Maduromycosis

Minutes of a meeting at PMCH's office on 5th April 1960.

Present: - Dr. I. G. Murray
Dr. I. A. Hussein
Dr. Khalil A/Rahman
Mr. I. M. Moghraby.

A general survey of the present Madura Fungus situation in the whole of the Blue-Nile-Province was made to enable Dr. Murray to gain a more comprehensive grasp of the problem, the object of his visit to the Sudan as representitive of Prof. Spooner. E.T.C.

The following are some of the scattered observations that transpired during the meeting.

I) RECORDS: - Hospital records for both inpatients and outpatients are to be standardised. Proformas are to be worked out by Mr. Moghraby. Khartoum Hospital Form does not suit the locality.

2) Dr. Murray, to assist in human implantation experiments, will send fortnightly fresh emulsions of Madurella Mycetome. For emulsion can only live for about one week.

The M. R. C. may not object to this practice.

The dose of the emulsion would be empericle.

3) Vascularity studies have so far failed. However, a fresh trial will be made when material for chemotherapy and antibiotic tests becomes available.

AMPHOTERICIN supplied by Squibbs was found to precipitate at the higher concentrations with Glucose 5% as solvent. Madura treatment will be resumed with the drug if this phenomenon stops recurring. Reference will be made to the manufacturers.

4) Meanwhile Dr. Murray will keep us informed of any new Antifungicidals in this line. He will carry out all in vivo experiments at his lab. in London.

5) Antigens.

Dr. Murray narrated his work of the past month. When he has produced a report on his results, he will send us a copy.

While he is away the medical staff of the surgical unit will undertake the follow up of some of his antigen-tested cases and add to them some more of their own. The idea behind following up is to observe the fading away of the antibodies, i. e. the falling of titre.

6) The question of secondary glandular involvement was discussed and Dr. Murray asked for material to be sent to the School of Medecine in London for Histopathology and biochemical analysis. TROPICAL

The nature of the Madura pigment is yet to be known.

7) Further cultures of the Nocardia Fungus have to be made, he having had no opportunity to do so while he was with us.

8) Dr. Murray asked if histological reports on operation specimens could be sent to him, or for that matter the material itself.

9) Epidemiology.

No further improvement on the current methods was suggested.

A proforma to be used by the dispensaries and Omdas was suggested to help collect figures on incidence. In fact the Omda of Hag Abdullah volunteered to supply such information on a type of form

10) The occurrence of Maduromycosis in animals in the Sudan has not been investigated before, at least no such information was passed to us by the vet's. The association of human cases with infected animals (for example, herds), if any, seems possible and needs investigation

Implantation into animals is being carried out by Prof. Lynch in Khartoum. Whether the monkey will prove susceptible remains to be seen.

THE VALUE OF SKIN TESTS IN DIFFERENTIATING BETWEEN MADUROMYCETOMA AND ACTINOMYCETOMA

BY

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As far as present knowledge goes mycetoma due to Madurella mycetomi is amenable only to surgical treatment and a number of authors have reported the failure of drug therapy in man (Abbott, 1956, Slade et al. 1956) and experimentally infected mice (Murray & Colichon 1962). On the other hand, there have been a number of hopeful reports regarding the medical treatment of mycetoma due to aerobic actinomycetes. Cures have been claimed by Dixon (1941), Peters (1945), Tucker & Hirsch (1949) and Dolan et al., (1960) using sulphonamides and Cockshott & Rankin (1960) using dapsone; most of these infections appeared to be due to Nocardia asteroides or Nocardia brasiliensis. In addition Mariat (1957), Mackinnon(1958) and Mariat & Satre(1961) have shown that most the aerobic actinomycetes are in some measure sensitive in vitro to such substances as penicillin, streptomycin, chloramphenicol, sulphonamides and dapsone. Extended clinical trials are wanting at the present time, although Gonzalez-Ochoa (1955) succeeded in curing 15 out of 21 patients infected with N. brasiliensis by giving dapsone over periods of 8 to 24 months.

The problem of differential diagnosis has to be faced. There is little if any clinical difference between mycetomas due to fungi and those due to actinomycetes, although the

colour of discharging grains, if present, gives a valuable clue. Absolute diagnosis can be made either by culturing the organism from the lesion or by histological examination of the infected tissue. Both these procedures are satisfactory but are relatively slow and call for equipment seldom available in the smaller hospitals of the tropics. It is also possible that biopsy is undesirable as it might conceivably promote lymphatic or local spread of the disease. If a rapid and reliable differential diagnosis could be made by skin tests the way would be open to medical treatment of actinomycetomas and surgical treatment of maduromycetomas. That such a reaction is feasible in nocardial mycetoma has been demonstrated by Gonzalez-Ochoa & Baranda (1953) and by Bojalil & Zamora (1963).

