Primary immunodeficiencies and Immune response to fungal infections.

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Abstract

Primary immunodeficiencies are genetic illnesses that damage one or more immune system parts and if ignored, greatly increase morbidity and mortality as well as the susceptibility to infection. It is crucial to differentiate between these conditions and acquired immunodeficiencies caused by immunosuppressive drugs, cancer, the Human Immunodeficiency Virus (HIV) and other reasons. Primary immunodeficiencies are diagnosed early in childhood in more than 80% of cases and are found before the age of 20. Therefore, paediatricians often do the initial diagnosis and management of these immunological diseases, which frequently present as persistent, severe infections caused by common organisms or illnesses caused by opportunistic pathogens.

Keywords: Inherited disease, HIV, Immunological diseases, Opportunistic pathogens

Introduction

Primary immunodeficiencies are inherited conditions affecting one or more immune system components that, if left untreated, increase infection susceptibility and significantly increase morbidity and mortality. It is important to distinguish between these illnesses and acquired immunodeficiencies brought on by immunosuppressive medications, cancer, the Human Immunodeficiency Virus (HIV) and other factors. More than 80% of instances of primary immunodeficiencies are identified before the age of 20 [1], with diagnosis occurring early in childhood. Therefore, in the majority of cases, paediatricians are responsible for the first diagnosis and treatment of these immunological diseases, which typically manifest as recurrent, protracted or severe infections brought on by common organisms or illnesses brought on by opportunistic pathogens [2].

Primary immunodeficiencies are grouped into broad groups, such as humoral, cellular, combined humoral and cellular, phagocytic, complement and other, well characterized immunodeficiency syndromes, depending on the immune system component that is predominantly impaired [3,4]. The scope, clinical manifestation and treatment of fungal infections related to primary immunodeficiencies are covered in the current review. A succinct summary of the host immune response to fungal infections is first offered in order to better comprehend the relationship between certain immunological deficiencies and fungal illnesses. Even though it is now known that *Pneumocystis jirovecii* (formerly known as *Pneumocystis carinii*) is a fungus [5], the unique epidemiology, clinical course and therapy of infection brought on by this organism are not included in this review.

Description

Immunity to fungus infections

Innate immune response: To establish a successful host defence against fungus in humans, both innate and adaptive immunity must work together in concert [6,7]. A range of cells that have phagocytic and antigen presenting activities mediate the innate response. Neutrophils, mononuclear leukocytes (macrophages and monocytes) and dendritic cells are some of these; to varying degrees, Natural Killer (NK), T cells, epithelial and endothelial cells may also be implicated [8]. Through the use of Toll Like Receptors (TLR, primarily TLR-2 and TLR-4) and other elements of the fungal cell wall, host cells with innate immunity can identify fungi as pathogens [9]. Inflammatory mediators including cytokines, chemokines and complement components work to attract more phagocytic cells to infection sites. Through oxidative and non-oxidative methods, fungal elements can be killed inside cells or injured outside cells. Opsonins and cytokines released from T cells can enhance these processes. Nitric Oxide (NO) synthase and NADPH oxidase are examples of enzymes in the oxidative pathway that produce reactive oxygen intermediates that have harmful effects on fungus cells. Through degranulation and the production of defensins, neutrophil cationic peptides and other fungicidal compounds, non-oxidative fungal death is accomplished [10].

Acquired immune response: Through differentiation of $CD4^+$ T cells along a T-helper (Th) cell type 1 (Th1) or type 2 (Th2) pathway, adaptive immune response against fungus can be induced. Interferon (IFN), Interleukin (IL)-2, IL-12 and IL-18 are cytokines that are produced during the Th1 response. These cytokines promote phagocytic activity, the development of cytotoxic $CD4^+$ T cells and the creation of opsonizing

antibodies. Creation of cytokines like IL-4 and IL-10, which promote the production of non-opsonizing antibodies and allergic reactions as well as the down regulation of the extensive inflammatory response brought on by Th1 cytokines, is linked to the development of the Th2 response. Predominance of Th1 over Th2 adaptive responses is correlated with effective defence against invasive mycoses [11].

