Case of Primary Nocardiasis of the Lachrymal Gland caused by a Species of Nocardia hitherto undescribed

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Case of Primary Nocardiasis of the Lachrymal Gland caused by a Species of Nocardia hitherto undescribed.

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Introduction.

The disease recorded in this paper represents a nocardiasis[1] or actinomycosis, in which the causal agent is a genus of fungus, characterized by having a mycelium composed of fine bacilliform hyphæ growing readily aërobically and producing anthospores.

In all probability it gained access to the lachrymal gland by settling on the surface of the eyeball, and working its way to the upper fornix of the conjunctiva, so entering one of the lachrymal ducts.

Clinical History and Description of the Case.

On May 12, 1918, the patient, M. B., a male, aged 22, from Dongola, was admitted to Khartoum Civil Hospital suffering from a swelling of the right eye, and an inability to open it. The swelling, which was of three and a half years' duration, and was gradually increasing in size, was attributed to a blow received from a native shoe. There was, however, no visible scar.

On examination, it was found that the eyelid could not be everted, but when raised, a thick yellow discharge poured out, and the whole of the conjunctival surface of the upper lid appeared to be rough and granular, with deeper ulceration in parts. On palpation, the swelling was painless, and of a doughy consistency, but without œdema; it

[1] Keratitis produced by mould fungi (kerato-mycosis-aspergillina) has been described in Fuchs's "Text-book of Ophthalmology," 4th ed. (translation), p. 259; also in Pyle's "System of Ophthalmic Practice" (Path. Bact., Collins and Mayou), p. 411.

extended between the eyeball and the roof of the orbit, causing a bulging forward of the fornix of the conjunctiva. There were no enlarged lymphatic glands, the eyesight was intact, the eyeball itself was not invaded, nor were its movements involved, and there was neither photophobia nor lachrymation. It was therefore evident that there was an intra-orbital growth lying between the eyeball and the bony roof, chiefly extending into the upper eyelid, and involving all the structures therein, except the skin and eyelashes, and ulcerating almost the whole of the palpebral surface of the conjunctiva.

A week after admission to hospital, the growth was dissected away

Fig. 1.

Fig. 2.

Fig. 1.—M. B., male, aged 22. *Nocardia lutea* of the right lachrymal gland. Upper eyelid swollen and firmly closed. Three and a half years' duration.

Fig. 2.—Eyelid raised with great difficulty so as to expose as much of the growth as possible. Shows eyeball pressed down ; also shows eyelid invaded.

under chloroform. In order to evert the eyelid, it was necessary to slit the external canthus, and so bring the growth into view. It appeared to have commenced in the lachrymal gland, and to have grown into the upper lid, invading the tarsal cartilage, and to have extended to a certain extent between the eyeball and the bony orbit along the ducts of the lachrymal gland.

The growth itself was a flattish lobulated body about $1\frac{1}{2}$ in. in length, and consisted of two ill-defined lobes, which were intimately

connected ; the one portion consisting of the lachrymal gland and the extension of growth into the eyelid, and the other probably consisting of a part of the growth and the orbital portion of the lachrymal gland. The conjunctiva was extensively affected.

When inspected with a hand lens the growth showed numerous light yellow gelatinous areas scattered throughout the lachrymal gland and the surrounding granulomatous-looking tissue. Some of these gelatinous areas were excised with aseptic precautions, and transferred to tubes containing sterile normal saline solution, thoroughly shaken,

Fig. 3.

M. B., male, aged 22. After removal of lachrymal gland and growth.

and emulsified. The emulsion was then examined with a lens, and found to contain minute yellow grains of a soft consistency, somewhat irregular in shape, and measuring about 0 2 mm. in diameter. These were removed with a platinum loop, and subjected to further washing with sterile normal saline solution, before being sown on suitable culture media.

The remainder of the growth was then placed in fixatives, and embedded for histological examination.

Pathological Histology.

Sections showed the morbid histological changes commonly associated with a fungus infection. There was marked vitreous degeneration of the tissues, with infiltration of plasma cells, and young connective tissue cells (fig. 4), and in the vicinity of the lachrymal ducts nocardial grains could be seen irregularly distributed, but in most instances separated from the surrounding tissue by a clear unstained

Fig. 4.

