

Research on Pathogenesis and Management Strategies for Pediatric Allergic Purpura from Both Chinese and Western Medical Perspectives

Qiling Yin¹, Weihua Zhang^{1,2,*}

¹Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

²Affiliated Rainbow Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China

*Correspondence Author

Abstract: *Henoch-Schönlein purpura (HSP) is a common systemic vasculitis in children, affecting small blood vessels in the skin, musculoskeletal system, gastrointestinal tract, and kidneys. Its primary clinical manifestations include non-thrombocytopenic palpable purpura, arthritis or arthralgia, diffuse abdominal pain, and renal involvement characterized by hematuria and/or proteinuria. Approximately 20% to 80% of pediatric HSP patients develop renal damage, including hematuria and proteinuria. Furthermore, childhood HSP exhibits a high recurrence rate; frequent and prolonged episodes of rash recurrence increase the susceptibility to renal injury. Therefore, early intervention in pediatric HSP is crucial for improving prognosis. The pathogenesis of allergic purpura remains unclear in modern medicine. While various indicators for assessing disease severity and prognosis are well-established, treatment typically involves symptomatic management. No specific therapy currently exists, and treatments like corticosteroids, immunosuppression, and blood purification are reserved for severe HSP. Crucially, children are in a critical growth and development phase, and certain immunotherapies may cause severe immunosuppression, serious complications, and increased risks of infection and organ damage. With the continuous development and advancement of traditional Chinese medicine (TCM), new treatment options have emerged for pediatric HSP patients. Multiple studies indicate that TCM treatment for childhood HSP can reduce recurrence rates, achieving satisfactory outcomes in both efficacy and safety.*

Keywords: Henoch-Schönlein purpura, IgA vasculitis, Traditional Chinese Medicine, Western medicine, Pathogenesis, Diagnosis, Treatment, Children.

1. Introduction

Henoch-Schönlein purpura (HSP), also known as IgA vasculitis (IgAV), is an IgA-mediated systemic vasculitis characterized by involvement of small arteries and capillaries in the skin, joints, gastrointestinal tract, kidneys, and other tissues and organs, accompanied by deposition of IgA immune complexes in affected tissues [1]. HSP ranks among the most common vasculitides in children, with an annual incidence of 14–20 cases per 100, 000 children. Recent studies indicate an upward trend in its prevalence [2,3]. Diagnosis is established when palpable purpura is present alongside any of the following: biopsy demonstrating predominant IgA deposition, arthralgia/arthritis, abdominal colic, or hematuria/proteinuria. Although HSP typically follows a self-limiting course, approximately 20–80% of affected children develop renal involvement. This may present as isolated microscopic (and/or gross) hematuria, with or without proteinuria, nephritis, and/or nephrotic syndrome. Overall, the prognosis for children with mild HSP is favorable. The long-term risk of permanent renal impairment is low (approximately 1.6%) in patients with mild urinary abnormalities. However, this risk significantly increases (up to 19.5%) in children with nephropathy and/or nephrotic syndrome. Furthermore, the risk of progression to chronic kidney disease ranges from 5% to 20% in children with >50% crescentic glomerulonephritis [4,5]. Traditional Chinese medicine(TCM) classifies this condition under the categories of “purpura disease,” “blood syndrome,” “purpura,” and “purpura-like disorders.” Its etiology often involves external pathogenic factors, dietary indiscretion, stasis i purpura, “grape epidemic,” or “purpura.” Its etiology often involves exposure to external pathogens, dietary indiscretion, stasis in

collaterals, and prolonged deficiency of qi and blood. Clinically, wind-heat toxins and damp-heat accumulation are most common, while blood stasis persists throughout the disease course. Deficiency of vital energy and qi-yin deficiency underlie the chronic, intractable nature of this condition [6].

Current HSP treatment primarily relies on corticosteroid therapy and intravenous immunoglobulin (IVIG) pulse therapy. Immunomodulatory therapy is typically employed for patients with renal involvement [7]. However, due to children’s developmental needs, current treatments often fall short of expectations and carry side effects. Furthermore, HSP exhibits high recurrence rates, with risks persisting for years post-remission, severely impacting patients’ physical and mental health as well as quality of life. Existing research indicates that frequent and prolonged rash recurrence constitutes a high-risk factor for renal injury.TCM demonstrates significant efficacy in treating HSP, effectively reducing rash recurrence frequency and lowering HSP relapse rates while offering stable therapeutic outcomes and high safety profiles. This provides a novel treatment option for pediatric HSP patients [8-10].

