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Malassezia furfur fungaemia in a ventilator-dependent patient without known risk factors

缺乏已知風險因素的依賴呼吸機患者的馬拉塞黴菌屬頭皮屑真菌血症

Malassezia furfur **is the lipophilic yeast which causes tinea versicolor and is an uncommon cause of fungaemia. It usually occurs in the context of hyperalimentation with lipid emulsion, immunosuppression, or the presence of a central venous catheter. We report a case of a ventilator-dependent patient who developed *Malassezia furfur* fungaemia in the absence of these known risk factors. A likely risk factor in this patient was receipt of multiple courses of broad-spectrum antibiotics. This case highlights the importance of recognising *Malassezia furfur* as a cause of fungaemia, as well as the need for special culture techniques to aid identification.**

馬拉塞黴菌屬頭皮屑是引起藓雜色的親脂性酵母，是引起真菌血症的罕見原因。馬拉塞黴菌血症主要發生在接受脂質乳劑治療、或免疫力受抑制、或有主要靜脈導管治療者身上。我們報告了一名依賴呼吸機的患者，在沒有已知風險因素下患了馬拉塞黴菌屬頭皮屑真菌血症的病例。對於這名患者，可能的風險因素是接受了多重廣譜抗生素療程治療。這病例突顯了馬拉塞黴菌屬頭皮屑作為真菌血症誘因的重要性，以及需要特殊培養物技術幫助鑒定的重要性。

Introduction

Malassezia furfur is an uncommon cause of fungaemia. It usually occurs in the context of the presence of a central venous catheter,[1] hyperalimentation with lipid emulsion,[2] and immunosuppression.[3] We report the case of a ventilator-dependent patient who developed *M furfur* fungaemia in the absence of these known risk factors. A probable risk factor in this case was the need for multiple courses of antibiotics. This case highlights the fact that *M furfur* fungaemia can occur in the absence of the classically described risk factors.

Case report

A 39-year-old man suffered an industrial accident in April 1999, resulting in facet dislocation of cervical vertebrae C2/3 and C3/4, fracture of the C5/6 anterior arch, and a burst fracture of C7 vertebral body. Complications of spinal shock and respiratory failure were evident and the patient was admitted to an intensive care unit (ICU) for mechanical ventilation and stabilisation of the cervical spine by halo-vest. Intravenous methylprednisolone (3 g in total) was given after admission on the recommendation of orthopaedic surgeons, for the management of spinal shock. An elective tracheostomy was fashioned in May 1999.

The patient suffered multiple episodes of sepsis during his ICU stay between April and September 1999. This included eight episodes of ventilator-associated pneumonia (respiratory tract secretions growing variously *Acinetobacter baumanii*, *Stenotrophomonas maltophilia*, *Candida* species, and methicillin-resistant *Staphylococcus aureus)*, three episodes of urinary catheter-related

Key words:
Fungemia;
Malassezia;
Risk factors

關鍵詞：
真菌血症；
馬拉塞黴菌；
風險因素

HKMJ 2002;8:212-4

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cystitis (isolates included *Staphylococcus epidermidis*, *A baumanii*, and *Candida* species), one episode of intravenous catheter-related enterobacter septicaemia, and one episode of culture negative gastroenteritis. He received multiple courses of antibiotic treatment with the following antibiotic agents: ampicillin/sulbactam, ceftriaxone, ticarcillin/clavulanate, vancomycin, gentamicin, amikacin, cefoperazone/sulbactam, ciprofloxacin, metronidazole, trimethoprim/sulphamethoxazole, rifampicin, and fusidic acid.

The halo-vest was removed after 3 months of ICU stay upon confirmation of good alignment and satisfactory fracture healing. However, the patient remained tetraplegic and ventilator-dependent. He was transferred to the Department of Medicine and Geriatrics for ventilator rehabilitation in September 1999.

