International Journal of Leprosy Volume 34, Number 1
Printed in U.S.A.

Granuloma Multiforme in Eastern Nigeria[1]

S. G. Browne, O.B.E., F.R.C.P.[2]

The recent report by Leiker *et al.* ([3]) of a chronic skin granuloma with polymorphic appearances may be supplemented by this record of the same condition as observed in the north of Eastern Nigeria not far from the focus in the Northern Region already described.

Fourteen years ago Garrett ([2]), the Area Superintendent, at the time, of the Oji River Leprosy Settlement, distinguished the condition from leprosy on clinical grounds because of the retention of tactile sensation in the patches, which, if they had represented tuberculoid leprosy, should have been characterized by well-marked loss. Garrett also made histologic investigations (unpublished), and observed the negative results of fungicidal and karyolytic treatments.

Subsequently, Felton Ross and Fern, successively Area Superintendents at Oji River, confirmed Garrett's observations. For the same reasons that led to designation of granuloma multiforme as Mkar disease in Northern Nigeria, it was called Nkanu disease in the Eastern Region. Further enquiries over the past few years have shown that the focus in the east is more extensive than was formerly believed.

While it is admittedly impossible to make an unassailable diagnosis from a photograph, it may be mentioned that figure 216 in a book by Clarke ([1]) over the caption "erythema annulare centrifugum (Darier)" resembles very closely one variety of granuloma multiforme. Clarke reported that histologically this lesion showed a tuberculoid structure, and that dapsone was without effect. He suggested that it might be described as an "annular sarcoid."

LOCATION OF FOCI IN EASTERN NIGERIA

The villages affected lie in the transitional belt to the north of the equatorial forest, in hilly country with wooded valleys and savannah uplands. The rainfall is about 50 inches annually, and there is a well-marked dry season extending from December to March. No example of granuloma has been encountered in the equatorial forest zone.

The Nkanu focus comprises three groups of villages (Amiri, Amagundze and Ugbako) about 20 to 30 miles south of Enugu, in Udi Division. Some 60 miles to the east of Enugu, there is another focus west and north of Abakaliki (Ezza, Umwesaka, Ezzambo). Further east still, in the Ogoja Province, foci exist near Yahe and Bansara, and to the north of Ogoja near the northernmost limits of the Eastern Region, abutting on the northern Region.

Since, because of difficulties of access, accurate whole-population surveys of the villages affected have not yet been made, no exact estimates of prevalence can be given. It is indicative of a high prevalence that several patients from a single village may present themselves at a medical center, and that at one leprosy clinic about 20 patients, out of 400 under treatment for leprosy, actually had granuloma multiforme and not leprosy.

Typical patients from these foci have been studied recently, but little can be added usefully to the excellent clinical description given by Leiker *et al.* ([3]).

Sex and age ratios. Of the 20 patients (all adults) in this series, 15 were women. Only three were 35 years of age or under; two were over 70, and five others over 60.

Distribution of the lesions. The lesions were found predominantly on the upper chest and suprascapular regions, the deltoid area and outer aspects of the arms, the

[1] Received for publication, September 21, 1965.
[2] Leprosy Service Research Unit, Uzuakoli, Eastern Nigeria. Present address: 16 Bridgefield Road, Sutton, Surrey, England.

face, scalp and neck; and then, in descending order of frequency, on the abdomen, the knees, and the outer aspect of the legs. The buttocks and drawers area were very rarely affected, nor was the inner aspect of the arms, or the inner and posterior aspect of the thighs and legs.

Number of lesions. In all patients, several or many lesions were present; in some, innumerable lesions were scattered over the entire exposed surface of the body as if the patient had encountered a flurry of falling snowflakes.

Description. All the varieties described by Leiker *et al.* ([3]) were seen in this series. Particularly noticeable was the extremely widespread eruption of small nodules, which, as they increased in size, produced rings and crescents of smooth or papular raised lesions. In some instances ring-like lesions encroached on neighboring lesions as they expanded, producing a picture of multiple interlocking rings; there was no immunity or refractory state, such as is observed when one tuberculoid leprosy lesion approaches another. In several patients a tendency to symmetry was noticeable, and lesions frequently straddled the midline. One patient presented a number of succulent lesions composed of shiny flat rings, well-raised above the level of the skin, and surrounding a central depressed area reminiscent of the immune area in borderline leprosy.

Histologically, the picture was that of a proliferating tumor of fibroblasts and round cells embedded in an edematous and fibrous stroma. Enquiry elicited the observation that such an acute form was not rare.

Symptoms. Itching is a common complaint in the initial stages, but not later. Eye lesions and systemic symptoms, such as glandular involvement, have not been noted.

In this small series, one female patient was found to be suffering also from major tuberculoid leprosy.