2. Pathogenesis

2.1 Pathogenesis of Western Medicine

The pathophysiology of HSP is multifactorial, involving complex interactions between the immune system, genetic susceptibility, and environmental triggers. A hallmark of HSP is the deposition of IgA1-dominant immune complexes in small blood vessels, leading to inflammation in the skin,

kidneys, joints, and gastrointestinal tract. Several mechanisms have been implicated in the pathogenesis of HSP: First, abnormal glycosylation of IgA1: In this context, IgA1—a subclass of IgA—undergoes glycosylation at its hinge region via a process called O-glycosylation. In IgA deficiency, a glycosylation defect results in the formation of galactose-deficient IgA1 (Gd-IgA1), predisposing individuals to the production and deposition of pathogenic immune complexes [11-13]. Second, Gd-IgA1 immune complex formation: Interaction between Gd-IgA1 and autoantibodies (IgA1 or IgG antibodies) leads to the formation of circulating immune complexes. These Gd-IgA1 immune complexes deposit in the walls of small blood vessels in the skin, kidneys, or gastrointestinal tract, triggering local inflammation. Thus, Gd-IgA1 and immune complex formation play a central role. Deposition of these complexes in small vessels triggers local inflammatory responses involving complement activation and immune cell recruitment, leading to the disease's characteristic clinical features [14]. HSP primarily manifests in five types: cutaneous, abdominal, articular, renal, and mixed. Approximately 15%–30% of HSP cases present as isolated cutaneous HSP [5]. Cutaneous HSP involving the kidneys progressively evolves into Henoch-Schönlein purpura nephritis (HSPN), a severe secondary glomerular disease posing significant threats to pediatric health [10].

2.2 Etiology and Pathogenesis in TCM

From the perspective of TCM, children possess a “pure yang” constitution, characterized by an inherent excess of yang and deficiency of yin. This manifests as their vigorous vitality and rapid growth, while also revealing a physiological state of abundant yang and deficient yin, with more activity than rest. Consequently, when children encounter pathogenic factors, they readily transform yang into heat. When exposed to cold pathogens, irregular eating habits, emotional fluctuations, or allergens, this pure yang vitality becomes disturbed. Excessive excitement and lack of restraint lead to internal and external interactions, causing internal accumulation of yang heat. This heat then agitates the blood, manifesting as purpura. The defensive qi (wei qi), belonging to yang, governs the protection of the skin and resistance against external pathogens. However, in children, the defensive yang is not yet fully developed and stable, often reacting with sudden and intense excitement. Once affected by pathogens, if the defensive barrier is compromised and yang heat escapes outward, it easily leads to the pathological changes of yang hyperactivity transforming into fire and heat injuring the nutritive blood. Thus, the pure yang constitution of children determines the characteristics of allergic purpura being susceptible to pathogens, prone to onset, and easily transforming into heat [15]. The Complete Works of Jingyue: Blood Disorders states: “Blood is the essence of yin and should not be disturbed; disturbance leads to disease. Blood nourishes qi and should not be depleted; depletion leads to disease. Disturbance often arises from fire; excessive fire forces blood to flow recklessly. Depletion often arises from qi; injured qi cannot retain blood.” HSP onset arises from dietary indiscretion, external pathogen invasion, chronic illness, febrile diseases, or multiple causes. Pattern differentiation includes: Wind-Heat Injuring Collaterals, Blood Heat Causing Uncontrolled Circulation, Damp-Heat Obstructing Collaterals, Yin Deficiency with Excessive Fire, and Qi

Inability to Retain Blood. Pathogenesis primarily involves internal blood heat causing blood to break and circulate uncontrollably [8]. The pathological location involves the Kidney and Bladder, with predominant pathogenic factors being Wind, Dampness, Heat, Toxin, and Stasis [16,17]. Among HSP children with renal involvement, the highest incidence of renal damage occurs in the Blood Heat Unrestrained Pattern, followed by the Damp-Heat Obstructing Pattern. When heat-toxin penetrates the lower jiao, disturbing the kidney collaterals, the lower part is primarily affected due to dampness injury. Consequently, hematuria and proteinuria may manifest, confirming that heat pathogens and damp pathogens are significant causative factors in the progression of HSP to HSPN [18].

