Subcutaneous infection due to *Aspergillus terreus*

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SYNOPSIS A case of subcutaneous infection by *Aspergillus terreus* is reported. Pus from the lesion contained spherules which did not appear to be related to the aspergillus. The nature of the spherules is discussed.

Aspergilli are capable of producing a variety of pathological conditions in man though infection of the subcutaneous tissues appears to be unusual. Organisms of this genus are widely distributed in nature and, while they may be frequent contaminants of wounds and abrasions, subcutaneous mycoses due to these or other fungi are extremely rare in Britain (Riddell, 1956). Aspergilli have been isolated from conditions such as maduromycosis in tropical countries though it is probable that in the majority of these cases their presence is due to secondary invasion (Franks and Guiducci, 1954). Infection of the subcutaneous tissues can occur in disseminated aspergillosis or by direct spread from deeper lesions, such as in bone (Cawley, 1947). These are, however, rare, and skin lesions were noted in only two out of 15 cases of disseminated aspergillosis reviewed by Grcevic and Matthews in 1959. The present case is reported as, in addition to being an example of infection due to *Aspergillus terreus*, a group not usually pathogenic to man, pus from the lesions contained spherules which do not appear to be related to the fungus or any other previously recognized pathogen.

CASE REPORT

The patient was a 58-year-old woman whose Wassermann reaction was found to be positive in 1957. A course of penicillin was given by injection into the buttocks, the last injection being given in September 1957. In October 1958 pain and tenderness were noticed in the left buttock and became progressively worse until March 1959, when a fluctuant swelling, surrounded by an area of induration, was found to be present at this site. The abscess was incised and 2 oz. of thick yellow pus was evacuated. At this time the patient's haemoglobin was 14.4 g./100 ml., the leucocyte count was 8,000/c.mm., with a normal differential count, and the E.S.R. (Wintrobe) was 5 mm./hour. The chest radiograph was normal.

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The wound healed in two weeks but during April 1959 two further abscesses developed in the surrounding tissues. The abscesses were incised after which the lesion healed and though there was some thickening of the surrounding tissues it has given no trouble since. Radiographs of the pelvis and left hip showed some fascial calcification extending posteriorly behind the neck of the left femur with the appearance of post-inflammatory calcification.

The patient's general health throughout this period was good and there were no significant previous illnesses. She had never been abroad and had no contact with pets or other animals.

INVESTIGATIONS Examination of the pus from each abscess gave essentially the same findings. Unstained films showed numerous fat globules and pus cells together with spherules, 20-200 μ in diameter, containing spore-like bodies, 5-10 μ in diameter (Figs. 1 and 2). Smears stained by the Gridley-Gomori method showed branching hyphae (Fig. 3). Culture of the pus on each occasion gave a heavy pure growth of *Aspergillus terreus*. The spherules were washed free from the pus and cultured separately but no growth was obtained. Samples of the pus were injected intraperitoneally into mice and guinea-pigs but no progressive lesions developed. On sacrificing the animals the only abnormalities were areas of thickening in the capsules of the liver or spleen. In section these were due to fibrosis surrounding spherules which were undergoing degeneration and provoking an inflammatory reaction (Fig. 4).

DISCUSSION

Aspergillus terreus appears to have a particularly low virulence for man. Only a few cases of infection due to this organism have been reported (Thom and Raper, 1945) though it produces pulmonary lesions in birds and is recognized as a cause of abortion in cattle (Ainsworth and Austwick, 1959). In the present case it is unlikely that the aspergillus was a contaminant or secondary invader as it was isolated in pure culture from each abscess that developed and

FIG. 1. Film of the pus showing the spherules and fat globules. Unstained, wet preparation $\times 140$.

FIG. 2. High-power view of the pus showing spore-like bodies within the spherules. Unstained, wet preparation $\times 550$.

FIG. 3. Smear of the pus showing a colony of the aspergillus. Gridley-Gomori stain $\times 310$.

FIG. 4. Section of spleen from a mouse injected intraperitoneally with pus from the lesion. There is fibrosis and an inflammatory reaction around degenerating spherules in the capsule of the spleen. Haematoxylin and eosin $\times 310$.

typical hyphae were identified in the pus. The infection was probably introduced during the course of penicillin injections after which it lay dormant, or only developed slowly, during the year before symptoms were first noticed. The rapid development of the lesion in the later stages may have been due to the appearance of a mutant more adapted to growth in the body than the original strain. Alternatively, minor trauma could have been responsible for spread of the infection to the superficial tissues, and in this connexion it may be significant that Henrici (1939) has shown that aspergilli can produce a toxin which will cause necrosis and pus formation on injection. Release of a toxin, such as this, from a localized lesion into the surrounding tissues might cause abscesses to form which could rapidly settle following evacuation of the toxic material.

A case with features resembling the present case was reported by Wybel in 1952. In this patient a granuloma developed around the cervical spinal cord following the intrathecal injection of penicillin for the treatment of pneumococcal meningitis. The symptoms, which were very indefinite in the early stages, gradually progressed until quadriplegia developed and death occurred three years after the meningitis. Hyphae, morphologically resembling those of aspergilli, were present in the granuloma. It was suggested that the penicillin therapy had assisted the establishment of the infection though in this case or the present case the mechanism by which this could occur is uncertain. Experimentally it has been shown that penicillin does not increase the susceptibility of mice to infection by the inhalation of aspergillus spores (Sidransky and Friedman, 1959) and though antibiotics increase the growth of candida *in vitro* (Huppert, Macpherson, and Cazin, 1953) this has not been demonstrated to occur with aspergilli. Aspergillus infections of the lungs are particularly liable to develop in patients treated with antibiotics, but this is usually considered to be due to the unrestricted growth of the fungus following the suppression of the normal flora by the antibiotics.

The identity of the spherules found in the pus has not been determined. All attempts at culture failed and there was no growth following inoculation into animals. It seems unlikely that they are related to the aspergillus because of their failure to grow and in addition no structure resembling them is found at any stage in the life cycle of the aspergilli. The general appearance of the spherules is similar to those found in coccidioidomycosis and rhinosporidiosis though there are differences in detail. The spherules of *Coccidioides immitis* have a thicker wall and culture is usually easy. In the sporangia of *Rhinosporidium seeberii* a pore can usually be identified but these sporangia, like the spherules in the present case, have not been cultured *in vitro*. If the spherules do indicate infection by a second organism then it is possible that there was symbiosis between the organisms and an increase in their pathogenicity.

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