Stem Cells Offer Option For Refractory Vasculitis

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Stem cell transplantation may be an option for patients whose lives are threatened by medically refractory vasculitis, Dr. Thomas Daikeler and his colleagues have reported.

Up to 20% of vasculitis patients don't respond to conventionally dosed immunosuppression, Dr. Daikeler said in an interview. Options for these patients are very limited, he said. However, his review of 20 patients who received the transplants showed that 93% responded positively, with 7 achieving sustained complete remission (Ann. Rheum. Dis. 2006 Sept. 1 [Epub doi:10.1136/ard.2006.056630]).

At the 44-month follow-up phase of one study, 93% of patients who failed immunosuppressive therapy responded to stem cell transplantation.

Dr. Daikeler, of the University of Basel, Switzerland, reviewed outcomes in 15 patients included in the European League Against Rheumatism (EULAR) database or the PROMISE international medical database, and 5 additional patients identified through a Medline search.

The report focused on the details of the 15 EULAR/PROMISE patients. Their median age was 37 years (age range 10-57 years). Four had cryoglobulinemia, three had Behçet's syndrome, three had Wegener's granulomatosis, and the others had Churg-Strauss angiitis, Takayasu's arteritis, polychondritis, and a polyarteritis nodosa. All patients had active disease and had failed intensive immunosuppressive therapy, including cytostatic drugs. Most of them (14) had an autologous stem cell transplant first; 1 had an allogeneic transplant first.

At the time of the analysis, the median follow-up for all patients was 44 months (range 16-84 months). The response rate was 93%. Overall, seven responded partially and needed maintenance immunosuppression for minor disease, seven patients were in complete remission, and one patient showed stable disease.

Three patients died. One patient with partial response relapsed 24 months after allogenic transplant and died of died of graft-versus-host disease; a second patient who achieved complete response of his underlying polyarteritis nodosa died of lung cancer 2 years after autologous transplant; the third patient showed no response to therapy and died of right ventricular failure due to severe preexisting pulmonary hypertension 26 months after the initial transplant.

Among the 14 patients who received an autologous transplant, there were 2 relapses—one at 2 months and one at 24 months post transplant. One of these patients then received an allogeneic stem cell transplant and relapsed again 2 years later with headache and aphthous disease. However, the patient was successfully treated with four cycles of rituximab and cyclophosphamide.

The second relapsed patient received another autologous transplant 24 months after the first one. This was followed by another relapse 4 months later, and then an allogeneic transplant, which led to partial remission lasting for 24 months. Six patients in the group experienced neutropenic fever, and two others had reactivation of cytomegalic and Epstein-Barr virus. One patient experienced transient pancytopenia and transient cardiotoxicity.

Among the five patients identified in the Medline search, the following outcomes occurred: complete remission 18 months after transplant in a patient with polyarteritis nodosa; cessation of all disease activity, no medication necessary, for a 4-year-old with intestinal Behçet's syndrome; cessation of all immunosuppressive therapy 18 months after transplant for a patient with Takayasu's arteritis; cessation of disease activity, no medication necessary, for a child with small-vessel vasculitis; complete remission 16 months after transplant for patient with Wegener' s granulomatosis.

Since the graft-versus-host disease is an issue only with allogeneic transplants, Dr. Daikeler suggested that autologous transplants for these patients be evaluated in larger clinical trials. ■

Reversible Loss

SLE *from page 1*

tients and 15 controls who were randomly selected from the center's patient database, and matched for age (55 years), gender (90% female), and coronary risk factors such as hypercholesterolemia (80%), hypertension (80%), tobacco use (33%), and family history of CAD (80%). All patients underwent gated SPECT scans, plus either exercise using the Bruce or modified Bruce protocols, or pharmacologic stress testing using dobutamine or adenosine.

Patients with SLE had significantly worse end-systolic volume indices (45 mL/m^2 vs. 32 mL/m^2), and a trend toward depressed ejection fractions (50% vs. 57%), the authors reported.

The study was prompted by a case in which gated-SPECT imaging was used to risk-stratify a 35-year-old male who came to the clinic with active lupus and chest pain, and was found to have significant stress and resting perfusion defects and inducible ischemia in the anterior wall. Aggressive treatment for SLE and cardiac risk factors with prednisone, mycophenolate, aspirin, and atorvastatin resulted in significant regression of the ischemia at 1 year. His ejection fraction recovered from 23% to 47% and stress-induced cavity dilation of the left ventricle improved from 1.68 to 1.25. ■

Rituximab Targets Systemic Complications of Sjögren's

BY DIANA MAHONEY
New England Bureau

Rituximab is a safe and effective treatment for the systemic complications of primary Sjögren's syndrome, judging from the findings of a small retrospective study.

