Metabolic Factors May Link Diabetes, Morphea

BY NANCY WALSH
New York Bureau

ABANO TERME, ITALY — The unexpected finding of increased rates of diabetes in patients with morphea suggests that metabolic factors may be involved in triggering the condition, Dr. Christiane Pfeiffer reported in a poster session at a congress on skin, rheumatism, and autoimmunity.

Several etiologic factors have been reported, though inconsistently, for morphea. Infection, particularly with *Borrelia burgdorferi,* has been suggested as a trigger, as have vaccination and trauma. But a questionnaire survey of 113 patients seeking care at a university-based dermatology department in Saxony, Germany, found twice the prevalence of diabetes in patients with morphea, compared with the normal population in the district. (See box.) This finding has not previously been reported for morphea, or cutaneous scleroderma, and the association may involve the effects of nonenzymatic glycosylation of extracellular matrix components in diabetes, she said.

Moreover, obesity was not implicated, because the increase in diabetes was seen even though body mass index was not significantly different in morphea patients than in age- and sex-matched controls, said Dr. Pfeiffer of the department of dermatology, University Hospital, Dresden, Germany.

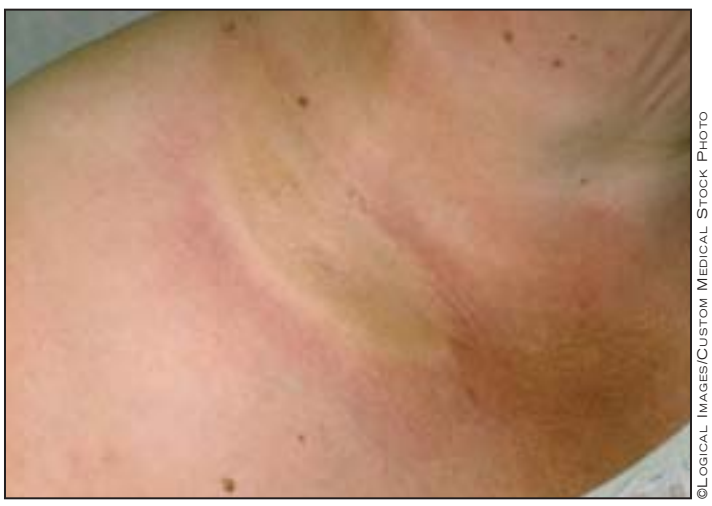
Analysis of responses to questionnaires filled out by patients also revealed that the number of plaques correlated with the severity of disease and extracutaneous involvement.

In patients with five or more lesions, arthralgias were reported by 23.9% of the patients, myalgias by 15.2%, contractures by 10.9%, and esophageal dysmotility by 6.5%. In those with fewer than five lesions, the same complications were reported by 7.1%, 9.5%, 2.4%, and 2.4% of patients, respectively, she said. High numbers of lesions also correlated with increases in erythrocyte sedimentation rate and C-reactive protein levels.

A total of 78% of patients had the plaque variant of morphea, with the rest having the guttate variant, idiopathic atrophoderma of Pasini and Pierini, linear scleroderma, and profound scleroderma. In patients with all variants of morphea, lesions were found on the trunk in 81%, whereas only 8 patients had facial lesions. Overlap syndromes also were reported; 8 patients had morphea and lichen sclerosus et atrophicus; and two had morphea with eosinophilic fasciitis.

"Our data also suggest the existence of variant-specific organ involvement in morphea," Dr. Pfeiffer said. Arthralgias were reported by 40% of patients with atrophoderma Pasini and Pierini, while linear scleroderma was associated with the presence of antinuclear antibodies, muscular atrophy, and contractures.

In patients with profound scleroderma, 45% had myalgias and myopathy. There were no increases in Raynaud symptoms, carpal tunnel syndrome, or lung disorders in patients with any of the variants, she said. ■



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The number of plaques in morphea, shown here on a patient's neck, was found to correlate with the severity of disease.

Diabetes Prevalence Higher in Morphea Patients

	Patients With Morphea	Normal Population
TOTAL	8.8%	4.4%
Females	11.9%	5.2%
Females >41 years old	21.3%	10.1%
Females >61 years old	29%	16%

Note: Survey responses of 113 dermatology patients were compared with those of a normal population.
Source: Dr. Pfeiffer

ELSEVIER GLOBAL MEDICAL NEWS

Paget's Patients Develop Resistance to Pamidronate

BY MIRIAM E. TUCKER
Senior Writer

FORT LAUDERDALE, FLA. — Reduced responsiveness to repeat bisphosphonate treatment in patients with Paget's disease of bone appears to be limited to pamidronate and may not be a problem with the newer, more potent agents, Dr. Socrates Papapoulos said at a meeting sponsored by the Paget Foundation for Paget's Disease of Bone and Related Disorders.

