Case Reports

Aspirin induced leukocytoclastic vasculitis, lower gastrointestinal hemorrhage and acute renal failure (mimicking systemic vasculitis)

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ABSTRACT

نستعرض في هذا التقرير حالة مريض يبلغ من العمر 60 عاماً يعاني من طفح وعائي جلدي شديد مع نزيف في الجهاز الهضمي السفلي وذلك بعد تناول جرعة صغيرة من الاسبرين (81 ملغ) وتحسنت حالته بعد التوقف من استخدام الاسبرين مباشرة. وبعد 3 أسابيع عانى من فشل كلوي حاد والذي يعتقد أنه نتيجة لأعراض التهاب وعائي عام ولكنه كان نتيجة النخر الأنبوبي الكلوي الحاد كمضاعفات متأخرة للاسبرين.

This is a case of a 60-year-old gentleman who presented with an extensive cutaneous vasculitic rash (leukocytoclastic) with lower gastrointestinal bleeding following a small dose of aspirin (81 mg). The aspirin was stopped immediately. Three weeks later, he had acute renal failure, which was initially thought to be secondary to systemic vasculitis, but proved to be acute renal tubular necrosis as a delayed reaction to aspirin.

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Analgesic and anti-inflammatory medications are widely used in all age groups for the treatment of pain, inflammation, fever of diverse etiology, and as antiplatelet agents. As an antiplatelet agent, aspirin is commonly used in cardiac patients due to its irreversible blockage of thromboxane-A, a large proportion of the population is exposed to these drugs. The various non-steroidal anti-inflammatory drugs (NSAIDs) inhibit enzyme cycloxygenase-1 (COX-1) and COX-2 to different degrees. Aspirin (ASA) is a strong inhibitor of COX-1.[1] Anti-inflammatory drugs including ASA, are associated with an array of diverse effects ranging from mild gastritis to life threatening allergic reactions, such as, bullous reaction, Steven Johnson syndrome, pneumonitis, aseptic meningitis, and nephritis.[2,3] Most cases of leukocytoclastic vasculitis are self-limited and usually result in complete recovery without sequel. This is a report of an adult male treated with aspirin who subsequently had systemic complications and cutaneous vasculitis. Our objective in presenting this particular case is to report a multiple serious side effects of small dose ASA that can coexist together to resemble a systemic vasculitis which is a rare presentation and should not be overlooked.

Case Report. A 60-year-old gentleman, presented to the emergency department, complaining of extensive cutaneous rash with abdominal pain and rectal bleeding. Symptoms started 20 days after taking aspirin 81 mg. When the patient developed the rash, he stopped taking aspirin. He reported similar attacks on earlier 2 occasions; 6 years and 5 years before, following 81 mg aspirin. He also complained of weight loss (undetermined), of a few kilograms. He had discomfort in the nose lately, but no history of epistaxes. He has a history of diabetes mellitus for which he is taking insulin. He was a smoker for 20 years and stopped recently. His clinical examination showed an extensive maculopapular rash all over the body mostly on the extremities, which was palpable

non-blanching purpelish in color, and resembled cutaneous vasculitis.

He was afebrile with a blood pressure of 134/66 mm Hg and a pulse rate of 100/minute. Systemic examination was unremarkable. Laboratory examination showed a white blood count of 21.5 (normal range (NR): 4.0-11.0 x 10^9/L, hemoglobin was initially 16g/dL (11.5-16.5g/dL) then dropped to 10g/dL, platelets count 484 x 10^9/L, eosinophil and immunoglobulin E was normal, albumin was low 25g/L (NR: 36-51g/L), urea 7.2mmol/L (NR: 2-6.7mmol/L), creatinine 74mmol/L (45-84mmol/L), serum glucose 22.2mmol/L (NR: 3.3-8mmol/L), C-reactive protein 120mg/L (0-6mg/L), erythrocyte sedimentation rate 60mm/hr (NR: 0-15mm/hr), stool was negative for ova and parasite, creatinine clearance was 77 ml per minute (NR: 66-143 ml per minute, and proteinuria was 0.3g per day (NR: 0.0-0.15g per day). Microscopic urinalysis for red blood cell (RBC) morphology showed 192,000 glomerular RBCs per cubic cc and 480,000 non-glomerular RBCs. Antinuclear antibodies and anti-neutrophil cytoplasmic antibody test were negative. The result of ENT examination for nasal mucosa was normal. The upper gastrointestinal (GI) tract was normal, lower GI endoscopy showed multiple erythematous patches seen at the rectum and terminal ileum. The stomach biopsy was normal. Terminal ileum biopsy showed multiple superficial ulcerations replaced by neutrophilic exudates, no obvious vasculitis, culture was negative, and the acid fast bacilli (AFB) was negative (**Figures 1 & 2**).

