

DIFFUSE CUTANEOUS MASTOCYTOSIS

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Over the last 20-25 years it has gradually become clear that urticaria pigmentosa is only a clinical form of mast-cell disease. Other cutaneous and visceral types have gradually been recognized, but the number of cases is so small that it is not easy to group them in a way that will show the prevailing clinical patterns in perspective. Marshall *et al.*¹ have contributed an important paper to the South African literature in which the mastocytoses and mastocytomas are discussed, with special reference to the association of cyclical attacks of flushing.

Since mast cells are known to contain important amounts of biologically potent substances (heparin, histamine, sometimes serotonin, and precursors of ground substance), the vasomotor and haemostatic aspects of mast-cell disease have attracted attention. In a personal communication, Marshall² states that cyclical flushing in children with mastocytomas recurs at 4-6 weekly intervals, and in adults at less regular intervals, varying from a few days to several months. One of his patients was Coloured, the others being White. The effects on blood coagulation have been noted in detail by Herzberg.³

The incidence of mast-cell infiltrations (solitary or multiple) in our experience in the Transvaal is about 0.1% in dermatological practice. So far the solitary mastocytomas and the multiple (urticaria pigmentosa) cases have occurred with equal frequency.

In the present paper the classificatory or functional problems will not be discussed. We are concerned only to present the features of a Bantu patient with diffuse cutaneous mastocytosis. Had it not been for the excellent illustrated account in Degos's *Dermatologie*⁴ the nature of the case would have eluded us. Although diffuse cutaneous mastocytosis was first described by Hissard *et al.*⁵ the special features of their case were brought into prominence by Degos^{4,6} and related to subsequent findings in such a way as to make a prompt clinical diagnosis possible. The diagnostic features in our case are as follows: Generalized pruritus with prurigo papules, a generalized shagreen-like skin surface, flexural giant pseudolichenification, flexural intracutaneous tumour formation unrelated to lymph glands, and areas of surface ulceration. Colour changes, while of help in a White skin, are of very little aid in our Bantu patient, whose skin also showed a widespread increase in pigmentation beyond the normal for his race.

Although the findings in our patient fit the account of Degos with precision, there was some delay in identifying the diagnostic cell type in haematoxylin-and-eosin stained sections. While the diagnosis was in histological doubt several alternative diagnoses were entertained. Firstly, foamy cells were seen in some sections, and xanthoma disseminatum was then suspected—a condition showing papules

round the eyes and flexural infiltrations. The foam, however, proved to be unstainable with fat stains on frozen sections. Secondly, the presence of some dilated vessels in the sections, the rough skin, and the corneal opacity, suggested Fabry-Ruiter's disease, angiokeratoma corporis diffusum. However, the intervening skin between papules was nowhere normal, the vessels were not ectatic enough, and there was no cardiovascular disease or any lipid storage to support this alternative. Thirdly, an epidermal dystrophy of hereditary or acquired type was considered. Lastly, a typical Darier's disease with flexural vegetations, generalized acanthosis nigricans, bullous and ulcerating erythroderma, and generalized confluent papillomatosis (Gougerot-Carteaud), were variously entertained, but the clinical and histological features of all of them fitted either poorly or not at all with the findings in our case. Retrospectively, onchocerciasis might also have been considered, though the patient had only lived in the Northern Transvaal.

The description of diffuse cutaneous mastocytosis may suggest a fairly constant picture, but this is perhaps deceptive. Firstly, our patient showed no demonstrable visceral involvement, and secondly other rather similar cases have more definite urticaria-pigmentosa lesions as well.⁷ It is at present difficult to arrive at a clear prognosis, since the described patients, in this and related groups of cases⁸, tend to languish in rather poor health for no easily explained reason. Perhaps the soundest attitude is to call the condition a mast-cell reticulosis, which groups it with other reticuloses, and the general symptoms will then fall in line with the diversity of complaints met with in the group of chronic but malignant reticuloses of other types.

CASE REPORT

We first saw this patient in 1959. He was a 60-year-old Bantu male, in whom an itching rash had developed on the thighs 23 years before at the age of 37. During the same year (1936) the rash spread to the rest of the trunk and limbs, where it persisted unchanged for 12 years. He then noted a gradual thickening and hardening of the skin, which was followed by recurrent ulceration of the palms and soles. In 1958, a year before admission, the face and ears became affected by the same itching thickened skin alteration for the first time, and then he also developed tumours behind the knees and in the groins. At the same time there developed ulcerations of the genitalia and an eye complaint that blinded him. Apart from colds, earache and a chronic cough, the history yielded little else of note.

