Scholars Journal of Medical Case Reports **ISSN 2347-6559 (Online)**
Sch J Med Case Rep 2015; 3(4)326-328 **ISSN 2347-9507 (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjmcr.2015.v03i04.013

Approach to Unknown Body Rashes in an Elderly: was it caused by Celecoxib? A Case Report and Literature Review

Zhi Xiong Chong[1*], Zainal Darus [2]
[1]School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Malaysia
[2]Department of Medicine, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Malaysia

***Corresponding Author:**
Name: Zhi Xiong Chong
Email: zhixiong17c@yahoo.com

Abstract: Approach to an elderly who presented with rashes can be difficult when he or she was irritable or drowsy and non-cooperative. Joint pain is a common musculoskeletal problem among the elderly and mainly is due to degenerative joint disease such as osteoarthritis. Celecoxib is a type of selective COX-2 inhibitor which is primarily designed for pain relieve with minimal risk of gastrointestinal bleedings. It has been widely used as a pain killer in the management of osteoarthritis and rheumatoid arthritis. The most common side effect reported are headache (15%) followed by hypertension (12%). We present a case of unknown body rashes in a 71 years old Malay woman with underlying osteoarthritis who was just started to consume Celecoxib.
Keywords: Celecoxib, COX-2 inhibitor, Osteoarthritis, Rheumatoid arthritis, Rashes.

INTRODUCTION

Joint pain and osteoarthritis are the most common musculoskeletal problem among the elderly [1].

Celecoxib is a selective COX-2 inhibitor which reduces inflammation and act as an analgesic agent [2]. Its mechanism of action is mainly inhibiting the cyclooxygenase 2 (COX-II) pathways [2]. For many years, Celecoxib has been used in modern medicine in treating osteoarthritis and rheumatoid arthritis [2, 3]. The advantage of Celecoxib compared to the conventional non-steroidal anti-inflammatory drug (NSAIDs) is that Celecoxib has lesser gastrointestinal side effects [3, 4]. The most common reported side effects caused by Celecoxib is headache (15%) followed by hypertension (12%) [2, 3, 5]. Other side effects are rare and seldom or never being reported in any literature. Rashes are one of the most common adverse effects of all drugs in the world but Celecoxib-induced rashes are very rare, only account about 2.1% [4, 5].

Approach to unknown body rashes in an elderly can be a difficult clinical task when the elderly is non-cooperative, irritable or drowsy [1]. Elderly has weaker immune system and many differentials diagnoses need to be excluded when they present with unknown body rashes [1]. The differential diagnoses include infection, malignancy, systemic illness and many more [1]. Unknown rashes in an elderly with underlying joint problem who was just started on analgesic raise the clinical suspicious of possible drug-induced rashes [2]. However, such diagnosis can only be made after excluding all possible differential diagnoses with the aid of laboratory investigations [2, 3].

We report a 71 years old Malay woman with underlying osteoarthritis who presented with unknown body rashes after she consumed oral Celecoxib for three days. Thorough history taking, physical examination and laboratory investigations excluded malignancy, infection, connective tissue diseases and systemic illness. She was treated with steroid and antihistamines and the rashes started to resolve after three days. Relationship between Celecoxib and body rashes was not known and there is still lack of previously published literature which had discussed on this issue.

Written informed consent has been obtained from the patient and her family members to publish her case scenario as a published case report.

CASE REPORT

This is a 71 years old Malay woman who is a known case of bilateral knee osteoarthritis diagnosed 2 years ago. She was initially started on tablet Paracetamol 1 gram when needed (PRN) and scheduled for regular physiotherapy. As time passed, the pain became progressively worsened and she was prescribed with tablet Celecoxib 200mg twice a day (BD) to relieve the knee pain. One day after she consumed the drug, she noticed several rashes appeared over her face

but she did not take seriously on it and continue to consume the drug. Few days later, the rashes spread to the trunk and the periphery and increased in number. The rashes were associated with pain and itchiness. She went to seek for medical attention at a local private clinic and was prescribed with oral loratadine 10mg once daily (OD) but the rashes just resolved minimally despite she had stopped taking Celecoxib. She was later on brought to Hospital of Universiti Sains Malaysia (HUSM) by her son for further management. Besides painful and itchy generalised body rashes, she also complained of intermittent low grade fever, irritability, loss of appetite and lethargy.