Specific skin reactions in guinea pigs sensitised to a variety of mycetoma causing organisms have been demonstrated (Murray, 1961) and in the present study two of the antigens (culture filtrate antigen and carbohydrate antigen) described in that paper were tested on man in Sudan. The carbohydrate antigen was found to be less effective than the culture filtrate antigen and reference to antigen in the following trials refers exclusively to the latter.

Culture filtrate antigens were prepared from Madurella mycetomi, Streptomyces somaliensis and Streptomyces pelletieri and were injected intradermally into the anterior of the forearms in 0.1 ml. quantities through No. 20 needles attached to Mantoux syringes. The diameters of any wheals produced were read at intervals thereafter up to 24 hours. A total of 19 patients were so examined on several occasions and the results are set out in the two tables. It is regrettable that in only 9 instances was the causal organism identified either by culture or histology or both but in every case grains were obtained and studied leaving little doubt that the first 6 cases in the table suffered from

actinomycetoma and the remaining 13 from maduromycetomi. The skin reactions were identical in every repetition of the tests.

Two things stand out from the tables. All 6 patients with actinomycetoma reacted strongly to the actinomycete antigens, particularly that from S. somaliensis but scarcely at all to the culture filtrate from M. mycetomi. Secondly, few of the maduromycetoma patients reacted to any of the antigens, No. 11 standing out as a notable and inexplicable exception. It seems from these results: 1. that patients with actinomycotic mycetoma react to intradermal tests with an antigen derived from S. somaliensis and 2. that patients with mycetoma due to M. mycetomi do not react to such antigens but may ~~ex~~occasionally react to an antigen derived from M. mycetomi.

SUMMARY

Six patients with actinomycetoma and 13 with maduromycetoma were injected intradermally with culture filtrate antigens derived from M. mycetomi, S. somaliensis and S. pelletieri. Those with actinomycetoma reacted to actinomycete antigens, especially that from S. somaliensis, but those with maduromycetoma either failed to react to any of the antigens or reacted only to that antigen derived from M. mycetomi.

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Table I

Skin reactions of people with actinomycetoma to intradermal injections of antigens from Madurella mycetomi (M), Streptomyces somaliensis (S) and Streptomyces pelletieri (P). The diameters of the wheals are recorded in millimetres.

No.	Colour of grains	Causal organism	Reaction diameter 5 & 24 hours after injection					
			5 hours			24 hours		
			M	S	P	M	S	P
1	Yellow	S.somaliensis	0	18	4	0	13	7
2	Yellow	Unknown	0	20	8	0	15	6
3	Yellow	Unknown	2	8	10	0	7	7
4	Yellow	S.somaliensis	0	10	10	0	9	6
5	Yellow	S.madurae	0	12	10	0	10	10
6	Tellow	Unknown	0	14	4	0	12	8

Table II

Skin reactions of people with madoromycetoma.

No.	Colour of grains	Causal organism	Reaction diameter 5 & 24 hours after injection					
			5 hours			24 hours		
			M	S	P	M	S	P
7	Black	Not cultured	0	0	0	0	0	0
8	Black	Not cultured	0	0	0	0	0	0
9	Black	Not cultured	0	0	0	0	0	0
10	Black	M. mycetomi	6	12	8	0	0	0
11	Black	M. mycetomi	50	10	9	50	0	0
12	Black	M. mycetomi	0	5	6	0	0	0
13	Black	M. mycetomi	0	4	2	0	0	0
14	Black	M. mycetomi	0	0	0	0	0	0
15	Black	Not cultured	14	0	0	0	0	0
16	Black	M. mycetomi	11	10	8	0	0	0
17	Black	Not cultured	0	0	0	0	0	0
18	Black	Not cultured	0	0	0	0	0	0
19	Black	Not cultured	0	0	0	0	0	0

Explanation of Therapeutic Result:

A very good or good result means that the chemotherapy led to a clinical cure or to the disappearance of the most important symptom or even bacteriologic sterilization.

The result is considered moderate if there is a marked regression of symptomatology or of the characteristic symptoms.

A bad therapeutic effect means no change in the evolution of the disease.