

Viral Infections In Immunocompromised Patients

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Objectives

- Understanding of conditions that increase the risk for severe complications due to viral infection.
- Assessment of the most common viruses affecting immunocompromised patients with cancer
- Knowledge of diagnostic measures
- Knowledge of pharmacological and cellular treatment options
- Insight into prevention strategies

Viral infections are a frequent cause of severe disease in children with hematological malignancies, cancer or patients undergoing allogeneic haematopoietic stem cell transplantation (HSCT). The reasons for the impaired immune responses are the underlying disease itself, antineoplastic therapy leading to granulocytopenia, lymphopenia, disruption of natural skin and mucosal barriers, reduced humoral immune function and colonization with nosocomial pathogens. High dose chemotherapy and autologous stem cell reinfusion and particularly allogeneic hematopoietic stem cell transplantation (HSCT) with the risk of graft versus host disease lead to a long lasting severe immunodeficiency.

The development of rapid diagnostic tools to detect viruses like shell-vial culture antigen detection assays and the highly sensitive and specific polymerase-chain-reaction (PCR) based techniques enables efficient and timely therapeutic decision. However, broad virus screening is cost intensive and thus should be restricted to high risk patients (e.g. patients undergoing T-cell depleted allogeneic HSCT or patients with chronic GVHD, respectively).

The most common viral isolates in children with cancer are herpes-simplex virus (HSV), varicella-zoster virus (VZV) causing chicken pox (varicella) and herpes zoster. After allogeneic HSCT cytomegalovirus Epstein Barr virus and adenovirus are the most relevant organisms for severe infectious complications and should be carefully monitored until immunoreconstitution. General prevention strategies to reduce the risk include isolation precautions (simple or reverse isolation, air filtration), water purification and careful hand disinfection practices. Pharmacological prophylaxis include application of antiviral drugs as acyclovir, ganciclovir, ribavirin and recently oseltamivir.

HSV infections results in most cases from reactivation of latent virus causing mucocutaneous lesions in seropositive patients. HSV pneumonia and encephalitis are life threatening events. In children intravenous or oral acyclovir is given as prophylactic or therapeutic measure to prevent severe disease during periods of profound immunosuppression.

Young immunocompromised children are at high risk for primary varicella-zoster virus infection which might be complicated by VZV pneumonia with fatality rates of about 10%. The use of intravenous acyclovir is the treatment of choice. Strict isolation of infectious patients are required to prevent immunocompromised patients from contamination. VZV hyperimmune globulins might be helpful for seronegative patients if administered within 96 hours after exposure. Herpes zoster is due to reactivation of latent VZV and is most frequently observed among patients with leukaemia or after allogeneic or autologous HSCT. To reduce incidence and severity of herpes zoster inactivated VZV vaccine might lead to a better reconstitution of the specific cellular immunity after HSCT. Especially in patients with impaired gastrointestinal function acyclovir should be applied intravenously as the absorption of oral formulations can be insufficient.

Cytomegalovirus (CMV) is still an important cause for morbidity and mortality after HSCT. Quantification of the viral load and the viral load kinetics influence the outcome after CMV infection, reinfection and reactivation. In patients undergoing HSCT the strongest predictor for mortality in patients with CMV viremia is the serostatus of the donor. Patients who develop CMV viremia have the highest risk for transplant related mortality if the donor is CMV IgG negative. In contrast, seropositive recipients grafted with a seropositive donor will need only a short time to develop a durable T cell response. Intravenous ganciclovir prophylaxis results in less frequent CMV disease but not in improved survival. Alternatively, pre-emptive treatment of CMV viremia is associated with both decreased incidence of CMV disease and better survival after allogeneic HSCT. One adverse side effect of ganciclovir application is hematotoxicity. Thus, foscarnet appears an efficient alternative drug with less myelosuppressive effects. Valganciclovir is an oral prodrug of ganciclovir with a superior bioavailability compared to oral ganciclovir and might become an attractive alternative to intravenous ganciclovir. However, valganciclovir has to be registered for children, the preparative investigations are currently investigated.

Adenovirus (AdV) infection in the course of allogeneic HSCT is associated with high transplant-related morbidity and mortality. Disseminated AdV disease is lethal in most instances. Early detection of AdV infection and identification of patients carrying a high risk of disseminated disease therefore remain a major challenge. Monitoring of PB specimens by real-time PCR permitted early diagnosis of invasive AdV infection in all instances. In patients who developed disseminated AdV disease, detection of the virus in PB preceded onset of clinical symptoms by a median of over three weeks. The observation of AdV in peripheral blood may therefore serve as a basis for early initiation of pre-emptive antiviral treatment. Recent reports discuss the possible beneficial role of ribavirin for the treatment of adenovirus infections, however these observations should be evaluated in prospective trials.

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