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VIRAL INFECTIONS IN IMMUNOCOMPROMISED PATIENTS

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ABSTRACT:

Immunocompromised patients have a decreased ability to fight infections and other diseases. This may be caused by certain diseases or conditions, such as AIDS, cancer, diabetes, malnutrition, and certain genetic disorders. Knowledge of viral infections in immunocompromised patients is sparse. We reviewed the incidence of different types of viruses in a well-characterized population of immunocompromised patients. All articles related to immunocompromised patients with suspicion of viral infection were included in the review. In general viral infections are common in a person who has general debility, immunosuppressive therapy, pregnancy, under treatment for allergy, and so on. Regardless of their specialties, physicians are increasingly confronted with many of the adverse effects of treatment that cause immune system suppression such as chemotherapy and stem cell transplantation for cancer, solid organ transplantation, and therapies for autoimmune and rheumatological diseases. The immunocompromised patients have weak immune systems and they are very much prone to infections and they can acquire infections from the community and also from the infected hosts. Herpesviruses, cytomegalovirus, and Epstein-Barr virus are most common of the viral infections affecting these patients, along with respiratory viruses. Antiviral drug therapies can be given combined with a reduction in a dose that cannot induce

immunosuppression. In this review, we discussed the epidemiology, pathogenesis, clinical features, and treatment plans of the viral infection in immunocompromised patients.

INTRODUCTION

Susceptibility to a viral infection depends on the virulence of the virus and the susceptibility of an individual. The defense against viral infection is mainly based on the spontaneous response of the host immune system. It is a coordinated effort of innate and adaptive immunity. As the age advances the potential of the immune apparatus is decreased due to various factors. Age is a secondary factor in many cases. The general debility resulting from multiple factors impair the immune function. Owing to the prolonged survival of patients with multiplemalignancies and advances in both solid-organ and hematopoietic stem cell transplantation, the spectrum of immunocompromised hosts has increasedin the last decade. Novel immunosuppressive therapies create diverse immune deficits that generate a substrate for opportunistic infections. (1) These patients are defined by higher susceptibility to infections by organisms with lower native virulence than in immunologically normal hosts.

The most common explanation for respiratory viral infections in immunocompromised patients was Influenza, parainfluenza, respiratory syncytial virus, coronavirus, human metapneumovirus, and rhinovirus. However, adverse outcomes are much more likely in immunocompromised patients individuals and include progression to pneumonia, respiratory failure, and increased mortality rates. In fact, the LRTI rates and mortality rates for hematopoietic stem cell transplant (HSCT) recipients and patients with hematological malignancies reportedly range from 10% to 50%. Long- term complications associated with respiratory viral infections.75% of the articles were positive for viral infection. The incidence of viruses was as follows: adenovirus 3.0%, bocavirus 1.1%, coronavirus 8.9%, human metapneumovirus 6.6%, H1N1 0.53%, influenza 6.1%, parainfluenza 10.3%, rhinovirus-enterovirus 35.4%, and RSV 8.2%. Other viruses included cytomegalovirus 25.1%, Epstein-Barr virus 0.85%, herpes simplex virus 12.6%, human herpes virus-6 0.32%, human herpes virus-7 0.1% and varicella-zoster virus 0.1%. Antiviral therapy was started in approximately 5.6% of the cases, continued in 17.0% and stopped in 0.4% of There is a high prevalence of respiratory virus infections in immunocompromised patients. This finding may influence patient management.

