Hematologic Disorders after Solid Organ Transplantation

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The evaluation of hematologic disorders after solid organ transplantation (SOT) must take into account issues unique to the post-transplant setting that influence the development of anemia and single or multi-lineage cytopenias. Attention to the time of onset of cytopenia(s) is important, because the disorders of passenger lymphocyte syndrome, transplant-related thrombotic microangiopathy, hemophagocytic syndrome, and graft-versus-host disease typically occur during the first few months after SOT, and post-transplant lymphoproliferative disorder usually occurs within the first year. Drug-related anemia and cytopenia(s) occur due to a variety of mechanisms, including drug-induced hemolysis and marrow suppression and perturbation of T-cell subsets by the immunosuppressive agents, leading to immune dysregulation and autoimmunity. Viral infections can cause direct suppression of hematopoiesis, and a variety of opportunistic infections can precipitate acquired hemophagocytic syndrome, a frequently lethal systemic inflammatory disorder. Early investigation of pancytopenia by bone marrow biopsy is warranted, because it is often the presenting symptom of one or multiple life-threatening pathologies after SOT, such as graft-versus host disease, post-transplant lymphoproliferative disorder, hemophagocytic syndrome, or severe opportunistic infections, and these entities may have a better prognosis if early interventions are undertaken.

The spectrum of hematologic disorders after solid organ transplantation (SOT) includes single or multilineage cytopenias of infectious, inflammatory, immune-mediated, or drug-related etiology; post-kidney-transplant erythrocytosis; thrombotic microangiopathy (TMA); infection-induced hemophagocytic syndrome (HPS); graft-versus-host disease (GVHD); post-transplant lymphoproliferative disorder (PTLD); venous thromboembolism; and coagulopathy. Anemia due to inappropriately low levels of erythropoietin or iron deficiency is common. This review will focus on the factors unique to SOT that influence the development of anemia and other cytopenias.

Etiologies of Anemia Uniquely Related to SOT

Passenger Lymphocyte Syndrome

ABO-mismatched SOT is often a necessity due to the limited availability of donor organs. A minor ABO-mismatched organ transplant is characterized by the presence in the donor plasma of preformed antibody (anti-A and anti-B isohemagglutinins) directed against the recipient's red blood cell antigens; for example, type-O donor organs transplanted into non-type-O recipients or type A or B donor organs transplanted into type-AB recipients. The complications that can arise from minor ABO-mismatched SOTs were reviewed by Yazer and Triuliz.[1] ABO-mismatched SOT leads to a unique immunological phenomenon, the passenger lymphocyte syndrome (PLS).[2] This syndrome occurs when viable lymphocytes of donor origin are adoptively transferred as "passengers" within the organ allograft, leading to alloimmune hemolysis of recipient red blood cells. As described in the review by Audet et al.,[2] PLS can be viewed as a type of "graft-vs.-host reaction" in which passenger memory B lymphocytes from the donor are stimulated after transplant by exposure to recipient or transfused red-cell antigens, and respond by producing antibody directed against these antigens, leading to hemolysis. PLS typically has an abrupt onset 1 to 3 weeks after SOT. The laboratory findings of PLS in the allograft recipient are an abrupt drop in hemoglobin level, elevated lactate dehydrogenase (LDH), and unconjugated bilirubin levels, decreased haptoglobin, a positive direct antiglobulin test, and detectable serum antibody against the target red cell antigen. Most cases of PLS are due to ABO mismatch, but cases due to antibodies against antigens in the Rh, Kidd, and Lewis blood group systems have also been reported. The process is self-limited, usually resolving within 3 months, because the passenger lymphocytes do not engraft and there is a finite time period during which the viable lymphocytes can proliferate. The hemolysis can be severe. As described in Hoffman's review of immune hemolytic anemia, the risk and severity of alloimmune hemolysis from PLS is related to the volume of lymphoid tissue in the organ allograft, and is highest with heart-lung transplants (hemolysis in 70%) and lower in liver (hemolysis in 29%) and kidney transplants (hemolysis in 9%).[3] Treatment is supportive and includes transfusion support with blood products selected in accordance with the guidelines reviewed by Petz[4] and, in some cases, red blood cell exchange to remove incompatible recipient-origin red blood cells.