3. Diagnosis

Based on the 2005 expert consensus [19], the European League Against Rheumatism (EULAR) and the Pediatric Rheumatology European Society (PReS) jointly proposed new classification criteria applicable to all pediatric vasculitides (including HSP). These criteria were validated through the Pediatric Rheumatology International Trial Organization (PRINTO) in 872 HSP cases (age \leq 18 years at onset). The EULAR/PReS/PRINTO diagnostic criteria for HSP [20] are based on clinical features, requiring the presence of purpura or petechiae (predominantly on the lower extremities) and fulfillment of one of the following four criteria: (1) Acute-onset diffuse abdominal colic (possibly with intussusception and gastrointestinal bleeding); (2) Histological evidence of leukocytoclastic vasculitis or proliferative glomerulonephritis with predominant IgA deposition; (3) Acute-onset arthralgia or arthritis; (4) Proteinuria or hematuria. These criteria demonstrate extremely high sensitivity (100%) and specificity (87%) in distinguishing HSP/IgAV from other vasculitides.

For diagnosing IgAV, SHARE recommends: (1) Biopsy: (a). Skin biopsy with IgA-specific immunofluorescence staining should be performed for atypical rashes and/or when excluding other diagnoses. Skin biopsy is not required for patients presenting with typical purpuric rashes on the lower limbs and buttocks. (b). Negative IgA immunofluorescence staining in biopsy does not rule out IgAV diagnosis. (2) Renal Evaluation: (a). Renal involvement should be assessed by estimating glomerular filtration rate (eGFR) and urine analysis (hematuria and urine protein/urine ratio or uric acid/urine ratio). (b). Pediatric nephrology consultation is indicated for IgAV patients with moderate proteinuria and/or impaired eGFR. (c). Renal biopsy is indicated in IgAV patients with severe proteinuria (\geq 250 mg/mmol persisting for at least 4 weeks; although shorter-duration severe proteinuria remains a relative indication for biopsy), persistent moderate proteinuria (100–250 mg/mmol), or impaired GFR. (3) Imaging: For patients with severe abdominal pain, ultrasound examination should be performed by an ultrasonographer with pediatric expertise to rule out intussusception [4].

4. Treatment

4.1 Treatment with Western Medicine

In the vast majority of HSP patients, no specific treatment is

required during the self-limiting phase of the disease. Approximately 78% of children experience joint pain and/or acute arthritis during the course of the illness, and about 60% may develop diffuse abdominal pain. If renal function is normal in HSP patients, nonsteroidal anti-inflammatory drugs (NSAIDs) are not contraindicated. Adequate analgesic therapy should be provided for HSP-related arthropathy and abdominal pain. Consider corticosteroid (CS) therapy in the following situations: (1) orchitis; (2) cerebrovascular vasculitis; (3) pulmonary hemorrhage; (4) other severe vasculitic manifestations threatening organs or life; (5) for patients with severe abdominal pain and/or rectal bleeding (after excluding intussusception), corticosteroid therapy may be considered. Oral corticosteroids (prednisolone/prednisone) should be administered at 1–2 mg/kg/day. For severe cases requiring corticosteroids, pulse intravenous methylprednisolone may be considered (e.g., 10–30 mg/kg daily for 3 consecutive days, with a maximum single-day dose not exceeding 1 g). Prophylactic corticosteroid therapy is not indicated for preventing IgA-associated nephropathy [4]. HSPN patients unresponsive to corticosteroids may be candidates for second-line therapies such as mycophenolate mofetil, cyclophosphamide, intravenous immunoglobulin, rituximab (RTX), methotrexate, colchicine, and hydroxychloroquine [21,22].

