Infectious Complications Post Transplant: How to recognize?

Transplant activities are increasing in Pakistan over last few years. In order to avoid graft rejections, transplant physician use drugs to reduce immunosuppression but that may come at cost of infections which in this era of drug resistance may be life threatening. Apart from transplant more physicians are using immunosuppressive drugs for variety of diseases like Rheumatoid arthritis, multiple sclerosis etc. Several factors may influence the types of infections that an immune suppressed population is likely to develop. These include the type and intensity of therapy and its temporal progression. Previous exposure to antimicrobials, presence of catheters, lines or drains, drug induced suppression of cell populations, technical complications related to surgery itself, any underlying immune condition/ viral infection and metabolic state all are factors that can interact to predispose a patient to an infection.

Antilymphocyte globulins that act against T-lymphocytes can result in activation of latent viruses while anti B-lymphocytes can predispose to encapsulated bacteria. Plasmapheresis is a risk factor for encapsulated bacterial and line infections while mycophenolate mofetil (antimetabolite) increases risk of early bacterial and late CMV infections.[1] Corticosteroids increase risk of bacterial, fungal, PCP and delay wound healing. Calcineurin inhibitors that reduce T cell differentiation increase risk of herpes and intracellular pathogens. mTOR inhibitors (inhibits cellular proliferation) in combination with other therapy further increases risk of infections with poor healing.

Immunosuppression, antimicrobial exposure, effects of surgery/ischemia can alter the host's normal microbiome. This results in an altered immune system which can lead to infections. Screening assays of potential recipients can help identify those at risk. Personal/ family history with emphasis on tuberculosis, pets and occupational exposure as well as review of microbiological data and vaccinations can be helpful.

Cytomegalovirus antibody, Epstein-Barr virus (EBV) antibody, measles, mumps, rubella serologies, Nontreponemal and treponemal testing, Human immunode?ciency virus serology (ELISA) or Hepatitis B (HBV) serologies, Hepatitis C antibody, Toxoplasma antibody (notably in cardiac recipients) and Tuberculosis by skin test or interferon-c release assay must be checked before transplant.[2]

Further testing includes Herpes simplex virus antibody, Varicella-zoster virus antibody, and some testing may depend upon travel exposure and may include Strongyloides stercoralis, Trypanosoma cruzi and Schistosoma mansoni. Rectal swabs can be taken for resistant bacteria depending on geographical epidemiology. If not immunized the vaccinations to be considered include Hepatitis B, Hepatitis, Influenza, Pneumococcal vaccine, Tetanus (Tdap), MMR (review serologies), Varicella zoster virus (>50 years), Meningococcal (including type B), Hemophilus influenzae and Human Papillomavirus.

The timeline for post transplant infections can be divided into three periods. In the initial 4 weeks, there is increased risk of nosocomial infections, infections related to donor- recipient discordance and due to surgical complications. Following this period, in the first-year post transplant there is higher risk of activation of latent infections and opportunistic pathogens. After 1-year, highest risk is of community acquired infections. Events such as graft rejection/ malignancy can modify an individual's risk of developing a certain infection. Antibiotic prophylaxis and vaccinations can often only delay infections but not stop them altogether.

Highest risk of CMV infection is in donor positive/ recipient negative in combination with induction using T cell depletion and in order to avoid it, valganciclovir prophylaxis is recommended for variable duration of 3-6 months depending on type of transplant.[3] Pre emptive therapy is an option in the recipient population that tests positive serologically before starting immune suppression. It is important that Donor negative/ recipient negative combination group patients must only be transfused CMV negative tested blood or leukocyte filtered blood.

In addition, one single-strength trimethoprim-sulfamethoxazole tablet (TMP-SMZ, containing 80 mg trimethoprim, 400 mg sulfamethoxazole) or one double-strength tablet po daily for 3–6 months must be given posttransplant for PCP prophylaxis which will be also cover Nocardia and UTIs.

In TB endemic countries like Pakistan, treating for Latent Tuberculosis is very important even when screening for it is negative. Standard protocol is to treat for 6 to 9 months but recent data in HIV patients suggest that prolonging for 36 months is more benficial.

So, Invasive infections in the immune suppressed population can be very variable and due to a variety of organisms that should be considered. Early intervention to obtain samples for culture biopsy and special testing of rarer organisms is imperative for reaching a timely diagnosis and initiating appropriate therapy.

References

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