

Benefits Persist Past 2 Years

Scleroderma from page 1

plus rabbit antithymocyte globulin. One additional patient was considered a mobilization failure because an adequate number of CD34+ stem cells could not be obtained during apheresis.

At baseline all patients had very high modified Rodnan skin scores, and all showed reduced carbon monoxide diffusion capacity (DLCO) on lung function tests. (See chart.) Two patients had mild to moderate pulmonary hypertension. High-resolution computed tomography revealed the presence of pulmonary fibrosis in three patients and ground glass areas in two, said Dr. Miniati of the University of Florence (Italy).

After the autologous stem cell transplantation, skin scores improved rapidly with the improvement persisting for at least 2 years. There also was a reduction in the ventricular-atrial gradient on Doppler echocardiography, stabilization of lung function, and improved quality of life as measured by the Health Assessment Questionnaire, she said.

None of the patients has developed opportunistic infections during the 2 years of follow-up. No arrhythmias occurred during the infusions, and despite concerns about cardiac toxicity with the adminis-

tration of cyclophosphamide to patients with underlying cardiac injury, no toxicity has been seen.

Data on capillaroscopy patterns in these patients were covered in an abstract she presented at last year's meeting of the European League Against Rheumatism (EULAR), Dr. Miniati said in response to a question. Nailfold videocapillaroscopy (NVC) is a technique for visualizing and evaluating microvascular damage in scleroderma using an optical probe connected to image analysis software. NVC patterns have been classified as early, active, and late (Rheumatology [Oxford] 2004;43:719-26).

In Dr. Miniati's EULAR presentation, she reported that all four patients in her series showed a typical late pattern before stem cell transplantation, with few giant capillaries, large avascular areas, and vascular architectural disorganization. Three months after the transplantation, the NVC pattern had improved and was classified as active, characterized by numerous giant capillaries, hemorrhages, an absence of avascular areas, and disorganization of the normal capillary array with ramified/bushy capillaries. This pattern suggests angiogenesis and has persisted for 2 years (Ann. Rheum. Dis. 2005;64[suppl. 3]:289). ■

Clinical Response to Stem Cell Transplantation

Patient	Rodnan Skin Score		DLCO	
	Baseline	2 years	Baseline	2 years
1	40	10	38%	44%
2	38	12	36%	42%
3	29	13	64%	72%
4	38	20	67%	73%

Source: Dr. Miniati

ELSEVIER GLOBAL MEDICAL NEWS

For Severe Lupus, Nonmyeloablative Stem Cell Transplant Shows Promise

An autologous hematopoietic stem cell transplantation technique that achieves lymphoablation without myeloablation proved effective against severe refractory systemic lupus erythematosus in a preliminary study.

Serology, complement, immunomediated hemolysis and thrombocytopenia, thrombotic events, and pulmonary function all improved while preserving renal function in a single-center study of 48 patients. This nonmyeloablative hematopoietic stem cell transplantation (HSCT) significantly improved SLE symptoms and gave patients a 50% probability of 5-year remission, reported Dr. Richard K. Burt of Northwestern University, Chicago, and associates.

These results justify a randomized clinical trial comparing autologous HSCT with standard care, Dr. Burt and his associates said (JAMA 2006;295:527-35).

Fifty "very ill" patients underwent the two-step procedure involving a lupus-specific conditioning regimen to eliminate self-reactive lymphocytes followed by stem cell infusion. All patients had glomerulonephritis, lung involvement, CNS in-

volvement, vasculitis, myositis, cytopenias, serositis, ulcerative mucocutaneous disease, and/or antiphospholipid syndrome refractory to optimal treatment.

One patient died from pulmonary and cerebral mucormycosis after stem cell mobilization commenced but before transplantation, for treatment-related mortality of 2%. A second patient died from active SLE after postponing transplantation.

The remaining 48 patients were followed for a mean of 29 months. Scores on measures of serology, complement, and disease activity all improved and remained so throughout follow-up. Pulmonary function also improved.

Eighteen of 22 patients were able to discontinue anticoagulation subsequent thrombotic events. Renal function remained stable or improved; 16 patients who had nephritis before HSCT were able to discontinue dialysis afterward. Idiopathic thrombocytopenic purpura cleared in five of seven patients, and autoimmune hemolytic anemia cleared in three of five patients.

