CUTANEOUS VASCULITIS DURING ANTI-TUBERCULOSIS TREATMENT IN TUBERCULOMA BRAIN – A REPORT ON 2 CASES

Rajeshwari Ramachandran, R. Balambal, V.D. Ramanathan and R Prabhakar

(Original received 20.7.1990, Accepted 23.10.1990)

Summary. **Two patients with tuberculoma of the brain developed purpura while on anti-tuberculosis and anti-convulsant therapy. Biopsy of the skin lesion revealed evidence of vasculitis. The relevance of the rare complication is discussed.**

Introduction

One of the rare but serious adverse reactions to rifampicin therapy is thrombocytopenia causing purpura. Nessi et al[1] in their review of allergic reactions during rifampicin treatment described purpura either with normal platelet count or with thrombocytopenia. Once rifampicin is withheld, platelet count returns to normal.[2,3,4,5] This rifampicin induced thrombocytopenia may be symptomless[1,6] or lead to spontaneous bruising.[4] There is another group of purpura namely, drug induced "allergic purpura" characterised by aseptic vasculitis of vessels in corium with normal or low platelet count.[7] However, no case of cutaneous vasculitis with purpura during rifampicin therapy has been reported so far. We report two cases of purpura with cutaneous vasculitis proved by skin biopsy in two children who were on rifampicin therapy for brain tuberculoma.

Case 1 : A ten year old girl, weighing 20 kg came with left focal convulsions and was diagnosed as a case of right parietal brain tuberculoma based on CT Scan appearance. Her initial platelet count was 2,80,000/cumm. She was started on treatment with rifampicin 200 mg, isoniazid 200 mg and pyrazinamide 500 mg on a thrice weekly schedule, along with prednisolone 5 mg thrice daily and eptoin. During the sixth week of therapy, she developed generalised joint pains associated with knee, ankle, wrist, elbow swelling and vomiting in association with generalised abdominal pain. Within 24 hours of onset of joint pains, purpuric spots developed in the upper and lower extremities. Echymosis was observed in the lower extremities over extensor aspect. A haemogram showed total WBC count 13,000 cells/cumm, differential WBC count P 78%, L 19%, E 3%; PCV 44%, Hb. 13.4 gms, RBC count 3.4 million and platelets 2,50,000/cumm. Peripheral blood smear was normocytic and normochromic and showed no immature cells. Bleeding time was 1 min 48 set and clotting time was 5 min 5 sec. ESR was 21 mm at 1 hour. Urine showed no albumin or RBCs. During the following two days, she developed hematochezia, hematuria and fresh purpuric spots in both the extremities in the next five days. Sigmoidoscopy done in view of hematochezia showed small purpuric spots 7 cms from the anal orifice. Rosewaaler test, ASO titre and LE cells, ANF were negative. Platelet count after live days was 92,000/cumm. Biopsy of the purpuric lesion showed vasculitis with fibrinoid deposits in some areas of dermis and in vessel wall. Renal functions were normal. A clinical diagnosis of allergic purpura was made and all anti-tuberculosis drugs were withheld. She was put on Prednisolone 30 mg along with antacids. Within a week, she improved well. The platelet count came up to 1,80,000/cumm. Rifampicin was terminated and she was given Ethambutol and Isoniazid daily during which period she has remained free from any adverse effect.

Case 2 : A six year old girl, weighing 25.5 kg came with left focal convulsions and a CT scan suggested right parietal brain tuberculoma. Pre-treatment platelet count was 2,70,000/cumm. She was started on Rifampicin 200 mg, Isoniazid 200 mg, and Pyrazinamide 500 mg daily along with Prednisolone 5 mg thrice daily and eptoin.

From Tuberculosis Research Centre, Spur Tank Road, Chetput, Madras 600 031.
Correpondence: Dr. R. Prabhakar, Director, Tuberculosis Research Centre, Spur Tank Road, Chetput, Madras 600 031.

Fig. 1. The presence of lymphocytes in the dermis; a vessel wall infiltrated with mononuclear cells (arrow) is also seen (Haematoxylin and eosin, 20 x 5).

