Transplantation in Rare Lymphoproliferative and Histiocytic Disorders

Alexis Cruz-Chacon, MD, John Mathews, MD, and Ernesto Ayala, MD

Background: Some uncommon lymphoproliferative and histiocytic disorders may present with an aggressive course and require hematopoietic stem cell transplantation (HSCT) as part of the therapeutic approach.

Methods: Published research on the use of HSCT for the treatment of these disorders was reviewed and summarized.

Results: Allogeneic HSCT may be indicated in patients with blastic plasmacytoid dendritic cell neoplasia, familial or secondary recurrent hemophagocytic lymphohistiocytosis, and resistant Langerhans cell histiocytosis. Autologous HSCT may be considered in patients with Castleman disease resistant to treatment. No role has been established for the use of HSCT for dendritic cell sarcoma.

Conclusions: HSCT has an evolving role in the treatment of select aggressive lymphoproliferative and histiocytic disorders.

Introduction

Atypical lymphoproliferative and histiocytic disorders are composed of several entities that have in common the presence of lymphoproliferative or histiocytic cells with variable degrees of atypia, a poorly defined natural history, and an unclear prognosis. Most of these entities are infrequent and, as a consequence, treatment is not dictated by well-designed prospective trials. Some are aggressive — similar to high-grade lymphoma — and transplantation is commonly used as initial therapy or following relapse. Nearly all transplantation-related data have been derived from case reports and small, uncontrolled series.1,5

In this review, selected entities, including blastic plasmacytoid dendritic cell neoplasm (BPDCN), hemophagocytic lymphohistiocytosis (HLH), Langerhans cell histiocytosis (LCH), dendritic cell sarcoma, and Castleman disease, were included for which data on transplantation outcomes were available. Whenever possible, the role of transplantation in the treatment of each entity was approximated. A summary of the indications for transplantation in these rare lymphoproliferative and histiocytic disorders is found in Table 1.

Blastic Plasmacytoid Dendritic Cell Neoplasm

BPDCN is a rare, clinically aggressive hematological malignancy. This tumor was initially described in...
Table 1. — Indications for Hematopoietic Stem Cell Transplantation in Select Lymphoproliferative and Histiocytic Disorders Among the Pediatric Population

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Type of Transplantation</th>
<th>Indication</th>
<th>Conditioning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blastic plasmacytoid dendritic cell neoplasia</td>
<td>Allogeneic Autologous (limited)</td>
<td>Consider in first remission for all patients</td>
<td>Myeloablative or reduced intensity</td>
</tr>
<tr>
<td>Hemophagocytic lymphohistiocytosis</td>
<td>Allogeneic</td>
<td>All patients with the familial form of disease</td>
<td>Myeloablative or reduced intensity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients with the recurrent or resistant secondary form of the disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients with the malignancy-associated form of the disease</td>
<td></td>
</tr>
<tr>
<td>Langerhans cell histiocytosis</td>
<td>Allogeneic</td>
<td>Resistant, recurrent, or high-risk disease</td>
<td>Myeloablative or reduced intensity</td>
</tr>
<tr>
<td>Dendritic cell sarcoma</td>
<td>Allogeneic or autologous</td>
<td>No role</td>
<td>—</td>
</tr>
<tr>
<td>Castleman disease</td>
<td>Autologous</td>
<td>Multicentric following the failure of systemic therapy</td>
<td>High-dose melphalan</td>
</tr>
</tbody>
</table>

1995 as acute agranular CD4+ natural killer (NK) cell leukemia; however, the term BPDCN was introduced by the World Health Organization following the discovery that the entity arises from the precursors of plasmacytoid dendritic cells (type 2 dendritic cells).

