Henoch-Schönlein purpura in children: its relation to oral and dental health

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ABSTRACT

Background: Henoch-Schönlein purpura (HSP) is a rare systemic small vessel vasculitis, which commonly occur in children between 2 and 10 years of age. The course of the disease is often self-limiting, although may manifest long-term renal morbidity. The severity of renal involvement decides about the prognosis of this disease. Many factors can trigger the disease attack, which is the most common is bacterial invasion. Since the oral cavity is often refer as infectious foci to other part of the body, it seemed rationally to be part that contribute the course of disease, thus management of these infectious foci, if possible, gives rise to an astoundingly good prognosis. Purpose: This paper will describe a review on HSP and the possible association with oral and dental health since it might be related to the prognosis of HSP. Reviews: Rashes in children are common; they may develop a rash after prescription of antibiotics. Nevertheless there are some childhood diseases that may manifest a rash presentation, such as HSP. It is important for pediatric dentist to have knowledge about HSP and consider the possibility of dental treatment or disease as potential triggers. Conclusion: Oral and dental condition may be the trigger cause of HSP attack. Therefore, it is important for pediatric dental practitioner to be aware of the course of the disease in order to limit the expanding complications.

Key words: Henoch-Schönlein purpura, infectious foci, children

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INTRODUCTION

Henoch-Schonlein purpura (HSP) is the most common type of systemic vasculitis in childhood and diagnosed when palpable purpura is present plus one of the following: diffuse abdominal pain, any biopsy showing predominant immunoglobulin A (IgA) deposition, arthritis or arthralgia, and renal involvement. Symptoms can begin in children, most commonly between the ages of 4 and 7 years, soon after an upper respiratory tract infection or streptococcal pharyngitis. Children may develop arthritis, leading to pain. A rash may start as urticaria or erythematous maculopapules on the legs and buttocks. Eventually these spots blend to form purpura in the skin. Abdominal pain that can be quite severe may also present in some cases. Children younger than 2 years with HSP are more likely to develop edema of various areas of their bodies, which is a result of leaky small blood vessels in the skin. Kidney involvement can also cause edema, hematuria or proteinuria. Although its cause is unknown, it is often associated with infectious agents such as group A streptococci and also as immune complex disease since IgA, which is caused by mucosal infections, is known to play an important role in its immune-pathogenesis. A high prevalence of infectious foci in oral as well as ear, nose, and throat diseases was revealed in children with HSP.

HSP is known to have a high probability of being spontaneously cured if supportive treatment is the primary intervention. However, it sometimes develops into severe conditions with a high rate of reoccurrence. No form of therapy has ever been shown to decrease the duration of the disease or prevent recurrences. Nephritis is the most serious long-term complication of HSP. Although early aggressive therapy has been recommended for children with such severe renal involvement, there is little evidence to indicate the best treatment for it.

Since the oral cavity is often refer as infectious foci to other part of the body, and also structured by mucous tissue, it seemed rationally to be related to HSP. Management of these infectious foci, if possible, gives rise to an astounding good prognosis in reducing the recurrent attacks of HSP. Tahmassebi in 2007 first reported a case of HSP following endodontic treatment. Inoue, et al. in 2008, reported that dental caries (70%) along with apical periodontitis (53%) was found in HSP cases and conclude that early and extensive treatment for these lesions may prevent the complication of HSP. This paper will discuss an overview of HSP and the possible relation of oral focal infection, which will be valuable to pediatric dentists, since, although HSP is generally a benign, self-limited condition, oral and dental health of the patient might be related to the prognosis of HSP.

Epidemiology and etiology

Henoch-Schönlein purpura (HSP) is an inflammatory disorder characterized by a generalized vasculitis involving the small vessels of the skin, gastrointestinal (GI) tract, kidneys, joints, and, rarely, the lungs and central nerve system. The syndrome takes its name from two German physicians. In 1837, Johan Schönlein first described several cases of peliosis rheumatica or purpura associated with arthritis. Thirty years later, Edouard Henoch described the GI manifestations, including vomiting, abdominal pain, and melena. Henoch-Schönlein purpura has also been referred to as rheumatic purpura, leukocytoclastic vasculitis, and allergic vasculitis.

