ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Leukocytoclastic Vasculitis Induced by Pyrazinamide in Children.

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ABSTRACT

We report a case of leukocytoclastic vasculitis induced by pyrazinamide in the course of anti - tuberculosis therapy which is a rare complication in children. A 14 year old girl was been diagnosed as pulmonary tuberculosis and started on anti-tuberculosis therapy with isoniazid, rifampicin, ethambutol and pyrazinamide. She developed purpuric lesions in the lower extremities after 4 days of anti-tuberculosis medications. Anti-tuberculosis drugs were stopped and the histopathology of purpuric lesions showed leukocytoclastic vasculitis. The skin lesions started to improve after the cessation of anti-tuberculosis drugs and treatment with low dose corticosteroids and anti-histamines. Anti-tuberculosis drugs were rechallanged one at a time over a week duration. Purpura recurred in the lower extremities after taking pyrazinamide. This case of leukocytoclastic vasculitis induced by pyrazinamide therapy is reported for its rarity in children.

Keywords: luekocytoclastic, pyrazinamide, children.

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ISSN: 0975-8585

INTRODUCTION

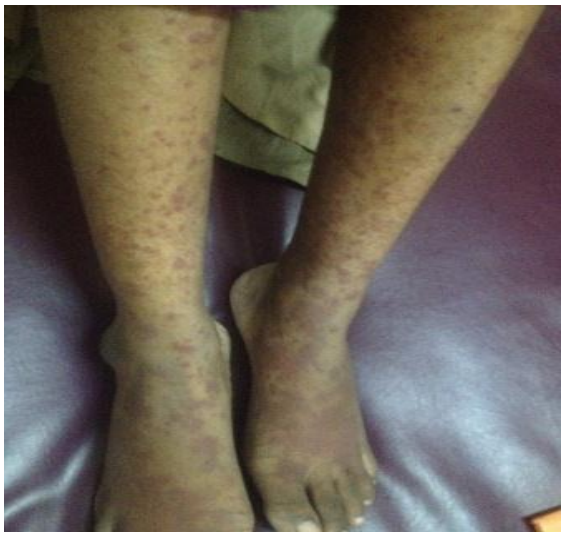
Leukocytoclastic vasculitis is also called as hypersensitivity vasculitis. It is histological process characterized by necrotizing inflammation around small dermal blood vessels composed of neutrophils and debris [1,2]. Hypersenstivity reactions to anti-tuberculosis drugs are reported rarely in children. The classical clinical lesions of leukocytoclastic vasculitis are purpuric lesions [3]. There are reports related to anti-tuberculosis drugs induced vasculitis with rifampicin [4].

We report a case of leukocytoclastic vasculitis induced by anti-tuberculosis drug with pyrazinamide. A very few cases have been reported in adults but to our knowledge it is rare in children.

Case report

A 14 year old girl was admitted in our hospital with consolidation of right lung and was treated with intravenous antibiotics. She also had history of contact with open case of tuberculosis. Initial evaluation for tuberculosis was done. Total count – 12400 cumm, neutrophils-80%, lymphocytes-20%, erythrocyte sedimentation rate was increased, platelets, liver function test, renal functional tests were within normal limits, Anti-HIV was negative, sputum smear was positive, mantoux was positive with induration, geneXpert MTB – RIF showed mycobacterium tuberculosis detected, rifampicin resistance not detected. Ophthalmologist opinion was sought fundus was normal. She was started on anti-tuberculosis drugs as per regimen with 4 drugs rifampicin, isoniazid, pyrazinamide and ethambutol. After 3 days of starting anti-tuberculosis drugs she started to develop purpuric skin lesions in the lower extremities (Picture:1). Anti-tuberculosis drugs was stopped and blood investigation was done. Complete blood count, liver function test , renal function test, urine complete analysis were within normal limits, C-reactive protein was negative. Skin biopsy was done, histopathology revealed upper dermal vessels with moderate perivascular infiltrates composed of degenerated polymorphic and eosinophilic infiltrate ,and nuclear debris with fibrinoid necrosis suggestive of leukocytoclastic vasculitis (picture:2). She was started on low doses of corticosteroids and anti-histamines. Once the purpuric lesions disappeared anti-tuberculosis medications was rechallenged over 1 week duration for each drug. All anti- tuberculosis drugs were started with low dose for first 3 days and then with the dose appropriate for weight for 4 days as showed in the table :1. Purpuric lesions developed in the lower extremities when pyrazinamide was started. Pyrazinamide was stopped. Low dose corticosteroids and anti-histamines given. Once the purpuric lesions disappeared anti- tuberculosis drugs isoniazid, rifampicin, ethambutol were started and in addition second line anti-tuberculosis drugs ofloxacin and streptomycin were also added. She has been observed for past one month and there is no recurrence of purpura.

