

Case Report

Ibuprofen induced hypersensitivity vasculitis: a case report and review of literature

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Abstract

Ibuprofen is one of the most commonly prescribed drugs used to reduce fever and relieve pain. Hypersensitivity vasculitis is a rare adverse effect of ibuprofen. Here, we report a case of a female patient who developed hypersensitivity vasculitis and acute renal failure following the use of ibuprofen.

Keywords: Ibuprofen, hypersensitivity vasculitis, acute renal failure.

INTRODUCTION

Non steroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of inflammatory condition. Ibuprofen is a NSAIDs and its pharmacological properties include antipyretic, anti-inflammatory and analgesic actions (Walker and Edwards, 2003). The mechanism of action of Ibuprofen is by inhibition of the enzyme cyclooxygenase involved in its anti-inflammatory activity (Walker and Edwards, 2003). The most common adverse effects of Ibuprofen are gastritis, peptic ulceration, renal impairment, angiodema. Hypersensitivity vasculitis is a rare adverse effect. Here, we report a case of hypersensitivity vasculitis and acute renal failure following the use of Ibuprofen.

CASE REPORT

A 45 years old woman not known to have any medical illness before presented to Emergency room of Assir central hospital (Abha, Saudi Arabia) with fever, abdominal pain of one week duration. She reported being doing well till one month ago when she started to have severe toothache for which she received ibuprofen 400mg, 10 tablets for two days. Three weeks later she

noticed the appearance of scattered red skin lesion on the lower limbs associated with fever, fatigability, wrist joints pain and a tea color urine. Few days later she developed severe upper abdominal pain associated with passage of black stool for which she presented to the hospital. Systemic review especially in regard to the connective tissue disease stigmata and other aspects of history were unremarkable. At emergency Room, the patient was looking ill, febrile (38.5 °C). However, other vital signs were stable. Chest and cardiovascular examination were unremarkable. Abdominal examination showed tender epigastrium. Joint examination showed painful wrist joint with passive and active movement but no swelling. Lower limbs examination showed scattered palpable red purpura over the anterior aspects of both legs (Figure 1). Her initial investigation revealed leukocyte count of $19 \times 10^3/L$, hemoglobin count of 14 g/dl, blood urea nitrogen count of 50 mg/dl, serum creatinine count of 1.9 mg/dl. The ESR was 20 mm/hr. Coagulation profiles were within normal range. The liver function test was normal apart from serum albumin of 2.5 g/dl. Urinalysis showed protein (++) , red blood cells count of 25 and white blood cells count of 10. Patient was admitted to general ward as a query vasculitis syndrome most likely drug reaction (hypersensitivity reaction) or Henoch-Schliën purpura (HSP). She was started on supportive therapy. Septic screening was sent along with autoimmune screening serology. Next day her creatinine increased to 2.8 mg/dl with evidence of active

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Figure 1. Clinical features. Scattered palpable, non-blanching red purpuric rash over the anterior aspects of both legs.

