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AMIKACIN- INDUCED CUTANEOUS SMALL VESSEL VASCULITIS

[1]Dr. Justina Princess G., [2]*Dr. Aruna Bhushan and [3]Harsha M. Naikwad

[1]Post Graduate, Department of Pharmacology, BIMS, Belagavi.

[2]Associate Professor, Department of Pharmacology, BIMS, Belagavi.

[3]Pharmacovigilance Associate, Department of Pharmacology, BIMS, Belagavi.

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***Corresponding Author**
Dr. Aruna Bhushan
Associate Professor,
Department of
Pharmacology, BIMS,
Belagavi.

ABSTRACT

Amikacin is an aminoglycoside, semisynthetic derivative of kanamycin and has bactericidal action against many gram-negative bacteria. All aminoglycosides have shared toxicity but hypersensitivity and cutaneous reactions are unusual. Here, we report a case of 20 year old female presenting with amikacin induced cutaneous small vessel vasculitis.

KEYWORDS: Amikacin, Vasculitis, Aminoglycoside, Young adult.

INTRODUCTION

Aminoglycosides are the agents which kill the micro-organisms by inhibiting protein synthesis. The common adverse effects are ototoxicity, nephrotoxicity, at higher doses neuromuscular blockade and can also cause hypersensitivity reactions. But number of cases reported with aminoglycoside induced hypersensitivity reaction is less than 2%, whereas with beta-lactam 15%.[1]

Cutaneous small vessel vasculitis is a rare condition which can be idiopathic or secondary. Secondary due to underlying infections such as upper respiratory infections caused by group A beta-hemolytic streptococcus, other infectious triggers include parvovirus etc, chronic infection such as hepatitis B and hepatitis C. Connective tissue disorders namely rheumatoid arthritis, systemic lupus erythematous etc and medications. Drug induced vasculitis is a secondary type which is defined as inflammation of blood vessels due to an adverse effect of a drug. 10-20 % of vasculitis is drug induced vasculitis. NSAIDS, antibiotics such as beta-lactam group, quinolones and sulfonamides commonly cause vasculitits. Others are tumor

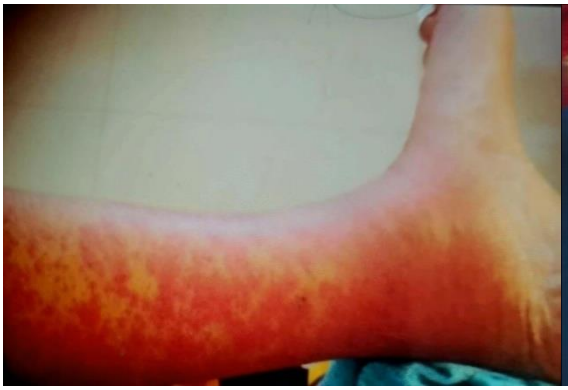
necrosis factor inhibitors, rituximab, tocilizumab, statins.[2] Here, is a rare case of amikacin induced cutaneous small vessel vasculitis in a 20 year old lady.

CASE REPORT

A 20 year old lady presented with history of cough, fever and chills of 2 weeks duration and she received the treatment from a private local practitioner with Inj. Amikacin 500mg and inj Ceftriaxone 1g intravenous and IV fluids. On 3rd of drug administration she developed tiny erythematous papules over the left foot which progressed to involve both feet within 2 hours. Later lesions progressed to multiple erythematous palpable papules and plaques, nonblanchable ranging from 0.5 cm to 2 cm involving the anterior and posterior aspect of both lower limbs and feet with xerosis "Fig. 1", dorsum of hands, web spaces of upper limbs, dependant areas sacral and gluteal region and the lesions were associated with itching, burning sensation. She also had complaints of multiple joint pain initially started in both knees and progressed to ankle and wrist joints due to which she had difficulty in walking.

