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Case Report

Sub-cutaneous phaeohyphomycosis caused by *Cladophialophora devriesii* in a United Kingdom resident

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An 83-year-old diabetic man receiving corticosteroids developed a forearm lesion. Histology confirmed the presence of a dematiaceous fungus, with associated granulomatous inflammation. Culture of a biopsy yielded fungal colonies with branching chains of single-celled, melanised, dry, sympodial conidia, which were identified as *Cladophialophora devriesii* on the basis of morphology and rDNA gene sequencing. To date, *C. devriesii* has been a relatively rare cause of human disease. To our knowledge, this is only the second case to be described, and the first report of infection in a UK resident.

Keywords *Cladophialophora devriesii*, fungus, cutaneous, infection

Introduction

The genus *Cladophialophora* was created to accommodate *Cladophialophora carrionii* and has since grown to encompass many species including *C. arxii*, *C. bantiana*, *C. boppii*, *C. carrionii*, *C. devriesii*, *C. emmonsii*, *C. minourae and C. modesta*. All members of the genus are characterized by the acropetal production of dry conidia in sessile, or ascending chains, without obviously differentiated conidiophores. Conidia are one-celled, sub-spherical or limoniform, and have smooth melanized walls. The various species of the genus *Cladophialophora* can be distinguished by the length and degree of branching of conidial chains, and their resistance to fragmentation, and also to some extent on the basis of biochemical assimilation tests and thermotolerance [1]. *Cladophialophora* has a marked tendency towards pathogenicity, with reports of human infections attributed to most of the species described to date [2]. *C. bantiana* shows unambiguous neurotropism, and is one of the most pathogenic fungi described to date, having caused fatal brain infections in many otherwise healthy mammals, including humans [3]. *C. devriesii* has been described from a case of fatal disseminated phaeohyphomycosis [4,5]. In contrast, *C. carrionii* has been associated with numerous cases of human chromoblastomycosis [6], a distinct clinical entity in which hyphae are reduced to sclerotial cells. Here we report the first UK case of infection with *C. devriesii* and discuss the classification of the organism and its close relatives in terms of its primary virulence potential.

Case report

An 83-year-old man was referred to the Dermatology service, Hope Hospital, Salford, UK with a two-month history of a swelling of the right forearm. It was not enlarging but discharged pus intermittently. He denied any recent trauma to the site and had not received any prior treatment for this condition but did have an adjacent scar suggesting earlier trauma. He had a previous history of a squamous cell carcinoma completely excised from his left shoulder. He was a non-insulin dependent diabetic and also suffered with steroid-dependent chronic obstructive airways disease which required prednisolone 15 mg daily at the time of presentation. He had also been previously treated for carcinomas of the prostate and colon. In addition to

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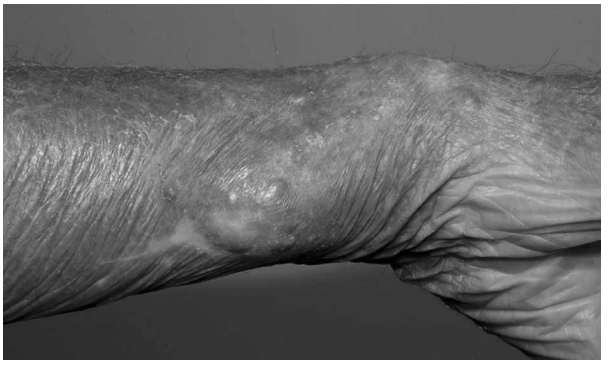

Fig. 1 Satellite papules of phaeohyphomycosis and nodule with associated scar ulnar border of right forearm.

prednisolone his medication included: verapamil, indapamide, risedronate, gliclazide, calcium carbonate, colecalciferol and inhaled salbutamol. He was allergic to penicillin. He had no contact with animals and as a result of his pulmonary disease found it difficult to venture outside his house.

On examination there was a firm fluctuant swelling over the ulnar border of the distal forearm measuring 3×3 cm (Fig. 1), which expressed pus upon application of gentle pressure to this area. He was also noted to have firm pink satellite papules along the ulnar border of the forearm. An atrophic scar was closely associated with the primary lesion but the patient could not remember how or when this injury had occurred. There was no lympadenopathy or organomegaly and his cardiorespiratory status was stable.