Although the exact cause of HSP is unknown, exposure to various infective pathogens, drugs, vaccines, food allergens and insect bites may be possible immunological triggers. An upper respiratory tract infection (URTI) preceding presentation with HSP by some days or weeks has been reported in up to 50% of cases and the occurrence of HSP in children particularly in the autumn and winter months suggests an infectious etiology. In patients with HSP, immunoglobulin A (IgA) immune complexes are deposited in small vessels, as a result of exposure to an antigen from an infection, medication, or other environmental factors. Group A streptococci, which can cause an upper respiratory tract infection, are the most common pathogenic microorganisms that cause HSP. Several dermatological or autoimmune diseases are thought to correlate with odontogenic infectious diseases. For example, Burger's disease has been linked to periodontitis, or palmoplantar pustulosis and chronic pigmented purpura have also been reported to have an association with an oral focal infection.

HSP is considered to be associated with odontogenic infectious diseases as well. There are a few reports that mention the correlation between HSP and odontogenic infectious diseases. Jinous et al. have reported a case of HSP that had developed after endodontic treatment. This report suggested that root canal treatment could be a trigger for HSP, as it assumed that trepanation of the apex may cause a streptococcal bacteremia. Environment and microbiological flora changes in the root canal may also cause a bacteremia. Inoue et al. have reported on the efficacy of dental treatment in preventing nephropathy in pediatric HSP. Igawa et al. reported that an oral focal infection could be a precipitating factor for adult HSP, as improvements in the skin lesions were observed after patients being treated for the oral infection.

HSP preferentially affects children aged 2–11 years. The median age is 5 years and occurs a slight predominance in males, which is twice as females. The condition has been reported to have an incidence of 10–20 cases per 100 000 school-aged children each year. More than 90 percent of patients are children younger than 10 years, with a peak incidence at six years of age. However, it is also seen in infants, adolescents, and adults. HSP is milder in infants and children younger than two years. Disease is more severe in older children and adults, especially with regards to renal involvement. The true prevalence may be underestimated because cases are often not reported. As seen in Indonesia, the exact data about the prevalence HSP is still unclear.
According to secondary data in Harapan Kita Hospital Jakarta during 6 years period (2004–2010), it was reported 70 cases of HSP in 2–16 years old children with the rate for boys are higher (55.7%) than girls (44.3%).

Based to ethnic groups, HSP has a higher prevalence in Caucasians and Asians than in those of African descent. The disease occurs more often in the colder months and is usually preceded by an upper respiratory infection, particularly streptococcal, but a recent study suggests that an occult malignancy may be the cause.

Despite the exact etiology of HSP remains unknown, histologically HSP exhibits an immune mediated leukocytoclastic vasculitis, with deposits of immunoglobulin A (IgA) and its immune complexes within the walls of involved vessels and organs. Patients have elevated serum levels of IgA, IgA immune complexes, IgA anticardiolipin antibodies, and transforming growth factor-β, as well as altered IgA glycosylation.

Antigen and antibody complexes, mostly IgA, form as a result of bacterial and viral infections, vaccinations, drugs, and autoimmune mechanisms. These antigen antibody complexes deposit in the small vessel walls and activate the alternate complement pathway that leads to neutrophil accumulation resulting in inflammation and vasculitis without a granulomatous reaction. This can involve multiple systems including skin, gastrointestinal tract, kidney, and joints but it can involve any organ system. Vasculitis causes extravasation of blood and its components into the interstitial spaces resulting in edema and hemorrhage.

Clinical feature

The major clinical manifestations of HSP are purpura, arthritis, abdominal pain, gastrointestinal bleeding, and Henoch-Schönlein purpura nephritis (HSPN). The most common clinical manifestations are illustrated in Figure 1. These can develop over days to weeks and may vary in the order that they present. It can masquerade as many different conditions, depending on the symptoms. Palpable purpura and joint pain are the most common and consistent presenting symptoms; initial diagnosis of HSP in the absence of these symptoms may not be obvious.

The classic rash (Figure 2) of HSP begins as erythematous, urticarial and macular wheals. It then coalesces and develops into the typical ecchymoses, petechiae, and palpable purpura. The rash occurs in 96% cases, often manifests in a symmetrical pattern at pressure dependent areas, such as the lower extremities and the

![Figure 2. Closer look of skin rash.](image)

Figure 3. Typical distribution of palpable purpura in Henoch-Schönlein purpura.