Drug-Induced Anemia and Other Cytopenias

The pharmacologic management of SOT recipients involves the administration of numerous drugs with the potential to cause anemia and cytopenias through a variety of pathophysiologic mechanisms. Some of these drug-induced cytopenias are not unique to SOT, such as the induction of folate deficiency from the administration of trimethoprim/sulfamethoxazole, hemolysis from the use of dapsone or trimethoprim/sulfamethoxazole in patients with unrecognized glucose-6-phosphate dehydrogenase deficiency, or drug-induced hemolytic anemia from beta-lactam antibiotics or trimethoprim/sulfamethoxazole. The drug toxicities that are more specific to SOT include the protean potential adverse hematologic effects of the growing armamentarium of immunosuppressive agents and the antiviral agents used for prophylaxis and treatment of the specific viral infections that threaten the outcomes of allograft and recipient survival. Ganciclovir and valganciclovir, which are commonly used for the prophylaxis and treatment of cytomegalovirus (CMV) in allograft recipients, frequently cause reversible leukopenia, but can

also lead to multilineage cytopenias or severe drug-related pancytopenia.

Controlled comparative trials of the calcineurin inhibitors cyclosporine versus tacrolimus in liver transplantation demonstrated rates of anemia that varied from a low of 1% to 5% in European trials to as high as 38% to 47% in a large US trial.[5] Calcineurin inhibitor-induced anemia has been attributed to marrow suppression and the decreased red-cell survival that results from calcineurin inhibitor-induced microangiopathy. Mycophenolate mofetil reversibly and non-competitively inhibits the enzyme inosine monophosphate dehydrogenase, the rate-limiting enzyme for de novo purine synthesis during lymphocyte proliferation. Although the pharmacologic effect of mycophenolate mofetil is relatively selective to proliferating lymphocytes, its use is associated with reversible cytopenias, primarily leukopenia, but anemia can also occur. The antimetabolite effect of azathioprine, a purine-analog drug, can also cause marrow suppression and cytopenias. In addition, there are case reports of pure red-cell aplasia associated with the use of mycophenolate mofetil, tacrolimus, azothioprine, and anti-thymocyte globulin.[6,7] A high incidence of sirolimus-induced anemia has been reported after kidney transplantation. Vanrenterghem's review of anemia after kidney transplantation discussed the postulated etiologies for sirolimus-induced anemia, including an effect on iron hemostasis, a direct antiproliferative effect on the marrow, and induction of a chronic inflammatory state via interleukin-10 (IL-10)-dependent inflammatory autoregulation.[8]

Recently, transplant physicians have developed immunosuppressive regimens for SOT that eliminate long-term corticosteroid use and avoid the chronic nephropathy associated with calcineurin inhibitors. Many of the newer immunosuppressive regimens incorporate monoclonal antibodies, including rabbit anti-thymocyte globulin (thymoglobulin); alemtuzumab, a humanized anti-CD52 antibody that depletes T cells and B cells; and daclizumab, a humanized anti-CD25 antibody that targets the IL-2 alpha subunit (Tac antigen) expressed on activated lymphocytes. An interesting recent report by Elimelakh et al. described their observation of a high incidence of red-cell aplasia and autoimmune hemolytic anemia in pancreas transplant recipients enrolled on clinical trials of alemtuzumab-based maintenance therapy.[9] They reported severe red-cell aplasia, autoimmune hemolytic anemia, and idiopathic thrombocytopenia purpura, alone or in combination, in 20 of 357 (5.6%) pancreas-transplant recipients 12 to 24 months after initiation of the immunosuppressive regimen. Between February 2003 and November 2005, they treated 357 pancreas transplant recipients with immunosuppressive regimens that included alemtuzumab for lymphocyte depletion, daclizumab as a T-cell activation inhibitor, thymoglobulin, and mycophenolate mofetil. Of the 357 patients, 65 had induction only, 156 had induction and maintenance with alemtuzumab and mycophenolate mofetil, 108 were converted to alemtuzumab and mycophenolate mofetil, and 28 were treated for rejection with alemtuzumab and mycophenolate mofetil. In 121 of the 367 patients, daclizumab was added. The incidence of PTLD in their patient cohort did not differ from historical controls, but there was an increased incidence of opportunistic infection and a high incidence of delayed onset red-cell aplasia. They reported the blood and bone marrow findings of four cases of red-cell aplasia, seven cases of red-cell aplasia with associated autoimmune hemolysis, and nine cases of autoimmune hemolytic anemia. One patient with red-cell aplasia and one patient with autoimmune hemolytic anemia were also diagnosed with idiopathic thrombocytopenia purpura. Sixteen of the 17 patients with a positive direct antiglobulin test had immunoglobulin and complement on their red blood cells. The authors speculated that the combination of a T-cell-depleting agent and a T-cell-proliferation antagonist impaired T-regulatory cell function disproportionately to other T-cell subsets, which led to immune dysregulation and autoimmunity.