Section showing nocardial grain *in situ* and plasma cell infiltration. (× 200.)

area (figs. 4 and 5). No sheath proper could be detected. In the tissues the grains showed little structure in detail, owing to the dense matrix present.

In Gram-Weigert stained sections, numerous cellular elements known as fuchsin or Russell's bodies were found scattered throughout the gland and adjacent tissue. They retained Gram's stain, were

circular in shape, and occurred singly or in clumps, and varied in size from 2 μ to 15 μ in diameter (fig. 6). Their exact nature is unknown. They have been previously recorded as occurring in actinomycosis and maduromycosis, and there can be little doubt they are fungous in origin.

FIG. 5.

Section showing grain in lachrymal duct. (× 160.)

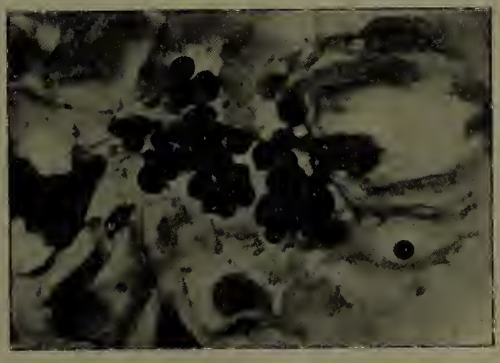

FIG. 6.

Section showing fuchsin (Russell's) bodies. (× 1,000.)

Structure of the Grain.

A portion of the grain flattened between a slide and cover-glass showed that it was composed of typical nocardial bacilliform hyphæ with rounded bodies or spores (fig. 7), the whole being held together in a dense matrix, which more or less concealed the hyphal and spore elements of the grain as seen in the tissues.

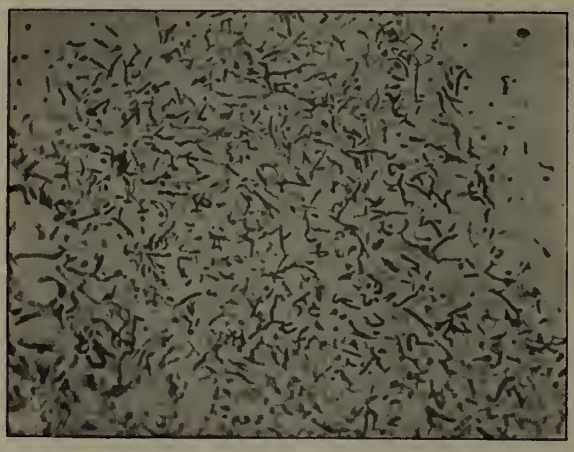

Fig. 7.

A portion of a crushed nocardial grain stained, showing bacilliform hyphal filaments and spores. (× 600.)

Cultivation.

When the grain was placed on suitable media growth readily occurred, and subcultures were carried out on various media. The fungus obtained from the grain was not only an aërobe, but also a facultative anaërobe. Under aërobic conditions growth readily occurred at 22° C. and 37° C., but ceased at 58° C. The optimum temperature appeared to be 30° C. In young cultures the hyphal filaments and spores were Gram-positive and acid-fast; in old cultures, however, the filaments and spores did not retain Gram's stain, and were non-alcohol fast. Well developed cultures invariably possessed a characteristic ochraceous orange colour (Ridgway's standards, Plate XV, 15, YO), gave off no odour, and showed no efflorescence.

In *Sabouraud's media* a raised convoluted ochraceous orange-coloured growth was produced without pigmentation of the surrounding medium (fig. 8). In *glucose agar* an ochraceous orange convoluted growth occurred without pigmentation of the medium. In *nutrient gelatine* stab cultures at 22° C. showed a greyish-coloured villous growth along the line of the stab, while the surface growth was convoluted and of a reddish-yellow colour. Neither pigmentation nor liquefaction of this medium occurred at the end of six weeks. In *inspissated ox-blood serum* the growth was convoluted, of a yellow colour, and more viscid

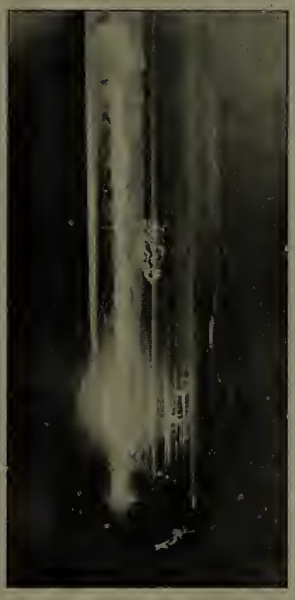

Fig. 8.