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Figure 4. Henoch-Schönlein purpura of the upper limb with swollen elbow joint.

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buttocks (Figure 3). In no ambulatory children the face, trunk, and upper extremities may be more affected. May be urticarial and cause edema, particularly in children.\textsuperscript{18}

Joints are involved in the majority of cases, involving lower limbs (ankles and knees) more commonly.\textsuperscript{21} Arthralgia occurs in 84% of HSP patients and often coexists with other symptoms. The large joints of the lower extremities are most commonly affected. It is none destructive arthritis. Transient oligoarticular arthritis and periartricular swelling may cause pain, tenderness and restricted movement (Figure 3).\textsuperscript{18}

GI pain is often the most debilitating of the HSP symptoms, and can be further complicated by GIT hemorrhage (14–38%), intussusception, obstruction or perforation.\textsuperscript{21,22} GI problems started as cramping abdominal pain, often with vomiting, appears about a week or more after the rash begins. Although there are cases where GI problems occur without a rash. 25% have GIB and 50% have occult blood loss. On endoscopy you see purpuric lesions +/- edema, ulceration, or bowel spasm (Figure 5).\textsuperscript{8}

Renal symptoms have a wide range of severity, from asymptomatic microscopic hematuria, to full-blown nephritic syndrome or nephritis. Most renal involvement occurs early, 85% within the first month, although it can develop later; follow-up to 6 months is recommended.\textsuperscript{21} Begins few days to weeks after other symptoms. Urine analysis can show proteinuria (mild), red blood cells, and cellular casts. Many patients will be asymptomatic, but others can develop nephritic syndrome.\textsuperscript{8}

Other symptoms are rare and usually involve the central nervous system or lungs, from pulmonary hemorrhage through to convulsions. Age does play a role in the symptomatology, with children younger than two years showing predominantly cutaneous symptoms and signs, as well as a much lower incidence of renal and gastrointestinal involvement. The peak incidence is in the 4–6 year-old age group with figures around 70/100 000 population, with a very slight male predominance. Recurrence is relatively common and 30% of patients will have one or more recurrences of acute vasculitis. The average duration of disease is 4 weeks and while steroids will shorten this period, current data suggest there is no correlation between steroid use and increased frequency of relapse.\textsuperscript{21}

**Diagnosis, differential diagnosis and prognosis**

Diagnosis of HSP depends on clinical findings and history. It is usually not difficult if the classic triad of rash, gastrointestinal complaints or hematuria, and arthritis is present. When symptoms are not typical, however, the differential diagnosis can become extensive. There is not a specific laboratory test for the disorder, although an elevated serum IgA level is suggestive. Some laboratory studies can also help in excluding other diagnoses and in evaluating renal function, including urinalysis.\textsuperscript{8}

HSP is a clinically obvious condition in the majority of cases, but laboratory investigation would include: full blood count, to exclude thrombocytopenia; most often thrombocytosis is found in HSP. Anemia may be present but is usually an indicator of GIT hemorrhage or severe hematuria. Renal function is obviously very important and assists in identifying some with a rapidly progressive glomerular disease. Erythrocyte sedimentation rate (ESR) is elevated in approximately 60%, but is a nonspecific inflammatory marker. IgA levels are elevated in 25–50% of patients. Albumen levels are diminished in cases of nephritic syndrome and/or protein-losing enteropathy, which may occur. Occult fecal blood is seen in 25%. Factor XIII plasma levels can be measured in atypical cases and are decreased in the majority, even prior to purpura formation. Skin biopsy is a useful diagnostic tool in atypical cases, and reveals a typical leukocytoclastic vasculitis with necrosis of the vascular wall and inflammatory cell infiltrate, accompanying IgA dermal deposition.\textsuperscript{21}

Vasculitis is not a common childhood condition and HSP is difficult to confuse with other small-vessel vasculitides, but a relatively short list of alternative possibilities, which includes Kawasaki disease. Most of these conditions can be excluded or diagnosed clinically, but immune serological markers and a full blood count will distinguish doubtful cases.\textsuperscript{21}

Generally the prognosis is good, with the exception of those with significant renal involvement.\textsuperscript{23} HSP is only fatal in the most rare of cases. Initial attacks of HSP can last several months, and relapses are possible. Kidney damage related to Henoch-Schoenlein purpura is the primary cause of morbidity and mortality. Overall, an estimated 2% of cases progress to renal failure; as many as 20% of children who have HSP and are treated in specialized centers require hemodialysis. The renal prognosis appears to be worse in adults than in children.\textsuperscript{24}

**Management**

Management is mainly supportive and symptomatic. Most patients can be managed as outpatients with treatment being directed at adequate oral hydration and pain relief.