The abscess was extensively debrided under local anaesthetic and tissue was sent for histological, bacteriological and mycological analysis. He was commenced on ciprofloxacin and rifampicin.

Histology demonstrated granulomatous inflammation (Fig. 2) and associated brown fungal elements on staining with haematoxylin and eosin (Fig. 3). PAS diastase and Grocott's stains also confirmed the presence of septate fungal hyphae. It was intended that the patient be commenced on oral voriconazole but he experienced an exacerbation of his chronic respiratory disease requiring hospitalization. He unfortunately succumbed to this longstanding problem before treatment of the abscess could be commenced. Residual dermal papules were still present on his last admission.

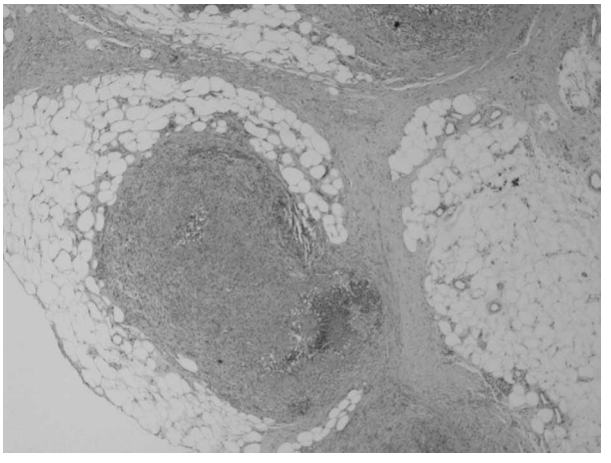

Fig. 2 Low power view of granulomas.

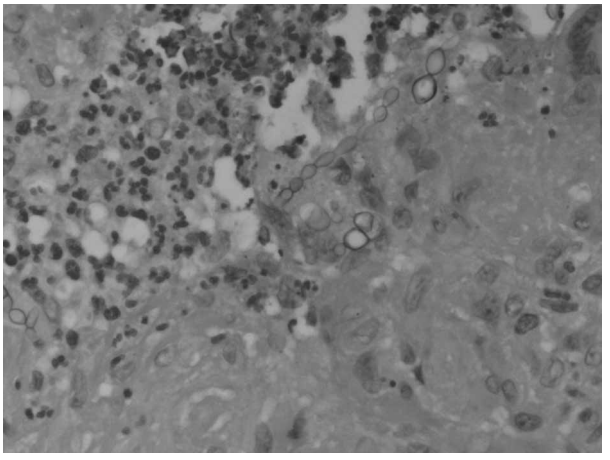

Fig. 3 Brown fungal elements of *Cladophialophora devriesii*.

Tissue subjected to mycological analysis yielded pure cultures of a powdery olivaceous fungus, which microscopically was consistent with *Cladophialophora*. Chains of limoniform conidia were relatively short (up to six conidia per chain), multiply branched, and formed on short denticles (Figs. 4 and 5). The organism grew well at 37°C, but very poorly at 42°C. These

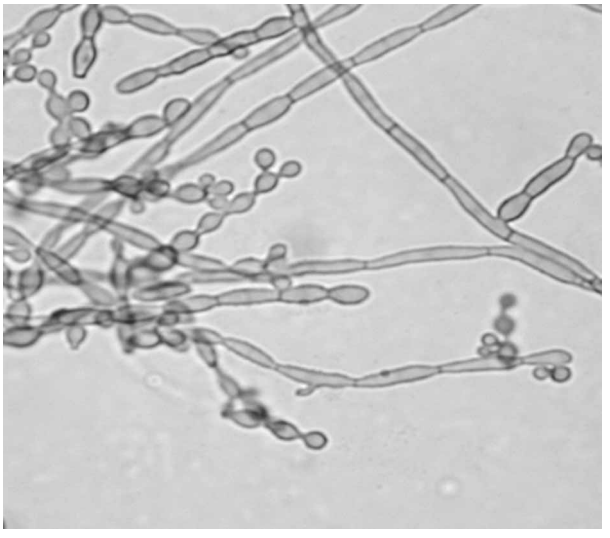

Fig. 4 Slide culture of NCPF 4275 on potato dextrose agar at 35°C (magnification ×40).

