Rifampicin-induced thrombocytopenia

J. W. HADFIELD
M.B., M.R.C.P.

Battle Hospital, Reading, Berkshire

Summary
Rifampicin occasionally causes thrombocytopenia when given as part of an intermittent regimen. A case is reported of severe thrombocytopenia developing after one dose of rifampicin, following a 4-month gap in daily therapy. The literature on rifampicin-induced thrombocytopenia is reviewed.

Case report
A 37-year-old man was referred for investigation of frequent bronchitis, haemoptysis and persistent morning cough. His chest X-ray showed faint mottling in the right upper zone, consistent with early tuberculosis. Although sputum microscopy and culture were negative for acid-fast bacilli, it was decided to give a 12-month course of rifampicin 600 mg and isoniazid 300 mg daily.

Ten months later he was admitted with a 24-hr history of a purpuric rash involving his arms, legs, face and tongue. Investigations were as follows: Hb 12.4 g/dl; WCC 6.5 x 10^9/l; platelet count 8.5 x 10^9/l.

The patient then admitted that having become asymptomatic he had stopped all medication after 6 months. When his cough returned 4 months later his wife persuaded him to restart the rifampicin and isoniazid, which he did the day before admission. Recovery was rapid and the platelet count being 60, 113, 157, 200, and 330 x 10^9/l on consecutive days.

Further investigations were as follows: Immuno-fluorescent antibody screen negative; bone marrow showed megakaryocytes present in normal numbers; rifampicin antibody test positive.

Discussion
Rifampicin is a well tolerated and highly effective anti-tuberculous drug when given in regular daily doses. Adverse reactions are uncommon, the most frequent being cutaneous reactions and gastrointestinal upsets although hepatotoxicity may occur (Girling, 1977). Intermittent regimens however are associated with a higher incidence of the 'flu' syndrome (fever, chills and malaise), thrombocytopenia, acute renal failure and haemolytic anaemia.

The rifampicin-dependent antibodies, which are responsible for the thrombocytopenia and more commonly the 'flu' syndrome have very rarely been found on well supervised daily therapy. There are 2 reports of thrombocytopenia occurring on daily rifampicin (Ferguson, 1971; Hong Kong Report, 1975). In the first report, no antibodies were found and in the second purpura occurred transiently during a cutaneous reaction, rifampicin was subsequently reintroduced uneventfully.

The incidence of these antibodies depends both on the size of dose given and the rhythm of rifampicin administration. A study in Singapore (Singapore Report, 1975) showed that 16% of patients given once weekly chemotherapy developed the 'flu' syndrome whereas only 6% developed this on twice-weekly treatment. There was also a 50% reduction in febrile episodes when 600 mg doses were used rather than 900 mg.

Bassi, Perna and Silvestri (1976) found rifampicin-dependent antibodies in 10 out of 32 patients 3 weeks after discontinuation of 600 mg daily having found no antibodies on the day after treatment was stopped. Their explanation was that continuous treatment resulted in neutralization of any antibodies formed, the complex being continuously removed without causing an allergic reaction. Any gap in therapy as in this case or with intermittent dose regimens 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 dangers of non-compliance in the treatment of tuberculosis with rifampicin are well illustrated in this case. However, when rifampicin is used in a re-treatment regimen, a careful check must be kept on the platelet count in the early stages since antibodies have been detected 16 months after cessation of treatment (Pujet, Homberg, and Decroix, 1974).

Other drugs that produce thrombocytopenia by an immunological mechanism include apronal, digitoxin, quinidine and quinine (de Gruchy, 1975).

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References


Report of the Hong Kong Tuberculosis Service (1975) A controlled trial of daily and intermittent rifampicin plus ethambutol in the retreatment of patients with pulmonary tuberculosis: results up to 30 months. Tubercle, 56, 179.
