Root Out All Causes of Secondary Osteoporosis

BY ROBERT FINN
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SAN FRANCISCO — Finding one possible cause of secondary osteoporosis does not mean there aren't other causes as well, Dr. Diana Antoniucci reported at a meeting on osteoporosis sponsored by the University of California, San Francisco.

"Having one secondary cause of osteoporosis does not preclude you from having another, so even if one contributor is obvious from the history, you can still consider laboratory testing," said Dr. Antoniucci, of UCSF. (See sidebar for suggestions on which tests to order.) She listed four frequent causes of secondary osteoporosis for physicians to consider.

Glucocorticoid Use

This is the most common cause of drug-induced osteoporosis. In these patients, prevention is the best strategy. All patients should be taking supplemental calcium and vitamin D, Dr. Antoniucci said, and if the patient has already been diagnosed with osteoporosis or is otherwise at high risk, the physician should measure bone mineral density (BMD) with dual-energy x-ray absorptiometry (DXA). Clinical trials have shown that bisphosphonates halt bone loss and reduce fractures in patients taking glucocorticoids, and alendronate and risedronate are both approved for this indication. They should be considered for any patient on glucocorticoids with low BMD.

Vitamin D Deficiency

This deficiency is common in the general population. Depending on the study population, the prevalence appears to range between 9% and 50%. When severe, vitamin D deficiency is associated with osteomalacia, which is indistinguishable from low bone density on DXA. Less-severe vitamin D deficiency is associated with secondary hyperparathyroidism.

One difficulty in the assessment and treatment of vitamin D deficiency is that there is no general agreement as to what constitutes a sufficient level of 25-hydroxyvitamin D, Dr. Antoniucci noted. A level of 20 ng/mL appears to be necessary for normal parathyroid dynamics, 32-36 ng/mL appears to be necessary for maximal intestinal calcium transport, and 30-40 ng/mL is the level that several randomized controlled trials have determined is necessary for fracture reduction.

"The good news is that vitamin D insufficiency is treatable," Dr. Antoniucci said. "Replacement reestablishes vitamin D stores, and it improves bone mineral density because it allows optimal calcification of preexisting osteoid."

Celiac Disease

Somewhere between 9% and 12% of patients with osteoporosis also have celiac disease. Conversely, about 50% of patients with celiac disease have a BMD that is two standard deviations or more under the mean. Among patients with celiac disease, those with a low BMD are more likely to have villous atrophy, an indication of more severe disease.

The pathogenesis of bone disease in these patients is likely multifactorial, according to Dr. Antoniucci. They tend to have worse calcium absorption from the gut, especially before their disease is diagnosed, which can be many years in some patients. They also can have vitamin D deficiency from secondary hyperparathyroidism. Some women with celiac disease also have infertility and amenorrhea, both of which can lead to poor bone health.

At least one study has demonstrated that among patients with celiac disease, a strict gluten-free diet over the period of a year can improve bone mass in both men and women (Arch. Intern. Med. 2005;165:393-9). The authors of that study concluded that it's worth screening patients with unexplained osteoporosis for celiac disease.

Dr. Antoniucci is not so sure that that's a good idea. "First of all, what exactly is 'unexplained osteoporosis'? And secondly, it might be a very expensive way to be treating the disease," she said.

Androgen Deprivation Therapy

This is a common treatment for men with prostate cancer, but the longer a man is on this therapy, the greater his BMD loss and the greater his chance of fracture. After 10 years on androgen deprivation therapy, about 20% of men will have experienced a fracture, a risk fivefold greater than in age-matched controls. Slender white men seem to be at greatest risk, she said, noting that both pamidronate and zoledronate have been shown to prevent bone loss caused by androgen deprivation therapy. ■

Telling Lab Tests To Keep on Hand

There is no consensus on whom to evaluate for secondary osteoporosis, said Dr. Antoniucci. However, "most people would agree that we should evaluate virtually all men with low T-scores, premenopausal women with low *z*-scores or fragility fractures, and postmenopausal women." A standard laboratory work-up should include:

- ► Electrolyte levels
- ► Renal and hepatic function
- ► Complete blood count
- ► 24-hour urine calcium excretion (can provide important information if the result is very high or low)
- ► 25-hydroxyvitamin D levels
- ► Testosterone levels
- ► Thyroid-stimulating hormone levels (in patients on thyroid hormone replacement)

Additional tests should be dictated by the patient's history and physical exam and the physician's clinical judgment.

Brothers of PCOS Patients Share Some Metabolic Characteristics

BOSTON — Brothers of women with polycystic ovary syndrome share with their sisters similar metabolic features that indicate they may be at increased risk for decreased insulin sensitivity and glucose tolerance, high triglycerides, and dysfibrinolysis, Dr. Jean-Patrice Baillargeon said at the annual meeting of the Androgen Excess Society.

These characteristics, which are independent of both fat percentage and body mass index, suggest that polycystic ovary syndrome (PCOS) may represent an inherited constellation of symptoms that are expressed differently in men and women, said Dr. Baillargeon of the University of Sherbrooke (Que.).

He compared insulin sensitivity and other metabolic measures in 17 brothers of women with PCOS and 28 men who had no first-degree relatives with PCOS. Their average age was 28 years. There were no significant differences in body mass index (average 26.5 kg/m^2) or percentage of body fat (average 22%). Levels of total and free testosterone and dehydroepiandrosterone sulfate were also similar for the two groups.

At baseline, brothers had slightly, but not significantly, higher diastolic blood pressures (74 vs. 68 mm/Hg). However, they had significantly higher levels of triglycerides (1.66 vs. 0.99 mmol/L), plasminogen activator inhibitor-1 (27 vs. 16 nmol/L), and factor VIII (27 vs. 16 nmol/L). "The increased PAI-1 and factor VIII show a dysfibrinolysis in the brothers."

Three of the brothers (18%) had decreased insulin sensitivity after an oral glucose tolerance test; insulin sensitivity values were normal in all controls. The 2-hour glucose levels, insulin area under the curve, and glucose area under the curve were also significantly higher in brothers of women with PCOS. "The insulin sensitivity of the brothers was 38% less than that of the controls. This was primarily due to a 65% decrease in insulin-stimulated nonoxidative carbohydrate metabolism."

All of these factors remained significant, even after adjusting for anthropomorphic measures. They were also significant in two matched-pair analyses, one of 13 pairs and one of only 7 pairs.

—Michele G. Sullivan

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