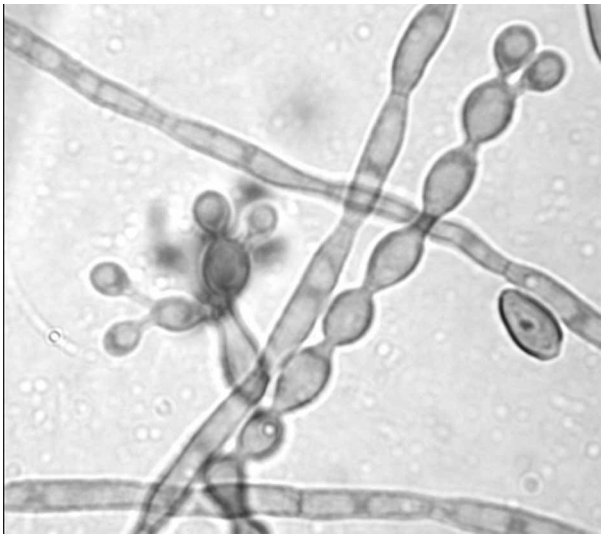

Fig. 5 As Fig. 4, magnification ×100, with oil.

features suggested a presumptive identity of *C. devriesii*, which was confirmed by sequencing of nuclear ribosomal repeat large subunit and internal transcribed spacer region 1 (ITS1) (EMBL accession numbers AJ 972912 and AM114417 respectively). This isolate was subsequently added to the National Collection of Pathogenic Fungi (NCPF), housed at the Mycology Reference Laboratory, Bristol, with the identifier NCPF 4275.

The isolate was initially handled on the open bench in the general microbiology laboratory at Hope Hospital, until its identity suggested a potential category (BSL) 3 pathogen. It was then transported to the HPA Mycology Reference Laboratory, where it was identified. One laboratory worker at Hope Hospital had several healing lacerations on his face, and was counselled with respect to post-exposure prophylaxis, which was not deemed necessary. Over a follow-up period of 6 months, he has remained well, with no development of skin lesions.

Discussion

Chromoblastomycosis is a chronic fungal infection caused by dematiaceous (pigmented) fungi, and characterized by the formation of clusters of small, round, thick-walled, brown sclerotic cells in tissue sections. It is rare in the United Kingdom with most cases being imported. The organisms responsible are soil saprophytes and are usually introduced into the skin following trauma [3]. Organisms known to cause chromoblastomycosis include *Fonsecaea pedrosoi*, *Phialophora verrucosa*, *Cladophialophora carrionii*, *Fonsecaea monophora* and *Ramichloridium cerophilum* [6–8]. Although the presentation of small, pink, painless papules is characteristic of chromoblastomycosis, the histological presentation in our patient did not fit with this condition as septate hyphae were observed, so it is better described as sub-cutaneous phaeohyphomycosis.

C. devriesii is a rare human pathogen and prior to this report has been isolated from only one individual when the organism was first described. That patient was a 26-year-old woman from Grand Cayman who had a breast lesion caused by *C. devriesii* infection [4], and which required surgical excision. This infection subsequently recurred locally and spread widely to eventually result in her death from disseminated infection [5]. She was HIV negative and no other evidence for a compromised immune system was reported.

In the present report, we isolated *C. devriesii* as the causative organism from skin nodules with macro- and microscopic appearances typical of phaeohyphomycosis. The individual in our case denied any traumatic antecedent event, although the presence of an old atrophic linear scar in close proximity to the abscess would seem the logical site for inoculation following relatively minor trauma. Interestingly, the individual had no history of foreign travel for many years preceding the development of the fungal lesion. Two possibilities exist. The first is that his age and the long-term immunosuppression with oral corticosteroids may have contributed to establishment of infection years after inoculation with the causative agent abroad. The second is that this infection was actually acquired in the UK.

Most *Cladophialophora* spp. (except those described from single infections of humans) have been isolated from wood in warm arid areas [9], it is impossible to speculate on the exact source of *C. devriesii* in this case as this organism has not previously been reported as a saprophyte in the UK. Regardless of the exact source of infection, this report is the first documented case of human infection with *C. devriesii* in the UK. Unlike those other members of *Cladophialophora* that have been frequently associated with cutaneous phaeohyphomycosis (*C. boppii, C. emmonsii* and *C. carrionii*) and which are classified as BSL 2 pathogens, *C. devriesii*, like *C. arxii* and *C. bantiana* also appears capable of causing systemic and local infection (albeit with localization outside the nervous system).

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