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Case Report

Aspirin Induced Leukocytoclastic Vasculitis: Case Report

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ABSTRACT

Acetyl salicylic acid is indicated for treatment and prophylaxis of many cardiovascular diseases. In some cases, it may cause cutaneous adverse reactions. In this case leukocytoclastic vasculitis was developed due to aspirin. A 70-year-old male patient had complaints of Bilateral lower limb swelling associated with swelling over scrotum and penis since 3 days. He was suffering from several medical conditions and for that he was taking multiple medications. 1 month ago, he had a cerebrovascular accident (CVA) and was taken to a private clinic where he was prescribed with a combination of Aspirin (125mg) and Atorvastatin (20mg) at the bed time (HS) (no documentation was found). He had mild renal impairment. During hospital he developed hematuria. On the 3rd day of admission, he was diagnosed with Leukocytoclastic vasculitis and admitted to ICU. Leukocytoclastic Vasculitis was suspected due to a combination of aspirin and atorvastatin and this combination drug was stopped and the patient was monitored. This dechallenge resulted in recovery of Leukocytoclastic Vasculitis. Leukocytoclastic Vasculitis may be caused by Aspirin and showed some reversible recovery of symptoms.

Key words: Acute renal failure, Haematuria, Cutaneous manifestation, Iatrogenic dermatological reaction, Aspirin.

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INTRODUCTION

Aspirin is acetylsalicylic acid [ASA]. It is indicated as Anticoagulant, Antiplatelet, Analgesic, fibrinolytics and non-Steroidal anti-inflammatory Drug (NSAID). Like other NSAIDs, Aspirin inhibits prostaglandin synthesis and platelet aggregation, but its potency is higher as compared to other molecules because of acetyl group in its structure. It exerts its effect by 2 mechanisms: converting itself in salicylic acid and acetylating certain macromolecules (i.e., cyclooxygenase). Due to acetylation, cyclooxygenase become inactivated and prevent conversion of Arachnoid acid to thromboxane A2. Thromboxane A2 is potent vasoconstrictor and stimulate platelet aggregation. Aspirin is indicated to prevent ischemic episodes in coronary artery disease patients and to check the restenosis of stented coronaries. Also, it is found to have synergistic activity along with clopidogrel.[1] Apart from this it is also indicated for Pain, Fever, Acute Coronary Syndrome, Ischemic Stroke and Transient Ischemic Attack and off-label, it is used in some cancers.[2] Normal dose of aspirin is 325mg. Aspirin toxicity is seen when serum aspirin level reaches >50mg. In Children aspirin should be avoided due to risk of development of Reye's syndrome. Side effects of aspirin include heartburn, allergic reaction (itching, rash, hives, difficulty in breathing, swelling on face), confusion, dizziness, diarrhoea, hearing loss, abdominal pain, vomiting, etc.[3] Cutaneous adverse effects of aspirin include urticaria, erythema nodosum, purpura, hives, Lyell's syndrome, etc.[4] Here in this case a patient developed Leukocytoclastic vasculitis (LCV). LCV is a small vessel disease. clinically, it is cutaneous disease with or without internal organ involvement.[5]

Histopathologically, it is a small-vessel vasculitis. It has an incident rate of 30 million/ years globally.[6] LCV can occur at any age group and is thought to affect men and women in equal numbers but few studies suggest male predominance.[7]

CASE DESCRIPTION

A 70-year-old male patient came to the surgery department of tertiary care hospital with complaints of Bilateral (B/L) Lower Limb (LL)swelling over shin and calf muscle of legs since 3-4 days (Figure 1)

Associated with (a/w) swelling over scrotum and penis since 3 days. Also, he had complaints of pedal (a/w pitting) edema with redness (big patches) for 4-5 days. He was suffering from several medical conditions and for that he was taking multiple medications. He had a history of metabolic syndrome. He was taking Sodium Bicarbonate (500mg) Twice a day (BD), Furosemide (20mg) BD, Tamsulosin (0.4mg) At bedtime (HS), Bethanechol (25mg) thrice a day (TDS), Nifedipine (20mg) 2-1-2, Clonidine (0.1mg) 2-1-1 for hypertension with hypertensive nephropathy since 5-6 years. He had diabetes for 10 years with diabetic neuropathy. He was on Human Insulin (12U-12U-12U) S/C, Insulin Glargine (16U) @10pm and Pregabalin (75mg) and methyl cobalamin

Figure 1: Disease severity on the day of admission.