—Mary Ann Moon

No Link Between Vasculitis, Leukotriene Modifiers Found

BY NANCY WALSH
New York Bureau

SAN DIEGO — The use of leukotriene modifiers to treat patients with asthma was not associated with the development of Churg-Strauss syndrome in a population-based, nested, case-control study.

Shortly after leukotriene modifiers were introduced in the mid-1990s, there were reports of more cases of this rare vasculitis than would be expected, suggesting there might be a link, Dr. Leslie R. Harrold said at the annual meeting of the American College of Rheumatology.

Subsequently, an investigation of reports of the syndrome in the Adverse Event Reporting System (AERS) database, maintained by the Food and Drug Administration, found a strong association with zafirlukast and montelukast, though not with zileuton (Clin. Ther. 2004;26:1092-104).

Several possible explanations for leukotriene modifiers being related to Churg-Strauss syndrome have been suggested, such as an increased awareness of the condition, and reductions in corticosteroid doses resulting in the unmasking of an underlying eosinophilic syndrome (J. Rheumatol. 2005;32:1076-80). It also is possible that patients receiving leukotriene modifiers tend to have more severe asthma, which may predispose them to Churg-Strauss syndrome.

"To investigate this relationship, we assembled a cohort of 382,377 adults who received three or more dispensings of an asthma drug during any calendar year be-

tween Jan. 1, 1996, and Dec. 31, 2002," said Dr. Harrold of the University of Massachusetts, Worcester. The cohort came from a national health plan and three managed care plans, with a combined patient population of 13.9 million.

Patient age, gender, drugs dispensed, diagnoses, and procedures information were obtained from automated databases, and cases of Churg-Strauss syndrome were identified through the databases and confirmed by chart reviews.

Each patient with Churg-Strauss syndrome was then matched with 100 controls for age, sex, health plan region, and year of cohort entry. Dispensing information for the patients before they were diagnosed with Churg-Strauss syndrome also was obtained.

A total of 47 possible, probable, or definite cases of Churg-Strauss syndrome and their 4,700 matched controls were identified and analyzed, Dr. Harrold said.

Compared with controls, patients were significantly more likely to have received a greater number of asthma drug classes overall, and to have been given prescriptions for oral steroids, inhaled steroids, and leukotriene modifiers.

On multivariate analysis, the number of asthma drug classes used within the previous 6 months and the use of leukotriene modifiers in the previous 2-6 months were not associated with Churg-Strauss syndrome. Only oral and inhaled steroids were associated with the syndrome, with odds ratios of 5.1 and 4.4, respectively.

The study was funded by Glaxo-SmithKline. ■

Transsternal Thymectomy Beneficial At Any Stage of Myasthenia Gravis

Transsternal thymectomy is safe and effective for patients with myasthenia gravis at any stage of the disease, according to Dr. Hassan Kattach of Radcliffe Infirmary, Oxford, England, and associates.

Dr. Kattach and his associates assessed outcomes in 85 consecutive patients who underwent transsternal thymectomy at their institution between 1987 and 1998.

Most of the patients chose surgery because their symptoms were refractory to all other treatment. The mean age at surgery was 31 years (range, 11-74 years), and mean follow-up was 5 years.

Transsternal thymectomy was performed through a full sternotomy. The resection borders were the thyroid gland above, the diaphragm below, and the phrenic nerves laterally. This resection is more extensive than that with standard transsternal thymectomy but less extensive than that with aggressive, extended transsternal thymectomy advocated by some clinicians, the investigators said (Ann. Thorac. Surg. 2006;81:305-8).

There were no patient deaths perioperatively or during follow-up. Of the patients, 67 reported clinical improvement, and 63 became asymptomatic or achieved

clinical stage I disease with no or minimal treatment required. This included 15 patients who achieved complete stable remission. After the surgery, 13 patients reported no symptom improvement.

Patients who had more advanced disease preoperatively showed the greatest improvement after the surgery.

Complications developed in 13 patients, including 8 patients with major operative complications. These were related to advanced thymomas that required extensive dissection and included two cases of phrenic nerve palsy in patients whose thymomas involved the phrenic nerves.

Neither improvement nor clinical remission were predicted by patient age, gender, duration of disease, or thymic pathology. As such, these factors should not be considered as indications or contraindications to the procedure, Dr. Kattach and associates wrote. Some clinicians have questioned the role of thymectomy in patients who show no evidence of thymoma on chest imaging, but these results show that the presence or absence of thymoma should not influence the decision to do the surgery.

—Mary Ann Moon