Efficacy of Tonsillectomy Plus Methylprednisolone Pulse Therapy for a Child with Henoch-Schoenlein Purpura Nephritis

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Efficacy of Tonsillectomy Plus Methylprednisolone Pulse Therapy for a Child with Henoch-Schoenlein Purpura Nephritis. Tohoku J. Exp. Med., 2007, 211 (3), 291-295 —— Henoch-Schoenlein purpura (HSP) is a systemic disorder characterized by a leukocytoclastic vasculitis involving small vessels with the deposition of immunoglobulin A (IgA) immune complexes. Renal involvement is the principal cause of morbidity and mortality in children with HSP. We report here an 11-year-old boy with Henoch-Schoenlein purpura nephritis (HSPN) accompanied by recurrent purpura and persistent nephropathy despite conventional therapy such as prednisolone, methylprednisolone pulse therapy and immunosuppressive agent (Mizoribine). The patient was treated with tonsillectomy plus methylprednisolone pulse therapy. This treatment decreased proteinuria, induced disappearance of microscopic hematuria, and improved renal pathological findings. Tonsillectomy plus methylprednisolone pulse is effective and useful therapy for some children with recurrent purpura and persistent nephropathy. ——— HSPN; methylprednisolone pulse; urokinase pulse; tonsillectomy; recurrent purpura

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Henoch-Schoenlein purpura (HSP) is an immunoglobulin (Ig) A-mediated immune-complex vasculitis that predominantly affects the skin, joints, gastrointestinal tract, and kidneys. It occurs most frequently in childhood, and its prognosis is mainly determined by the severity of renal involvement (Habib et al. 1994). Treatment with methylprednisolone pulse therapy and oral prednisolone does not always induce complete remission in patients with Henoch-Schoenlein purpura nephritis (HSPN) (Niaudet and Habib 1998; Foster et al. 2000; Flynn et al. 2001; Kawasaki et al. 2005). Approximately 20% of patients exhibit persistent nephropathy or progressive end-stage renal failure despite the treatment (Yoshikawa et al. 1987; Habib et al. 1994; Kawasaki et al. 2005).

The pathogenesis of HSP remains unknown. However, HSP is generally believed to be an immune complex-mediated disease characterized...
by the presence of polymeric IgA1 (pIgA1)-
containing immune complexes predominantly in
dermal, gastrointestinal, and glomerular capillar-
ies (Rai et al. 1999). It has been suggested that
HSPN and IgA nephropathy (IgAN) comprise a
spectrum of clinical presentations of similar
disorders. The granular IgA and C3 immune
deposits found predominantly in the mesangium
are indistinguishable from those seen in IgAN.
Frequent association between upper respiratory
tract infection and the development of HSP has
also been suggested (Yoshikawa et al. 1987;
Habib et al. 1994; Rai et al. 1999). Recently,
there have been reports of the efficacy of tonsil-
llectomy and tonsillectomy plus methylprednisol-
one pulse therapy (tonsillectomy pulse therapy)
in treating IgAN (Sanai and Kudoh 1996; Hotta et
al. 2001; Xie et al. 2003). In addition, there had
been a few reports on the efficacy of tonsillecto-
my pulse therapy for HSPN in adult (Sugiyama et
al. 2005). However, there have been no reports
on the efficacy of tonsillectomy pulse therapy for
HSPN in pediatric patients.

We report here a child with HSPN accompa-
nied by recurrent purpura and persistent nephrop-
athy despite conventional therapy who was suc-
cessfully treated with tonsillectomy followed by
intravenous pulse methylprednisolone and oral
prednisolone.

CASE REPORT

The patient first had abdominal pain and pur-
pura at 9 years of age in May 2001. His family
physician diagnosed HSP on the basis of abdomi-
nal pain, purpura, and arthralgia of the right ankle.
He had no urinary abnormality, and had not con-
sulted his family physician since August 2001. In
June 2002, proteinuria and hematuria were detect-
ed on a school urinary screening. He experienced
abdominal pain and purpura again in addition to
urinary abnormality, and was referred to a hospi-
tal and admitted in July. Results of laboratory
investigations are shown. Laboratory tests
revealed a leukocyte count of 6,650/mm³, erythro-
cyte count 443 × 10⁶/mm³, platelet count 25.5 ×
10⁵/mm³, erythrocyte sedimentation rate (ESR) 10
mm/hr, serum total protein 6.1 g/dl, serum albu-
min 4.0 g/dl, serum creatinine 0.45 mg/dl, and
serum total cholesterol 184 mg/dl. Urinalysis
revealed protein of 0.92 g/day, with sediment con-
taining 100 erythrocytes per high-power field, 50
leukocytes, and many granular casts. Creatinine
clearance (24-hr) was 154.2 ml/min per 1.73m².
Immunology studies revealed C3 159 mg/dl, C4
29 mg/dl, CH50 35.8 U/ml, antinuclear antibody
titer < 80X, negativity for anti-DNA antibody, and
negativity for titers of serum anti-neutrophil cyto-
plasmic antibodies.