Thrombotic Microangiopathy

TMA following SOT and bone marrow transplantation was initially recognized as a complication of cyclosporine therapy in the 1980s. TMA is characterized by intravascular platelet aggregation, leading to thrombosis in the microcirculation, thrombocytopenia, and microangiopathic hemolysis. The onset of TMA is usually within the first few weeks after SOT, although it can occur months or years after SOT. The clinical features include anemia, reticulocytosis, rising LDH levels, fragmented and nucleated red blood cells on the peripheral blood film, varying degrees of renal dysfunction, and, in severe cases, multi-organ system dysfunction analogous to idiopathic thrombotic thrombocytopenia purpura. It is thought that direct endothelial injury by calcineurin inhibitors initiates TMA, although the pathogenesis of post-transplant TMA is incompletely understood. The phenomenon of microvascular thrombosis can be limited to the vasculature of the allografted organ or it can be systemic. Typically, TMA resolves with discontinuation of cyclosporine. TMA also occurs with the use of tacrolimus, although in both SOT and hematopoietic cell transplantation, it has been reported that some patients with cyclosporine-induced TMA can be re-challenged with tacrolimus and not develop recurrent calcineurin inhibitor-induced TMA. The combination of sirolimus with either cyclosporine or tacrolimus is associated with a higher incidence of TMA.[10]

The mechanism for platelet consumption in some cases of de novo thrombotic thrombocytopenia purpura is an acquired severe deficiency of ADAMTS 13, the von Willibrand factor-cleaving metalloproteinase that degrades the larger von Willibrand factor multimers in the circulation, thereby preventing them from accumulating and leading to platelet aggregation and clumping.[11] An inhibitory antibody directed against ADAMTS 13 is found in high frequency in patients with idiopathic, de novo thrombotic thrombocytopenia purpura. In contrast, it has been reported that SOT-related TMA is usually not associated with a severe deficiency of ADAMTS 13, and most authors have postulated that direct endothelial damage by the immunosuppressive drugs, vascular rejection of the allograft, CMV infection, or other insults are the mechanisms that lead to post-transplant TMA. In 2002, Pham et al. described a case of acquired severe deficiency of ADAMTS 13 associated with TMA in a renal transplant recipient.[12] Later, Mal et al. reported two lung allograft recipients who developed TMA associated with an acquired severe deficiency of ADAMTS 13 due to an inhibitor; both patients also had diffuse alveolar hemorrhage.[13] The authors concluded that acquired severe deficiency of ADAMTS 13 may be the underlying pathophysiology in some cases of SOT-related TMA, and diffuse alveolar hemorrhage may be a manifestation of TMA after SOT. Management of post-transplant TMA includes primarily the withdrawal of the suspected immunosuppressive agent and evaluation for CMV or other viral infections. Severe cases may benefit from plasma exchange.

Hematologic Disorders Associated with Opportunistic Infections

Viral Suppression of Hematopoiesis

Immunosuppressed SOT recipients are vulnerable to a panoply of opportunistic infections, but of particular relevance to the issue of

infection-induced cytopenias and pancytopenia are parvovirus B19 (PV B19) and the DNA herpes viruses CMV, human herpes virus-6 (HHV6), human herpes virus-8 (HHV8), and Epstein-Barr virus (EBV). The hematologic manifestations of CMV infection and the recommended strategies for viral surveillance, universal antiviral prophylaxis, preemptive therapy, or treatment of CMV disease are well established in the SOT literature and will not be reviewed herein. Reactivation of HHV6 from latency after SOT is a common occurrence, but the development of significant clinical disease is infrequent, so there are no recommended approaches for its prevention.[14] The most common hematologic manifestation of clinically significant HHV6 infection after SOT is leukopenia, but other cell lines can be affected as well. Standard polymerase chain reaction (PCR) on tissue or peripheral blood mononuclear cells will not discriminate between latent and active HHV6 infection. Viral isolation by culture is not rapid and is less sensitive than analysis of the peripheral blood viral load by quantitative PCR, which is the preferred diagnostic method for confirming HHV6 reactivation. The antiviral agents used to treat HHV6 infection are the same as those used to treat CMV infection, although no agent has formal Food and Drug Administration approval for this indication due to the absence of controlled trials. Ganciclovir or foscarnet are used for first-line therapy; it is unknown which agent is preferred due to the absence of comparative, prospective data. Cidofovir is highly active against HHV6 in vitro, but it is reserved for second-line therapy of infections resistant to ganciclovir or foscarnet because it is nephrotoxic. In 2000, Luppi et al. described an acute syndrome of primary HHV8 infection in two recipients of kidney allografts from an HHV8 seropositive donor.[15] One of the kidney recipients developed fever, splenomegaly, and marrow aplasia with plasmacytosis, with the presence of HHV8 latent nuclear antigen in immature progenitor cells. The reader is referred to the comprehensive reviews by Fischer[16] and by Allen and Green[17] regarding the viral pathogens associated with hematologic disorders in SOT recipients.