Skin biopsy showed leukocytoclastic vasculitis (**Figure 3**). Echocardiography was normal. Computed tomography angiogram of the abdomen was normal (no evidence of vasculitis). During the work-up, which took around 2 weeks, the symptoms improved. The rashes disappeared, and his condition started to normalize without any treatment. Our impression was that the symptoms are secondary to aspirin allergy. There was some concern regarding the weight loss. He was discharged and given a follow-up appointment within 2 weeks. Two weeks later, he came back with abdominal pain and recurrence of rashes, but no lower GI bleeding. Further investigations indicated that he was in acute renal failure. Laboratory examination showed an increase in urea to 13 mmol/L, creatinine of 280 mmol/l, sodium of 133 mmol/L, and potassium of 4.8 mmol/L. During examination, we suggested the possibility of systemic vasculitis; thus, he was started on methylprednisolone pulse 1 g intravenously daily for 3 days followed by 60 mg daily. A kidney biopsy was carried out (**Figure 4**) and the resulted indicated diabetic changes and acute tubular necrosis. He had already received high dose steroids for 10 days and his condition had normalized. The administration of steroids was stopped, and he was given a follow-up appointment. He was seen in the clinic one month later where urea and creatinine levels were all normal. On the second follow-up (3 months later), he reported in good condition with normal urea and creatinine levels.

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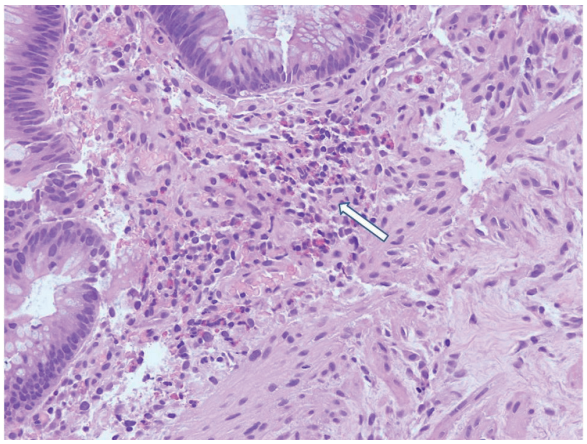

Figure 1 - Oesinophilic infiltration in the colon lamina propria.

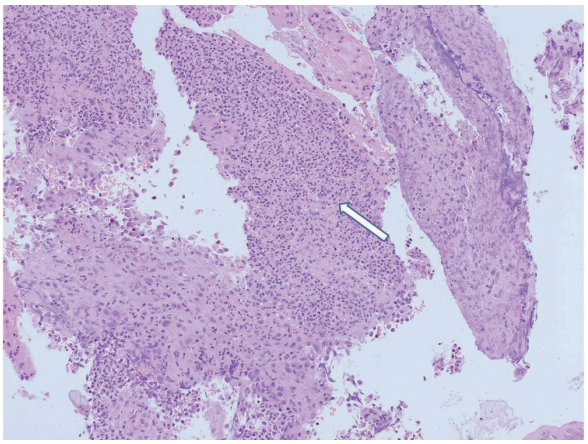

Figure 2 - Neutrophilic exudates in the terminal ileum.