The most common presentation in patients with BPDCN is brown to violaceous cutaneous lesions, plaques, or tumors with or without bone marrow involvement and leukemic dissemination. Some patients may have a leukemic presentation without skin involvement. Most patients present with cytopenias, lymphadenopathy, and/or splenomegaly. Liver, tonsil, paranasal cavity, lung, eye, central nervous system, and paravertebral involvement have all been reported. Identifying the specific immunophenotype of tumor cells is essential for diagnosis. BPDCN malignant cells coexpress CD4 and CD56, and the expression of other plasmacytoid dendritic cell–associated markers, including CD123, blood dendritic cell antigen 2, T-cell leukemia 1, and SPIB, is useful for the diagnosis of BPDCN. Differential diagnoses include CD56+ acute myeloid leukemias, nasal-type extranodal NK/T-cell lymphoma, subcutaneous panniculitis-like T-cell lymphoma, and cutaneous T-cell lymphoma. About two-thirds of patients with BPDCN have genetic abnormalities, but no diagnostic cytogenetic or molecular changes have been identified.

BPDCN is characterized by an aggressive behavior with rapid systemic dissemination. Despite an initial response to systemic chemotherapy, most patients relapse and have a poor rate of overall survival (median, 12–14 months). The optimal treatment for BPDCN is unknown and small retrospective analyses alone are available to guide therapy. Studies found that the clinical course and response to therapy differ among children compared with adults. Children have a good response to similar treatment regimens used for high-risk acute lymphoblastic leukemia without the need for hematopoietic stem cell transplantation (HSCT); by contrast, BPDCN is more aggressive in adults. Prospective studies defining the most optimal frontline therapy in adults are lacking, whereas retrospective studies favor acute lymphoblastic leukemia or aggressive non-Hodgkin lymphoma therapies for the initial treatment of adults diagnosed with BPDCN. However, most patients responding to initial therapy will relapse within 2 years irrespective of the type of chemotherapy received.

For additional information on BPDCN, please see the article by Dr Riaz and colleagues on page 279.

**Hematopoietic Stem Cell Transplantation**

Due to the reported poor and transient responses to initial chemotherapy, adults with BPDCN are frequently offered allogeneic HSCT. Most of the available data regarding the outcomes following allogeneic HSCT come from small retrospective studies. The largest retrospective study included 34 patients from a European database who received myeloablative conditioning for allogeneic HSCT. The majority of patients received stem cells from a sibling or matched unrelated donor. The overall survival rate was 41% at 3 years, and no relapses were observed 27 months following HSCT. Receiving transplantation in the first complete remission was associated with a more favorable outcome than in those transplanted with more advanced disease. When the analysis was restricted to this group of patients, the 3-year disease-free survival and overall survival rates were 45% and 60%, respectively.

Age, donor, source, and presence of chronic graft-vs-host disease had no impact on survival on univariate analysis.

A smaller, single institution case series demonstrated the feasibility of allogeneic HSCT in older patients with the use of reduced intensity conditioning.
Four of the 6 adults studied with BPDCN (median age, 67 years; range, 55–80 years) underwent reduced intensity conditioning for allogeneic HSCT. Two patients who received transplants before the age of 21 years were found to have active disease relapsed at 6 and 18 months following transplantation. Therefore, these data suggest that reduced intensity conditioning may be considered for older or comorbid patients who are not candidates for myeloablative conditioning for allogeneic HSCT. Several small case series and reports with single cases have been reported of autologous HSCT for the treatment of patients with BPDCN. Patients with chemosensitive disease and early disease presentation alone have been found to benefit from autologous HSCT.

Few case reports exist of patients with BPDCN who have undergone cord blood stem cell transplantation. However, one such case was reported by Ramanathan et al who described successful cord blood HSCT in a patient with BPDCN using a preparative regimen of thiotepa, fludarabine, and melphalan.