Recent investigations have linked high levels of B-cell autoreactivity with high levels of disease activity and the development of a range of systemic complications, including arthritis; vasculitis; lymph node enlargement; thyroid, lung, kidney, nerve, and muscle problems; and an increased risk of developing B-cell lymphoma.

To assess the safety and efficacy of rituximab (Rituxan), an anti-CD20 antibody that targets B cells, for treating the systemic manifestations of primary Sjögren's syndrome (pSS), Dr. Raphaèle Seror of Bicetre Hospital, Paris, and colleagues obtained records from six referral centers in France for 16 female patients (median age 59 years) diagnosed with the condition who had been treated with rituximab for either lymphoma or other complications (Ann. Rheum. Dis. 2006 Sept. 1 [Epub doi:10:1136/ard.2006.057919]).

All of the patients included in the evaluation received a 100-mg pulse of methylprednisone and either 20 mg of oral cetirizine or an intravenous pulse of 5-mg dexchlorpheniramine before each rituximab infusion, and four of the patients received concomitant immunosuppressants.

Rituximab therapy induced complete remission in four of the five lymphoma patients but was not effective in one patient with salivary lymphoma. Among the 11 patients with systemic features, rituximab was effective in 9, including 4 with cryoglobulinemia, 2 with pulmonary involvement and polysynovitis, 2 with polysynovitis, and 1 with mononeuritis multiplex. Despite rituximab therapy, one patient with cryoglobulinemia experienced a worsening of peripheral nerve involvement, and the platelet counts of the patient with thrombocytopenia remained below 10,000/mm^3, the authors reported.

The investigators also assessed laboratory outcomes, including changes in erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, cryoglobulinemia, B-cell biomarkers, and, for some patients, serum B-cell activating factor of the tumor necrosis factor family (BAFF) levels from retrospective ELISA assessment of frozen samples. B-cell depletion was achieved in 14 of the 15 patients, and median ESR and CRP levels decreased from 60 to 20 mm/h and from 11.4 to 4 mg/L, respectively.

Median rheumatoid factor decreased from 124 to 7.5 IU/mL, disappearing completely in five patients. Median gammaglobulin, IgG, and beta-2 microglobulin levels also decreased, while median BAFF levels increased, possibly as a consequence of B-cell depletion, the authors hypothesized.

During the median 14.5-month follow-up, five patients relapsed, four experienced a flare of pSS, and lymphoma was diagnosed in one patient treated initially for cryoglobulinemia. Clinical relapse was associated with the reappearance within 3 months prior to relapse of peripheral blood B cells and an increase in B-cell biomarkers. Rituximab was effective in all but four of five patients treated for relapse. Only three of the patients experienced moderate adverse events, including delayed, infusion-related flulike reactions, the authors wrote. ■

Cutaneous Neonatal Lupus May Signal More Serious Outcomes

SAN ANTONIO — All cases of congenital heart block are caused by neonatal lupus, Dr. Bernice Krafchik said at a meeting sponsored by Skin Disease Education Foundation.

About half of neonatal lupus babies will have congenital heart block. Part of the challenge in diagnosis is that most often the mothers are asymptomatic, added Dr. Krafchik, professor emeritus of pediatrics and medicine, the Hospital for Sick Children, University of Toronto.

The heart block is usually complete heart block. "These patients often require a pacemaker—you have to really watch these kids closely; the pacemaker itself can have adverse events and cause death."

In general, babies with just cutaneous lesions from neonatal lupus erythematosus respond well to therapy, according to Dr. Krafchik.

"Skin patients really do very well and the lesions disappear. But they may develop systemic lupus erythematosus [SLE] later." Babies with neonatal lupus skin lesions usually are born to mothers with SLE, which she said is one of the new facts emerging about neonatal lupus.

About 50% of babies born with neonatal lupus have skin lesions. There are four presentations: periorbital lesions that produce a "raccoon" face, annular erythema with atrophy, central erythema with an edge, and telangiectasias.

The telangiectasias are less common but might persist into adulthood. Some telangiectasias respond to laser treatment, although scarring can be problematic, said Dr. Krafchik.

Neonatal lupus can cause thrombocytopenia and hepatitis as well. Hepatitis occurs in approximately 10% of affected neonates and is usually mild with "excellent recovery," she said at the meeting.

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—Damian McNamara