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Candidiasis Treatment Should Pay Attention to the Immune Changing Patients

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Abstract

The guideline of the Infectious Diseases Society of America (IDSA) about candidiasis is a key standard for clinical doctors to treat patients, and textbook to teach medical students. However, in the progress of clinical treatment and documents checking, the immune changing patients, who suffered candidiasis, may be mismatched to the clinical treatment guidelines. The opinion could be shown by the literature of gastrointestinal system, and respiratory system, which suffered severely fungal infection mostly, mainly connected with the outside world and inside organ systems of the human body. They could show some patients have been excess treatment, and we should pay attention to the immune changing patients.

Keywords

Candidiasis, Infectious Diseases Society of America, Esophageal Candidiasis

1. Introduction

Candida is widespread exit on an animate object in nature, which is normal commensal of humans, and inhabits even in the inner of human body like the gastrointestinal tract, the female genital tract, etc. [1]. Candidiasis can present a wide variety of symptoms which include fatigue, allergies, gastrointestinal system, neurological system, genito-urinary system, respiratory system, skin, and so on. As the first case of candidiasis has been described in debilitated patients, the advent of candida species as common human pathogens, dates to the introduction of modern therapeutic approaches that suppress normal host defense mechanisms [2]. Numerous reviews of cases of candidiasis have identified the following predisposing factors or conditions: antibacterial agents [3],

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indwelling intravascular catheters [4], hyperalimentation fluids [5], indwelling urinary catheters [3], parenteral glucocorticoids [6], respirators [7], neutropenia [4], abdominal and thoracic surgery [7], gastroesophageal reflux [8] [9], cytotoxic chemotherapy, immunosuppressive agents for organ transplantation [3], severe burns [8] [9], low-birth-weight neonates [10], using illegal drugs [11], HIV infection [10], and so on. Of these relatively recent advances, the most important are the use of antibacterial agents that alter the normal human microbial flora and allow nonbacterial species to become more prevalent in the commensal flora, and the host's immune response is comprised [12]. Candidiasis is the most common opportunistic fungal infection as a result of both the ubiquity of the organisms and the increasing number of patients with the above mentioned risk factors for infection with these organisms [13]. Candida species cause a wide spectrum of diseases ranging in severity from localized mucous membrane infection to life-threatening disseminated disease [14]. Local infections are often related to overgrowth of Candida as a result of changes in the normal flora. In an immunosuppressed host, especially a patient with neutropenia or AIDS, general fungal infection is common [15]. At present, the medical therapeutics is commonly used. Candida species are now among the most common nosocomial pathogens, which have a trend of increase [16]. In the United States, these species are the fourth most common isolates from the blood of hospitalized patients [17].

2. Candidiasis Treatment of the Immune Changing Patients

We could discuss the neglected immune changing patients form the esophageal candidiasis of gastrointestinal system firstly. The recommend treatment of IDSA (Infectious Diseases Society of America) to esophageal candidiasis is systemic antifungal therapy is required [18]. Oral arrange fluconazole at a dosage of 200 - 400 mg (3 - 6 mg/kg) daily for 14 - 21 days. Their references are almost completely based on HIV patients or cancer patients, which neglect other patients [19]-[21] (we will show all the neglected patients in behind, and their condition are different with the selected candidiasis patients). Yakoob J and colleagues have reported that candida esophagitis patients responded well to treatment with nystatin in in non-HIV population [22]. These candida esophagitis patients were treated with either nystatin 5 ml DS/fluconazole 100 mg a day by mouth for 5 days. None of these candida esophagitis patients were found to be resistant to this treatment. As treatment with fluconazole was expensive, fewer patients were prescribed with fluconazole treatment. The implications of their study are that in Pakistan candida esophagitis is associated with chronic diseases and those on treatment with corticosteroids and antibiotics are redisposed to it. If the immune changing candida esophagitis patients suffered fungal infection by gastroesophageal reflux, or the above mentioned condition, and this condition was corrected by treatment, their immune condition should be considered to be normal. So they should be primarily treated by cystatin not fluconzazole.

