**INTRODUCTION**

A thrombocyte count of < 1,50,000/mm$^3$ is defined as thrombocytopenia (TCP). However, 2.5 % of the normal population may have thrombocyte level lower than this value. The causes of TCP include viral infection, immune disorders, collagen vascular diseases, lymphoproliferative disorders and drugs. Drug induced TCP can be caused by quinidine, sulphonamide, chemotherapeutic agents, penicillin, barbiturates, heparin, digoxin and estrogen. Thrombocytopenia is a serious side effect of rifampicin although it is rare. There are very few reported cases of TCP due to Isoniazide also. Rifampicin induced thrombocytopenia was first reported in 1970. It is usually reversible if detected early and treated appropriately. Although Isoniazide induced TCP has been define previously, there are only four previous cases in the literature.

**CASE REPORT**

A 30 years old male, who was known case of sputum positive pulmonary tuberculosis was presented with complaints of gum bleeding and purpuric rash over right forearm one month after starting antituberculosis treatment under RNTCP. He does not have present or past history of any medical illness and he was not taking any other medication except ATT. On physical examination orodental hygiene was poor. There was purpuric rash over right forearm, left shoulder and left leg. On chest examination crepts were ausculted over both infraclavicular regions, other system examination does not reveal any positive finding. Chest X-ray PA view shows inhomogeneous opacities in both upper zones suggestive of active disease. Haemogram only demonstrate low platelets counts (62000 cells/cumm). Blood sugar was normal, HIV test was nonreactive, M P QBC was negative and his bleeding time, clotting time and INR were within normal limit. Rifampicin and Isoniazide assumed to be the causative factor of thrombocytopenia so both of these drugs were withheld. Next day again hemogram was done and this time platelets count became normal (2, 50000 cells/cumm) and rashes subsided. Among the two antituberculosis drugs rifampicin is the frequent cause of TCP, although it is rare, so we started rifampicin first. After starting of rifampicin gum bleeding started and platelets counts drops to 30000 cells/cumm. So again rifampicin was withheld and other antituberculosis drugs continued, platelets counts again became normal. Patient did not experience gum bleeding, purpuric rash and low platelets count after challenge with Isoniazide. Diagnosis of rifampicin induced TCP was suspected and rifampicin was replaced with the quinolone.

**Figure 1:** Purpuric rashes on the volar aspect of right forearm just below the elbow joint.

**Keywords:** Rifampicin, Tuberculosis, Thrombocytopenia (TCP), RNTCP

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Rifampicin induced thrombocytopenia under RNTCP

DISCUSSION

Rifampicin is a well tolerated and highly effective bactericidal antituberculosis drug but does not devoid of side effects. Common side effects are cutaneous symptom, an abdominal symptom, a flu syndrome, a respiratory symptom, purpura and elevated transaminase serum level. Thrombocytopenia is the well known, potentially fatal side effect of rifampicin although it is rare and occurs in both daily and intermittent therapy but more commonly with intermittent therapy. Pool et al (8) reported three cases of TPC with twice weekly therapy with rifampicin and Ferguson and the Hong Kong trial reported TCP even with daily rifampicin. It has been postulated that with daily administration of rifampicin, there is neutralization of any antibody formed and the immune complex are continuously removed without causing any allergic reaction. Any gap in therapy allows a sufficient quantity of antibody to be built up during the antigen free interval so that when rifampicin is re-administered an intense reaction takes place. The mechanism of TCP with rifampicin hypothesized is that, in the presence of the drug the immune complexes non specially adsorb to the platelet membrane causing platelets damage and rapid removal from the circulation. The binding epitope of the IgG antibody was found in the glycoprotein Ib/IX complex which is the target in rifampicin induced immune thrombocytopenia. Conformation of rifampicin induced TCP requires demonstration of rifampicin dependent antiplatelet antibodies. Unfortunately this test is not available in most laboratories. George et al collected case report of drug induced TCP and defined the standard criteria with whom to explain the association between the drugs and TCP. They defined four criteria: 1) The suspected drug preceded TCP and recovery was complete and sustained after the drug withdrawal. 2) The suspected drug was the only drug used prior to the onset, or other drugs were continued or reintroduced after discontinuation of the suspected drug with a sustained normal thrombocyte count. 3) Other etiologies of TCP were excluded. 4) re-exposure to the suspected drug resulted in recurrent TCP. If the suspected drug meets all criteria, then the level of evidence is definite. If it meet the first three, it is probable; if it meets only the first criterion, it is possible; and if the first criterion is not met, then it is unlikely that it is the responsible agent. Our patient meet the all four criterion so diagnosis of rifampicin induced TCP was definite. We are unable to find rifampicin induced antiplatelet antibodies because of lack of facility available. Attention should be paid if rifampicin induced thrombocytopenia suspected. Apart from bleeding in to superficial site like skin and mucus membrane, thrombocytopenia may also cause intracranial haemorrhage. U. Zuzarte Cheryllan et al reported a case of rifampicin induced thrombocytopenia who developed left sided hemiplegia probably because of intracranial haemorrhage and went into comatose stat and finally succumbed. Although most patient of rifampicin induced TCP recover within seven to ten days and do not requires therapy. Occasionally patients with platelets counts below 10,000 to 20,000 cells/ cumm have severe haemorrhage and may require temporary support with glucocorticosteroid, plasmapheresis or platelets transfusion. We did not prescribe any temporary support to our patient because platelets counts did not come down to such critical level and patient recover completely after stopping the offending drug alone.

CONCLUSION

If thrombocytopenia develops in a patient who are taking ATT including rifampicin either daily or intermittent regimen in absence of other known cause of thrombocytopenia, rifampicin should be stop immediately and never include in the treatment regimen even in small dose. Clinician must be aware of this rare complication which is life threatening but if detected early is completely reversible.

REFERENCES