While the significance of phagocytes and T-cells is well known, there has long been debate over the function of humoral immunity in the immune response to fungus infections. Fungi have a variety of carbohydrate and other antigens in their cell walls that cause immune system reactions. There is not much proof that these antibodies alter the pathogenesis of fungi, though [12,13]. For instance, whereas *Candida albicans* and *Cryptococcus neoformans* antibodies are developed early in development, they do not appear to provide infection protection [14]. Patients with hypo or agammaglobulinemia also do not have a high susceptibility to fungus infections. It is now well known that the multiple antibodies produced by a certain fungus species during colonisation or infection target distinct epitopes and exhibit a variety of, sometimes conflicting, actions that can be protective, non-protective or neutral. Antibodies produced against unrelated fungal components can occasionally even mask protective epitopes [16,15].

Conclusion

Therefore, the idea that protective antibodies are produced is not ruled out despite the likelihood that this polyclonal antibody response may not give protection. However, finding these antibodies involves searching at the monoclonal level and has recently garnered a lot of scientific attention since it could result in the creation of new medicinal interventions or vaccines.

References

1. Lindegren ML, Kobrynski L, Rasmussen SA, et al. Applying public health strategies to primary immunodeficiency diseases: a potential approach to genetic disorders. MMWR Recomm Rep. 2004;53(RR-1):1-29.
2. Kumar A, Teuber SS, Gershwin ME, et al. Current perspectives on primary immunodeficiency diseases. Clin Dev Immunol. 2006;13(2-4):223-59.
3. Buckley RH. Primary immunodeficiency diseases due to defects in lymphocytes. N Engl J Med. 2000;343(18): 1313-24.
4. Lekstrom-Himes JA, Gallin JI. Immunodeficiency diseases caused by defects in phagocytes. N Engl J Med. 2000;343(23):1703-14.
5. Edman JC, Kovacs JA, Masur H, et al. Ribosomal RNA sequence shows *Pneumocystis carinii* to be a member of the fungi. Nature. 1988;334(6182):519-22.
6. Romani L. Immunity to fungal infections. Nat Rev Immunol. 2004;4(1):1-23.
7. Shoham S, Levitz SM. The immune response to fungal infections. Br J Haematol. 2005;129(5):569-82.
8. Huffnagle GB, Deepe GS. Innate and adaptive determinants of host susceptibility to medically important fungi. Curr Opin Microbiol. 2003;6(4):344-50.
9. Netea MG, van der Graaf C, Van der Meer JW, et al. Recognition of fungal pathogens by toll like receptors. Eur J Clin Microbiol Infect Dis. 2004;23(9):672-6.
10. Mansour MK, Levitz SM. Interactions of fungi with phagocytes. Curr Opin Microbiol. 2002;5(4):359-65.
11. Mencacci A, Cenci E, Bacci A, et al. Cytokines in candidiasis and aspergillosis. Curr Pharm Biotechnol. 2000;1(3):235-51.
12. Casadevall A, Cassone A, Bistoni F, et al. Antibody and/or cell mediated immunity, protective mechanisms in fungal disease: an ongoing dilemma or an unnecessary dispute? Med Mycol. 1998;36(1):95-105.
13. Cutler JE, Deepe GS Jr, Klein BS, et al. Advances in combating fungal diseases: vaccines on the threshold. Nat Rev Microbiol. 2007;5(1):13-28.
14. Bode CP, Schroten H, Koletzko S, et al. Transient achalasia like esophageal motility disorder after *Candida* esophagitis in a boy with chronic granulomatous disease. J Pediatr Gastroenterol Nutr. 1996;23(3):320-3.
15. Cassone A, de Bernardis F, Torososantucci A, et al. An outline of the role of anti-*Candida* antibodies within the context of passive immunization and protection from candidiasis. Curr Mol Med. 2005;5(4):377-82.
16. Pachl J, Svoboda P, Jacobs F, et al. A randomized, blinded, multicentre trial of lipid associated amphotericin B alone versus in combination with an antibody based inhibitor of heat shock protein 90 in patients with invasive candidiasis. Clin Infect Dis. 2006;42(10):1404-13.

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