**Hemophagocytic Lymphohistiocytosis**

HLH is a hyperinflammatory disorder characterized by the nonmalignant, reactive, uncontrolled proliferation of histiocytes. The disease results from the underlying immune dysfunction either from a primary immune deficiency (called familial HLH) or from an acquired failure of immune hemostasis associated with infection, autoimmunity, or malignancy (called reactive or secondary HLH). HLH is a clinical syndrome biologically characterized by a highly stimulated but ineffective immune response. The activation and proliferation of T cells and macrophages are uncontrolled and inflammatory cytokines are overproduced. Although the trigger for hyperinflammation varies, the final pathway is commonly the infiltration of multiple organs by activated CD8+ T lymphocytes, macrophages, and hypercytokinemia, resulting in end-organ damage. Clinically, patients with HLH typically present with high fever, hepatosplenomegaly, cytopenias, liver and pulmonary dysfunction, and, frequently, signs of neurological involvement. Multiorgan failure typically occurs during the final stage of progressive organ injury.

HLH is commonly divided into 2 types: familial and secondary. Familial HLH is an inherited disorder characterized by various defects on granule-dependent cytotoxicity. Known genetic mutations include the *PRF1* and *hMunc* genes, which account for approximately 20% to 40% of familial HLH cases. Others include X-linked lymphoproliferative disorder, Chédiak–Higashi syndrome, Griscelli syndrome, and severe combined immunodeficiency. The trigger for HLH is typically infection. Secondary HLH is a broad category that includes autoimmune disorders and infections associated with HLH (commonly viral, although bacterial, fungal, and protozoan infections have been reported) as well as malignancy associated with HLH. Malignancy-associated HLH is typically associated with hematological disorders, particularly lymphoma. The most common types of lymphoma associated with HLH are NK/T-cell and diffuse large B-cell lymphoma.

No single diagnostic test will confirm HLH; rather, clinical and laboratory data must be used to confirm the diagnosis. In the first prospective study of HLH performed internationally, a diagnosis was based on the presence of 5 criteria (fever lasting > 7 days, splenomegaly, bicytopenia, hypertriglyceridemia and/or hypofibrinogenemia, and hemophagocytosis). In yet another study, 3 additional criteria were introduced: low or absent NK cell activity, hyperferritinemia, and a high level of soluble interleukin 2 receptor. Currently, a diagnosis of HLH can be made either by molecular diagnosis via the detection of a genetic mutation characteristic of familial HLH or by fulfilling 5 of the 8 criteria discussed above.

**Treatment**

The therapeutic strategy for HLH involves treatment of severe inflammation while also addressing the underlying trigger. If the patient is acutely ill, then prompt care at an intensive care unit and the initiation of HLH-specific treatment are required. Alternatively, if the patient is stable, then a search for the trigger is initiated and treatment is provided. Typically, decisions on how to treat HLH in adult patients are extrapolated from pediatric data. Malignancy-associated HLH has a worse prognosis than other types of HLH and, generally, successful treatment of the underlying malignancy is needed prior to the resolution of HLH.

In a prospective study performed on an international level, Henter et al showed that combined chemotherapy and immunotherapy (etoposide, steroids, and cyclosporine A) improved rates of survival among patients with HLH. A total of 113 patients who were 15 years of age or younger were included. At a median follow-up of 3.1 years, the estimated 3-year overall survival rate was 55% (51% in cases of familial HLH). Patients with persistent, recurrent, or familial HLH underwent bone marrow transplantation and had a 3-year survival rate of 62%. In another study, patients receiving combination cyclophosphamide/vincristine/prednisone had a 1-year overall survival rate of 66.7%, and the treatment was especially favorable for those with infection and autoimmune disease–associated HLH. In yet another study, patients receiving treatment with combination cyclophosphamide/doxorubicin/vincristine/prednisone had a median overall survival rate of 18 weeks and a 2-year overall survival rate
of 43.9%. However, one-half of patients will relapse with standard HLH therapy. A review of 22 pediatric and adult patients who received alemtuzumab for the treatment of refractory HLH showed that 14 patients (64%) experienced a partial response and 77% of patients survived to undergo allogeneic HSCT.