Fig. 9.

Fig. 8.—Three days old culture of nocardial grain on Sabouraud's medium showing the convoluted growth.

Fig. 9.—Culture on potato seven days old. Natural size.

in character than in other cultures. Neither liquefaction nor pigmentation of the medium was present. In *peptone broth* there occurred after forty-eight hours a general turbidity with pellicle formation, and a luxuriant growth of greyish-coloured cohering flocculi, followed later by a yellow pigmentation of the medium. In *litmus milk* neither acid formation nor clotting occurred. Old cultures showed a yellow pigmentation of the medium. On *agar agar* a raised moist ochraceous orange-coloured growth with paler edges was produced, without

pigmentation of the surrounding medium. The fungus did not show the same tendency to form a convoluted growth on this medium, as on glucose or Sabouraud's agar. On *potato* a luxuriant raised viscid ochraceous orange-coloured growth occurred with pigmentation, but no eroding of the medium (fig. 9). In *fluid sugar media* the growth was similar to the growth in peptone broth. Neither acid nor gas formation occurred in the various sugars employed.

Mycology.

Cultures showed, as in the grain, the presence of non-septate fine bacilliform hyphae with spores (fig. 10), which appear to be held

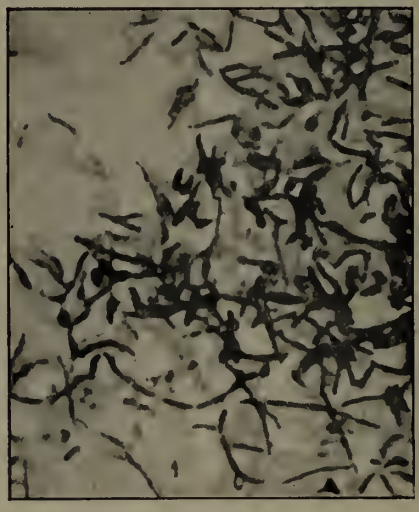

Fig. 10.

Smear preparation of a culture five days old. (× 1,000.)

together by a viscid pigmented substance apparently secreted by the fungus.

Some of the hyphal filaments, more especially in older cultures, showed irregular branching (fig. 11), and contained within their walls dark staining areas representing chains of spores (fig. 12), which apparently became detached or shed as the culture increased in age. Fig. 13 represents a section of a culture eight days old. Fig. 14 represents a section of a culture twenty-one days old, and shows the large number of spores with comparatively few hyphal filaments.

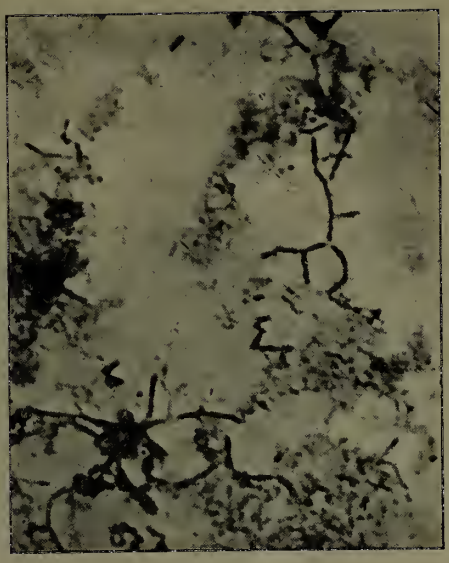

FIG. 11.

Smear preparation of a culture seven days old, showing the irregular branching of the hyphal filaments. (× 1,000.)