On further questioning, she denied previous history of drug and food allergy or any insect bites. Besides, there was also no relevant family history of drug allergy. There was no personal history of systemic musculoskeletal disease such as rheumatoid arthritis and had no contact with people infected with scabies recently. She also denied of recent traveling to dengue or malaria endemic area and had no history of prolong fever prior to the appearance of these rashes. Apart from osteoarthritis, she is healthy and had no diabetes mellitus, hypertension, family history of malignancy and connective tissue disease.

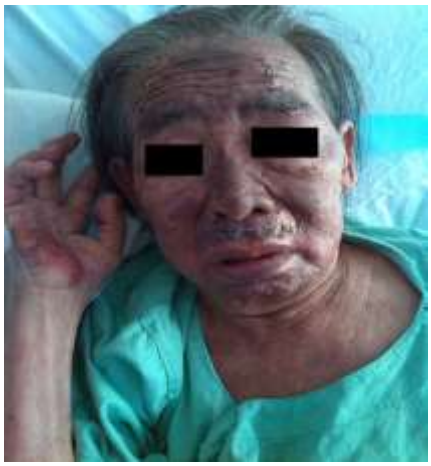

Fig. 1: Showed the patient had multiple irregular maculo-papules over the face and palm. Some rashes were healed with dry scars while some rashes were wet with reddish-brown discharge.

On physical examination, the patient was alert, conscious but irritable and in pain. Generalised skin rashes were noted predominantly over the face, periphery, palm and sole of foot. The rashes were tender maculo-papules which were non-blanching. Some rashes were healed with dried scars. Some rashes were wet with red-brown discharges. All rashes were of various irregular sizes. Upper and lower limbs were affected more compared to the trunk. The mucosa areas like the oral cavity and lips were spared and the rashes did not look to be bullous. Steven-Johnson syndrome was less likely as the mucosa was spared. Both liver and spleen were 2 finger breaths palpable below the costal margin, soft and non-tender. Examinations of other systems such as cardiovascular, neurology and respiratory systems were normal and unremarkable.

Complete blood count revealed that she had normocytic normochromic anemia (Hb:9.6g/dL) and reticulocytosis of 5%. There was no eosinophilia and change in white cells counts. Direct and indirect coombs tests were positive and highly suggestive of immune-mediated hemolytic anemia. Liver function test showed slight elevation of Alanine Transaminase (ALT) (53 iU/L) and Aspartate Transaminase (AST) (49 iU/L). Erythrocyte sedimentation rate (ESR) was raised (35mm/hour). Blood culture and sensitivity did not isolate any bacteria. Renal function test, coagulation profile, autoimmune autoantibodies and other relevant investigation results were all normal. Skin biopsy and immunology tests were not done as the patient refused it.

Since infection, malignancy, systemic illness, vasculitis and other differential diagnoses have been ruled out; she was treated as possible drug-induced rashes. In the ward, she was advised to stop taking Celecoxib and she was given intravenous hydrocortisone 100g three times a day (TDS) and oral Chlorpheniramine 4mg twice a day (BD) to reduce the inflammation. The intravenous steroid was then changed to oral prednisolone 30mg from day 2 of hospitalisation onwards till she was discharged. She was also given intravenous Pantoprazole 40mg BD as a prophylaxis against peptic ulcer. She was hospitalised for 5 days and her condition improved after the anti-inflammatory agents were given. The number and severity of rashes was reduced by the steroid. The rashes almost completely disappeared on day 5 of hospitalisations. Besides, Betamethasone Valerate cream (BVC) was also applied over the skin to reduce the rashes and was effective.

Before discharge, she was advised on never taking Celecoxib again and should inform any doctor who she will meet in future to not to prescribe her with Celecoxib again. In addition, she was referred to the orthopaedics unit for the management of joint pain. The orthopaedics colleagues were reminded to prescribe her with other type of analgesic.

DISCUSSION

Celecoxib-induced rashes are very rare [6]. Previous literature reported that rashes caused by Celecoxib are maculo-papules exanthema [6], which is consistent with the clinical finding in this case report. The rashes caused by Celecoxib are generally benign unless the patient is immunocompromised and secondary infection sets in [6].

