RIFAMPICIN INDUCED PLATELET DYSFUNCTION

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Drug induced purpura is known to be caused by different mechanisms. We came across a patient who presented with purpura in the absence of either thrombocytopenia or haemolytic anaemia, hence being reported. Paucity of literature on Rifampicin affecting platelet function prompted us to report this case.

Case Report

A 30 year old male soldier was admitted to this chest hospital as a case of pulmonary tuberculosis on 18th May 1999. After initial evaluation he was clinically, radiologically and bacteriologically proved to be suffering from pulmonary tuberculosis and on 29th May 1999 he was started on conventional antitubercular treatment (ATT) regime with Ethambutol, Isoniazid, Rifampicin and Pyrazinamide (EHRZ). He was responding well to treatment up to three weeks, when he developed purpuric rashes over both lower legs in symmetrical distribution (Fig-1).

Complete blood count (CBC) revealed haemoglobin of 128 gm/l, total leucocyte count of $14.8 \times 10^9/l$, with predominant neutrophils, platelet count $258 \times 10^9/l$, bleeding time 1 min 53 sec, clotting time 5 min 5 sec. Platelet aggregometry with different agonists like ADP, epinephrine, collagen, ristocetin showed reduced aggregation with ADP and epinephrine. The Platelet Rich Plasma (PRP) of the patient was further subjected to Flow Cytometric assay on Coulter EPICS-XL for Platelet Glycoprotein Ib/IX and GP IIb/IIIa and Granule Membrane Protein 140 (GMP-

140)P-Selectin antigens utilizing the monoclonal antibodies procured from Pharmingen/Becton Dickinson USA.

The study revealed normal expression of GP IIb/IIIa and P selectin but significant reduction of GP Ib/IX, when compared to normal controls thus suggesting a platelet functional disorder affecting the platelet glycoprotein Ib/IX. Patient plasma incubated with each of the ATT drugs separately in vitro showed similar response to aggregation with the drug Rifampicin. The offending drug Rifampicin was withdrawn. The purpuric rash disappeared after three days and repeat investigation revealed return of platelet functions to normal. The aggregation showed normal pattern and the flow cytometric assay for platelet glycoprotein Ib/IX showed 64.3% expression, when compared to 7.4% expression at presentation of symptoms thus confirming the diagnosis of Rifampicin induced reversible platelet dysfunction, which resulted in purpura in this patient.

TABLE 1

Receptor analysis of platelets by flow cytometry-coulter EPICS-XL

Time of analysis	Expression of platelet GP Ib/IX	Expression of platelet GP IIb/IIIa	Expression of P-Selectin/ GMP-140
During the Episode	7.4%	16.8%	10.5%
After the Episode	64.3%	25.5%	15.4%

Fig. 1 : Symmetrical distribution of purpura while on Rifampicin

Fig. 2 : Flow cytometric analysis of platelet glycoprotein Ib/IX on PRP with and without Rifampicin analysed on Coulter EPICS-XL (UK) using Pharmingen (US) monoclonal antibodies

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Discussion

Non thrombocytopenic purpura has been reported [1] due to administration of variety of drugs like aspirin, alcohol, allopurinol, atropine, belladonna, carbamazepine, chloral hydrate, chlordiazepoxide, cimetidine, desipramine disopyramide, doxepin, gold salts, indomethacin, isoniazid, meclofenamate sodium, mefenamic acid, morphine, naproxen, nifedipine, nitrofurantoin, penicillamine, penicillin, phenacetin, phenytoin, piroxicam, quinine, quinidine, sulfonamides, thiouracils, tolmentin. Some of these reactions are caused due to allergic hypersensitivity mechanism. Drugs are known to induce platelet abnormalities by different mechanisms [2]. Most of the drugs are known to cause quantitative defects of platelet and thereby induce thrombocytopenia. Rifampicin [3] is known to cause thrombocytopenia and/or auto immune haemolytic anaemia [4] in rare cases. Rifampicin has not yet been documented to produce qualitative platelet disorders in order to produce platelet function defects. Here in our case we found significant deregulation of the expression of platelet glycoprotein Ib/IX during the episode of illness/symptoms, thereby inducing platelet dysfunction leading to purpura. The present report demonstrates that rifampicin can affect

selectively the glycoprotein receptor Ib/IX where as IIb/III is spared. Further more, the marker of activation of platelets i.e. P selectin (GMP-140) is also not elevated indicating that there is no activation of the platelets. The withdrawal of the drug for a period of 3 days reverted the situation to normal.

The paper therefore reveals that rifampicin besides producing thrombocytopenia can also produce platelet dysfunction by inhibiting the GP Ib/IX receptor of the platelets. This is important because rifampicin is an anti tubercular drug extensively used by the physicians world over.

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