Picture 1: Purpuric Skin Lesions in the Lower Extremities



ISSN: 0975-8585

Picture 2: Upper dermal vessels with moderate perivascular infiltrates composed of degenerated polymorphic and eosinophilic infiltrate, and nuclear debris with fibrinoid necrosis suggestive of leukocytoclastic vasculitis.

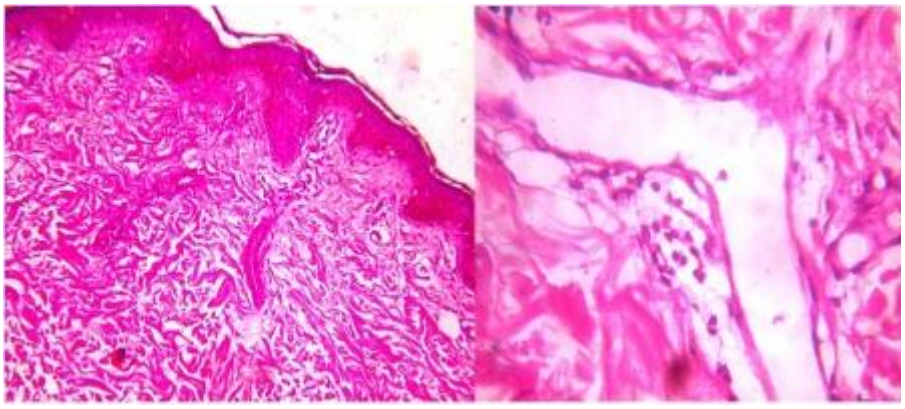


Table 1: Rechallenge of anti - tuberculosis medications

Drugs	First 3days Dose	Symptoms	Next 4 days Dose	Symptoms
Isoniazid	150 mg	none	300 mg	none
Rifampicin	225 mg	none	450 mg	none
Pyrazinamide	375 mg	purpura	-	-
Ethambutol	400 mg	None	800 mg	none
Ofloxacin	400 mg	None	800 mg	none
Streptomycin	0.75gm	None	0.75 gm	none

DISCUSSION

Allergic drug induced vasculitis has been reported with drugs like sulfonamides, penicillin, NSAIDs, etc [5]. Cutaneous adverse effects of anti-tuberculosis therapy are well recognized and has been reported upto 5% of patients treated [4]. Leukocytoclastic vasculitis associated with rifampicin therapy has only a few reports [6]. However with pyrazinamide therapy there are very few reports in adults. It is a rare complication in children upto our knowledge. The combination of vasculitis and pulmonary tuberculosis is rare and was first described in 1967 [7]. There are two types of pulmonary tuberculosis – related vasculitis. They are leukocytoclastic vasculitis as a manifestation of pulmonary tuberculosis and anti-tuberculosis drugs associated vasculitis [8]. In our case it is anti-tuberculosis drug associated vasculitis.

In case of leukocytoclastic vasculitis, mycobacterium tuberculosis is not found in the vessel wall, which differentiates it from cutaneous tuberculosis in which micro organisms are seen in biopsy. Pulmonary tuberculosis related vasculitis will improve with the introduction of the anti-tuberculosis medications [9,10]. In anti – tuberculosis drug induced vasculitis the skin lesion typically improve upon withdrawal of medication. Studies have described rifampicin associated vasculitis [4]. But there has been no report regarding association between pyrazinamide and vasculitis. The mechanism behind pyrazinamide induced vasculitis remains unclear.

CONCLUSION

We described a case of pyrazinamide induced leukocytoclastic vasculitis which is confirmed by histopathology and drug rechallenge. Although it is rare in children it should also be considered as a cause of drug induced vasculitis.

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