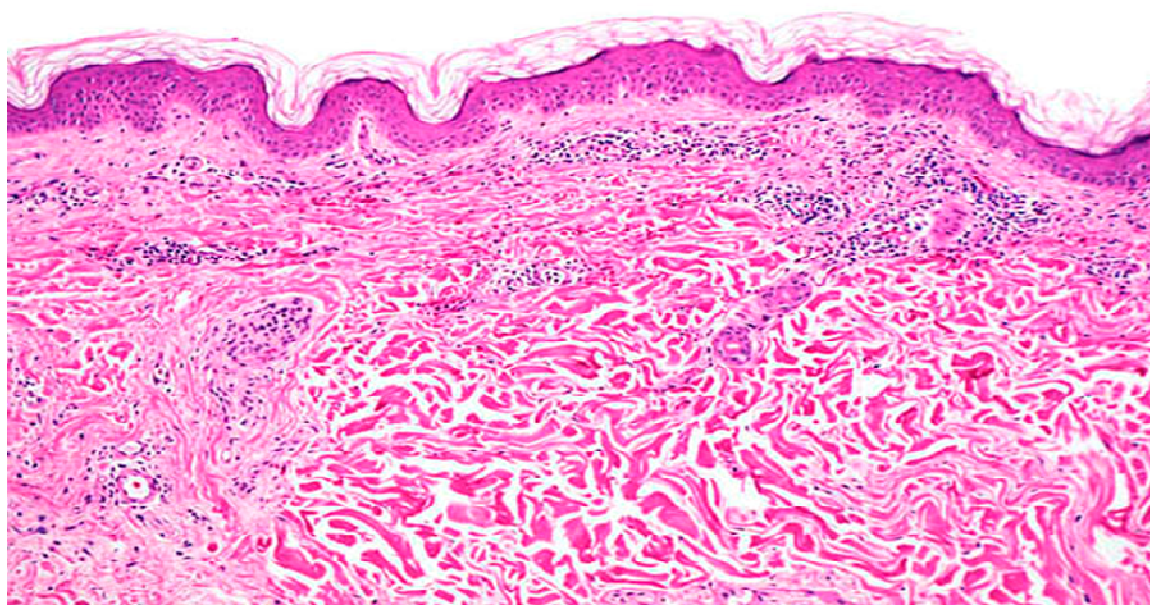


Figure 2. Histological changes in the skin biopsy. On histology, there were extravasation of RBCs, nuclear dust (leukocytoclasia) and destruction of the walls of the blood vessels.

urinary sediment and white blood cells jumped to $26,000 \times 10$ with predominant neutrophils 80%. Bearing in mind rapid progressive glomerulonephritis. We started her on pulse methylprednisolone 1 gm intravenous for three days with broad coverage antibiotic. Creatinine continued increasing to 3.2mg/dl and then 3.6mg/dl but the patient

started to improve clinically from the next day to the systemic steroid and all parameter retained to normal by the third day (creatinine 1.5mg/dl, white blood cells 11×10^3). Skin biopsy showed leukocytoclastic vasculitis (Figure 2) and immunofluorescence showed no IgA deposits. Antinuclear antibody, antineutrophil cytoplas-

mic antibodies and anti-double strand DNA were negative with normal complement levels. Hepatitis, HIV serologies and rheumatoid factor were negative. Echocardiogram was normal. Patient refused to do renal biopsy and was shifted to oral prednisone 50 mg per day and azathioprine 50 mg oral daily. Patient was discharged on good condition with follow up with nephrology.

DISCUSSION

Non steroidal anti-inflammatory drugs are widely used throughout the world. Ibuprofen, is a widely used non steroidal anti-inflammatory drugs. Ibuprofen is used to reduce fever and to relieve headache, muscle aches, menstrual pain, backache, and pain after surgery or dental work (Walker and Edwards, 2003; Huskissan et al., 1971). It has many side effects including ulcer disease, gastrointestinal bleeding, renal insufficiency and mild hepatic injury and rare side effect is hypersensitivity vasculitis (Huskissan et al., 1971; Davies and Avery, 1971). Hypersensitivity vasculitis may be idiopathic, directly caused by a drug or occur in association with a known disorder such as infection. Drugs are the most common cause of hypersensitivity vasculitis particularly penicillins, cephalosporin, sulfonamides, pheytoin, and diuretics (Calabrese and Duna, 1996; Martinez-Taboada et al., 1997). Recently, NSAIDs have been ranked second only to antibiotics in causation of skin reactions (Sanchez-Borges et al., 2005). Hypersensitivity vasculitis due to drugs can be identified on the basis of five defining characteristics: age >16 years, use of possible offending drug in temporal relation to the symptoms, palpable purpura, maculopapular rash, and biopsy of a skin lesion showing neutrophils around an arteriole or venule (Calabrese et al., 1990). In case reported here, the patient has four out of five criteria of hypersensitivity vasculitis and deterioration of renal function, so the diagnosis of "ibuprofen induced hypersensitivity vasculitis and acute renal failure" was established. Henöch-Schonlein purpura (HSP) is unlikely possibility as the skin biopsy with immunofluorescence showed absence IgA deposition. Vasculitis with rheumatoid arthritis and other forms of vasculitides are also unlikely in view of negative rheumatoid factor, ANA, ANCA with normal complement levels. Negative hepatitis serology, HIV serology and normal echocardiogram ruled out the possibility of vasculitis secondary to infection. In 1996, Lie and Dixit described a case of hypersensitivity vasculitis of the temporal artery induced by etodolac (Lie and Dixit, 1996). In 2000, Clénin et al. described a case of ibuprofen induced transient ANA and anti-histone positive