Duration. While spontaneous regression and complete resolution may occur, it is the chronicity of the condition that is characteristic. The raised papular ring surrounding a slightly dyschromic area may cease to extend and may diminish in elevation, but records exist that indicate that many lesions have remained apparently unchanged for long periods, up to ten years or longer.

ETIOLOGY

A most pressing problem in granuloma multiforme is its etiology. Many attempts have been made to elucidate the cause, so far without success.

Examinations by the scraped-smear technic have been made on scores of occasions, but no acid-fast organisms have ever been found. The inhabitants themselves distinguish the condition from leprosy: they know that it is never followed by neuropathic ulceration of the extremities, and have observed the inefficacy of dapsone treatment, which has been available in this district since the early 1950's.

Scrapings from the surface of the lesions, put up in 25 per cent caustic potash, have yielded no spores or mycelial elements.

Histology. No microscopic structure has been seen that might account for the development of the granuloma. Fluorescent microscopy has disclosed no organism or particulate matter demonstrable by this technic. No fungi have been detected. Nerve twigs are never infiltrated. No stained bodies have been detected in the numerous foreign-body giant cells examined.

No microfilariae either of normal morphology or disintegrating, have been seen in sections, but several artifacts resembling microfilariae have been noticed, formed of histiocytes or fibroblasts arranged end to end.

No acid-fast material, as, for instance, pollen grains, has been recognized microscopically in sections of early lesions.

The local application of fungicides (chrysophanic acid, dithranol, salicylic acid, resorcin, and iodine) has caused blistering and exfoliation, but the march of the granuloma has not been halted. Caustics, e.g., Izal, carbolic acid, and cashew nuts, are often used by the local population in attempts to cure the condition. Expensive systemic fungicides have not been tried.

The investigation continues.

DISCUSSION

The distribution of lesions and the increased prevalence with age, may be associated with an air-borne agent acting perhaps intermittently over long periods. Exhaustive inquiries made in the districts affected have disclosed no unique phenomenon that might account for this disease, such as social habits and customs, or the presence of peculiar biting insects or matter of vegetable origin. Granuloma multiforme has not been seen in association with onchocercal or streptocercal microfilariae in districts where these are present in the dermis.

Dust falling from the poles and leaves used in roofing and ceilings is a possibility, but the dusts appear to be no different from those found in villages where granuloma multiforme is not found. Similarly, irritant matter capable of producing a chronic granulomatous or sarcoid response might conceivably fall from forest trees. Lizard droppings appear to be similar in these villages to those found elsewhere. The Kveim reaction has not been investigated.

Cosmetics in use include antimony for eye shadow, and various earths and vegetable stains obtained and prepared locally, but the distribution and multiplicity of the lesions virtually excludes such recognized granuloma-producing agents as causative factors in these districts.

The only fact of possible etiologic importance that has emerged so far is that all the villages affected are the resort of a veritable plague of bats. It may be that some agent from their droppings or lodging in their skin might be responsible.

SUMMARY

Several scattered foci of granuloma multiforme (recently reported from Northern Nigeria) are now shown to exist in the Eastern Region, where the entity has been recognized for some years. The clinical features are very similar to those described.

Despite intensive investigation, the etiology of the condition remains unknown. The only new possibility, it is suggested, is an agent present in bat droppings.

RESUMEN

Varios focos esparcidos de granuloma multiforme (recientemente comunicados en el Norte de Nigeria) han mostrado su existencia en la region del Este, donde la entidad ha sido reconocida por varios años. Los aspectos clínicos son muy similares a aquellos descriptos.

A pesar de la investigación intensiva, la etiología de la condición permanece desconocida. La única nueva posibilidad, se sugiere, es un agente presente en las heces de los murciélagos.

RÉSUMÉ

Le granulome multiforme a été récemment signalé au Nigéria du Nord. Il est à présent démontré qu'il en existe plusieurs foyers éparpillés dans le Nigéria de l'Est, où l'entité avait été reconnue pour de nombreuses années. Les caractéristiques cliniques sont fort semblables à celles qui ont été décrites.

Malgré des recherches intensives, l'étiologie de cette condition demeure inconnue. La seule possibilité nouvelle apparaît être, ainsi qu'on le suggère, un agent présent dans la fiente de chauve-souris.

Acknowledgment. My thanks are due to Dr. S. O. Egwuatu, Chief Medical Officer, Ministry of Health, Eastern Nigeria, for permission to publish this article.

REFERENCES

1. Clarke, G. H. V. Skin Diseases in the African. London, H. K. Lewis and Co., Ltd. 1959.
2. Garrett, A. S. Personal communication.
3. Leiker, D. L., Kok, S. H. and Spaas, J. A. J. Granuloma multiforme, a new skin disease resembling leprosy. Internat. J. Leprosy **32** (1964) 368-376.