The pathogenesis on how Celecoxib causes rashes was still unknown but based on the laboratory investigations of this case; it is believed that immune mediated mechanism has taken place evidenced by positive direct and indirect coombs tests and hemolysis [6, 7]. Our hypothesis is that the drug stimulates the body antibodies production which attacked the red blood cell and skin tissue, causing hemolysis and skin rashes. Hepatosplenomegaly of two finger breaths below the costal margin are also believed to be related to this postulated hypothesis.

Another interesting point is that Celecoxib-related rashes have been reported to cause eosinophilia which was absent in this case [2, 6]. Eosinophilia suggested presence of on-going allergy-mediated inflammation [2, 3, 6]. This remains a mystery in this case. Apart from Celecoxib-induced rashes, could the rashes be caused by other reason such as some viral-induced exanthem? Therefore, it is impossible to 100% confirm the diagnosis of this case as Celecoxib-induced rashes as there is no definitive diagnostic criteria and test [7, 8].

In this case, steroid as the universal anti-inflammatory agent [4] was employed to reduce the body inflammatory reaction as to reduce the rashes and was found to be effective. The role of steroid in adverse drug reaction has been proven to be effective in most other cases [7, 8]. However, it should be used with caution as steroid may immunosuppress the patient and causes other side effects such as peptic ulcer [4, 5].

Besides, previous literature and case study also highlighted the possibility of severe Celecoxib-induced toxiderma: a hypersensitivity syndrome with multi-organ failure and an acute generalized atypical exanthematous pustulosis [8]. Therefore, all patients with suspected Celecoxib-induced rashes should be monitored carefully to prevent the happening of unwanted fatal situation [8]. Even though it is rare, but it does not mean that it will not happen [8].

CONCLUSION

In conclusion, cutaneous lesion caused by Celecoxib is extremely rare. Apart from excluding other causes such as infection, malignancy and systemic illness, patient who presents with body rashes of unknown causes after newly taking Celecoxib should be suspected to develop Celecoxib-related rashes until proven otherwise. Diagnosis of Celecoxib-induced rashes is mainly a clinical diagnosis and diagnosis of exclusion till today as there is no definitive laboratory test being introduced yet.

ACKNOWLEDGMENT

We would like to express deepest gratitude to the patient, Madam FI and the family for their willingness to participate in this case studies.

REFERENCES

1. John WE, Mary SS; The generalized rashes: Part I. Differential diagnosis. Am Fam Physician, 2010; 81(6): 726-734.
2. Moore RA, Derry S, Makinson GT, McQuay HJ; Tolerability and adverse events in clinical trials of celecoxib in osteoarthritis and rheumatoid arthritis: systematic review and meta-analysis of information from company clinical trial reports. Arthritis Res Ther., 2005; 7(3): R644–665.
3. Chan FKL, Lanas A, Scheiman J, Berger MF, Nguyen H, Goldstein PJL, Celecoxib versus omeprazole and diclofenac in patients with osteoarthritis and rheumatoid arthritis (CONDOR): a randomised trial. Lancet, 2010; 376(9736): 173–179.
4. Silverstein FE, Faich G, Goldstein JL, Simon LS, Pincus T, Whelton A *et al.*; Gastrointestinal toxicity with celecoxib vs non-steroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: a randomized controlled trial. Celecoxib long-term arthritis safety study. JAMA, 2000; 284(10): 1247–1255.
5. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ *et al.*; Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. BMJ, 2004; 329: 15–19.
6. Marquès S, Milpied B, Foulc P, Barbarot S, Cassagnau E, Stalder JF; Severe cutaneous drug reactions to celecoxib (Celebrex). Ann Dermatol Venereol., 2003; 130(11): 1051–1055.
7. Sullivan JR, Shear NH; The drug hypersensitivity syndrome: what is the pathogenesis. Arch Dermatol., 2001; 137(3): 357–364.
8. Forman R, Koren G, Shear NH; Erythema mutliforme, Stevens-Johnson syndrome and toxic epidermal necrolysis in children: a review of 10 years' experience. Drug Saf., 2002; 25(13): 965–972.