(100mg) HS. He also had mixed retinopathy. On his last admission to hospital, he had Hypertensive emergency 4 month ago. But 1 month ago, he had a cerebrovascular accident (CVA) and for that he was taking a combination of aspirin and Atorvastatin (125mg/20mg) HS (not exactly known to relatives/no documentation found/diagnosed from a private clinic). Additionally, he was taking Tab. Calcium (500mg) Once Daily (OD) and Syrup Lactulose 30cc HS. His laboratory findings show decreased Hb; increased urea, creatinine and C- Reactive Protein (CRP). And then Haematuria was noticed on 2nd day. On the 4th day, his total count was found highly increased but started decreasing by the next day (Table 1).

Ultrasonography (USG) of abdomen and pelvis showed a small right kidney with mild nephrolithiasis, hepatomegaly and cholelithiasis. Initially he was diagnosed with cellulitis and sent to a surgery ward but on the 3rd day of his admission he was diagnosed with LCV by a dermatologist and sent to Intensive Care Unit (ICU). LCV was suspected due to a combination drug of aspirin and atorvastatin. So, it was stopped on the 4th day, but he did not put on any treatment for LCV and just monitored. As such no major drug-drug interaction was found to cause LCV. During his hospital stay, his routine medication was continued, some antibiotics and supportive medication was given (Table 2).

Table 1: Laboratory investigation during hospital stay.

Parameter	16/11	17/11	18/11	19/11	20/11	21/11
Hb (%)	10.1	9.5	9.3	8.8	8.7	10.5
Tc (cells/mm)	7100	9000	10300	16000	14200	13000
Plt (mil/lit)	2.07	1.83	1.75	1.67	1.6	1.5
Urea (mg/dl)	160	175	193	182	177	190
Creatinine (mg/dl)	4.4	6.1	6.0	5.6	5.3	4.5

MEDICATION CHART

His condition was monitored after stopping a combination drug, on the 4th day LCV was recovered (Figure 2).

On the 7th day of admission, he took Discharge Against Medical Advice (DAMA). As on 4th day patient LCV was recovered, this might be suggestive of Aspirin induced LCV as aspirin was started a month prior and drug induced LCV take days to develop. But the rechallenge of aspirin was not done to confirm as patient took DAMA.

DISCUSSION

Leukocytoclastic vasculitis (LCV) is vascular damage, which is caused by nuclear debris from infiltrating neutrophils.[7] It is also known as hypersensitivity vasculitis and hypersensitivity angiitis.[8] It is a group of clinical syndromes with inflammatory involvement of venules, capillaries and arterioles. Clinically, it presents as a cutaneous disease with or without internal body organ involvement. LCV presents as a palpable purpuric rash associated with burning sensation or pain and is most commonly observed on the legs, but any surface may be involved. It affects internal as well as external organs and tissues. The tissues and organs most commonly involved are the skin, joints, mucous membranes, lungs, brain, heart, gastrointestinal tract, kidneys and muscle. The prognosis of LCV is typically good if internal organs aren't affected. Rarely LCV may present as completely asymptomatic lesions, nodular lesions or ulcerations.[9] Multiple etiologic factors are associated with LCV includes drugs, infections, foods, autoimmune diseases, collagen vascular diseases and malignancies have been suggested to

Table 2: Treatment given during hospital stay.

