Severe Thrombocytopenia and Intermittent Use of Rifampin

TO THE EDITOR:

Multidrug therapy for leprosy has been implemented in Brazil since 1986 ([2]). The recommended schedules for adults include daily dapsone and a monthly supervised dose of rifampin for paucibacillary cases and daily dapsone and clofazimine with monthly supervised rifampin plus clofazimine for multibacillary cases ([2]).

Intermittent use of rifampin has been associated with a flu-like syndrome that has been reported in up to 20% of patients ([4, 5]). More severe complications, such as shock, hemolysis, acute renal failure, and thrombocytopenia, have also been described ([6]).

We herein report a patient who developed two episodes of severe thrombocytopenia after receiving his monthly dose of rifampin 600 mg plus clofazimine 300 mg.

The patient, a 22-year-old male, had a known diagnosis of lepromatous leprosy since 1986, and had been treated initially with daily rifampin for the first 3 months, with dapsone for 5 years, and with thalidomide while experiencing type 2 reactions (erythema nodosum leprosum). In May 1991 multidrug treatment was introduced because he still had clinical and bacteriological evidence of active disease. Two days after the fourth monthly doses of rifampin and clofazimine, the patient had severe epistaxis. His platelet count was 7000/mm^3 at the time of admission. The hematocrit was 39.7%; the white-cell count was 11,100, with 47% neutrophils, 2% band forms, 18% lymphocytes, 1% monocytes, and 32% eosinophils. A bone-marrow aspirate revealed an increased number of eosinophils and megakaryocytes.

Treatment of the epistaxis required postnasal packing and transfusion of platelets. His platelet count was 9000/mm^3 on day 2, and 210,000/mm^3 on day 5 when the patient was discharged.

One month later the patient inadvertently was given another dose of 600 mg of rifampin, and 1 day later he was admitted to the emergency department of the teaching hospital with epistaxis that again required postnasal packing. His platelet count was 12,000/mm^3 and increased to 230,000/mm^3 after 5 days. Eosinophilia persisted, but larvae of *Strongyloides stercoralis* and ova of *Hymenolepis nana* were seen on stool examination.

The patient has had no other episode of bleeding after a follow up of 4 months without receiving rifampin.

Thrombocytopenia is a rare side effect of the intermittent use of rifampin, and platelets are said rarely to drop below 100,000/mm^3 ([6]). It has been recognized since 1970 ([1]), and it has been reported in patients taking rifampin for the treatment of either leprosy or tuberculosis. Taking into consideration that 48,282 patients were under multidrug therapy for leprosy in Brazil in 1990 ([3]), and with an estimated prevalence of thrombocytopenia of 6% ([8]), we can expect about 2897 cases of thrombocytopenia each year in Brazil, at least some of them developing hemorrhage.

Attention must be given to hemorrhagic manifestations in the first few days after the supervised monthly dose of rifampin in leprosy patients. Platelet count monitoring can hardly be recommended since it probably would not be cost effective even in the very few institutions where it could be done. An alternative way of detecting thrombocytopenia would be to perform a tourniquet (capillary fragility) test ([7]) on the day after the dose of rifampin. Although not highly specific, the tourniquet test requires only a sphygmomanometer to be performed, and it can be a valuable and inexpensive screening test. Patients with a positive test would either be referred for a platelet count or an alternative schedule for the treatment of their leprosy instituted.

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REFERENCES

1. BLAJCHMAN, M. A., LOWRY, R. C., PETTIT, J. E. and STRALING, P. Rifampicin induced immune thrombocytopenia. Br. Med. J. **3** (1970) 24–26.
2. BRAZIL. MINISTÉRIO DA SAÚDE/FUNDAÇÃO NACIONAL DE SAÚDE. Normas técnicas e procedimentos para utilização dos esquemas de poliquimioterapia no tratamento da hanseníase. Brasília: Ministério da Saúde, 1990.
3. BRAZIL. MINISTÉRIO DA SAÚDE/FUNDAÇÃO NACIONAL DE SAÚDE. Relatório da Avaliação Nacional do Programa de Controle da Hanseníase. Brasília: Ministério da Saúde, 1991, p. 21 (mimeogr.).
4. FLYNN, C. T., RAINFORD, D. J. and HOPE, E. Acute renal failure and rifampicin: danger of unsuspected intermittent dosage. Br. Med. J. 2 (1974) 482.
5. GIRLING, D. J. and HITZE, H. L. Adverse reactions to rifampicin. Bull. WHO 57 (1979) 45–49.
6. JACOBSON, R. R. Treatment. In: *Leprosy*. Hastings, R. C., ed. London: Churchill Livingstone, 1985, pp. 193–222.
7. KOLMER, J. A. *Clinical Diagnosis by Laboratory Examinations*. New York: Appleton-Century-Crofts, 1949, pp. 39 and 665–666.
8. POOLE, G., STRADLING, P. and WORLLEDGE, S. Potentially serious side effects of high-dose twice weekly rifampicin. Br. Med. J. **3** (1971) 343–347.

Giant Histoid Tumor

TO THE EDITOR:

Histoid leprosy, originally described by Wade in 1963 ([5]), is characterized by the development of discrete, firm, dome-shaped nodules that stimulate benign skin tumors both clinically and histopathologically. They develop on an apparently normal skin in patients with lepromatous leprosy who have relapsed after prolonged monotherapy with dapsone. Histoid lesions tend to arise at unusual body sites, and their sizes range up to 3 cm in diameter ([4]).

A 45-year-old man with histoid leprosy is reported. He presented with a well-defined, nontender, large, raised, tumor-like lesion of 6 × 4 × 3 cm on the left elbow. The "tumor" was not fixed to the underlying bone or muscle and its surface was shiny with softening and crusting at four points (Fig. 1). A few, scattered, discrete, firm, dome-shaped, well-defined, hemispheric, shiny papules and nodules were seen on the trunk and upper arms (Fig. 2). Their size varied from 0.5 to 2 cm, and most of these nodules showed central depression due to necrosis and crusting. There were multiple, diffusely infiltrated, shiny macules and patches on the face, trunk, and limbs. The ulnar nerves and the common peroneal (lateral popliteal) nerves on both sides were

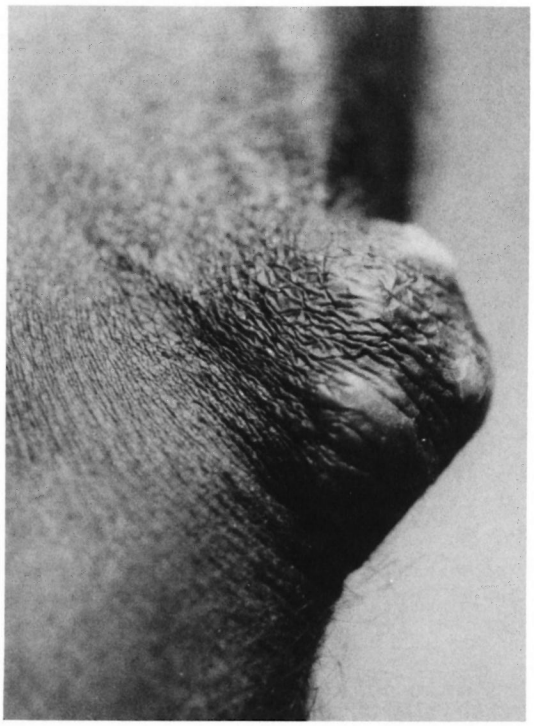

Fig. 1. "Giant histoid tumor" at the elbow. Note areas of softening, crusting, and depression on the surface.