Two weeks after transfer, the patient developed a high, swinging fever of up to 40°C. Blood and urine cultures were taken. The urine was sterile. The patient did not have an intravenous catheter in the preceding week and there was no sign of phlebitis in previous intravenous sites. Chest radiography revealed collapse of the left lower lobe of the lung. A bronchoscopic toilet of the airway was performed. Purulent secretion was found obstructing the left lower lobe bronchus which was suctioned clean, and the left lower lobe re-expanded. The patient was given intravenous piperacillin/tazobactam and amikicin as empirical treatment. His fever did not respond to this treatment. Subsequently, bronchial washing showed a pure growth of *Haemophilus parainfluenzae* and the antibiotic regimen was changed to intravenous cefuroxime in accordance with sensitivity testing. Despite this antibiotic regimen and bronchoscopic toilet, the fever persisted. Cefuroxime was discontinued temporarily after 5 days to eliminate the possibility of drug-induced fever. The intravenous site showed no evidence of phlebitis, but the catheter was changed and the catheter tip sent for culture, which was later reported to be negative. Fever persisted with a peak of 40°C. Altogether three specimens for blood culture were taken during this febrile episode.

One week after the collection of blood culture specimens, turbidity was noted in the two aerobic bottle sets, and budding yeast cells were shown on Gram stain. The culture was then subcultured to Sabouraud agar, blood agar, and McConkey agar and incubated at 35°C. Dust-like colonies grew on the McConkey and Sabouraud agar after 2 days of incubation but not on the blood agar culture. Gram staining of the colonies showed 'bottle shaped' budding yeast cells, with a collarette-like thickening seen at the junction of the mother and daughter cells (Fig). The yeast cells could not be identified with the API 20 C AUX (BioMerieux, Marcy l'Etoile, France) and the Vitek Yeast Biochemical card (BioMerieux, Marcy l'Etoile, France). However, the growth of colonies of approximately 2 mm in diameter could be obtained by subculturing to Tween 80 blood agar. Based on the characteristic cell morphology seen and the growth requirement of long-chain fatty acids, *M furfur* was identified.

The patient was reviewed after *M furfur* was identified. Wood's light examination of the skin showed no evidence of tinea versicolor and skin scrapings did not grow the organism. Blood counts and a peripheral blood smear were normal, and serology for human immunodeficiency virus was negative. Total lymphocyte counts were normal. CD4 and CD8 counts were not requested as these are not reported as specific risk factors in the literature. A transoesophageal echocardiogram showed no evidence of endocarditis. Ultrasonogaphy of the abdomen and computed axial tomography of the brain, thorax, and abdomen showed no evidence of systemic or metastatic fungal infection.

Intravenous amphotericin B 0.7 mg/kg body weight was given for 10 days, with a prompt reduction in the fever seen. However, the patient developed severe hypokalaemia. Consequently, amphotericin B was substituted with oral fluconazole 200 mg daily for 14 days, which was discontinued due to hepatic dysfunction. The patient remained afebrile afterwards and four repeated blood cultures in the subsequent 2 weeks did not recover any organism.

Discussion

The genus *Malassezia* has three member species: *M furfur*, *M sympodialis* (a skin flora yeast of humans), and *M pachydermatis* (a skin flora yeast of other warm-blooded animals). *Malassezia furfur* and *M sympodialis* can be differentiated from *M pachydermatis* by their obligatory growth requirement of long-chain fatty acids. *Malassezia furfur* can be further differentiated from *M sympodialis* by the fact that *M furfur* can have its lipid requirements supplied by oleic acid or Tween 80.

Malassezia furfur is the causative agent for tinea versicolor and is an occasional cause of fungaemia. It would seem that *M furfur* was the pathogen responsible for this patient's prolonged febrile illness given that it was grown repeatedly from blood culture specimens and no other likely infection was identified. Moreover, *M furfur* does not appear to be an important contaminant of the hospital's blood culture specimens, as no other positive blood cultures have been encountered over the past 5 years. As skin scrapings from this patient were also sent for culture and were negative, contamination from the patient's own skin was unlikely. The patient responded promptly to antifungal therapy, after failing to improve after guided antibiotic therapy, further supporting the role of *M furfur* in causing this patient's illness.