Generic Name	Dose	Frequency	ROA	16/11	17/11	18/11	19/11	20/11	21/11	22/11
Amoxicllin+Clavunic acid	625 mg	12 hrly	IV	+	-	-	-	-	-	-
Human insulin	12 u	1-1-1	IM	+	+	+	+	+	+	+
Insulin	16 u	@ 10 pm	IM	+	+	+	+	+	+	+
Aspirin+Atorvastatin	150/20	HS	PO	+	+	Stop	-	-	-	-
Nicardipine	20 mg	1-1-1	PO	+	+	+	+	+	+	+
Clonidine	0.1 mg	2-1-1	PO	+	+	+	+	+	+	+
Calcium	500 mg	1-0-0	PO	+	+	-	-	-	1-0-1	+
Sodium bicarbonate	500 mg	1-0-1	PO	+	+	-	-	-	-	-
Pregabalin+mt.cobalamin	75 /100	HS	PO	+	+	-	-	-	-	-
Tamsulosin	0.4 mg	HS	PO	-	+	-	-	-	+	+
Bethanecol	20 mg	1-1-1	PO	-	+	-	-	-	+	+
Lactulose	30 cc	HS	PO	-	+	-	-	-	-	-
Pantoprazole	40 mg	12 hrly	PO	-	-	+	+	+	+	+
Ondansetron	4 mg	8 hrly	PO	-	-	+	+	+	+	+
Normal saline with multivatimin	500 ml 1 amp	@ 20 – 40 ml/hr	IV	-	-	+	+	+	+	+
Pipercallin + tazobactum	2.25 g	8 hrly	IV	-	-	D1	D2	D3	D4	D5
Tab. Clindamycin	600 mg	8 hrly	IV	-	-	D1	D2	D3	D4	D5
Clindamycin ointment	-	BD	Topical	-	-	+	+	+	+	-
Linezolid	800mg	12 hrly	IV	-	-	-	D1	D2	D3	D4
Ethamsylate	600mg	1-1-1	PO	-	-	-		+	+	+
Furosemide	20 mg	1-0-1	PO	-	-	+	+	+	1-0-1	+

Figure 2: Recovering state of disease.

associate with LCV. The exact mechanism of action remains idiopathic, but it is believed that circulating immune complexes are associated with this condition. It could result from immunologic response to an identifiable antigen and fibrinoid necrosis with neutrophilic infiltrate in the vessel wall. Many of the neutrophils are fragmented. This form is found in vasculitis caused by deposits of immune complexes. Various etiological factors which can cause this condition include infections, drugs, collagen vascular disorder, autoimmune conditions, foods, and malignancies.[10] Drugs which aggravate or induce this condition includes antibiotics, antipsychotic agents, anti-tumor necrosis factor alpha agents, diuretics and other agents such as lithium and allopurinol.[11,12] There is limited literature available which shows aspirin causes LCV. Presentation of symptoms of LCV may be seen within 1 month to 1 year. A case reported by Fahdah A. A. *et al*. LCV was seen within 20 days of aspirin therapy, similar to this in present patient symptoms were seen within 20 days of aspirin dose.[13]

There are some reported cases in which other NSAIDS causes LCV are celecoxib, rofecoxib, naproxen, clopidogrel, NSAID.[1,7] Garcia *et al*. reported that 15% of patients who presented with drug induced vasculitis had evidence of renal impairment.[14] NSAID having some cutaneous as well as renal adverse effects. Cutaneous reaction could be present as vasculitis and renal impairment as proteinuria and hematuria. In this patient, renal impairment and hematuria was present but proteinuria was not found. The renal involvement is secondary to NSAIDs use is mediated via inhibition of prostaglandin synthesis from arachidonic acid by non-specific blocking of the enzyme cyclooxygenase resulting in vasoconstriction and reversible mild renal impairment in volume contracted states. When it is unopposed, this may lead to acute tubular necrosis and acute renal failure.[13]

As such there is no therapy established for LCV. But plasmapheresis and some agents having limited success in some cases. Drugs involve in the treatment of LCV includes, colchicine, dapsone, corticosteroids, cyclophosphamide, azathioprine, plasma exchange, intravenous immune globulin and NSAIDS.[14]

CONCLUSION

The present case of Aspirin induced Leukocytoclastic Vasculitis, drug was stopped during mild symptoms of LCV, but if in any case drug would not stop and it causes severe vasculitis, then patients should undergo amputation and other treatment strategies. So physician should be vigilant before prescribing aspirin.

Strength of the study

The present study explains the adverse effect of aspirin.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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