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5

Risk assessment in haematopoietic stem cell transplantation: Viral status

Per Ljungman* MD, PhD
Professor, Head
Hematology Center, Karolinska University Hospital, Karolinska Institute, SE-14186 Stockholm, Sweden

Viral infections have been important complications in the transplant procedure from the early days of stem-cell transplantation, causing significant morbidity and mortality. It is important for the management of patients to assess the risk for viral infections that might develop after the stem-cell transplantation. This can be exemplified by cytomegalovirus (CMV) and other herpesviruses, but risk assessment is also important for other viral infections. The aim of this review is to describe current knowledge regarding recipient and donor serological status for viral infections.

Key words: viral infections; serology; CMV; stem-cell transplantation; donors.

Viral infections have been important complications in the transplant procedure from the early days of stem-cell transplantation, causing significant morbidity and mortality. Over the years, major improvements in the post-transplant management of viral infections have been achieved. One of these achievements is the recognition that it is of major importance to assess the patient's risk for developing post-transplant viral infections. For several viruses this risk assessment is made through pre-transplant detection of the viral status of the patient and for several viruses also of the donor. The aim of this review is to assess available evidence about when to perform pre-transplant detection of viral markers, and the recommendations are made as minimum-level recommendations.

DIAGNOSTIC TECHNIQUES

For many viruses, the use of serology to detect antibodies is the diagnostic technique of choice. The presence of IgG antibodies against a virus indicates a previous infection and, for some latent or persistent viruses, the possibility of post-transplant reactivation. IgM antibodies might indicate a recent infection, although false-positive reactions

* Tel.: +46 8 58582507; Fax: +46 8 7748725.
E-mail address: per.ljungman@ki.se

and cross-reactions do occur. However, serology is usually not useful for diagnosis of active virus infections after SCT since many patients are unable to mount antibody responses. For some viruses, techniques able to detect parts of the virus, such as nucleic acids or viral antigens, are indicated. This applies for example for hepatitis B virus and HIV, but might also be applicable in a situation where a recent primary infection — for example with cytomegalovirus (CMV) — is suspected.

DONOR ISSUES

As a principle it can be stated that ongoing viral disease — i.e. symptomatic infection for example with respiratory syncytial virus (RSV), herpes simplex virus (HSV), or varicella–zoster virus (VZV) — in the donor should be seen as a contraindication for donation. The aims are both to eliminate the possible risks to the donor by performing the harvest procedure during active infection and to reduce the risk of transfer of the virus to the patient. The situation with asymptomatic viral infections in the donor is more difficult and will be dealt with below under the respective viral pathogens.

CYTOMEGALOVIRUS

CMV-seronegative patients

The ideal situation is to have a CMV-seronegative patient and a CMV-seronegative stem-cell donor since the risk for CMV disease in this combination is very low.[1,2] In seronegative patients with seropositive stem-cell donors (D^+/R^-), primary CMV infection develops in about 30%. Although the risk for CMV disease is low with current preventive strategies, Nichols et al showed recently that there was an increased mortality in bacterial and fungal infections in seronegative patients receiving grafts from seropositive donors; this shows the importance of CMV as an immunosuppressive agent after allogeneic stem-cell transplantation, increasing the risk for both bacterial and fungal infections after transplantation.[3] Attempts should therefore be made to find a CMV-seronegative donor for a CMV-seronegative patient. False-negative results of serological testing do occur, and either the patient or the donor can be in the incubation phase before antibodies can be detected. One question to be considered is the case where only a seropositive sibling donor is available but there might be a possibility of finding a CMV-seronegative unrelated donor. There is no available information regarding the relative risks comparing these two transplant options. However, Nichols et al showed no impact on mortality by using a CMV-seropositive donor for a CMV-seronegative patient receiving an HLA-identical sibling donor transplant, whereas there was a significant impact in unrelated donor transplants.[3] This would suggest that a sibling donor is still the preferred alternative, even if the donor is CMV-seropositive, compared to a CMV-negative unrelated donor for a CMV-seronegative recipient. The situation might be different in a setting comparing a family HLA-mismatched, CMV-mismatched donor with an unrelated CMV-matched donor, but the data are lacking to make a recommendation.

CMV-seropositive patients

Reactivation of CMV occurs in approximately 80% of patients who are seropositive before transplantation. Seropositivity of the patients still remains a risk factor for