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**Figure 5.** Endoscopic finding on esophagus showing inflammation, sub mucosal hemorrhage, and small ulceration.\textsuperscript{19}
Edema of the lower extremities, buttocks, and genital area are improved with bed rest and elevating the affected area. Non-steroid anti inflammations drug also may reduce the inflammation. No effective therapeutic protocol to reduce recurrent attacks of HSP or prevent the complication of nephropathy has been established.

**DISCUSSION**

Although HSP is a rare inflammatory disorder of childhood, it has clinical significance. The most serious sequel of HSP is renal involvement. This complication occurs in 50% of older children, but only 25% of children younger than 2 years of age. Less than 1% of cases progress to end-stage renal disease. Patients who develop renal involvement generally do so within three months of the onset of rash.

HSP is a self-healing benign disorder, but renal and gastrointestinal involvement can lead to poor prognoses. Odontogenic focus infection (OFI) as one of several trigger cause to HSP attack need to be consider as one of the risk factors that determine the prognosis of HSP. OFI is a bacterial infection that tends to be overlooked by dermatologists. Dental screening of HSP patients could help to decrease the risk of renal and/or abdominal complications and facilitate treatment.

The concept that focal infection may produce chronic systemic diseases has now been generally accepted. Local, septic, or mucosal infections foci anywhere in the body can be sources of systemic diseases. To date, foci of specific infections of the gums and the presence of abscesses around the roots of the teeth, often unsuspected, have not received attention in the treatment of pediatric diseases.

The etiological role of chronic oral infection in HSP is supported by several other studies. The antigens of the outer membranes of Haemophilus parainfluenzae, a common bacterium within apical periodontitis, and antibodies against these have been identified in the glomerular mesangium and sera of HSP and IgA nephropathy patients. In one case, endodontic dental therapy coincidentally induced HSP. Given that IgA nephropathy and HSPN are pathologically identical diseases, all of these data suggest that chronic infections in the oral cavity may play pathogenic roles in HSP. The high caries levels of HSP children may support this view. Dental caries in premature teeth easily invade through infected root canals into surrounding bony tissues, forming apical periodontitis.

The most commonly identified OFI in HSP patients was apical periodontitis in association with dental caries. Although both are infectious diseases by nature, apical periodontitis, which is mostly initiated from dental caries by oral bacteria invading through infected root canals, is a much more complex disorder in regard to infection as well as inflammation. A thousand billion bacteria colonize a single lesion, and more than 300 species of aerobic and anaerobic bacteria can be isolated. Within the associated lesions, various inflammatory cytokines are produced by cellular components of the periapical lesion, resulting in the persistence of active immune reactions.

Many degraded bacterial products and the decomposition products of pulp tissue stagnate there. Meanwhile, bacteria and their toxic derivatives and destroyed peripheral tissues may egress through the apical foramen and be captured continuously within tonsils through their surface epithelium. However, the innate secretory IgA-mediated oral mucosal defense system may fail to eliminate bacterial antigens owing to the presence of a tremendous amount of bacteria. On the other hand, bacterial pathogens may enter the blood stream during transient bacteremia, damaging the inside smooth lining of the blood vessel walls. Collectively, chronic and long-standing apical periodontitis have the potential to trigger HSP.

It is concluded that HSP is the most common systemic vasculitis primarily affecting children aged 3–15 years. HSP is characterized by palpable purpura without thrombocytopenia or coagulopathy, arthritis or arthralgia, abdominal pain, and renal disease. Diagnosis depends on clinical manifestations and no single diagnostic test can confirm the disease. Management is mainly supportive and symptomatic and can usually occur in the ambulatory setting. Oral and dental condition may be the trigger cause of HSP attack. Therefore, it is important for dental practitioner to be aware of the course of the disease in order to limit the expanding complications.

**REFERENCES**


