抗真菌藥 Fluconazole 對白色念珠菌臨床菌株形態學影響之探討

Surveillance for Morphological Effect of Antifungal Agent, Fluconazole, on Clinical Isolates of Candida albicans

中文摘要

白色念珠菌是二倍體真菌，生活史中沒有被發現有性生殖，它是造成伺機性感染的最常見真菌。已有研究發現白色念珠菌的致病能力主要就是來自白色念珠菌能自由的在酵母菌形 (Yeast) 與菌絲形(Hyphae) 之間做轉換。最近又有研究指出此菌株在 White-Opaque 表現形態之間的轉換是與生物膜形成以及特殊致病毒性有相關。可自發、可逆性且高頻率的形態轉換是白色念珠菌在人體最主要的致病機制，而形態間的轉換受環境條件影響。Triazoles 類抗真菌藥物中的 Fluconazole 最常被用來治療白色念珠菌感染。而作者觀察以 Fluconazole 治療失敗的白色念珠菌臨床菌株 CaF，發現它與標準菌株 ATCC 22816 在 Fluconazole 環境下的形態學變化不一樣。本研究發現 Fluconazole 會引發菌株 CaF 與 ATCC 22816 進行高頻率的 White-to-Opaque 轉換，由大約 5x10-4 與 4x10-3 提昇至 17.6% 與 15.0%。菌株 CaF 會產生有內涵體的大細胞及長串型酵母。這些發現尚未曾在文獻中被提到過。經由在 Lee’s medium 中以 E-test 實驗，發現在抑制圈內形成 Opaque 菌落高達 100%。這些形態學變化是否與致病毒性或是抗藥性有關聯，還需要更進一步的研究才能瞭解。

英文摘要

Candida albicans is a diploid, apparently asexual fungus. C. albicans is most common fungal pathogen of opportunistic infections. Pathogenic virulence of C. albicans was reported depending on morphogenesis between yeast and hyphal forms. One study found that morphologic switching of White-Opaque phase was related to biofilm-formation and pathogenic virulence. Automatic, reversible and frequent morphological switching is the important virulent factor for human infection of C. albicans. Morphological switching could be induced by environmental factors. Fluconazole, one of the triazoles, is the most common agent prescribed for candidiasis. The author found one clinical isolate of C. albicans, CaF, which was failed to be treated with fluconazole. This clinical isolate had different morphological change, compared to isolate of C. albicans ATCC 22816, under environment containing fluconazole. This study disclosed that fluconazole induced high frequent White-to-Opaque switching in both CaF and ATCC 22816, from frequency of 5x10-4 and 4x10-3 to 17.6% and 15.0%, respectively. Large cells containing inclusion bodies and yeast in chain were found in CaF. These findings were never described in the

literatures before. Our study of E-test on Lee’s medium, both isolates were found with 100% of Opaque colonies in inhibitory zone. The role of these morphological changes in pathogenesis and drug resistant is still unknown. This study might point out a new way for further studies on clinical pathogenesis and drug resistance.