"The issue of bisphosphonate resistance does not appear to be of primary importance for our clinical practice, especially with the more potent agents now available," said Dr. Papapoulos, professor of medicine and director of bone and mineral research at Leiden (the Netherlands) University Medical Center.

For most patients with Paget's disease of bone, short courses of bisphosphonate treatment typically result in remissions of 2 years or longer, and recurrences usually respond well to a new course of treatment. However, there have been reports of reduced responsiveness on repeat treatment. This so-called acquired resistance is characterized by a decrease in the magnitude of response, a need for higher doses to achieve the same response, and a shortening of the remission period compared with the initial treatment, he explained.

Previous literature on the subject has been confusing, particularly in the way responsiveness is measured. Some consider fractional decreases in serum alkaline phosphatase (AP) to be indicative of responsiveness, which is not valid because those values will almost always be lower on retreatment than at baseline, he said, adding that absolute serum AP values must be reported in order to assess the phenomenon of resistance.

To examine this issue, Dr. Papapoulos and his associates reviewed the records of 205 Paget's disease patients who had received two or more consecutive courses (up to nine courses) of either pamidronate or olpadronate. They received a total of 807 treatment courses with a mean follow-up per treatment of 29 months.

Overall, there was no difference in responsiveness—defined as a progressive increase in nadir serum AP—after initial versus subsequent treatment, nor was there a shorter period of remission following treatment. However, when the patients who had received only pamidronate were examined separately, there was a trend toward reduced responsiveness with pamidronate.

When the pamidronate patients were divided into those who had three or more affected bones versus those with two or fewer affected bones, the trend was seen only among those with more extensive disease. This finding is consistent with previous reports of acquired resistance to pamidronate in patients with extensive Paget's disease, Dr. Papapoulos noted. ■

Duration of Bisphosphonate Therapy Frequently Extended in Paget's Disease

BY MIRIAM E. TUCKER
Senior Writer

FT. LAUDERDALE, FLA. — Bisphosphonate treatment is often extended beyond the duration recommended by the label in patients with Paget's disease of bone, Mohamed Omar, Ph.D., and his associates reported in a poster at a meeting sponsored by the Paget Foundation for Paget's Disease of Bone and Related Disorders.

After the end of the recommended treatment course, patients with the bone disease should be evaluated to determine whether they need a second course.

Paget's disease is the second most common bone disorder among elderly persons, after osteoporosis; about 70-90% of patients are asymptomatic and diagnoses are typically made from incidental findings of elevated lab values or radiographic abnormalities. Bisphosphonates are the standard treatment, said Dr. Omar, of Novartis Pharmaceuticals Corp., East Hanover, N.J., and his associates.

For patients diagnosed with the disease, risedronate therapy is recommended for 2 months and alendronate and etidronate for 6 months. After the recommended treatment course, patients should be evaluated to determine whether they need retreatment. Claims data from a large nationally representative health care database were reviewed for the years 1996-2004. At least one prescription for a bisphosphonate had been written for 433 Paget's disease patients (mean age 65 years, 64.3% female). None had osteoporosis, which would require ongoing bisphosphonate therapy. One-third (33.9%) had been prescribed by general practitioners/internists, followed by endocrinologists (12.5%) and rheumatologists (9.8%).

The most frequently prescribed bisphosphonates were alendronate (53%), followed by risedronate (35%) and etidronate (7%). Additional use, defined as receipt of medication after the recommended treatment regimen for each product's approved label, was most often seen with alendronate (45%), followed by risedronate (41%), and etidronate (18%).

Among the patients with additional use, those taking etidronate had the highest number of mean incremental days' supply (143), followed by risedronate (142), and alendronate (139). Incremental costs of those additional supplies were $995 for those on etidronate, $2,697 for risendronate, and $828 for alendronate, Dr. Omar noted. It's not clear whether increased use of drug therapy reflected a true need for retreatment or inappropriate prescribing, he said.

Novartis is the maker of zoledronic acid, a bisphosphonate under consideration by the Food and Drug Administration for the treatment of Paget's disease. ■