Case Study of Malassezia pachydermatis in an adolescent undergoing chemotherapy

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Introduction

Malassezia are basidiomycetous yeasts that are mostly lipid dependent, inhabiting the mucosa of humans and other mammals, as well as forming a major part of the normal skin microbiome (Findley et al. 2013, *Nature* 498 (7454); 367; Theelen et al. 2018, *Medical mycology* 10 (1): S10). There are 17 species within the genus *Malassezia* (Figure 1). *Malassezia* in humans are often involved in common dermatological conditions, such as atopic eczema, folliculitis, pityriasis versicolor and seborrheic dermatitis (Velegraki et al. 2015, *PLoS pathogens* 8;11).

Malassezia pachydermatis falls under the genus *Malassezia*, and is considered a zoophilic, being the most common veterinary *Malassezia* species found on the skin and in the ear canal of dogs and cats, frequently causing seborrhoic dermatitis and otitis externa. *M. pachydermatis* is only occasionally found on human skin and, if it is, it is normally associated with pet owners (Theelen et al. 2018, *Medical mycology* 10 (1) : S10). *M. pachydermatis* is a rare cause of systemic infection, and if it does occur it is most commonly associated with neonates receiving lipid supplementation (Chen et al. 2017, *Journal of Microbiology, Immunology and Infection* 50 (4): 514; Iatta et al. 2013, Medical mycology 52 (3): 264-9) As far as we know *M. pachydermatis* is very rarely implicated in systemic infection in adults.

Systemic infections caused my *Malassezia* require prompt identification, removal of any central lines or sources and discontinuation of lipid supplementation or total parental nutrition (TPN) (Velegraki et al. 2015, *PLoS pathogens* 8;11). It is widely thought that the pathogenicity of developing *Malassezia* lesions in all mammals is inversely related to the host immune system (Cafarchia et al. 2008, *Acta tropica* 107 (1): 25-9). Importantly *M. pachydermatis* has been found to persist on the surfaces of incubators for long lengths of time (A Van Belkum et al. 1994, *Journal of Clinical Microbiology* 32: 2528-2532).

Topical antifungal agents are recommended for the management of localized skin disease, while more widespread infections requires administration of systemic anti fungal treatment, the preferred agents being fluconazole or liposomal amphotericin B (Gaitanis et al. 2012, *Clinical microbiology reviews* 25 (1): 106-41; Lortholary et al. ESCMID/ECMM guideline 2013, *Mycoses* 1;56:35-6). Limited cases of systemic infections caused by *M. pachydermatis* have been documented in adults, two of which were being treated for acute myeloid leukaemia and one in an adult with multibacillary leprosy (Choudhury et al 2014, *Journal of the RCPA* 1;46(5):466-7; Roman et al. 2016, *Medical mycology* 1;12:1-3).

Here we describe a case of *M. pachydermatis* fungaemia in an adolescent undergoing chemotherapy.

Microscopic appearance

The typical microscopic appearance of *Malassezia* is a flask-shaped appearance due to the monopolar budding of the round or oval cells (Lortholary et al. ESCMID/ECMM guideline 2013, *Mycoses* 1;56:35-6). The microscopic examination of the lipid-dependent strains showed ellipsoidal yeast cells with buds formed on a broad base, characteristic of *M. pachydermatis*.

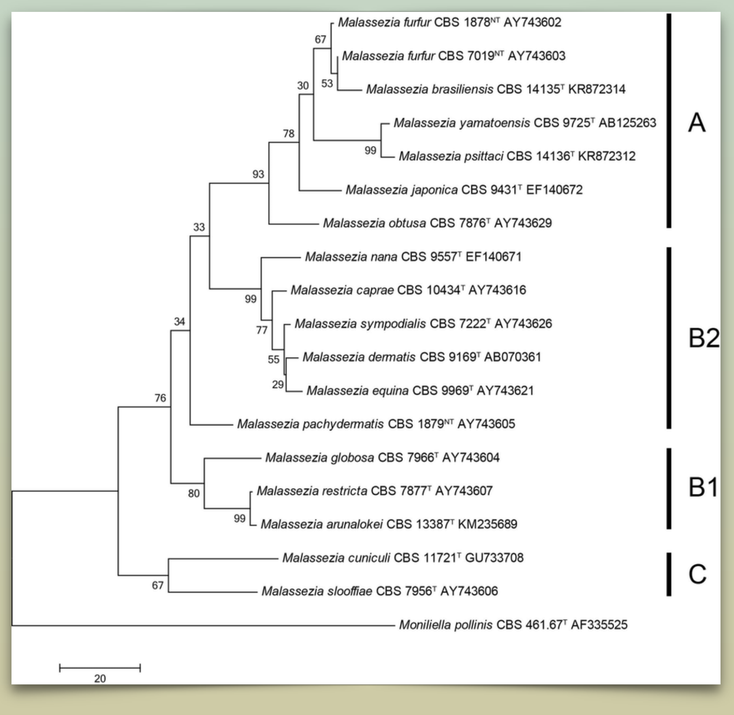

Figure 1. *Malassezia* genus (Theelen et al. 2018, *Medical mycology* 10 (1): S10)