So the immune changing patient should not suffer long period of expensive treatment and high expenditure. What is more, in the land of the blind, the one-edged man is king. In the area of antibiotics, when penicillin is lost its corona after the appearing of imipenem and cilastatin sodium to treat severe infection disease in no more than two hundred years, imipenem and cilastatin sodium has lost its corona after the appearing of fungus in no more than several decades. We may conclude even if the antibiotics or antifungal drug not to perplex us, another new microorganism will be appeared, because human body is perfect to culture life apart from ourselves. In fact, with the introduction of antifungal agents, the causes of Candida infections shifted from an almost complete dominance of *C. albicans* to the common involvement of *C. glabrata* and the other species [15]. The non-*albicans* species now account for approximately half of all cases of candidemia and hematogenously disseminated candidiasis [23] [24]. So, if the nystatin could treat some esophageal candidiasis patients, the guideline should not advise fluconazole is the primary drug. CDC also noted that some OPC (Oropharyngeal Candidiasis, Esophageal Candidiasis) patients can be treated by clotrimazole troches or lozenges and swishing and swallow of nystatin suspension.

3. Candidiasis Treatment of the Agranulocytosis

The excess expenditure condition also appear in agranulocytosis, for example primary malignant hematologic disease, myelodysplastic syndrome, aplastic anemia, rare aleukemic leukemia, some acute lymphoid leukemia, some lymphomas of bone marrow, tumor which caused by radiotherapy or chemotherapy and so on (**Table 1**) [25]. We should pay attention to these phenomenon that once these patients' primaries diseased have been cured, their immune condition is also changing to normal, and should be treated as immune normal people [26].

Table 1. Common pathogen of candidiasis caused by immune deficient.

Candidiasis caused by long/general term immune deficient	Candidiasis caused by short/local term immune deficient
agranulocytosis	antibiotic abuse
myelodysplastic syndrome	severe burn
hereditary or acquired aplastic anemia	gastroesophageal reflux
rare aleukemic leukemia	invasive treatment
some acute lymphoid leukemia	indwelling intravascular catheters
some lymphomas of bone marrow	hyperalimentation fluids
tumor which caused by radiotherapy or chemotherapy	indwelling urinary catheters
tuberculosis	Respirators
yyelophthisis	using illicit IV drugs
Severe infection	etc.
systemic lupus erythematosus	
hypersplenism	
etc.	
Ill-conditioned of white cells disease	
juvenility white cells	
low-birth-weight neonates	
abdominal and thoracic surgery	
critical disease	
corticosteroid treatment	
immune inhibitor treatment after transplantion	
AIDS	
Hematologic disease	
etc.	
antibiotic abuse	
severe burn	

4. Candidiasis Treatment of Chemotherapy or After-Transplant

Another immune changing disease is after-transplant, whether it is liver, pancreatic, small bowel, multivisceral organ, thoracic organ, stem cells, or other organ. These patients have to treated by corticosteroid, ciclosporin, or other immune inhibition agents, though the amount of their white cells may be normal, if treated by guidelines of community acquired Pneumonia, hospitals acquired pneumonia or lower respiratory tract infections, they have little change to live [27].

If the patients have abnormal of quantity and quality of white blood, we should treat they as long term immune deficient patients. If the pathogens of candidiasis have been recovered, we should them as long term immune patient, because their immune conditions are normal and they are health people at least a short period. The guideline of American Thoracic Society about fungal infections in adult pulmonary and critical care patients has already pay attention to the difference between immune deficiency patients and un-immune deficiency patients in respiratory system [28]. Lung nodules and majority bronchial calculus of healthy immune persons are not recommended general antifungal therapy.

If their pathogen disease could not be recovered, they should be name long term immune deficient patients. Therefore, the after-transplantation patients have received ciclosporin or other immune deficient drug, though the amounts of white blood cells are normal, they immune are comprised, so we should be treated positively.

5. Discussion

Previous guidelines about candidiasis are mainly based on the long term immune deficient patients who are the

main and severe group [15] [17] [29], and neglected these temporary immune deficient, and the patients' immune condition could be changed with the treatment. The long term immune deficient patients are mainly agranulocytosis, ill-conditioned of white cells disease (**Table 1**).