In past reports, *M furfur* fungaemia has been identified in neonates or adults requiring a central venous catheter,[1] with the use of intravenous fat emulsions,[2] in patients who were immunocompromised,[3] or in patients with a combination of these risk factors.[4-8] There have been three cases of

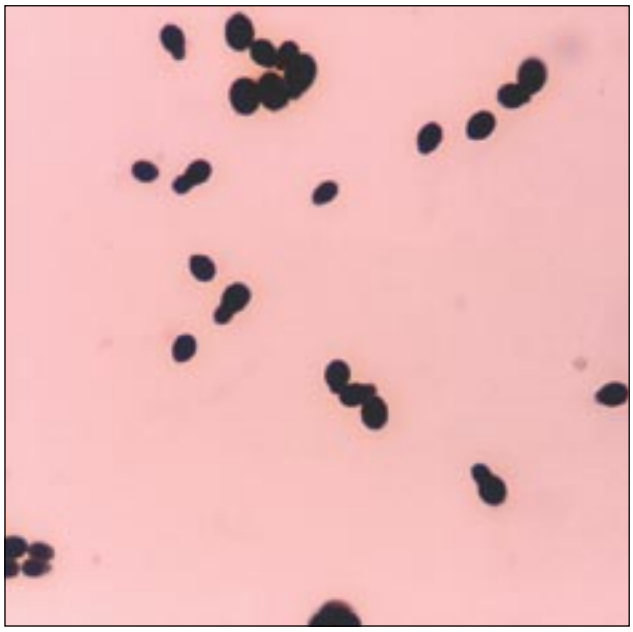

Fig. Bottle-shaped, budding yeast cells evident in blood culture (Gram stain, x100)

M furfur fungaemia reported in patients without these risk factors. However, one patient had a history of hairy cell leukaemia, splenectomy, and metastatic adenocarcinoma of the prostate,[9] another had lung cancer, and the third was diabetic and had a central venous catheter in situ for haemodialysis.[10] It could thus be argued that these patients were, in fact, immunocompromised.

This patient did not have any of the accepted risk factors for *M furfur* fungaemia. Although he had been given methylprednisolone, as he developed *M furfur* fungaemia almost 5 months later, it is difficult to directly attribute the current episode of fungaemia to corticosteroid use. This contrasts with a previous report of seven patients in whom immunosuppression was considered a risk factor for *M furfur* fungaemia. These latter patients had a combination of risk factors, including neutropenia, intravenous lipid emulsion intake, chemotherapy and/or corticosteroid intake in the same month as *M furfur* was cultured.[3] All four patients who had received corticosteroid therapy in the month *M furfur* was cultured, also had some other risk factor for fungaemia, such as neutropenia, intravenous lipid intake, or chemotherapy.[3] For the current patient, it remains speculative whether corticosteroid use 5 months previously contributed to this episode of fungaemia. Other known risk factors were not present. It would seem that the major risk factor for fungaemia in this case was the use of multiple courses of broad-spectrum antibiotics received for treatment of other infections. The portal of entry was most likely a contaminated peripheral intravenous catheter, despite the fact that the organism was not recovered from either the catheter or the skin.

Conclusion

This case serves to illustrate that *M furfur* fungaemia can occur in the absence of usual risk factors such as hyperalimentation, indwelling central venous catheter use, or immunosuppression. A probable risk factor for this patient was treatment with multiple courses of broad-spectrum antibiotics. Whether corticosteroid use 5 months before this episode was contributory is debatable. This case also highlights the value of subculturing suspicious yeasts to long-chain fatty acid overlaid Sabouraud agar or Tween 80 blood agar to confirm the identity of the infective organism.

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