**Allogeneic Hematopoietic Stem Cell Transplantation**

In 1986, Fischer et al. showed that allogeneic HSCT was curative in patients with familial HLH, a finding confirmed by other reports. In their international study, Henter et al. recommended allogeneic HSCT, which was part of the treatment for all study participants with persistent, recurrent, or familial types of HLH. Of the 113 patients who entered the study, 65 underwent allogeneic HSCT (15 matched related, 25 matched unrelated, 4 mismatched unrelated, 14 haploidentical, 5 cord blood, and 2 unsnknown). The most common conditioning regimen included myeloablative doses of busulfan, cyclophosphamide, and etoposide. The 3-year overall survival rate was 62%, which is notable because a small number of patients had a related donor. Acculated data have established that, for individuals with familial HLH, HSCT is the only long-term curative therapy option and should be offered to all patients. Table 2 summarizes the largest published studies in pediatric patients.

Table 2. — Selected Studies on Allogeneic Transplantation for Hemophagocytic Lymphohistiocytosis

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of Patients</th>
<th>Conditioning</th>
<th>Graft Failure (%)</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Henter et al</td>
<td>65</td>
<td>Busulfan/cyclophosphamide/etoposide ± antithymocyte globulin</td>
<td>Not reported</td>
<td>62% at 3 y</td>
</tr>
<tr>
<td>Baker et al</td>
<td>91</td>
<td>Busulfan/cyclophosphamide/etoposide ± antithymocyte globulin</td>
<td>9</td>
<td>53% at 5 y</td>
</tr>
<tr>
<td>Ouahé-Chardin et al</td>
<td>48</td>
<td>Busulfan/cyclophosphamide/etoposide ± antithymocyte globulin</td>
<td>22</td>
<td>58% at 5.8 y</td>
</tr>
<tr>
<td>Cooper et al</td>
<td>12</td>
<td>Fludarabine/melphalan/alemtuzumab</td>
<td>0</td>
<td>75% at 2.5 y</td>
</tr>
<tr>
<td>Cesaro et al</td>
<td>61</td>
<td>Busulfan/cyclophosphamide ± etoposide</td>
<td>5</td>
<td>58% at 8 y</td>
</tr>
</tbody>
</table>

Although the outcomes among patients with HLH have improved with the use of allogeneic HSCT, several limitations are apparent. For example, every effort should be made to achieve HLH remission prior to HSCT; if not, transplantation-related mortality rates will increase. Graft failure is also more frequent (~10%) in HLH than other nonmalignant disorders and is a cause for concern. In addition, transplantation-related mortality rates remain high (eg, recurrent HLH, graft failure, veno-occlusive disease, pneumonitis); therefore, new approaches for HSCT are needed. One such development is the introduction of reduced intensity conditioning in allogeneic HSCT for HLH. In 24 patients with HLH, Marsh et al. used reduced intensity conditioning for fludarabine and melphalan with variable doses and a novel, intermediate schedule of alemtuzumab. The regimen was associated with a low incidence of graft-vs-host disease, the absence of graft failure, and a low need for subsequent stem cell products.

Compared with children, very few adults with HLH are treated with allogeneic HSCT. In 2 published case reports, allogeneic HSCT was used for the treatment of an underlying hematological malignancy or Epstein–Barr viral infection with associated HLH. At the Moffitt Cancer Center, a 22-year-old woman presented with hepatosplenicomegaly, fever, and severe hypotension. Bone marrow biopsy and pathology from splenectomy showed the presence of γ/Δ hepatosplenic T-cell lymphoma and HLH. Upon presentation, her ferritin level was 20,700. Initially, the patient required aggressive treatment for HLH; however, once she was clinically stable, the patient received chemotherapy and achieved a partial response and subsequently underwent allogeneic HSCT. The conditioning regimen used included fludarabine, cyclophosphamide, thiopeta, and 200 cGy of total body irradiation, followed by double umbilical cord blood transplantation. One year following HSCT, the patient remained on remission from HLH and hepatosplenic lymphoma.