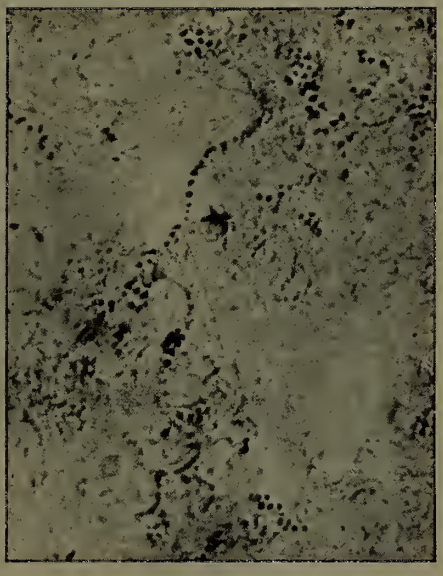

FIG. 12.

Smear preparation of a culture specially stained to demonstrate spores within the hyphal filaments. (× 1,000.)

In young cultures the hyphal filaments averaged 2 μ to 4 μ in length and 0·5 μ in breadth; some longer filaments measuring 12 μ in length were frequently present.

The spores, which apparently represented anthospores, were more or less circular in shape, and measured 0·7 μ to 1 μ in diameter.

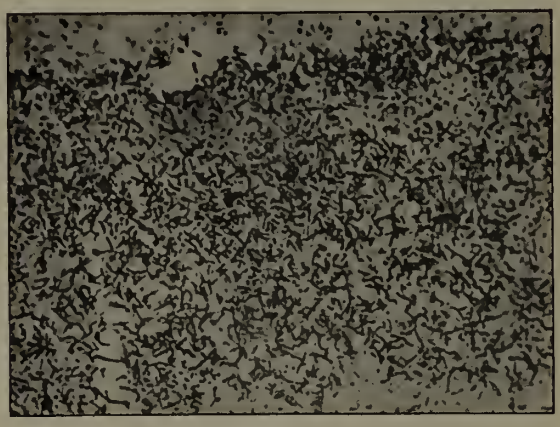

FIG. 13.

Section of a culture eight days old, showing hyphal filaments and spores. (× 300.)

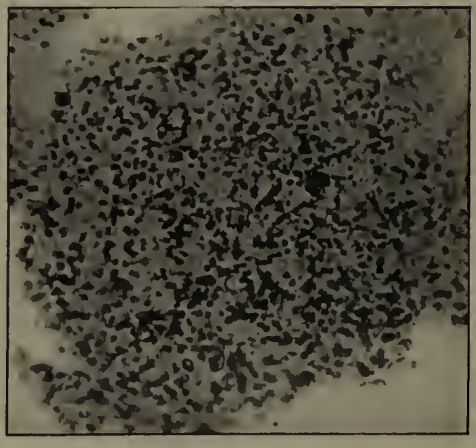

FIG. 14.

Section of a culture twenty-one days old, showing the large number of spores compared with hyphal filaments. (× 300.)

Animal Inoculation.

Experiments to prove the pathogenicity of this fungus have not been completed. The result of one experiment showed that it was not pathogenic for a grey monkey (*L. callitrichus*), when inoculated subcutaneously.

Classification of Fungus.

The fungus described belongs to Fuckel's class of *Fungi imperfecti* order *Microsiphonales*, genus *Nocardia* (De Toni and Trevisan 1889), section *Parasitica* (Foulerton 1910). It appears to be a new species and does not correspond with any fungus described in the literature available here. Recently Chalmers and Christopherson recorded a new species of nocardia, *Nocardia convoluta*, as occurring in the Sudan. *Nocardia convoluta*, however, differs from the above described fungus in: (1) Being non-acid fast, (2) liquefying inspissated ox-blood serum, (3) producing efflorescence, (4) producing buff-coloured growths.

Conclusions.

The fungus from this case represented a nocardia which was found parasitic in man. In young cultures it was Gram-positive acid-fast, and did not show club formation. It was readily cultivated, growing aërobically and anaërobically, without odour or efflorescence, producing ochraceous orange-coloured growths, which were convoluted on Sabouraud's medium, glucose agar, gelatin and blood serum. This nocardia neither liquefied gelatin nor inspissated ox-blood serum, produced no diastatic action on sugar media, and did not ferment milk.

As far as it is known it represents a species of nocardia new to human parasitology, and in view of its characteristic ochraceous orange-coloured growths in cultures the name *Nocardia lutea* (Christopherson and Archibald 1918) is suggested.