On examination there was a generalized velvety to rasp-like papillomatosis with increased pigmentation, and on the face, trunk and perineum a picture resembling papular eczema-prurigo. In the groins this papillomatosis resembled lichenification. On the palms, soles and genitalia and over the flexural tumours (see below) there were septic macerated ulcerations which healed slowly, leaving depigmentation. Depigmentation of the scratched prurigo papules was also noted. The tumours in the knee flexures and upper thigh mentioned in the history were observed. Dermo-

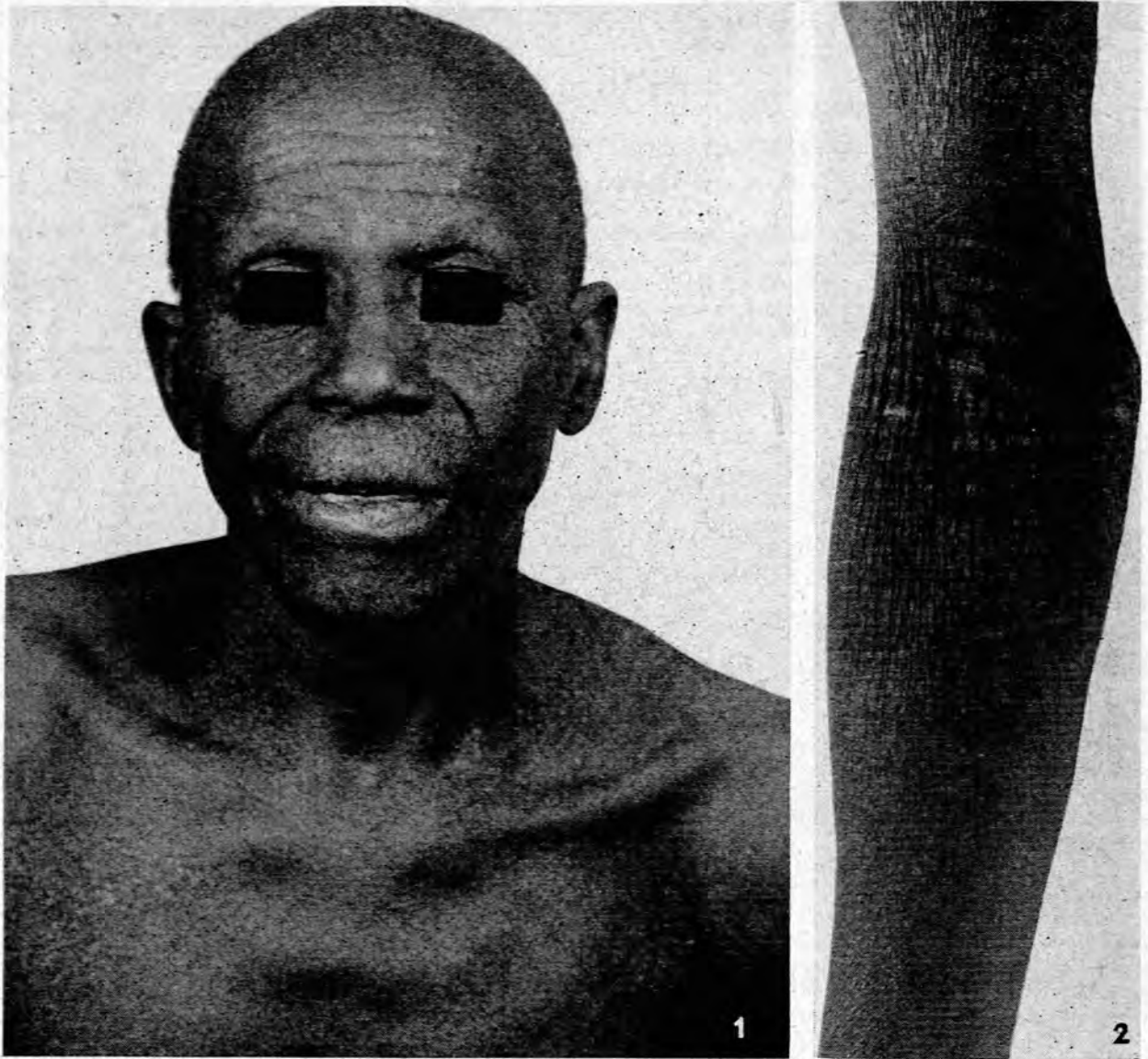


Fig. 1. Diffuse mastocytosis. Diffuse papulation, pigmentation and infiltration of skin (opaque corneas).
 Fig. 2. Diffuse mastocytosis. Flexural papillomatosis with pseudolichenification in the elbow.

graphism with palpable urtication was present. There was a vascularizing and non-ulcerating keratitis in both eyes, with conjunctival pigmentation of the palpebral conjunctiva. Both ear drums had been destroyed by otitis media. There was a productive cough yielding *Diplococcus pneumoniae* in the sputum, without any radiological changes of importance in the chest. There was no detectable cardiac abnormality. The abdomen was normal and no radiological enlargement of liver or spleen was noted. Disturbed liver function, in keeping with the common findings among the Bantu, was present, there being an inverted A/G ratio, raised zinc-sulphate test and a 50% prothrombin value. The blood calcium was not raised. Blood cholesterol 241 mg. % and total lipids 416.4 mg. %. Kolmer and Price reactions negative.