According to SHARE treatment recommendations, HSPN is categorized into mild, moderate, and severe based on three parameters: proteinuria, estimated glomerular filtration rate (eGFR), and percentage of crescent formation on renal biopsy. Children without renal impairment or proteinuria typically require no specific therapeutic intervention. For mild HSPN, defined as proteinuria ≤ 2.5 g/day in a 24-hour urine collection with normal eGFR, oral glucocorticoids are usually sufficient as first-line therapy. However, if proteinuria persists, second-line agents such as azathioprine, mycophenolate mofetil, or glucocorticoid pulse therapy may be used. For moderate HSPN, defined as renal biopsy showing $< 50\%$ crescent formation with impaired estimated glomerular filtration rate (< 80 mL/min/1.73m²) or severe persistent proteinuria (24-hour urine collection protein > 2.5 g/d for over 4 weeks), First-line therapy involves glucocorticoids (typically administered parenterally and in pulse doses). If no effect is observed, second-line agents are added: azathioprine, mycophenolate mofetil, or cyclophosphamide (parenteral administration). Treatment for severe HSPN comprises two phases: Phase I (Induction Therapy): Combination of glucocorticoid pulse therapy with intravenous cyclophosphamide pulse therapy. Phase II (Maintenance Therapy): Low-dose glucocorticoids combined with an immunomodulator (azathioprine or mycophenolate mofetil). Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are recommended to prevent or limit secondary glomerular damage in HSPN patients with persistent proteinuria (lasting over 3 months) [4,23]. RTX, an anti-CD20 monoclonal antibody, has been successfully used to treat ANCA-associated vasculitis. In a small case series of children with corticosteroid-dependent HSPN, RTX treatment reduced corticosteroid usage frequency, decreased hospitalizations, and achieved remission in most patients [24]. Currently, due to the lack of evidence regarding RTX efficacy on renal outcomes or Gd-IgA1 levels, and the limited use of RTX for HSP primarily confined to isolated clinical reports

and case series in pediatric and adult patients, RTX is currently reserved as an alternative therapy for refractory or recurrent HSPN [25,26].

4.2 TCM Treatment

The course of HSP is typically self-limiting, with most affected children having a favorable prognosis. However, long-term outcomes are primarily determined by the presence and severity of renal involvement. Currently, modern medicine lacks specific treatments for HSP, with therapeutic goals primarily focused on rapid resolution of clinical symptoms [27,28]. Studies have confirmed that immunosuppressive agents used in pediatric patients may cause adverse reactions such as liver dysfunction and gonadal suppression. Combining these agents with TCM may reduce the incidence of such adverse effects [29,30]. Clinical studies confirm that integrating TCM syndrome differentiation into HSP management improves pediatric outcomes and has gained clinical recognition. For preventing and treating recurrent HSP, TCM primarily addresses pathomechanisms such as “excessive toxins,” “damp-heat,” and “blood stasis.” Treatment involves herbal formulas targeting heat-clearing and toxin-resolving, blood-cooling and hemorrhage-stopping, or blood-activating and stasis-resolving actions, tailored to specific syndromes [6]. A 2023 multicenter clinical study on pediatric HSPN enrolled 316 children, dividing them into TCM and Western medicine groups. The TCM group received Tripterygium glycosides + sodium danetide IIA sulfonate injection + a heat-clearing and hemorrhage-arresting formula, with dosage adjusted based on disease severity. The Western medicine group administered low molecular weight heparin calcium + benazepril + dipyridamole + a Chinese medicine simulant for mild-to-moderate cases, while severe cases received prednisone in addition to the Western medicine regimen for mild cases. Results demonstrated that the comprehensive TCM regimen alone reduced proteinuria and hematuria in both mild and severe HSPN cases, with earlier onset of efficacy and fewer adverse reactions compared to the Western medicine group. Thus, the stepwise treatment regimen combining Tripterygium glycosides with TCM formulas for clearing heat and stopping bleeding, tailored to syndrome differentiation, demonstrated efficacy with fewer adverse reactions [9]. Commonly used formulas for HSP treatment include modified Rhino Horn and Rehmannia Decoction. Rehmannia root, sweet and cold in nature, enters the heart and liver blood divisions to clear heat, cool blood, nourish yin, and generate fluids, thereby restoring depleted yin and blood. Peony root, with its bitter, pungent, and slightly cold properties, enters the blood divisions of the heart and liver to clear heat, cool the blood, activate blood circulation, resolve stasis, and clear heat from the ying and blood divisions; Lithospermum root clears heat, cools the blood, dispels wind, and unblocks collaterals, collectively achieving the effects of clearing heat, cooling the blood, activating blood circulation, and detoxifying. Modern research indicates that components in rehmannia, such as polysaccharides and phenolic acids, may possess anti-inflammatory and immunomodulatory effects [31]. Multiple studies confirm that combined traditional Chinese and Western medicine treatment yields superior efficacy and lower clinical recurrence rates in HSP patients compared to Western medicine alone. Examples include Yu Ping Feng