The temporary immune deficient patients are mainly suffered antibacterial agents, gastroesophageal reflux, severe burns, and invasive treatment, which including indwelling intravascular catheters, hyperalimentation fluids, indwelling urinary catheters, respirators, using illicit IV drugs, etc. The difference between long term and short term should not be defined by time completed. Once the risk factors are corrected they should be named short term, once the risk factors are not corrected they should still name long term. Besides, we could difference the immune deficient patients to general deficient patients and local deficient patients too (**Table 1**). The meaning is the general immune deficient patients mostly are long term immune deficient patients, and the local immune deficient patients mostly are short immune deficient patients. Apart from the antibiotic abuse and severe burns could be sorted by both of the two groups (**Table 1**). The goals of these names are going to be remaining the clinical doctors paying attention to the changing immune condition about candidiasis easily and usually. These may guide the clinical doctors about the candidiasis to a preliminary evaluation. If the candidiasis is caused by long term immune deficient or general immune deficient factor, should be given heaven hit, vice versa. Once the immune deficient condition is changed, the treatment vigor should be adjusted too.

Different with HIV patients, who suffered immune deficient for whole life at least from the now point, the short term immune deficient patients would be immune changing patients. The immune changing patients are these patients who suffered immune comprised and fungal, once their pathogenic condition is corrected, they should not treated as the immune deficient patients, who treated by antifungal drug for so long. At present, we have not pay attention to these patients completely. So they have been excessive treatment usually.

The immune changing principle is easy to understand, and the ignored diseases are not fatal illness, was overshadowed by excessive medical treatment. In addition, it could be hard to make out fateful findings, and cannot put out series high-quality articles if only study this, so there are few in-depth researches in this area, except several reports in infamous magazine of developing countries. Therefore, this is not valued by people when searching literature or formulates clinical guidelines.

6. Conclusion

The immune deficient patients of candidiasis include the long term immune deficient patients, temporary immune deficient patients and immune changing patients. The patients' immune condition could change with time, treatment, age, and so on. Saving the life of patients is important, however, we should not arrange excess treatment, and not be careless about the cost and the backlash of anti-fungal drug resistance. The treatment of candidiasis should pay attention to the immune changing patient.

References

[1] Nucci, M. and Anaissie, E. (2001) Revisiting the Source of Candidemia: Skin or Gut? Clinical Infectious Diseases. *Infectious Diseases Society of America*, **33**, 1959-1967. http://dx.doi.org/10.1086/323759

[2] Anthony, S.F., Dennis, L.K., Dan, L.L., *et al.* (2008) Harrison's Principles of Internal Medicine. 17th Edition, Chapter 196—Candidiasis. McGraw-Hill Companies, USA.

[3] Hermsen, E.D., Zapapas, M.K., Maiefski, M., Rupp, M.E., Freifeld, A.G. and Kalil, A.C. (2011) Validation and Comparison of Clinical Prediction Rules for Invasive Candidiasis in Intensive Care Unit Patients: A Matched Case-Control Study. *Critical Care* (*London, England*), **15**, R198. http://dx.doi.org/10.1186/cc10366

[4] Hindupur, S. and Muslin, A.J. (2005) Septic Shock Induced from an Implantable Cardioverter-Defibrillator Lead-Associated Candida Albicans Vegetation. *Journal of Interventional Cardiac Electrophysiology*, **14**, 55-59. http://dx.doi.org/10.1007/s10840-005-3246-x

[5] Sobel, J.D., Fisher, J.F., Kauffman, C.A. and Newman, C.A. (2011) Candida Urinary Tract infections—Epidemiology. Clinical Infectious Diseases. *Infectious Diseases Society of America*, **52**, S433-S436. http://dx.doi.org/10.1093/cid/cir109

[6] Mayercik, V.A., Eller, A.W. and Pihlblad, M.S. (2011) Fungal Endophthalmitis Developing in Asthmatic Individuals Treated with Inhaled Corticosteroids. *Archives of Ophthalmology*, **129**, 952-953. http://dx.doi.org/10.1001/archophthalmol.2011.184

[7] Motloch, L.J., Rottlaender, D., Darabi, T., Joost, I., Erdmann, E. and Hoppe, U.C. (2011) Conservative Management of

Candida Infection of Prosthetic Aortic Graft by Means of Caspofungin and Fluconazole Alone. *Texas Heart Institute Journal*, **38**, 197-200.

