

action, mediated by activated T lymphocytes (⁶). The generation of toxic metabolites like nitrosamines and possibly other compounds through the N-hydroxylation pathway of dapsone metabolism coupled with genetic and environmental factors are also believed to be involved in the genesis of the dapsone syndrome (²). The clinical features include constitutional symptoms, cutaneous lesions in the form of papular exanthem or exfoliative dermatitis or, rarely, as erythema multiforme, toxic epidermal necrolysis or Stevens-Johnson Syndrome, jaundice, hepatitis, lymphadenopathy and mononucleosis (the last two have been attributed by Lowe to activation of the Epstein-Barr virus) (^{3,4}). Management includes avoidance of dapsone and the prompt institution of corticosteroid therapy which is life saving. Steroids should be tapered gradually over a period of more than 1 month, because dapsone is found to persist in the body for up to 35 days. The condition usually lasts for 2 to 4 weeks and recovery is the rule; however, it can end fatally in some patients.

Three out of four of our patients were detected to have associated hepatitis-B as a risk factor for the dapsone syndrome. So screening for this infection is essential before starting dapsone in any patient, whatever the indication may be. Many reports indicate that there has been an increased incidence of dapsone syndrome in recent years (^{3,7}). Among 180 patients treated during 1 year, four developed the dapsone syndrome (4/180). All of the cases were initially wrongly diagnosed as infectious mononucleosis or infective hepatitis. Other factors contributing to the re-

emergence of the dapsone syndrome could be a heightened awareness of the condition, the use of multidrug regimens in leprosy, and wider use of dapsone.

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Granuloma Multiforme (Called Nkanu Disease in the 1940s and Mkar Disease in 1964)

TO THE EDITOR:

I was interested to hear about a poster presentation at the recent 15th International Leprosy Congress in Beijing in September 1998, (Huskinson, R. A. C. Granuloma multiforme (GM): a nonleprosy disease with a

difference; no known chemotherapy to cure it. Session 11) drawing attention to granuloma multiforme (GM) and the need to include this disease in the differential diagnosis of leprosy in many countries. The original publication of this disease was by Leiker in 1964 (¹). Further reports have appeared in

the literature (^{1-8, 10, 11}) describing its occurrence, not only in Nigeria but in many other countries, mostly tropical or subtropical. R. A. C. Huskinson and A. C. McDougall have encouraged me to record my reflections and observations of this perplexing disease as seen in Nigeria in the early 1940s, over 20 years before the first published account.

I first began to notice these cases, which are now referred to as GM, early in the 1940s soon after posting to the Oji River Leprosarium in 1940. Among many thousands of leprosy patients, I noticed, particularly in the Nkanu subdivision of the Onitsha Province near Enugu, the capital of Eastern Nigeria, a type of rash which resembled minor tuberculoid leprosy in having raised, clearly defined edges, a healing center and sometimes erythema. There were never enlarged nerves or anesthesia or loss of sweating. Leprosy and GM often co-existed. It had some resemblance to some fungal diseases, and when I questioned patients they said it was called "Ununo Enyi" (elephant ringworm) and not "Ekpenta" (leprosy). Inevitably, the patches were treated with hydnocarpus oil, which had a good effect on leprosy but not on GM. Various treatments for fungal diseases were tried, with no effect. In those days, most early leprosy sufferers had caustics applied, which covered the disease until it extended beyond the scar. The same happened to GM. At that time, steroid tablets and ointments did not come our way. We never tried them, even later. When dapsone came, it had no effect. Patients and relatives were worried by the failure to cure GM since it superficially resembles leprosy. I took biopsies and sent them to Yaba Laboratory in Lagos, where the histology was reported as "typical tuberculoid leprosy." No bacilli were ever found, and GM's response to treatment was totally different. It also occurred in completely healthy people.