FACTORS LEAD TO VIRAL INFECTION IN IMMUNOCOMPROMISED PATIENTS

To prevent or get rid of diseases our body's immune system uses a number of defenses. The infections can be caused by various microorganisms such as bacteria, viruses, fungi, etc,.An immunocompromised host may be a patient who doesn't have the power to normally get an infection due to an impaired or weakened system. This inability to fight infection was often caused by a

variety of conditions, including diseases (e.g., diabetes, human immunodeficiency virus [HIV] infection), malnutrition, and drugs. (2-4)

Viral infections in an immunocompromised host have the power to cause severe disease at much higher rates than within the healthy population. Careful attention to viral epidemiology and viral outbreaks within the community, diagnostic screening of symptomatic patients with the onset of latest respiratory symptoms, and therefore the use of careful infection control methods that are rigorously enforced in both the outpatient and inpatient setting was important in limiting viral spread to those high-risk patients. The utilization of antiviral therapy before the event of respiratory failure can also be of benefit in these patients. The efficacy of immunoglobulin products or antibody products to limit the spread of infection within individual patients is usually utilized but has yet not been proven in rigorous trials during this patient population.(5)

The problems faced by immunocompromised patients

Deficiencies of host defense systems result in an immunologic imbalance that can lead to susceptibility to infection, an autoimmune disease, or a predisposition to malignancies. Immunodeficiency can be primary, acquired, or iatrogenic. Causative agents are commonly extracellular organisms because patients are deficient in serum opsonin. The challenges of managing infections in immunocompromised patients continue to evolve. People with weak immune systems are susceptible to infections and they also take a longer time to recover compared to other patients. Chemotherapy can be used to treat cancer but it weakens the immune system. Bone marrow transplantation, HIV infections also compromised the immune system. (6)

EPIDEMIOLOGY AND CLINICAL ASPECTS OF COMMUNITY-ACQUIRED RESPIRATORY VIRUSE

Viruses that cause acute respiratory illness in the general population and are responsible for hospitalizations in persons of all ages with underlying medical conditions are also a common cause of respiratory disease in transplant recipients. With the widespread availability of sensitive and reliable molecular detection methods, common respiratory viruses including respiratory syncytial virus (RSV), influenza and parainfluenza viruses (PIVs), adenoviruses, rhinoviruses (RhV), and coronaviruses have been detected worldwide in transplant recipients. More recently, newly identified viruses such as human metapneumovirus (HMPV) (7) new strains of coronaviruses (8) and bocavirus have also been detected in symptomatic transplant recipients.(9)

Community-acquired respiratory viruses (CRV) have a significant impact on the morbidity and mortality of the transplant recipient, causing a variety of diseases ranging from self-limited upper respiratory tract illnesses (URIs) to life-threatening lower respiratory tract infection (LRTI) and occasionally disseminated disease. (10) Disease manifestations are dependent on the specific virus, the type of transplant, and the type, degree, and duration of immune deficiency. Some respiratory viruses, such as parainfluenza viruses, may also have higher associated rates of pathogens.

Nosocomial transmission of CRVs is common, and widespread hospital outbreaks of CRVs have occurred with sometimes devastating sequelae. (11-14) Because these viruses are so easily transmitted from person to person in both inpatient and outpatient settings, infection control measures and enforcement of these measures are critical in controlling the spread of these infections (15) Community outbreaks of RSV infections typically occur during the late fall, winter, and early spring, frequently followed by outbreaks of human metapneumovirus. Influenza outbreaks typically occur during the winter in temperate climates but may occur throughout the year in more tropical areas. Parainfluenza virus infections occur throughout the year, with outbreaks occurring primarily in the spring, summer, and fall. Other viruses, such as rhinoviruses, coronaviruses, and adenoviruses, tend to take place throughout the year, although sporadic outbreaks of all these respiratory viruses may occur. (16)

T Cell Therapy for Adenovirus Infections

Adenoviruses (ADV) are non enveloped lytic DNA viruses. Fifty-two different human serotypes have been identified divided into 7 subgroups or species. (17, 18)During the last decade, ADV infection in the context of allogeneic hematopoietic stem cell transplantation (HSCT) has been increasingly recognized as a cause of transplant-related mortality (TRM), especially in children and the most severely immunocompromised adults, such as those undergoing haploidentical or T cell-depleted transplants.