[8] Kinoshita, Y., Ishimura, N., Oshima, N. and Ishihara, S. (2015) Systematic Review: Eosinophilic Esophagitis in Asian Countries. *World Journal of Gastroenterology*, **21**, 8433-8440. http://dx.doi.org/10.3748/wjg.v21.i27.8433

[9] Brusselaers, N., Monstrey, S., Snoeij, T., Vandijck, D., Lizy, C., Hoste, E., *et al.* (2010) Morbidity and Mortality of Bloodstream Infections in Patients with Severe Burn Injury. *American Journal of Critical Care*, **19**, e81-e87. http://dx.doi.org/10.4037/ajcc2010341

[10] Mikulska, M, Bassetti, M., Ratto, S. and Viscoli, C. (2011) Invasive Candidiasis in Non-Hematological Patients. *Mediterranean Journal of Hematology and Infectious Diseases*, **3**, Article ID: e2011007. http://dx.doi.org/10.4084/mjhid.2011.007

[11] Nacher, M., Adenis, A., Hanf, M., Adriouch, L., Vantilcke, V., El Guedj, M., *et al.* (2009) Crack Cocaine Use Increases the Incidence of AIDS-Defining Events in French Guiana. *AIDS* (*London, England*), **23**, 2223-2226. http://dx.doi.org/10.1097/QAD.0b013e32833147c2

[12] Berdal, J.E., Haagensen, R., Ranheim, T. and Bjornholt, J.V. (2014) Nosocomial Candidemia; Risk Factors and Prognosis Revisited; 11 Years Experience from a Norwegian Secondary Hospital. *PLoS One*, **9**, e103916. http://dx.doi.org/10.1371/journal.pone.0103916

[13] Marchetti, O., Bille, J., Fluckiger, U., Eggimann, P., Ruef, C., Garbino, J., *et al.* (2004) Epidemiology of Candidemia in Swiss Tertiary Care Hospitals: Secular Trends, 1991-2000. Clinical Infectious Diseases, **38**, 311-320. http://dx.doi.org/10.1086/380637

[14] Pfaller, M.A. and Diekema, D.J. (2007) Epidemiology of Invasive Candidiasis: A Persistent Public Health Problem. *Clinical Microbiology Reviews*, **20**, 133-163. http://dx.doi.org/10.1128/CMR.00029-06

[15] Trick, W.E., Fridkin, S.K., Edwards, J.R., Hajjeh, R.A. and Gaynes, R.P. (2002) Secular Trend of Hospital-Acquired Candidemia among Intensive Care Unit Patients in the United States during 1989-1999. *Clinical Infectious Diseases*, **35**, 627-630. http://dx.doi.org/10.1086/342300

[16] Arendrup, M.C., Fuursted, K., Gahrn-Hansen, B., Jensen, I.M., Knudsen, J.D., Lundgren, B., *et al*. (2005) Semination-al Surveillance of Fungemia in Denmark: Notably High Rates of Fungemia and Numbers of Isolates with Reduced Azole Susceptibility. *Journal of Clinical Microbiology*, **43**, 4434-4440. http://dx.doi.org/10.1128/JCM.43.9.4434-4440.2005

[17] Zaoutis, T.E., Argon, J., Chu, J., Berlin, J.A., Walsh, T.J. and Feudtner, C. (2005) The Epidemiology and Attributable Outcomes of Candidemia in Adults and Children Hospitalized in the United States: A Propensity Analysis. *Clinical Infectious Diseases*: *An Official Publication of the Infectious Diseases Society of America*, **41**, 1232-1239. http://dx.doi.org/10.1086/496922

[18] Pappas, P.G., Kauffman, C.A., Andes, D., Benjamin Jr., D.K., Calandra, T.F., Edwards Jr., J.E., *et al*. (2009) Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*: *An Official Publication of the Infectious Diseases Society of America*, **48**, 503-535. http://dx.doi.org/10.1086/596757

[19] Wilcox, C.M., Darouiche, R.O., Laine, L., Moskovitz, B.L., Mallegol, I. and Wu, J. (1997) A Randomized, Double-Blind Comparison of Itraconazole Oral Solution and Fluconazole Tablets in the Treatment of Esophageal Candidiasis. *The Journal of Infectious Diseases*, **176**, 227-232. http://dx.doi.org/10.1086/514028

[20] Ally, R., Schurmann, D., Kreisel, W., Carosi, G., Aguirrebengoa, K., Dupont, B., *et al*. (2001) A Randomized, Double-Blind, Double-Dummy, Multicenter Trial of Voriconazole and Fluconazole in the Treatment of Esophageal Candidiasis in Immunocompromised Patients. *Clinical Infectious Diseases*: *An Official Publication of the Infectious Diseases Society of America*, **33**, 1447-1454.