PV B19, a single-stranded DNA virus with target specificity for human erythroid-lineage cells, causes a rare clinical syndrome of anemia with reticulocytopenia and erythroid maturation arrest at the pro-normoblast stage in immunocompromised patients. Confirmation of the diagnosis of PV B19 red-cell aplasia can be made by enzyme-linked immunoabsorbent assay (ELISA) for anti-B19 specific antibody in patient sera, PCR assay for PV B19 DNA, or by the pathognomonic bone marrow biopsy finding of giant pro-erythroblasts with prominent intranuclear inclusions and cytoplasmic vacuolations and the absence of intermediate- and late-stage normoblasts.[18,19] Red-cell aplasia from PV B19 is treated by reduction of immunosuppression, infusions of intravenous immunoglobulin and erythropoietin. Recently, Guo et al. reported experimental results that provided insight into the mechanisms of PV B19 inhibition of erythropoiesis.[20] They demonstrated selective inhibition of erythroid growth and down-regulation of the expression of erythropoietin receptor mRNA in human CD34+ cells by CpG (cytosine linked to guanine by a phosphate bond) oligodeoxynucleotide-2006 (CpG-ODN 2006), a toll-like receptor-9 (TLR9) ligand that shares a consensus sequence with the PV B19 genome. Viral and bacterial pathogens or pathogen-derived products are recognized via TLR9, which has evolved to recognize unmethylated CpG dinucleotides that are commonly found in bacterial and viral genomes. Guo's team extracted PV B19 genome from serum and showed that it also inhibited erythroid growth and down-regulated expression of erythropoietin receptor.

Infection-Induced Hemophagocytic Syndrome

Acquired HPS is a life-threatening systemic inflammatory disease in which there is hemophagocytosis by proliferating, activated, non-neoplastic macrophages in the bone marrow, liver, lymph nodes, and spleen. The clinical features of HPS include fever, hepatosplenomegaly, lymphadenopathy, pancytopenia, skin rash, jaundice, cough, dyspnea, cachexia, and neurological dysfunction. Acquired HPS is an aberrant immune response of abnormal T-cell activation in reaction to a precipitating cause, leading to elaboration of macrophage-activating, pro-inflammatory cytokines such as IL-2 and gamma-interferon. The activated macrophages in turn secrete the T-cell-activating cytokines IL-1, IL-6, IL-12, and tumor necrosis factor-alpha (TNFα), which leads to further loop amplification of the pro-inflammatory process, a phenomenon also known as "cytokine storm." The laboratory findings of acquired HPS reflect the underlying pro-inflammatory pathophysiology, and include anemia, thrombocytopenia, leukopenia, high levels of soluble IL-2 receptor, abnormal liver tests, elevated LDH, hypofibrinogenemia, elevated ferritin, and hypertriglyceridemia, the latter attributed to inhibition of lipoprotein lipase enzyme by IL-1 and TNFα. In non-transplant patients, the underlying diseases associated with acquired HPS include viral infections, most frequently EBV, mycobacterial infection, non-Hodgkin's lymphoma, and systemic lupus erythematosus, as described in Takahashi's report of 52 adult patients with acquired HPS.[21] The form of HPS found in association with autoimmune diseases, most typically in systemic juvenile rheumatoid arthritis where it develops in up to 7% of patients, is referred to in the rheumatology literature as the "macrophage activation syndrome."[22]

