"Flu" Syndrome on Monthly Rifampin Dose; First Case Reported from Yemen

TO THE EDITOR:

"Flu" syndrome frequently appears in intermittent rifampin administration given in tuberculosis, but it is very rare in the monthly dose treatment of leprosy (¹). It is believed to be a result of a hypersensitivity reaction (⁴) which appears with the first dose or with repeated doses(⁵). Its low incidence in leprosy is attributed not only to the interval of rifampin administration, but also to the dose employed (600 mg for adults) in the World Health Organization (WHO) regimen^{(3, 5}). Also, it is less common when intermittent monthly rifampin is preceded by a period of daily intensive therapy for multibacillary cases in which 600 mg of rifampin is administered daily along with other drugs (dapsone and clofazimine)(⁵). The syndrome classically starts 1 to 2 hours after the administration of rifampin.

Drug-induced hepatitis has been reported with daily rifampin doses, but it was considered unlikely that such a reaction would occur when rifampin was given only once monthly⁽²⁾, especially for patients who had no history of pre-existing liver disease, alcoholism or old age.

We report here the first case from Yemen who manifested "flu" syndrome features on the once-monthly rifampin regimen.

A 22-year-old, male, borderline tuberculoid leprosy patient from Al-Zidia, Hodeidah governorate, completed 35 monthly doses of rifampin as per the WHO multidrug therapy (MDT) regimen without a fixed period (changed in 1995 into fixed period regimen as 24 doses in 36 months).

The patient presented to a primary health care worker with the following history: Starting from the 27th monthly dose of rifampin, 2 hours after ingestion of the drug, he had developed abdominal discomfort, fever, generalized body pain and chills lasting for 24 hours. He continued having the same side effects for the last nine monthly rifampin doses and was mistreated for malaria every month even though his malaria smear was negative.

More than 5385 patients are now taking and have been taking rifampin once monthly in our leprosy control program. Until now we have not encountered a case with such serious side effects.

The patient was admitted to the City of Light Hospital for confirmation of the diagnosis and treatment. With his consent, the patient was given a provocative dose of rifampin (600 mg) 20 days after his last dose. At the time of admission, a clinical examination was done including biochemical investigations as follows: Malaria smear = negative; chest X-ray = normal; blood pressure = 120/70 mm Hg; temperature = 37.8° C; pulse = 88 beats/min., regular with normal volume; heart sound = normal with double rhythm, no murmur.

Physically, he was quite normal, free of influenza symptoms, sore throat, urinary tract infection, and no history of pre-existing liver disease, and he had never tasted alcohol. Respiration showed normal vesicular breathing and no added sound. In conclusion, there were no underlying causes of fever.

Family history: The patient comes from a family in which his father, mother and sister are known leprosy patients and none of them had a similar history.

The patient was given 600 mg rifampin on an empty stomach, and was kept under close observation. One hour later, the patient complained of a feeling of tightness in breathing, had malar flush, redness of the face, a feeling of hotness at the epigastric region, a pulse of 74 beats/min and a temperature of 37.8°C.

Two hours later, the patient became more irritable, had redness of the face, had a feeling of thirst, was nauseated (impending vomiting), had generalized muscular aches, was shivering, had a pulse of 80 beats/min and a temperature of 37.9°C, and complained of blurred vision.

Three hours later, the patient was vomiting and unable to stand, had severe generalized body ache with malaise, chills, (even rigors) and redness of the face with a pulse of 95 beats/min and a temperature of 38.2°C. The patient refused any

further physical examination and looked exhausted and lethargic.

He was given a metamizol (dipyrone, analgin, Novalgin[®]) injection with an antihistamine (H1 antagonist). All symptoms disappeared and the patient started to recover.

In one such previous trial to diagnose the "flu" syndrome 24 hours after rifampin administration, the patient developed yellowish discoloration and the blood sample taken was normal.

In this trial, two blood samples were taken for liver function tests. The first sample was taken 8 hours after administration of rifampin and showed an increase in total serum bilirubin to 3.3 mg/dl, an increase in direct bilirubin to 2.0 mg/dl, a SGPT of 50 U/L and a SGOT of 60 U/L.

The second blood sample was taken 48 hours later. His liver function test was normal. The patient was given 600 mg rifampin with 500 mg metamizol every 6 hours. He experienced some malaise but did not have

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any of the other symptoms he previously experienced.

The patient has been released from treatment since he has completed 35 doses of the WHO MDT regimen.

-Abdul Rahim Al-Samie, M.B.B.Ch. Medical Officer/Field Supervisor

-Yasin Al-Qubati, M.B.B.Ch., M.Sc.

Director

National Leprosy Control Programme P. O. Box 55722 Taiz, Republic of Yemen NAAFS, B and MATEMERA, B. O. A possible "flu" syndrome on once-monthly rifampicin.(Letter) Lepr. Rev. 57 (1986) 271-272.

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Reprint requests to Dr. Al-Qubati.

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