Runde et al. reported a significantly higher incidence of ADV-infection in patients receiving anti-thymocyte globulin (ATG), and a study by van Tol et al. (19) found the risks of ADV infection and disease were increased in patients with more intensive T cell depletion. Other studies found a strong correlation between the presence of ADV-specific T cells and the clearance of ADV infection.] (20, 21). In a pilot study, (22) treated 6 patients with ADV-viremia with virus-specific donor T cells generated by INF-γ secretion assays. In 3 of 4 evaluable patients receiving this adoptive T cell transfer, the infused T cells underwent an in vivo expansion and the viral load decreased in peripheral blood. (23) In vivo expansion of specific T cells was dose-independent, suggesting that even very low numbers of ADV-specific donor T cells expand easily in vivo in the presence of viremia.

Vaccination of Stem Cell Transplant Recipients Against Viral Pathogens

Influenza

The mortality rate following influenza infections in HSCT recipients was previously reported to be around 15% (24-26) although recent data reporting outcome after more widespread utilization of neuraminidase The recent outbreak of new pandemic strain A/H1N1 stressed the importance of having strategies in place for the management of these patients.

Influenza infection is controlled by different parts of the immune system including both the innate and adaptive immune systems. After vaccination, both T cell and B cell responses are activated. The clearance of the primary infection depends on CD8 cells. These cells recognize epitopes from both the

hemagglutinin (HA) and the internal proteins of the influenza virus. Following recovery from influenza, antigen-specific T cells maintain long-lasting immunologic memory that responds quickly to restimulation. (27-29) The B cells produce antibodies to the influenza proteins and HA-specific antibodies appear within 2 weeks of the infection. In contrast to antibodies directed to HA, antibodies directed to NA do not neutralize the virus but reduce the release of virus from infected cells. A problem specific for influenza viruses is the antigenic shifts and drifts of circulating influenza virus that regularly occur, requiring adaptation of the seasonal trivalent influenza vaccines that must be administered to provide protection. (30, 31)

Two main types of influenza vaccine exist: inactivated and live, a cold-adapted vaccine for intranasal administration. (32, 33) Safety and efficacy of the intranasal live vaccine have not been evaluated in HSCT recipients but were safe in HIV-infected adults and children. (34-36) Because influenza infection occurring early after HSCT might result in severe disease, it would be logical to immunize candidates before HSCT. (37) However, most studies show that adult patients with hematologic malignancies respond poorly to vaccination. (38) In addition, the likelihood that whatever immunity that does exist will be lost is very high. (39)

Measles, mumps, and rubella (MMR) vaccine

Although severe and fatal measles have been reported in HSCT recipients the risk for serious infection after allogeneic HSCT is likely to be below. However, with more patients undergoing transplantation after reduced-intensity conditioning (RIC) regimens, the pregnancy potential for patients is likely to increase and thereby the risk of congenital rubella syndrome. The available MMR vaccines are live, attenuated vaccines, and are not recommended for use in immunocompromised patients. Immunization can be considered in allogeneic HSCT patients without chronic graft-versus-host disease (cGVHD) or ongoing immunosuppression. Data indicates that measles vaccine can be given to such patients without severe adverse effects at 2 years after SCT (40) During an epidemic in Brazil, patients were safely immunized 1 year after SCT (41)

Varicella vaccines

Although data are limited, varicella vaccine might be considered for seronegative HCT recipients who meet the criteria for live virus vaccination delineated above for the measles vaccine. The zoster vaccine should not be used. Two new inactivated varicella vaccines are under development. (42, 43)

Other vaccines

There is no data regarding vaccination of HSCT recipients with the recently licensed vaccines against human papillomavirus, and vaccination cannot yet be recommended. (44, 45)

CONCLUSION

Viral infections in an immunocompromised host have the ability to cause severe disease at much higher rates than in the healthy population. Control methods that are rigorously enforced in both the outpatient and inpatient

setting are important in limiting viral spread to these high-risk patients. The use of antiviral therapy prior to the development of respiratory failure may also be of benefit in these patients. The efficacy of immunoglobulin products or monoclonal antibody products to limit the spread of infection within individual patients is frequently utilized but has yet not been proven in rigorous trials in this patient population. Further clinical studies of agents to both prevent and treat these important viral infections are urgently needed.

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