Acquired HPS has been reported after renal, liver, heart, and pancreas-kidney SOT. The largest case series on HPS in SOT, reported by Karras et al., was 17 cases of HPS after cadaveric kidney transplant distributed among eight transplant units in Paris, with a denominator of 4230 renal transplants and an incidence of 0.4%.[23] The median time for onset of HPS was 52 d after kidney transplant. In 15 of the 17 patients, the following causes of HPS were identified: CMV (n = 3), EBV (n = 3), HHV6 (n = 1), HHV8 (n = 1), hepatitis C (n = 1), mycobacterium tuberculosis (n = 2) *Bartonella henselae* (n = 1), *Pneumocystis carinii* (n = 1), disseminated toxoplasmosis (n = 1), and PTLD (n = 2). The prognosis for this patient cohort was poor, with a fatal outcome in eight patients (47%) despite broad-spectrum antibiotic therapy, tapering of immunosuppression, supportive care, and graft nephrectomy. Secondary bacterial and fungal infections due to prolonged neutropenia, often associated with septic shock and acute respiratory distress syndrome, were common. The authors commented that HPS may be misdiagnosed due to its rarity and varying presentations, and they emphasized the need to perform early bone marrow biopsy whenever HPS is suspected. In 2010, Lo et al. reported two cases of HPS due to disseminated histoplasmosis after kidney transplantation in an Ohio River valley SOT unit.[24] In both cases, the patients underwent diagnostic bone marrow biopsy for investigation of a febrile illness with pancytopenia, and the biopsy disclosed hemophagocytosis in the marrow. Histoplasmosis was an unexpected finding in the bone marrow biopsy in one patient and in the lymph node biopsy from the other patient, whose marrow fungal culture later grew histoplasmosis. Both patients recovered with antifungal therapy and reduction of immunosuppression, and neither patient had graft rejection. The authors commented that HPS due to disseminated histoplasmosis after kidney transplant was previously unreported, although there was a prior reported case in a heart-transplant recipient. The good outcome in their two patients illustrates the importance of early diagnostic bone marrow biopsy

and an intensive search for opportunistic infections in the evaluation of SOT patients with unexplained fever and pancytopenia. No specific therapy can be recommended for post-transplant HPS other than treatment of the precipitating infection or PTLD and supportive care. In published cases, treatment with intravenous immunoglobulin and high-dose corticosteroids has been used, but with inconsistent outcomes. To date, there are no published reports using monoclonal antibody therapy directed against TNFα or IL-6 to treat HPS after SOT, although such an approach would seem logical given the pro-inflammatory nature of the disease process. It is of interest that etanercept, a TNFα inhibitor, was used to successfully treat acute HPS associated with systemic lupus erythematosus, as reported by Takahashi et al. in 2008.[25]

EBV-Driven PTLD

Hypoproliferative anemia or pancytopenia after SOT can be due to marrow infiltration with PTLD. Autoimmune hemolytic anemia can also be a manifestation of PTLD after SOT. PTLD after SOT occurs because impairment of EBV-specific, cyotoxic T-cell function by systemic immunosuppression permits the expansion of recipient-origin B cells latently infected with EBV. The spectrum of PTLD after SOT ranges from an infectious mononucleosis-like, EBV-driven polyclonal lymphocyte proliferation to life-threatening, aggressive non-Hodgkin's lymphoma. Most cases of PTLD occur in the first year after SOT. The risk of PTLD varies with the degree of immunosuppression administered, so it is more common in heart and lung transplant recipients (up to 10%) and less frequent in renal transplant recipients (1%–2%). The reader is referred to recent comprehensive reviews by Heslop[26] and by Gross et al.[27] for a discussion of PTLD biology, varied clinical presentations, and recommendations for viral surveillance strategies, preemptive therapy, and treatment. The published evidence-based guidelines for management of PTLD from both US and European task forces emphasize the need for immediate reduction in immunosuppression to the minimal level that will preserve survival of the transplanted organ, an intervention that may lead to complete remission. Rituximab monotherapy is recommended for PTLD that does not respond to reduced immunosuppression based on data from phase II studies demonstrating remission in 44% to 65% of PTLD patients. Rituximab + anthracycline-based chemotherapy is used to treat PTLD progression or relapse after reduced immunosuppression and rituximab monotherapy, or in selected cases for the initial treatment of high-grade histology PTLD that is clinically aggressive.

