

‘Flu’ syndrome on once monthly rifampicin: a case report

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Summary ‘Flu’ syndrome as a complication of intermittent weekly administration of rifampicin is well documented. The rare occurrence of ‘flu’ syndrome on once monthly rifampicin is reported in this paper.

Case report

A 54-year-old male patient completed 11 monthly doses of rifampicin as part of the WHO multibacillary multidrug regimen uneventfully. Following administration of the twelfth dose the patient reported that about 2 hr later he had developed malaise, fever and body aches lasting for approximately 12 hr. The patient reported this to the clinical team a month later at the time of the thirteenth pulsed MDT clinic. A presumptive diagnosis of ‘flu’ syndrome was made, the patient admitted for investigation, and with his consent, given a provocative dose of rifampicin.

At the time of admission, the patient was asymptomatic. Clinical examination as well as routine blood and urine tests and chest X-rays were done to rule out any underlying cause for the symptoms. All tests were normal.

A dose of rifampicin 600 mg was administered 5 days after the last therapeutic dose in hospital on an empty stomach. Two hours later the patient complained of malaise followed by chills, body ache and headache. Six hours after the administration of rifampicin the patient developed fever and 2 hr later the oral temperature reached 101·8°F. At this stage, with the diagnosis of ‘flu’ syndrome due to rifampicin established, the patient was given an injection of Paracetamol following which the symptoms and temperature subsided.

Two days after the challenging dose of rifampicin, a second dose of rifampicin 600 mg was given to the patient along with tablets of Paracetamol 500 mg 6 hourly for 24 hr. Six hr after the rifampicin administration the patient experienced some malaise, which lasted for 1 hr, but was otherwise asymptomatic. There was no rise in temperature.

At the time rifampicin was administered in the hospital a decision was taken to continue the standard WHO multibacillary multidrug regimen along with oral antipyretics. The patient has completed 18 doses to date without further problems and has shown a satisfactory response to treatment.

Discussion

Several syndromes resulting from intermittent rifampicin therapy have been described, cutaneous, abdominal, flu, respiratory and purpura. These may occur singly or in combination, the severity being greater when they occur in combination.¹

'Flu' syndrome is unlikely to complicate once-a-month rifampicin administration² and reports of its occurrence as a result of antileprosy therapy are few.³ Its low incidence in leprosy is attributable not only to the interval of administration, but also to the dose employed (600 mg for adults, WHO regimen) the highest incidence of the syndrome being recorded in intermittent regimens for tuberculosis employing doses of between 20 and 30 mg/kg bodyweight.⁴ 'Flu' syndrome is also less common when intermittent rifampicin administration is preceded by a period of daily administration⁵ and is therefore even less likely to be seen in India where, as per the Government of India guidelines, intermittent monthly rifampicin is preceded by a period of daily intensive therapy for multibacillary cases in which rifampicin is administered 600 mg daily along with other drugs (DDS and clofazimine).⁶

The syndrome as classically described begins 1–2 hr after administration of the drug and lasts for 8 hr, the symptoms coinciding with the period of maximum rifampicin plasma concentration. It is now known that the syndrome has an immunological basis, and that it is caused by the formation of rifampicin-antibody complexes.⁵ Antibodies to rifampicin have been detected from 4 months after starting therapy but have also been detected for the first time as late as the 16th month. While patients with rifampicin-dependent antibodies have a significantly higher incidence of side-effects, those who have no detectable antibodies are also known to develop adverse reaction.⁷ On the other hand, patients with rifampicin dependent antibodies may remain asymptomatic.⁸

It has been proposed that the drug acts as a hapten, which in the presence of plasma macromolecules induces the formation of antibodies against it. It has been suggested that symptoms of the 'flu' syndrome might be due to a minor degree of haemolysis, a haemolytic anaemia appearing with higher titres of rifampicin dependent antibodies.⁵ Other studies have, however, shown no direct correlation between antibody titres and the presence or absence of symptoms.⁷

While potentially dangerous reactions to rifampicin such as purpura, shock and renal failure are clear indications to stop the drug,² management of 'flu' syndrome is ill defined. Episodes of the syndrome are known to stop spontaneously, after temporary interruption of treatment, after reduction of the dose, or following institution of daily therapy. In this patient daily therapy was not considered because of the cost involved and the inability to supervise intake. Reduction of dose is particularly appropriate to high dose tuberculosis regimens where the reduction in the dose does not markedly effect therapeutic efficacy. As this patient's symptoms were well controlled with symptomatic treatment a decision was taken to continue treatment. This is in accordance with advocated procedures.¹

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