4. [PMID: 24799911]
15. Boyer EM TM, O'Neil KM. Partial response to anakinra in life-threatening Henoch-Schonlein purpura: case report. *Pediatric Rheumatology Online Journal*. 2011. [PMID: 21834965]