GVHD after SOT

GVHD after SOT is a very rare and frequently lethal complication caused by the engraftment and proliferation of allograft-associated lymphocytes in the immunosuppressed recipient, with subsequent immune-mediated attack by donor-origin effector cells directed against HLA-disparate host tissues. A recognized risk factor for the development of SOT-GVHD is the quantity of lymphoid tissue in the donor organ; therefore, SOT-GVHD occurs most frequently following small bowel and liver transplantation, followed by lung and kidney transplantation in decreasing order of frequency.[28] Other reported risk factors for SOT-GVHD are greater degrees of HLA match between donor and recipient and recipient age over 65 years.[29] Approximately 80 cases of GVHD after liver transplant were reported in 2008, with published incidence rates of 0.1% to 2%.[30] A 2008 report by Worel et al. of GVHD after lung transplantation stated that fewer than 10 cases of GVHD had been reported in the denominator of over 21,000 lung transplants worldwide.[31]

Kohler's review of GVHD after liver SOT made the interesting observation that the number of lymphoid cells in a liver allograft is comparable to a hematopoietic cell transplantation because approximately 10^9 to 10^{10} donor lymphocytes remain in the portal tract of the graft after perfusion with the preservative solution.[32] It is known that transient lymphocyte chimerism occurs in recipients of SOT, and in fact it is thought to be necessary for the establishment of organ tolerance; however, lymphocyte chimerism usually rapidly decreases over time so that by the third postoperative week, macrochimerism (>1% donor cells in peripheral blood) is abolished.

GVHD typically occurs early after SOT, with a median onset of 33 d reported in the analysis by Assi et al. of 30 cases of SOT-GVHD in organ transplants other than isolated liver transplants.[34] However, the author noted that GVHD onset was later after kidney transplant, with a median of 77 d. The typical clinical presentation of SOT-GVHD is fever, rash, diarrhea, and multilineage cytopenias or pancytopenia occurring 2 to 8 weeks after SOT. Profound marrow aplasia due to "graft-vs.-hematopoiesis" is a feature common to transfusion-associated GVHD and SOT-GVHD that is different from the presentation of GVHD after allogeneic hematopoietic cell transplantation. The diagnosis is often delayed because the cytopenias and rash that are the first symptoms of SOT-GVHD are attributed to viral infection or are thought to be drug related. The diagnosis of SOT-GVHD is made by demonstration of the histological features of GVHD in biopsies of affected tissues and confirmation of lymphocyte macrochimerism in the peripheral blood, marrow, and/or affected tissues. Prognosis is poor, with death due to infectious complications of prolonged marrow aplasia and multi-organ failure. SOT-GHVD reported mortality rates are 75% in liver-transplant recipients, 100% in lung-transplant recipients, and 30% in the report of 30 patients following SOT other than isolated liver.[33] The initial therapy for SOT-GVHD in the majority of published reports was high-dose corticosteroids. Some authors also reduced immunosuppression to enable the recipient immune system to recover and reject the allografted donor T cells. There are single case reports of successful treatment for SOT-GVHD after liver transplant using infliximab,[34] etanercept,[35] and alefacept,[36] but, given the rarity of SOT-GVHD, no evidence -based treatment guidelines exist.

The literature on SOT-GVHD frequently opines that the prognosis might improve with early diagnosis and interventions to prevent infectious complications of prolonged marrow aplasia. Therefore, the diagnosis of SOT-GVHD should be investigated by analysis for lymphocyte macrochimerism when recipients of SOT develop pancytopenia, especially in the first 2 months after organ allograft. Finally, although SOT-GVHD typically presents early post-transplant, a case report by Pollack et al. of severe late-onset GVHD 8 months after liver SOT illustrates the importance of considering SOT-GVHD in the differential diagnosis any time an SOT recipient presents with unexplained pancytopenia.[38]

Evaluation of Anemia and Cytopenias after SOT

In summary, the evaluation of anemia and single or multilineage cytopenias after SOT must take into account the unique features of the SOT setting.[38,39] Attention to the time of onset of the cytopenia(s) is important, because PLS, GVHD, HPS, and TMA are more likely to occur in first few months after SOT, and PTLD is most common in the first year after SOT. Opportunistic infections, especially viral infections, should always be investigated as a potential precipitating cause of cytopenia(s), either as the direct agent of marrow suppression or as the trigger for HPS or immune

cytopenia(s). Drug-related anemia and cytopenia(s) due to a variety of mechanisms, including perturbation of T-cell subsets by the immunosuppressive regimen leading to autoimmune cytopenia, should be considered. Early investigation of pancytopenia by diagnostic bone marrow biopsy is warranted, because pancytopenia is often the presenting symptom of one or multiple life-threatening pathologies such as SOT-GVHD, PTLD, or unsuspected opportunistic infections, conditions that may have a better prognosis if early interventions are undertaken.

Disclosures

Conflict-of-interest disclosure: The author declares no competing financial interests. Off-label drug use: Rituximab for the treatment of PTLD.

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