The blood count and bone-marrow findings were completely normal. The bleeding and clotting times were normal. A slight plasmocytosis was seen on sternal puncture, and no basophil cells. There was no general adenopathy. A suppurative adenitis developed in the left groin and pelvis from a *Staph. aureus* infection. It required surgical drainage and came presumably from the genital and foot ulcerations. No evidence of mastocytomas could be found on X-ray examination of the entire bony skeleton.

Histological Findings

The material examined consisted of 9 skin biopsies and 1 superficial corneal biopsy. Of the skin biopsies 6 were taken before therapeutic irradiation and 3 after completion of the treatment. The post-irradiation biopsies were taken from the tumours in the knee flexures and upper thigh; those taken before treatment were from the same tumours and also from the lesions on the face, neck, groins and shoulders.

The specimens were all fixed in 10% neutral formalin and processed in the usual way, and paraffin sections were cut at 4 μ . In addition to the haematoxylin-and-eosin preparations, sections from each block were stained with 0.5% aqueous toluidine blue and also with pinacyanol erythrosinate according to the method of Bensley.⁹ The Scharlach R method for fat was used on selected blocks.

Histological examination of the sections from the flexural tumours showed a well-marked hyperkeratosis, papillomatosis and follicular plugging of the epidermis. An irregular acanthosis was also present and some of the acanthotic processes projected fairly deep down into the dermis. In the middle and upper thirds of the



Fig. 3. Diffuse mastocytosis. Healed ulceration of penis and quadrillated skin thickening over groin tumours.



Fig. 4. Diffuse mastocytosis. Tumours in popliteal fossa.

dermis there was a fairly diffuse cell infiltration composed of numerous histiocytes and plasma cells with a few lymphocytes, eosinophil leucocytes, and a very occasional polymorphonuclear leucocyte. Some of the histiocytes showed a vacuolated cytoplasm, but neutral fat could not be demonstrated in these cells with the fat stain that was used. A number of angiectatic capillaries, venules and lymphatics were seen in the vicinity of the infiltrate. In the deeper part of the dermis the cellular infiltrate was much less pronounced and the few cells seen were arranged mainly around the blood-vessels.

The specially stained preparations showed the presence of numerous mast cells throughout the thickness of the dermis. These cells were mostly fully granulated, but varied considerably in size. Although the majority of cells were of the globular type, occasional dendritic and spindle-shaped forms were also present. Some of the smaller, globular mast cells were poorly granulated and these, especially, were much more clearly demonstrated with the pinacyanol erythrosinate method than with toluidine blue.

Examination of the biopsies taken from other areas showed essentially similar appearances except that the epidermal changes such as the papillomatosis and acanthosis varied in degree from one biopsy to the other. In the dermis the inflammatory-cell infiltrate was much less pronounced, but the number of mast cells appeared to be about the same. It would therefore appear as if the major part of the tumours is composed of the inflammatory infiltrate.

The mast cells in the individual biopsies were counted in a series of 10 adjacent fields immediately below the epidermis and also in 10 adjacent fields immediately below the first row of fields. The magnification used was 800. The mean number of mast cells per 20 fields of the different biopsy specimens was 195. In the post-irradiated lesions the mean mast count was 125 per 20 fields and

the cells as a whole were more sparsely granulated. Otherwise the appearances were essentially similar.

Section of the specimen of cornea showed the presence of a bandlike infiltrate in the subepithelial area. The infiltrate consisted of lymphocytes, plasma cells, and a few eosinophil leucocytes, but only a very occasional mast cell could be demonstrated in the specially stained preparations.

COMMENT

In this patient with a clinically typical, diffuse mastocytosis (type Hissard-Degos) the mast cells were not predominant in the cellular infiltrate. Prakken and Woerdeman¹⁰ have published figures of the mast-cell counts in sections from urticaria pigmentosa. By recalculating their values, our mast-cell count of 195 cells in 20 fields of a magnification of 800 at a section thickness of 4μ falls within their range of 110 - 290 cells in 10 fields of 690 magnification at 7μ for urticaria pigmentosa.

