Graft versus host disease (GVHD) arises when immunocompetent T-lymphocytes from the graft (i.e. donor tissue) cause an inflammatory reaction against the host (i.e. transplant recipient). T-lymphocytes are a part of the adaptive immune system. They function to recognize and destroy foreign pathogens, which are commonly thought of as viruses or bacteria. However, these lymphocytes are programmed to recognize any “non-self” material as foreign. This contributes to their ability to destroy tissue and organs that they recognize as foreign during transplantation.

GVHD is most likely to occur in recipients of lymphocyte rich organs. These include, but are not limited to, transfusion of non-irradiated blood products, liver transplantation, and allogeneic hematopoietic stem cell transplantation (HSCT). There are two types of HSCT, autologous and allogeneic. Autologous HSCT is the removal of the recipient’s own stem cells with the intent to reinfuse them after chemotherapy. Allogeneic HSCT is the transfer of stem cells from a sibling or unrelated donor to the recipient. Human leukocyte antigen (HLA) matching is completed prior to allogeneic HSCT. Despite HLA matching, the risk of GVHD is still higher in recipients of allogeneic HSCT because HLA matching is not always perfect, and the donor lymphocytes are more likely to react against “non-self” tissue.

The classification of GVHD can be further divided into acute and chronic. Acute GVHD occurs within 100 days of transplantation. Chronic GVHD occurs after 100 days following transplantation. Without prophylaxis (i.e. high dose chemotherapy and/or total body irradiation), acute GVHD occurs approximately 70-100% of the time. Prophylaxis decreases that risk to 9-50%. When it occurs, acute GVHD is thought to be triggered by a type IV hypersensitivity reaction. This reaction is essentially a delayed period of time in which the donor lymphocytes begin mounting an immune response that ultimately leads to inflammation and destruction of the hosts’ organ systems. The mechanism of chronic GVHD is not currently known, but it is thought to involve both T and B lymphocytes reacting against host tissue.

Common clinical features seen in acute GVHD include gastrointestinal symptoms like nausea, vomiting, and diarrhea. Hepatic dysfunction is seen in the form of an enlarged liver and "yellowing" of the skin referred to as jaundice. The increased concentration of bilirubin, a liver breakdown product, is what causes jaundice. Another common feature that patients may present to their dermatologist for is an itchy, painful rash that develops over the body. This rash most commonly forms on the ears, shoulders, neck, and over the palms and soles. Most commonly, the rash consists of lesions that both can and cannot be felt when touching the affected areas. In medical terms, this would be described as a pruritic (itchy), maculopapular rash. The chronic form of GVHD presents with similar gastrointestinal and liver symptoms seen in acute GVHD, but also exhibits a wider range of symptoms. Chronic GVHD can present with dry eyes and dry mouth, referred to as Sicca syndrome. A cough with wheezing and shortness of breath is also seen in chronic GVHD. A key distinguishing characteristic between acute and chronic GVHD is the skin changes. Chronic GVHD is more likely to present scleroderma-like and lichenoid changes of the skin. Scleroderma-like changes are characterized by fibrotic skin thickening, while lichenoid changes involve itchy, plaque-like lesions on the body.

Treatment focuses on optimizing GVHD prophylaxis by monitoring cyclosporine levels, which is a common immunosuppressant used in organ transplant recipients. The severity of the symptoms ultimately helps guide further treatment. In acute GVHD with a skin rash involving < 50% of the body surface, topical steroids are the first line of treatment. If the rash is > 50% of the body surface, and/or there is gastrointestinal symptoms and signs of liver damage, systemic steroids can be considered. Octreotide is another medication that can be used in patients experiencing severe diarrhea. This medication is a somatostatin analog that is often used in the treatment of secretory diarrhea, hence its’ use in acute GVHD. The treatment for chronic GVHD is relatively similar. Corticosteroids are the first line of treatment for patients experiencing symptoms like those previously discussed. Second line options include either increasing the steroid dose or using cyclosporine.

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