leukocytoclastic vasculitis (Clénin et al., 2000). In 2001, Davidson et al. described a case of ibuprofen induced leukocytoclastic vasculitis (Davidson et al., 2001). In 2007, Ansari et al. described a case of etodolac induced hypersensitivity vasculitis with digital gangrene (Ansari et al., 2007). Renal involvement is usually mild and is manifested by hematuria, proteinuria and cellular cast. Acute renal failure is rare. NSAIDs inhibit prostaglandin synthesis leading to renal vasoconstriction and decreased renal perfusion which can progress to acute renal failure. Acute interstitial nephritis is another form of NSAID induced acute renal failure and the exact mechanism is unknown (Huerta et al., 2005; Abraham and Keane, 1984). To conclude, Ibuprofen is considered as a safe NSAID. It can produce serious adverse effects (vasculitis). This drug can be easily purchased as the over the counter drug. Therefore, the awareness of the physician to this widely used drug on its rare adverse effect is necessary.

REFERENCES

- Abraham PA, Keane WF (1984). Glomerular and interstitial disease induced by nonsteroidal anti-inflammatory drugs. *Am. J. Nephrol.*;4:1-6.
- Ansari JK, Hussain T, Nasseem A (2007). Etodolac induced hypersensitivity vasculitis with digital gangrene. *J R Coll physician Edinb*;37:205-06.
- Calabrese LH, Duna GF (1996). Drug induced vasculitis. *curr opin rheumatol*;8:34.
- Calabrese LH, Michel BA, Bloch DA, Arend WP, Edworthy SM, Fauci AS, Fries JF, Hunder GG, Leavitt RY, Lie JT (1990). The American college of rheumatology 1990 criteria for classification of hypersensitivity vasculitis. *Arthritis Rheum*;33:1108.
- Clénin GE, Van Rooijen MM, Braathen LR (2000). Ibuprofen induced transient ANA and anti-histone positive leukocytoclastic vasculitis. *Hautarzt*;51(9):678-81.
- Davidson KA, Ringpfeil F, Lee JB (2001). Ibuprofen induced bullous leukocytoclastic vasculitis. *Cutis*;67:303-7.
- Davies EF, Avery GS (1971). Ibuprofen: a review of its pharmacological properties and therapeutic efficacy in rheumatic disorders. *Drugs*;2:416-46.
- Huerta C, Castellsaque J, Varas-Lorenzo C, Garcia Rodriguez LA (2005). Nonsteroidal anti-inflammatory drugs and risk of ARF in the general population. *Am. J. Kidney Disease*;45:531-9.
- Huskissan EC, Hart FD, Schenfield GM, Taylor RT (1971). Ibuprofen, A review practitioner; 207: 639-43.
- Lie JT, Dixit RK (1996). Nonsteroidal anti-inflammatory drugs induced hypersensitivity vasculitis clinically mimicking temporal arthritis. *J. Rheumatol.*;23:183-5.
- Martinez-Taboada VM, Blauco R, Garcia-Fuentis M, Rodriguez-Valverde V (1997). Clinical feature and outcome of 95 patient with hypersensitivity vasculitis. *Am. J. Med.*;102:186.
- Sanchez-Borges M, Capriles-Hulett A, Caballero-Fansecas F (2005). Risk of skin reactions when using ibuprofen – based medicine. *Expert opin Drug Saf*;4(5):837-48.
- Walker R, Edwards C (2003). Clinical pharmacy and therapeutics. 3rd ed. Scotland, IMH;795-99.