Since her skin lesions kept progressing she was referred to the district hospital. A detailed history was taken. She had no previous history of drug allergy or food allergy. There was a past history of cough and loss of appetite since 4 months, sputum was AFB positive and patient was on ATT. Both ATT and antibiotics were suspected and were stopped immediately. All routine laboratory investigation were done, complete hemogram showed Hb 9.6 %, peripheral smear showed neutrophilia and histopathological report of punch biopsy of skin confirmed neutrophilic small vessel vasculitis. She was treated with steroids Inj. Dexamethasone 6mg for 3 days, then switched to topical clobetasol ointment and supportive treatment like Tab. Cetrizine 10mg once daily, Tab. Paracetamol 500mg twice daily, Tab. Iron, calamine lotion for external application. Later the reactions regressed slowly leaving behind post-inflammatory hyperpigmentation "Fig. 2".

Inj Ceftriaxone for two days and ATT drugs were re-challenged and patient was observed for new skin lesions but there were none, indicating amikacin to be the suspected drug. So, the patient was advised to continue with ATT and was discharged without any sequel.



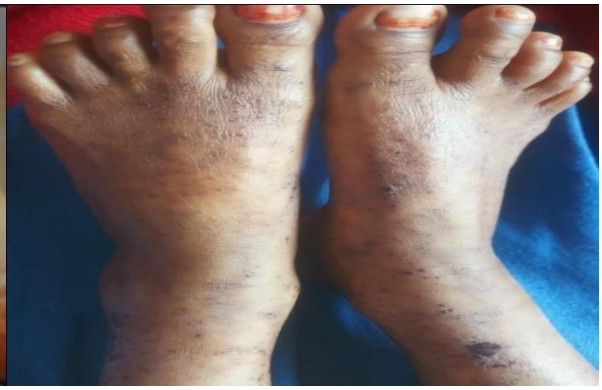


Fig. 1: showing lower limb with xerosis. Fig. 2: Post-inflammatory hyperpigmentation.

DISCUSSION

Small vessel vasculitis is a Type III hypersensitivity reaction known as immune complex mediated reaction. It manifests when IgG or IgM antibodies form immunological complexes with medications. Activation of neutrophils and macrophages by complement activity, leads to tissue inflammation and damage. The antigen-antibody complex in the kidneys, joints, blood vessels manifest as nephritis, arthritis and vasculitis. This reaction takes 7-10 days or weeks to develop.

Small vessel vasculitis, frequently damages the cutaneous tissue. It is known as leukocytoclastic vasculitis, neutrophils acts as the inflammatory mediator, infiltrates the cells is seen in antibiotic-induced vasculitis. Purpura and or petechiae may be associated with urticaria. Beta lactams antibiotics are mostly linked to this kind of reactions. If the offending antibiotic is discontinued reaction improves, but if serious then corticosteroid are administered.[3]

Aminoglycoside is categorized into two major classes: streptidine (streptomycin) and deoxystrepatamine (gentamicin, tobramycin, amikacin, kanamycin, neomycin, and plazomicin). They have significant postantibiotic effect due to concentration dependent killing and have narrow safety margin. Amikacin is a kanamycin derivative has a special feature as they are resistant to aminoglycoside inactivating enzyme and thus used in gentamicin and tobramycin resistant cases. They are used in various nosocomial infections. They cause adverse effects but skin reactions are rare.[1]

For drug-induced vasculitis there must be temporal association between the onset of drug intake and the reversibility with discontinuation of the drug. A case of amikacin induced drug reaction with eosinophilia and systemic symptoms syndrome (DRESS) [4] and streptomycin

induced skin manifestation when combined with isoniazid administration and few cases of ATT induced vasculitis are reported.[2]

In our case according to Naranjo's adverse drug reaction probability is the criteria with score 6[5] as there was no previous conclusive report, the adverse event appeared after 3 days of amikacin administration, the adverse reaction improved on discontinuation of the drug, Rechallenge with amikacin was not done and there were no alternative cause as ATT was rechallenged but no reaction was seen, the adverse event was confirmed by histopathological evidence. Therefore the reaction is probable caused by amikacin. According to WHO-UMC causality assessment system also is probable. Based on Hartwig's severity assessment scale reaction level is 4 with moderate severity.

So, in our case amikacin might be the most probable drug which induced vasculitis. And to best of our knowledge this is the first case of amikacin induced vasculitis. Recognition of such reactions is important as it leads to fatal consequences; discontinuation of the offending drug is a major part of the management.

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