Granules combined with conventional Western treatment, and a proprietary Chinese formula for clearing heat, draining dampness, promoting blood circulation, and detoxifying, combined with conventional Western treatment for HSP [32,33]. Modified Zhibai Dihuang Pills for pediatric HSPN with liver-kidney yin deficiency promote resolution of proteinuria and hematuria, improve T-lymphocyte subsets, reduce inflammatory responses, and correct hypercoagulable states [34]. Modified Yinqiao Powder enhances or modulates humoral immunity to suppress Gd-IgA1 secretion, thereby reducing multiple immune complex attacks on the kidneys and exerting renal protective effects [35]. Some scholars suggest that Taohong Siwu Tang may improve renal inflammation and fibrotic damage in rats by inhibiting ERK1/2 and HIF-1 α pathway activation [36]. Shenqi Dihuang Tang has also been demonstrated to reduce renal immune injury by lowering systemic inflammatory cytokine levels [37]. A 2025 data mining analysis of TCM syndrome-based treatment patterns for HSPN revealed that heat-clearing herbs were most frequently used, followed by tonic herbs, hemostatic herbs, diuretic and dampness-draining herbs, and blood-activating and stasis-resolving herbs. Among tonic herbs, qi-tonifying and yin-tonifying herbs predominated. Analysis of herbal properties showed that the four natures were predominantly cold, warm, and neutral, Cold-natured herbs cool the blood, clear toxins, nourish yin, and eliminate steaming sensations. Warm and neutral herbs warm the meridians, unblock collaterals, and tonify. Bitter, sweet, and pungent tastes collectively accounted for 83.4% of the formulas. Bitter taste clears and drains fire-heat, sweet taste tonifies, and pungent taste promotes blood circulation. This indicates that the primary therapeutic principles for HSPN involve clearing heat and detoxifying, tonifying qi and yin, and promoting blood circulation. As recorded in Suwen: Discourse on Meridians, "When fluids enter the stomach, they disperse vital essence upward to the spleen. The spleen disperses essence upward to the lungs, regulates water pathways, and transports downward to the bladder. Thus, water essence spreads throughout, and the five essences flow together. When these vital essences fail to be transported, stored, and excreted properly, proteinuria occurs. Therefore, clinical treatment primarily targets the liver, lung, spleen, and kidney meridians to direct the therapeutic effects directly to the affected areas and maximize efficacy [38].

5. Conclusion

HSP is highly prone to recurrence, with the risk persisting for years after remission, severely impacting children's physical and mental health as well as their quality of life. The high recurrence rate leads to prolonged illness and various complications. While Western medicine is essential for treatment, drugs like corticosteroids only temporarily reduce rashes and alleviate symptoms, accompanied by numerous adverse effects. Thus, in treating HSP—particularly in children—clinicians consistently face numerous difficulties and challenges. Beyond addressing the inevitable and persistent kidney damage and the difficult-to-relieve gastrointestinal symptoms, they must also consider that pediatric patients are in a critical period of growth and development. While traditional therapies like long-term glucocorticoid and immunosuppressive agents can alleviate symptoms, they often result in severe immunosuppression,

serious complications, increased infection risks, and organ damage. All these factors significantly impact the child's quality of life. In recent years, multiple clinical studies have demonstrated that TCM fundamentally regulates the physical condition of pediatric HSP patients. Numerous investigations confirm TCM's unique advantages in reducing HSP recurrence rates, controlling renal damage, and minimizing adverse reactions. Consequently, the integrated approach combining Chinese and Western medicine offers promising efficacy and high safety for treating pediatric HSP.

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