Allogeneic HSCT is a curative treatment option that should be offered to all patients with familial, recurrent, or persistent types of HLH. In adults with HLH, allogeneic HSCT is frequently used to treat an underlying hematological malignancy.

**Langerhans Cell Histiocytosis**

LCH is characterized by the idiopathic proliferation of histiocytes within the reticuloendothelial system and can infiltrate virtually any organ system. It can afflict any age group, although it is predominantly seen in children. Its clinical presentation and natural history range from benign unifocal to aggressive multifocal systemic disease. Diagnosis and treatment for adults are based on pediatric data.
Data from an international registry that included 269 patients who were 18 years and older revealed slightly more affected men than women (143 vs 126) with mean ages at diagnosis of 33 years and 35 years, respectively. Single-system LCH was found in 86 patients (31.4%) and isolated pulmonary LCH was found in 44 cases. A total of 188 patients (68.6%) had multisystem disease and 81 (29.6%) had diabetes insipidus.

The diagnosis is made via biopsy of the suspect lesion. The classic histopathological feature of LCH is the presence of lesional Langerhans cells with varying proportions of macrophages, multinucleated giant cells, T-lymphocytes, and eosinophils. A definitive diagnosis is based on the histopathological finding of at least 1 of the following: langerin (CD207) positivity, CD1a positivity, or the presence of Birbeck granules on electron microscopy. Given the minimal symptoms upon presentation, a thorough initial workup is recommended to evaluate the exact extent of involvement, including a complete history, physical examination, laboratory studies, and radiographic evaluation.

Treatment is based on a risk stratification system that was adopted by an expert panel of the Euro-Histio-Net. Stratification depends on the extent and severity of disease at diagnosis. LCH can be divided into 2 major categories: single-system LCH is subdivided further into single-site and multisite disease, and multisystem LCH is defined as the involvement of 2 or more organs at diagnosis with or without organ dysfunction. In the pediatric population, low-risk patients account for 20% of all multisystem LCH and have an excellent prognosis; they also are characterized by the absence of “risk organ” involvement, including the liver, lungs, and spleen, the hematopoietic system, and tumors of the central nervous system. Patients at high risk make up 80% of patients with multisystem LCH, have 1 or more risk organs involved, and have a high mortality rate.

In the setting of single-system LCH, unifocal involvement may be treated with careful observation and local therapy, which includes the total excision of the lesion with or without radiation therapy. Systemic therapy is required for multisystem LCH, single-system LCH with multifocal lesions, and single-system LCH with “special site” lesions, which are lesions in critical anatomical sites (e.g., intraspinal, craniofacial bone). Studies focused on the treatment of adult populations with LCH are limited. However, several chemotherapeutic agents have shown to be effective. A retrospective study of 58 adult patients with a mean age of 32 years compared 3 commonly used regimens. Cytarabine was shown to have better efficacy and lower toxicity rates when compared with vinblastine/prednisone and 2-chlorodeoxyadenosine. In addition, 84% of patients treated with vinblastine/prednisone and 59% of patients treated with 2-chlorodeoxyadenosine either did not respond or relapsed within 1 year, whereas 21% of patients given cytarabine failed to respond to treatment. In a prospective trial, 7 adult patients with multisystem LCH (n = 3) or single-system, multifocal LCH (n = 4) were given a short-course, intensive chemotherapy regimen that consisted of methotrexate, doxorubicin, cyclophosphamide, vincristine, prednisone, and bleomycin. The overall response rate was 100%, with 5 complete responses and 2 partial responses seen among the participants. After a median follow-up of 6.5 years, 4 patients were in first continuous complete responses and 3 patients had relapsed after 5, 8, and 62 months.

Single-agent chemotherapy represents the treatment strategy used for multisystem LCH with or without the involvement of “risk organs,” single-system LCH with multifocal lesions, and single-system LCH with “special site” lesions. Intensive regimens are reserved for aggressive presentations. Other treatments may include imatinib for cerebral LCH, zoledronic acid for bone disease, or lenalidomide.