His urinary protein excretion was 1.8 g/day,
and macroscopic hematuria was noted. First renal
biopsy was performed. The patient and his par-
ents gave their informed consent in renal biopsy.
On immunofluorescence (IF) microscopic exami-
nation, IgA deposits were found in the mesangial
region (Fig. 1A). Light microscopy (LM)
revealed mesangial cell proliferation and moder-
ate mesangial matrix accumulation. Two of 20
glomeruli showed cellular crescent formation (Fig.
1B). The activity and chronic index by Andreoli
and Bergstein (1989) were 4 and 3, respectively.
He was therefore diagnosed with HSPN with the
International Study of Kidney Disease in Children
(ISKDC) IIIb, and was treated with methylpredni-
solone pulse, prednisolone (PDN, 30 mg/day) and
angiotensin receptor blocker (Blopress, 4 mg/
day). Proteinuria gradually decreased. However,
he subsequently developed proteinuria and
macroscopic hematuria on tapering of PDN. In
November 2002, a second renal biopsy were per-
formed and revealed ISKDC IIIb. The activity
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and chronic index were 4 and 4, respectively.
Following discharge, he was given prednisolone
15 mg/day, and his urinary protein excretion was
0.5 g/day. Thereafter, his urinary protein excre-
tion was 0.4-0.8 g/day, and microscopic hematuria
persisted at visits to the outpatient clinic. In
October 2003, following an episode of acute ton-
sillitis, purpura and exacerbation of urinary find-
ings including increase of proteinuria and macro-
scopic hematuria were found. He was treated with
methylprednisolone pulse, prednisolone (PDN, 20
mg/day), and mizoribine (150 mg/day). Subsequently, purpura re-appeared and his urinary
protein excretion increased to 2.4 g/day. He was
admitted to our hospital, and a third renal biopsy was performed and revealed ISKDC IIIb. LM revealed increased lobulation, hypercellularity in the mesangium, fibro-cellular crescent formation and inflammatory infiltrations (Fig. 1C). The activity and chronic index were 7 and 7, respectively. In otolaryngology, provocation test was performed and it was positive.

Tonsillectomy pulse therapy was performed. Both tonsils were moderately hypertrophied. The resected tonsils displayed lymphoid hyperplasia, distended the crypts contained keratin plugs, which had resulted from keratinization and desquamation of the lining epithelium. The parenchyma of the tonsils exhibited mild fibrosis. These findings indicated the presence of chronic tonsillitis. Following tonsillectomy pulse therapy, the patient’s purpura, macroscopic hematuria, and proteinuria disappeared promptly, and have not recurred despite discontinuation of PDN. In addition, there have been no episodes of purpura or exacerbation of urinary findings. At 24 months
after tonsillectomy, a fourth renal biopsy was performed and revealed ISKDC II, and showed slightly mesangial matrix accumulation and no mesangial proliferation (Fig. 1D). The activity and chronic index were 3 and 4, respectively. There were no side effects of tonsillectomy pulse therapy. No proteinuria, macroscopic hematuria, or purpura has been noted during 36-month follow-up after tonsillectomy.

**DISCUSSION**

We have reported the efficacy of tonsillectomy pulse therapy in an 11-year-old boy with HSPN with recurrent purpura and persistent nephropathy.

In general, HSP itself is known as acute, not chronic disease. However, some of patients with HSPN were refractory. Niaudet P reported that recurrences of vasculitis episodes were predictive of poor outcome in HSPN (Niaudet et al. 1994). The mechanism of this refractory was obscure.

In addition, recurrence of disease in patients with HSPN who have received allografts was recognized soon after the demonstration that this form of glomerulonephritis has predominantly IgA in the immune deposits. Meulders et al. (1994) reported recurrent glomerular deposits of IgA in 53%, clinical nephritis occurred in only 18% of the grafts and was expressed as hematuria, often with proteinuria and occasionally with acute renal insufficient. In present study, our patient had recurrent purpura and persistent nephritis, and LM on the third renal biopsy revealed ISKDC III (active index 7, chronic index 7). Thus, we speculated that the prognosis of our patient might be poor.

For treatment of severe HSPN, some reports have described the use of multiple, combined agents, including immunosuppressive drugs (Niaudet et al. 1998; Foster et al. 2000; Flynn et al. 2001). We previously reported that methylprednisolone and urokinase pulse therapy with cyclophosphamide significantly reduced urinary protein excretion and prevented any increase in crescentic and sclerosed glomeruli in patients with HSPN of at least type IV (Kawasaki et al. 2005). However, immunosuppressive drugs including cyclophosphamide have side effects such as oncogenesis, myelosuppression, hemorrhagic cystitis, and interstitial pneumonia (Foster et al. 2000; Flynn et al. 2001). These drugs do not always induce complete remission in all patients with HSPN.

Recently, there have been reports on the efficacy of tonsillectomy for IgAN in adults (Sanai and Kudoh 1996; Hotta et al. 2001; Xie et al. 2003). Hotta et al reported that tonsillectomy plus methylprednisolone pulse therapy led to clinical remission in adult patients with IgAN (Hotta et al. 2001). In addition, we reported that tonsillectomy pulse therapy was effective for severe IgAN in childhood (Kawasaki et al. 2006). Wyatt and Hogg (2001), on the other hand, claimed that tonsillectomy cannot be recommended for IgAN by evidence-based criteria.

It is generally reported that the pathological findings of HSPN are similar to those of IgAN (Habib et al. 1994; Rai et al. 1999). Sugiyama et al. (2005) reported that tonsillectomy followed by intravenous pulse methylprednisone and oral prednisone resulted in a decrease in proteinuria, improvement of renal function and the disappearance of macrohematuria. We have reported here that tonsillectomy pulse therapy was effective in an 11-year-old boy with HSP with recurrent purpura and persistent nephropathy. Pathologic examination of the tonsils revealed chronic tonsillitis including lymphoid hyperplasia, distension of crypts containing keratin plugs, and fibrosis of the parenchyma. Following tonsillectomy, the purpura and urinary abnormalities disappeared. These findings suggested that the chronic tonsillitis played a role in the pathogenesis of HSPN.

In conclusion, tonsillectomy pulse therapy is effective and useful for some patients with recurrent purpura and persistent nephropathy.

**References**


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