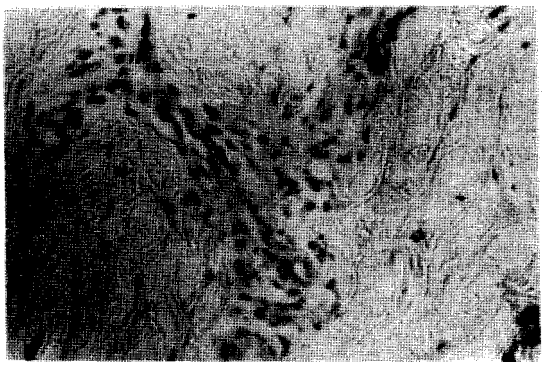

Fig. 2. Higher power view of the dermal blood vessel with mononuclear cell infiltration of its walls.

During the second week of therapy, she developed purpuric rashes over the chest, trunk and limbs. Her face appeared flushed and puffy. During the next 48 hours, generalised rash was observed. The investigations showed Hb. 10.2 gm, WBC 9,900 cells/cumm, DC :-N 37%, L 57%, E 6%, platelet count 1,10,000/cumm, bleeding time 1 mn 35 sec, and clotting time 9 min 15 sec. Biopsy of the rash revealed normal epidermis. Dermis showed dilated blood vessels with surrounding lymphocytic infiltration. There were features of cutaneous vasculitis (Fig. 1). All drugs were withheld. A week later, the platelet count was 5,10,000/cumm. Three weeks later she was started on Ethambutol and Isoniazid and she completed the 12 months' treatment period without any untoward effects.

Discussion

Allergic drug induced vasculitis has been reported with drugs like sulfonamides, penicillin, non-steroidal anti-inflammatory drugs, diphenyl-hydantoin, etc.[8] This presents clinically as palpable purpura. Rifampicin, however, is known to cause purpura due to thrombocytopenia.

In the two cases reported above, case 1 had received Rifampicin, Isoniazid and Pyrazinamide thrice weekly alongwith Phenytoin and steroids. During the 6th week, the patient presented with purpura when the platelet count was normal. When the platelets count became low, the patient developed systemic involvement in the form of hematuria and rectal bleeding.

In case 2, the patient was on daily treatment with Rifampicin, Isoniazid and Pyrazinamide along with Phenytoin and steroids. During the 2nd week of therapy, she developed purpura. Though thrombocytopenic purpura is described with intermittent Rifampicin regimens,. this patient presented with purpura on daily Rifampicin.[5]

Since the possibility of eptoin induced purpura cannot be ruled out, eptoin was withheld in these two cases and anti-convulsant was changed. Whether Rifampicin and eptoin drug interaction can precipitate such a reaction is also to be considered. It- is surprising that these two cases were also on steroids when they developed purpura and one of the two cases needed higher doses of steroids to control purpura. This may be due to rapid metabolism of corticosteroids resulting in lower serum levels of steroids, an interaction of rifampicin on the basis of microsomal enzyme induction in the liver.[9]

In both the cases, skin biopsy showed lymphocytic infiltration of vessels in dermis. In our Centre, Rifampicin is used in combination with various other anti-tuberculosis drugs for pulmonary and extra-pulmonary tuberculosis, like tuberculous lymphadenitis, abdominal tuberculosis, spinal tuberculosis, etc. This is the first time this complication of purpura with cutaneous vasculitis has occurred in the Centre.

In conclusion, one should be wary of this dreaded complication in a patient who receives Rifampicin daily or intermittently along with eptoin.

References

1. Nessi et al. Allergic reactions to Rifampicin

treatment-a review of published cases. Scan J Resp Dis. Supplement, 1973 84 : 15.

2. Girling, D.J., Hitze, K.L. Bulletin WHO No. 1, 1979, Vol. 57 : 45.
3. Eule, H. et al. Intermittent chemotherapy of pulmonary tuberculosis using Rifampicin and Isoniazid for primary treatment. The influence of various factors on the frequency of side-effects, Tubercle, 1974, 55, Ipid 1974, 55 : 193.
4. Fergusson OC. Rifampicin and thrombocytopenia, British Medical Journal, 1971, 3 : 638.
5. Rajendra Prasad and Mukerji, P.K. Rifampicin induced thrombocytopenia; Indian Journal of Tuberculosis. 1989, 36 : 44.
6. Poole G. et al. Potential sideeffects of high dose twice-weekly Rifampicin, British Medical Journal 1971,3 : 343.
7. Bruce U. Wintroube, Robert S. Stem and Kenneth A Arnot. Dermatology in Internal Medicine. 3rd Edition. 1987, Vol. 1, 1360.
8. Arian J. Gottlies, Williams J. Williams Hematology 3rd edition. 1983, 1373.
9. Dukes, MNG, Mayler's side effects of drugs, 1980, 9th edition, 530.