[21] Vazquez, J.A., Skiest, D.J., Nieto, L., Northland, R., Sanne, I., Gogate, J., *et al*. (2006) A Multicenter Randomized Trial Evaluating Posaconazole versus Fluconazole for the Treatment of Oropharyngeal Candidiasis in Subjects with HIV/AIDS. *Clinical Infectious Diseases*: *An Official Publication of the Infectious Diseases Society of America*, **42**, 1179-1186. http://dx.doi.org/10.1086/501457

[22] Yakoob, J., Jafri, W., Abid, S., Jafri, N., Islam, M., Hamid, S., *et al*. (2003) *Candida* Esophagitis: Risk Factors in Non-HIV Population in Pakistan. *World Journal of Gastroenterology*, **9**, 2328-2331. http://dx.doi.org/10.3748/wjg.v9.i10.2328

[23] Kamai, Y., Maebashi, K., Kudoh, M., Makimura, K., Naka, W., Uchida, K., *et al*. (2004) Characterization of Mechanisms of Fluconazole Resistance in a *Candida albicans* Isolate from a Japanese Patient with Chronic Mucocutaneous Candidiasis. *Microbiology and Immunology*, **48**, 937-943. http://dx.doi.org/10.1111/j.1348-0421.2004.tb03623.x

[24] Moudgal, V., Little, T., Boikov, D. and Vazquez, J.A. (2005) Multiechinocandin- and Multiazole-Resistant *Candida parapsilosis* Isolates Serially Obtained during Therapy for Prosthetic Valve Endocarditis. *Antimicrobial Agents and*

Chemotherapy, **49**, 767-769.

[25] Kenneth, K., Marshall, A.L., Ernest, B., Thomas, J.K., Uri, S. and Josef, T.P. (2010) Chapter 34. Aplastic Anemia: Acquired and Inherited. In: Kenneth, K., Marshall, A.L., Ernest, B., Thomas, J.K., Uri, S. and Josef, T.P., Eds., *Williams Hematology*, 8th Edition, the McGraw-Hill Companies, Inc., Shanghai.

[26] Woodhead, M., Blasi, F., Ewig, S., Garau, J., Huchon, G., Ieven, M., *et al*. (2011) Guidelines for the Management of Adult Lower Respiratory Tract Infections—Full Version. *Clinical Microbiology and Infection*: *The Official Publication of the European Society of Clinical Microbiology and Infectious Diseases*, **17**, E1-E59. http://dx.doi.org/10.1111/j.1469-0691.2011.03672.x

[27] Harrison, N., Mitterbauer, M., Tobudic, S., Kalhs, P., Rabitsch, W., Greinix, H., *et al*. (2015) Incidence and Characteristics of Invasive Fungal Diseases in Allogeneic Hematopoietic Stem Cell Transplant Recipients: A Retrospective Cohort Study. *BMC Infectious Diseases*, **15**, 584. http://dx.doi.org/10.1186/s12879-015-1329-6

[28] Limper, A.H., Knox, K.S., Sarosi, G.A., Ampel, N.M., Bennett, J.E., Catanzaro, A., *et al*. (2011) An Official American Thoracic Society Statement: Treatment of Fungal Infections in Adult Pulmonary and Critical Care Patients. *American Journal of Respiratory and Critical Care Medicine*, **183**, 96-128. http://dx.doi.org/10.1164/rccm.2008-740st

[29] Goldman, M., Cloud, G.A., Wade, K.D., Reboli, A.C., Fichtenbaum, C.J., Hafner, R., *et al*. (2005) A Randomized Study of the Use of Fluconazole in Continuous versus Episodic Therapy in Patients with Advanced HIV Infection and a History of Oropharyngeal Candidiasis: AIDS Clinical Trials Group Study 323/Mycoses Study Group Study 40. *Clinical Infectious Diseases*: *An Official Publication of the Infectious Diseases Society of America*, **41**, 1473-1480.