Ibuprofen-induced Henoch–Schönlein purpura nephritis: First reported case

Christopher Lim Thiam Seong, Malini Shanmuganathan

Abstract:
Ibuprofen is a nonsteroidal anti-inflammatory drug that is used widely in treating pain, fever, and inflammation. Its side effects are mainly due to acute renal impairment and gastric discomfort. We hereby report a rare case of Henoch–Schönlein purpura nephritis secondary to ibuprofen consumption which has not been reported in literature before.

Key words:
Henoch–Schönlein purpura, ibuprofen, nephritis

Henoch–Schönlein purpura (HSP) nephritis is a rare kidney disease leading to chronic kidney disease in a small percentage of patients. It usually presents as acute episode followed by complete healing in the majority of patients. However, persisting proteinuria and progressive chronic kidney disease occur in a minority of patients if treatment is not started promptly. There are few known triggers, but ibuprofen-induced HSP nephritis has never been described before.

Case Report
A 62-year-old female with known hyperlipidemia developed acute purpuric rashes over her lower limbs and abdomen 3 weeks after consuming ibuprofen for her right shoulder pain. She was seen by a dermatologist for the rash who diagnosed HSP [Figure 1]. The lesion was managed conservatively. She did not take any other medication or supplement apart from five tablets of 200 mg ibuprofen over 5 days period. Four weeks later, she developed new onset of leg edema, frothy urine, and hypertension. Laboratory test confirmed mixed nephritic-nephrotic syndrome.

Laboratory test results were as follows: Urea: 3 mmol/L, creatinine: 83 μmol/L, hemoglobin: 11.4 g/dL, white blood cell: 10.1 × 10⁹ platelet: 344 × 10⁹, albumin: 26 g/L, total cholesterol: 5.64 mmol/L, triglyceride: 2.61 mmol/L, low-density lipoprotein: 3.05 mmol/L, and erythrocyte sedimentation rate: 116 mm/h. Urinalysis revealed red blood cell: 4+, protein: 4+ with 24 h urine protein of 1.8 g. Serum complements (C3 and C4) were normal. P-anti neutrophil cytoplasmic antibody (ANCA), C-anti ANCA, antinuclear antibody, and anti-double stranded DNA antibody were negative. Hepatitis B, hepatitis C, and human immunodeficiency virus screening were negative. Ultrasonography revealed that both kidneys were of normal size with no significant abnormality.

Serum immunoglobulin showed markedly elevated serum IgE level at 2077 kU/L (normal, <100 kU/L) and slightly raised serum IgA level at 4.6 g/L (normal, <2 g/L). Renal biopsy revealed changes consistent with either IgA nephropathy or HSP nephritis with 34% active cellular crescents and sclerosing pattern with 13% global glomerulosclerosis. There was also tubulointerstitial inflammation with acute tubular necrosis-like changes and mild chronic tubulointerstitial damage. She was started on azathioprine, angiotensin receptor blocker, and prednisolone. Her skin lesion resolved after 4 weeks of treatment. Six months into treatment, her nephritis went to full remission.

Discussion
IgA nephropathy and HSP nephritis represent a spectrum of clinical presentations of similar disorder. The pathogenesis of HSP remains unclear, but it is generally considered to be an immune complex-mediated disease characterized by the tissue deposition of...
polymeric IgA1-containing immune complexes.[1] The pathognomonic granular IgA and C3 deposits in the mesangium are indistinguishable from those seen in IgA nephropathy. However, the presence of characteristic skin lesion, an elevated serum IgE level, and the presence of crescents in histopathology favor HSP over IgA nephropathy.[2] HSP usually affected patient younger than 10–years old with a 2:1 male preponderance. In one series, HSP was the most common cause of crescentic glomerulonephritis in children.[3] Genetic factors may play a role in HSP pathogenesis.[4] Triggers for HSP include upper respiratory infection, neoplastic disease such as leukemia, and myelodysplastic disorder and medications such as captopril, diclofenac, and vancomycin. In this case, we believe that the episode is likely triggered by ibuprofen consumption which has never been reported before. The patient has not consumed any other supplement or medications apart from ibuprofen. In this case, according to the objective causality assessment by the Naranjo adverse drug reaction probability scale, the causal association between ibuprofen and the adverse event was probable (Naranjo score = 6).[5] The adverse drug reaction was evaluated for causality assessment using the World Health Organization-Uppsala Monitoring Center (WHO-UMC) criteria. The assigned causality category with WHO-UMC criteria for this adverse drug reaction was “certain.” As mentioned earlier, HSP nephritis is associated with high IgE level which may be attributed by immunoallergic response to external stimuli.

Although the average natural course of the disease is 1 month with good recovery, there are cases that have a protracted course that may end up as end-stage renal failure.[6] Management is controversial and ranges from conservative to the addition of steroids to various immunosuppressants such as azathioprine, plasmapheresis, and cyclophosphamide.[7] In this case, since there is the presence of abundance of crescents which usually denotes a more aggressive disease progression, we decided to use oral azathioprine at a dose of 2 mg/kg and full dose oral prednisolone at 1 mg/kg as the preferred first-line immunosuppressants therapy. The presence of tubulointerstitial inflammation, fibrosis, and glomerulosclerosis in this patient was also independent risk factors for renal function decline in various renal models. We believe that these immunosuppressants together with angiotensin-converting enzyme inhibitor have a role in preventing the fibrotic transformation of the lesion.[8]

**Conclusion**

Ibuprofen-induced HSP nephritis has to be suspected when there is the presence of nephritic-nephrotic syndrome together with the classical skin rash over the extensor surfaces. Prompt diagnosis, withdrawal of the offending drug, and instituting the correct immunosuppressant are key to prevent the possible deterioration of the renal function.

**Financial Support and Sponsorship**
Nil.

**Conflicts of Interest**
There are no conflicts of interest.

**References**
1. Feehally J, Allen AC. Pathogenesis of IgA nephropathy. Ann Med Interne (Paris) 1999;150:91-8.
2. Davin JC. Henoch-Schönlein purpura nephritis: Pathophysiology, treatment, and future strategy. Clin J Am Soc Nephrol 2011;6:679-89.
3. Jardim HM, Leake J, Risdon RA, Barratt TM, Dillon MJ. Crescentic glomerulonephritis in children. Pediatr Nephrol 1992;6:231-5.
4. Amoroso A, Berrino M, Canale L, Coppo R, Cornaglia M, Guerrera S, *et al.* Immunogenetics of Henoch-Schoenlein disease. Eur J Immunogenet 1997;24:323-33.
5. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.
6. Fogazzi GB, Pasquali S, Moriggi M, Casanova S, Damilano I, Mihasch MJ, *et al.* Long-term outcome of Schönlein-Henoch nephritis in the adult. Clin Nephrol 1989;31:60-6.