**Hematopoietic Stem Cell Transplantation**

Kudo et al reported their experience with 15 children who had refractory LCH and underwent HSCT in Japan. The median age at transplantation was 23 months and all of the participants had previously failed conventional chemotherapy. Myeloablative conditioning was used in 10 patients and reduced intensity conditioning was used in 5 patients. Umbilical cord blood was the graft source in 10 patients. Eleven patients became long-term survivors; a 10-year overall survival rate of 73% was seen for the entire group and a 10-year survival rate of 55% was seen among patients with high-risk disease. HSCT from parental haploidentical donors was reported in 2 girls (aged 26 months and 5 months) with refractory multisystemic LCH. Conditioning included myeloablative doses of busulfan, cyclophosphamide, fludarabine, and etoposide. Prophylaxis to prevent graft-vs-host disease included cyclosporine, methotrexate, mycophenolate, daclizumab, and antithymocyte globulin. Both patients survived and remained free of disease for 54 and 44 months, respectively, following HSCT.

Allogeneic HSCT has been reported in an adult patient with LCH, thrombocytopenia, and no radii. Reduced intensity conditioning for allogeneic HSCT incorporated fludarabine, busulphan, and alemtuzumab prior to transplantation. Three years following transplantation, the patient had stable donor cell engraftment, a normalized platelet count, no evidence of disease progression, and no graft-vs-host disease.

These limited data suggest that allogeneic HSCT may be effective therapy for patients with LCH who...
Dendritic Cell Sarcoma

Dendritic cell sarcoma is a rare, malignant neoplasm that arises in follicular dendritic cells that form a meshwork in the lymph node follicles and are critical for antigen presentation. Hyaline Castleman disease has been implicated as precursor of this entity. It typically occurs in young adults and most commonly begins in the lymph nodes of the neck or mediastinum; however, it can also be found in extranodal sites as the gastrointestinal tract, the liver, spleen, and bone. Diagnosis depends on a clinical examination, imaging, and pathological assessment.

The clinical behavior of the disease is similar to low-grade sarcomas with local aggressiveness. Treatment for dendritic cell sarcoma involves the complete resection of the primary lesion; however, significant risk exists for local relapse and metastatic disease. In patients with advanced or unresectable disease, chemotherapy has been used with mixed results. In case reports, selected patients with disseminated disease responded to lymphoma-oriented chemotherapy regimens.

A single case report of high-dose chemotherapy and autologous HSCT for the treatment of dendritic cell sarcoma was found in the literature. In this case, a 25-year-old man with a primary tumor of the tibia and surrounding soft tissues was treated with cyclophosphamide/doxorubicin/vincristine/prednisone and achieved minimal response. Subsequently, the patient underwent chemotherapy mobilization with etoposide/cisplatinum/methylprednisolone sodium succinate/cytarabine, followed by stem cell collection. The patient then received high-dose carmustine/etoposide/cytarabine/melphalan followed by autologous stem cell infusion. He achieved a partial response but the disease subsequently progressed to his regional lymph nodes.

At this time, data are insufficient to recommend the routine use of HSCT in patients with dendritic cell sarcoma.

For a more detailed description of dendritic cell sarcoma and histiocytic neoplasms, please see the article by Dr Dalia and colleagues on page 290.

Castleman Disease

Castleman disease is a rare lymphoproliferative disorder and 2 major histological variants of the disease have been identified. Abnormal follicles with regressed germinal centers characterize the hyaline vascular variant, whereas the plasma cell variant is characterized by hyperplastic germinal centers and the massive accumulation of polyclonal plasma cells in the interfollicular region. A mixed form demonstrates areas with both histological patterns.