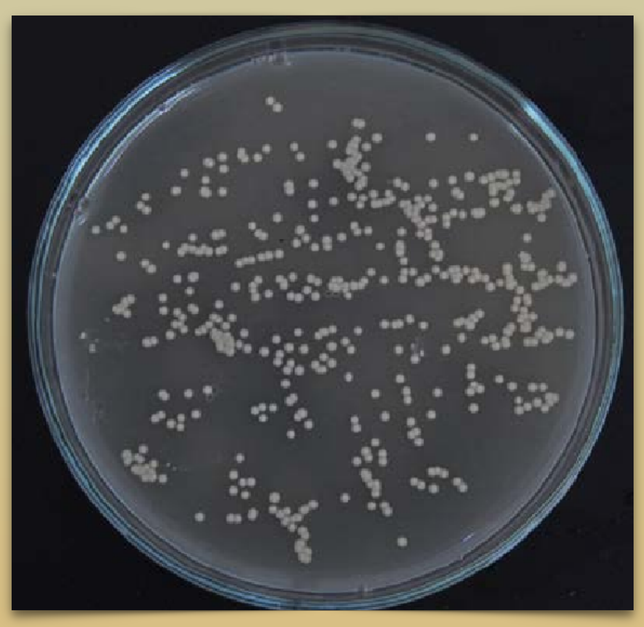

Figure 2. Colony morphology of *M. pachydermatis* on SGA (Metiner et al. 2016, Journal of veterinary medicine 42 (2) 117-121

Case Presentation

A 16-year-old white British male presented with a one week history of a rapidly enlarging neck swelling, progressing to the development of cervical and inguinal lymphadenopathy with an enlarged right testis. A computed tomography (CT) scan of his neck, chest, abdomen and pelvis demonstrated multifocal large lymph nodes in the neck, inguinal region and mesentery. A left cervical biopsy was performed that demonstrated a lymphoid malignancy, with CD20 positive cells in keeping with a high grade B non-Hodgkin cell lymphoma: Burkitts lymphoma. He was started on steroids and a combination of cyclophosphamide and vincristine (COP) chemotherapy via a peripherally inserted central catheter (PICC). The chemotherapy was subsequently converted to Rituximab, Cyclophosphamide, Vincristine, Prednisolone, Doxorubicin and Methotrexate (R-COPADM) as part of the Inter B-NHL Ritux 2010 strategy with curative intent. He had a suboptimal response to this and so his regimen was escalated to group C: cyclophosphamide, vincristine, doxorubicin and methotrexate (CYVE).

Eighteen days after initiating the first cycle of CYVE the patient was admitted with febrile neutropenia (temperature 38.1*C, white cell count 0.36 x 10^9/L (4.0-11.0), neutrophil count 0.01 x 10^9/L (1.5-8.0), lymphocytes 0.32 x 10^9/L (1.0-4.0), CRP 17mg/L. (<6). There were no localising symptoms or signs. Blood cultures (BacT/ALERT®, bioMérieux) were taken from his PICC line and he was initiated on empirical treatment of piperacillin/tazobactam (4.5g every 8 hours). After 3 days of incubation a yeast was isolated from the aerobic bottle. His PICC line was removed and he was commended on intravenous (IV) micafungin 100mg once a day (OD) via a peripheral cannula empirically pending identification of the yeast. The isolate was referred to the Mycology Reference Laboratory, Bristol. The isolate was purple on CHROMagar™, and confirmed to be *Malassezia pachydermatis* by matrix-assisted laser desorption time-of-flight (MALDI-TOF) mass spectrometry (ID score 2.063).

His treatment was subsequently rationalised to IV fluconazole 400mg OD, and he completed 4 days IV via a peripheral cannula, following which he had a further 10 days of the same dose orally (PO), completing a two week course in total. The isolate was found to be susceptible to amphotericin B (MIC=0.125mg/L), itraconazole (MIC<0.03mg/L) and voriconazole,(<0.03mg/L), but had intermediate susceptibility to fluconazole (MIC=4mg/L). He clinically improved and subsequent blood cultures were sterile following this.

On further questioning the patient reported that his dog had a sore and it was recommended that the animal be reviewed by the local veterinary team, it was thought that this was the original source of infection.

Discussion

Information about *M. pachydermatis* fungaemia in humans remains limited, particularly, beyond the neonatal age.

Due to the lipid-dependent nature of the species, diagnosis of *Malassezia* remains challenging. Special media are required such as Dixon or modified Leeming and Notham agar (Lortholary et al. ESCMID/ECMM guideline 2013, *Mycoses* 1;56:35-6). The species may then be confirmed and distinguished using MALDI-TOF mass spectrometry, as it was in this case. *M. pachydermatis* is easier to grow than the more commonly found *M. furfur.* Unlike other *Malassezia* species, *M. pachydermatis* has the ability to grow without fat, and hence it is able to grow on Sabouraud glucose agar (SGA) without lipid supplementation (15). However, precisely due to the ability of *M. pachydermatis* to grow without lipids, it can often be misidentified as a *Candida* species which can then lead to inappropriate therapy, which becomes problematic as *Malessezia* spp. are intrinsically resistant to echinocandins. As observed in our isolate, most strains of *M. pachydermatis* also exhibit reduced susceptibility to fluconazole and flucytosine. Pachydermatis may even be more resistant but bigger doses of azoles are thought to be adequate.

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