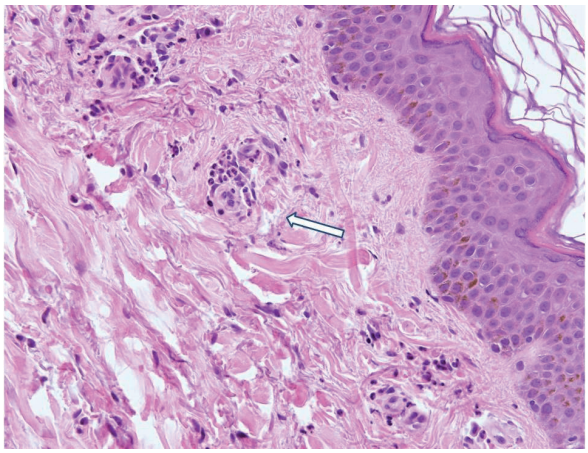

Figure 3 - Neutrophil surrounding a superficial dermal vessel (leukocytoclastic vasculitis).

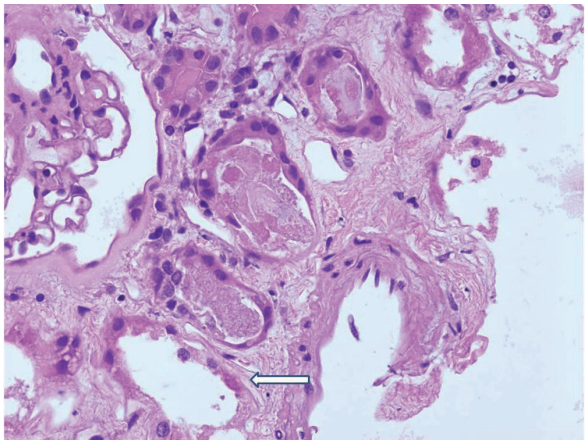

Figure 4 - Kidney biopsy shows acute tubular necrosis (ATN).

Discussion. A drug allergy refers to immunologically mediated hypersensitivity reactions, and non-allergic hypersensitive reactions refer to an adverse reaction that is not mediated by immunological mechanisms. The confirmation of diagnosis of this condition is generally obtained by oral provocation tests. For aspirin exacerbated respiratory disease, nasal challenge with lysine-aspirin has been shown. Other recently introduced tests include basophil activation test (BAT).[4] Our patient reported a history of food allergy (allergic to fish) acquired in the last few years, and this is consistent with his predisposition to a drug allergy.

There are limited data in the literature on aspirin causing leukocytoclastic vasculitis. The study reported by eHealthMe[5] was based on 93 reports from the Federal Drug Association (FDA) on patients who have leukocytoclastic vasculitis after exposure to aspirin. The time of occurrence is usually one month to one year after exposure, and our patient displayed symptoms 20 days after exposure. However, there are many records of cutaneous vasculitis with other NSAIDs ([COX-1]6 [COX-2]).[7,8] The allergic vasculitis reaction to VIOX (roficoxib) and Celebrex (celecoxib) was thought to be due to the sulfa component in celecoxib and roficoxib. Presentation of symptoms to those agents was in the form cutaneous vasculitis, and renal involvement in the form of proteinuria and hematuria. Garcia et al[9] reported that 15% of patients who presented with drug induced vasculitis had evidence of renal impairment. The renal involvement secondary to NSAIDs use is mediated via inhibition of prostaglandin synthesis from arachidonic acid by non-specific blocking of the enzyme cyclooxygenase leading to vascoconstruction and reversible mild renal impairment in volume contracted states. When unopposed, this may lead to acute tubular necrosis and acute renal failure.[10] Another case of severe leukocytoclastic vasculitis secondary to the use of naproxine was reported in a patient with digital gangrene.[7]

In conclusion, our patient presented a diagnostic dilemma, especially when he had a recurrence of symptoms after 2 weeks of recovery without any offending agent during this period. This phenomenon could not be explained; and created confusion with the possibility of systemic vasculitis.

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Ethical Consent

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.