In a major retrospective review of 113 patients, 48% of whom were men with a median age of 43 years (range, 4.2–78 years), 53% of patients studied had multicentric disease. Patients with the plasma cell variant were more likely to have multicentric disease, and these patients were more likely to be older, have B symptoms, palpable disease, peripheral neuropathy, extravascular volume overload, coexisting polynuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin abnormality (POEMS) syndrome, bony sclerosis, anemia, leukocytosis, thrombocytosis, a high sedimentation rate, hypergammaglobulinemia, a low albumin rate, and an elevated creatinine level. The 2-, 5-, and 10-year survival rates for the entire group were 92%, 76%, and 59%, respectively. The 5-year overall survival rates among patients with unicentric and multicentric Castleman disease were 91% and 65%, respectively. A total of 80% of patients with unicentric disease was treated with surgery; of these patients, 89% achieved a partial or complete response. Patients with multicentric disease were treated with prednisone alone, alkylator-based chemotherapy, interferon, anthracycline-based chemotherapy, or rituximab.

Patients with multicentric disease may have an associated human herpesvirus 8 infection (up to 50% of the cases) and they frequently present with elevated levels of interleukin 6. Antibodies against interleukin 6 or its receptor have become available and have been tested in clinical trials.

Hematopoietic Stem Cell Transplantation

The use of HSCT in the setting of Castleman disease is limited to a few case reports, particularly among patients with multicentric disease who have failed other systemic therapies. The first mention of high-dose therapy concurrently with autologous HSCT was published by Repetto et al. They reported on the case of a patient with aggressive Castleman disease who received high-dose melphalan and autologous HSCT. The patient achieved a complete remission that lasted 15 months at the time of publication. Ganti et al reported on the case of a 39-year-old man who presented with peripheral neuropathy, lymphadenopathy, pleural effusions, hepatomegaly, and splenomegaly. Monoclonal immunoglobulin A was identified in the serum and a diagnosis of POEMS syndrome was made. The initial treatment included rituximab; following a poor response to treatment, cyclophosphamide/mitoxantrone was added. The patient then underwent mobilization with cyclophosphamide and granulocyte-colony stimulating factor. Subsequently, he received high-dose chemotherapy with melphalan.
followed by an autologous stem cell infusion. Fourteen months following transplantation, the monoclonal spike had nearly disappeared, peripheral neuropathy had improved, and the patient was functional and free of symptoms.5

Tal et al71 reported on the case of a 52-year-old man who presented with diarrhea, weight loss, and abdominal masses. Lymph node biopsy confirmed the plasma cell variant of multicentric Castleman disease. The initial treatment was cyclophosphamide, vincristine, prednisone, and rituximab, and the patient achieved complete remission and a resolution of all his symptoms. Eighteen months later, the disease recurred and the patient was treated with vinblastine and rituximab.71 Subsequently, he received conditioning with etoposide, thiopeta, cytarabine, cyclophosphamide, and melphalan, followed by autologous peripheral blood stem cell transplantation. Fifty months following transplantation, the patient remained in remission.71

Although the evidence is limited, data suggest a role for autologous HSCT in patients with Castleman disease. Remissions have been long lasting and morbidity rates have been limited despite patients undergoing transplantation with active disease. Therefore, HSCT should be considered in patients with multicentric Castleman disease who have failed systemic therapies and, in particular, among those with associated POEMS syndrome.

For a more detailed description of Castleman disease, please see the article by Dr Soumerai and colleagues on page 266.

Conclusions

Acknowledging the paucity of the data, allogeneic hematopoietic stem cell transplantation has an accepted indication in patients with blastoid plasmacytoid dendritic cell neoplasia and in those with familial, recurrent, or persistent hemophagocytic lymphohistiocytosis. It may also be considered in patients with recurrent or high-risk Langerhans cell histiocytosis. Autologous hematopoietic stem cell transplantation may be considered in patients with Castleman disease, in particular with associated polynuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin abnormality syndrome, and also in patients with blastoid plasmacytoid dendritic cell neoplasia who have chemosensitive disease and are not suitable candidates for allogeneic hematopoietic stem cell transplantation. Published data do not support the routine use of hematopoietic stem cell transplantation in patients with dendritic cell sarcoma.

References