I reported it to my leprosarium neighbors at Uzuakoli and Mkar, but it had not been recognized at either location. Subsequently, it was found at both. Why did I not publish it? The answer was the pressure of work. Oji River Leprosarium had over 1000 patients and about 3000 outpatients in four clinics in 1940. We were responsible for about 5000 square miles of Onitsha Province, roughly 75 miles square, with

over a million population and an estimated 3% leprosy prevalence. We steadily increased our clinics to about 80 and our numbers, despite discharges, reached nearly 15,000 patients. The most new patients presenting on any one day for diagnosis was 240 at one clinic and 120 at another. We had a 40-bed hospital and a normal medically qualified staff of two doctors and one nursing sister. Our job was to discover, control, and treat this immense population with leprosy; spare time for research on a relatively harmless skin rash was not available.

Hydnocarpus oil was ineffective for GM but good treatment for leprosy, and it saved thousands from a miserable fate. It also rendered lepromatous forms of the disease much less infective. Dapsone was an enormous improvement and a year after we changed to its use, patient numbers went down rapidly in the 1950s.

Leiker's accounts of GM in the INTERNATIONAL JOURNAL OF LEPROSY (⁹) and in *Leprosy in Theory and Practice* (⁵), both published in 1964, were the first descriptions of the disease and later (⁶) he found it elsewhere, as far away as Indonesia, where he confirmed a) that it was confused with tuberculoid leprosy and b) it did not respond to treatment.

In 1987-1988 I returned to Oji River, but had much restricted transport and did not see many patients. Among the few I did see, I can confirm that GM was often confused with leprosy and was still present.

A word about the name the disease has acquired. Granuloma multiforme is a perfect description of most forms of leprosy! In fact, leprosy is much more multiform than GM. No local name, like "Nkanu" or "Mkar" disease, is appropriate for such a widely observed phenomenon. They only describe where it was first noticed and described in print. Its histological similarity to forms of leprosy and tuberculosis suggest that it may be infectious. Puzzle—find the causal organism! It is widespread in tropical and subtropical countries and, as far as I know, has not been found in temperate or cold climates.

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Histoid Leprosy; Report of Three Cases

TO THE EDITOR:

Histoid leprosy, originally described by Wade in 1960, is regarded as a distinct clinico-pathological entity, presenting as cutaneous or subcutaneous nodular- and/or plaque-like lesions arising from apparently normal skin and characterized histologically by tumorous collections of spindle-shaped cells arranged in criss-cross fashion, giving them a resemblance to neurofibromatosis (1).

CASE REPORTS

The three cases of histoid leprosy seen within 1 year were: a 25-year-old housewife (Case 1), a 28-year-old daily wage worker practicing earpiercing (Case 2), and a sugarcane cutter 32 years of age (Case 3). All three cases were of low socioeconomic status without any family history of Hansen's disease among close relatives or in their immediate neighborhoods. Cases 2 and 3 were from the Beed District of the state of Maharashtra, India, an area endemic for leprosy. None of the three patients had received any form of treatment for their disease when first seen. The durations of their symptoms were 6 months, 3 months and 2 months, respectively.

All three patients presented with asymptomatic, firm, well-defined, ½ cm to 1½ cm, erythematous-to-skin-colored, oval-to-round, shiny papulonodules over the pinnae, forehead, face, neck, trunk and extremities (Fig. 1). A few nodules were subcutaneous in location while the majority were cutaneous. In addition, Case 3 showed lesions over the scrotum and glans including around the external urethral opening (Fig. 2), a very rare site for leprosy lesions. Associated features of lepromatous leprosy, including multiple peripheral nerve thickening and patchy glove-and-stocking anesthesia, were present. However, none of these three cases showed trophic ulcers or madarosis.

Systemic examination of the three cases revealed no abnormalities. Routine blood and urinalysis, liver and renal function tests, blood VDRL and ELISA for HIV were all negative. Slit-skin smears from the nodules in all patients showed a bacterial index (BI) of 6+ (Ridley scale), and histopathology was consistent with the diagnosis of histoid leprosy with a thinned out epidermis, nodular infiltrate of spindle-shaped histiocytes arranged in whorls, and innumerable acid-fast bacilli found on Fite-Faraco staining.