If we had had only our own patient to conclude from, the importance of the mast cells might readily have been overlooked. The absence of visceral mast-cell disorder after more than 20 years, the lack of frank urticaria-pigmentosa lesions, and the presence of the histiocyte, lymphocyte and plasma-cell infiltration would have classed the condition as an obscure chronic inflammation. This last possibility would

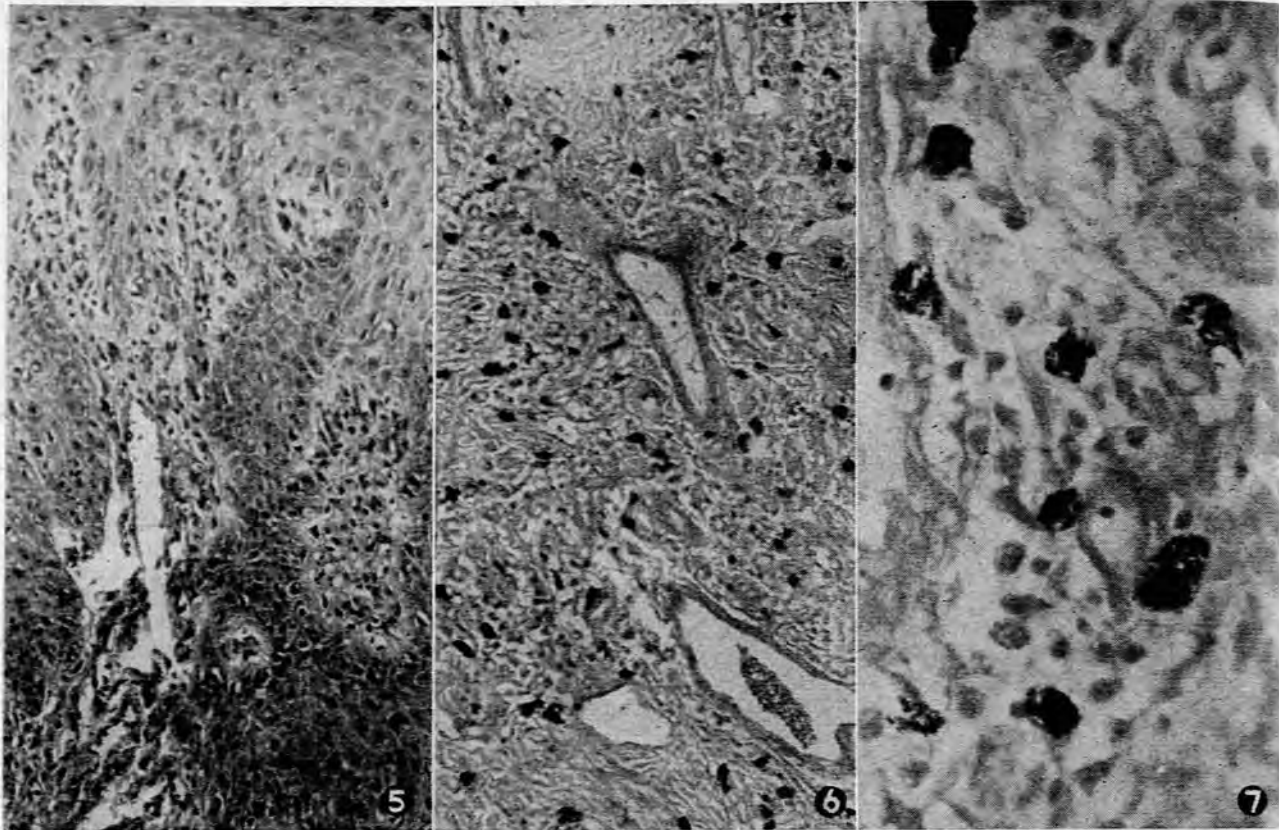


Fig. 5. Diffuse mastocytosis. Section of the tumours in the popliteal fossa showing hyperplastic and acanthotic epidermal changes with underlying inflammatory cell infiltration and slight angiectases. H & E $\times 80$.

Fig. 6. Diffuse mastocytosis. The section demonstrates the increase of mast cells in the dermis. Pinacyanol erythrosinate $\times 80$.

Fig. 7. Diffuse mastocytosis. Fully granulated mast cells, which are mainly of the globular type. Pinacyanol erythrosinate $\times 320$.

still have been entertained had the clinical distinctiveness of the condition not overruled the histological obstacles to the diagnosis.

SUMMARY

A case of diffuse cutaneous mastocytosis of 23 years' duration in a 60-year-old Bantu male is presented.

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