Lupus/CT Diseases

Takayasu’s Arteritis Remits With Minocycline

BY BRUCE JANCIN

Minocycline may provide an effective alternative to conventional treatments for active Takayasu’s arteritis, Akifumi Matsuyama, M.D., reported at a meeting sponsored by the International Academy of Cardiology.

While glucocorticoids have long been viewed as first-line therapy in Takayasu’s arteritis, roughly half of treated patients don’t respond adequately and require additional immunosuppressive therapy. And a significant fraction of patients experience disease progression despite such therapy.

The presumed mechanism of minocycline’s benefit is independent of the drug’s antimicrobial effect. Rather, the benefit hinges upon the matrix metalloproteinase-inhibiting action of tetracyclines, explained Dr. Matsuyama of Osaka University Hospital (Japan).

He reported on 11 patients with active Takayasu’s arteritis despite long treatment with systemic corticosteroids who were placed on oral minocycline at 100 mg b.i.d. for 3 months. Their steroid dosing remained unchanged.

Nine of the 11 patients went into remission according to American College of Rheumatology criteria. Their National Institutes of Health disease activity score dropped from a baseline mean of 2.8 to 0.7. Their erythrocyte sedimentation rate went from 30 to 33 mm/hr. Mean C-reactive protein fell from 1.78 to 0.89 mg/dL.

During the same 3-month period, the group’s mean serum matrix metalloproteinase-3 (MMP-3) level went from 149 to 65 mg/L. Their MMP-9 dropped from 116.6 to 47.1 mg/L. In contrast, their MMP-2 levels remained high and unchanged.

While these results are quite promising, Dr. Matsuyama stressed that they must be viewed as nondefinitive.

Until these findings are confirmed in a properly controlled trial, minocycline should be reserved for patients who don’t respond adequately to conventional therapy with glucocorticoids and additional immunosuppressive agents as needed, the physician added.

Since Takayasu’s arteritis is a remitting and relapsing disease, we can’t completely the possibility that the positive responses observed in our patients might have been due to spontaneous remission rather than the effect of the drug. However, the long-stand history of steroid dependency suggests that the clinical improvement was due to minocycline,” the physician continued.

Dr. Matsuyama and coworkers decided to test the therapeutic efficacy of minocycline as a result of their recent observation that circulating levels of MMP-3 and MMP-9 are significantly higher in patients with active Takayasu’s arteritis than in those whose disease is in remission or in normal controls.

This finding raised the possibility that MMPs might be useful markers of disease activity. They can be easily measured at low cost, which makes for an attractive noninvasive potential alternative to coronary angiography in patients with the disease.

From there it was a short leap to the hypothesis that MMPs might provide novel therapeutic targets.

The thought is that increased production of cytokines in the arterial lesions of Takayasu’s arteritis might induce production of MMP-3 and MMP-9 by mononuclear cells or smooth muscle cells, with resultant destruction of the elastic fibers in the media of the aorta and other large elastic arteries, according to Dr. Matsuyama.

Pharmaceutical companies are busily developing a novel variety of MMP inhibitors. But the tetracyclines are also known to suppress MMP activity, and minocycline is a drug largely free of serious toxicity.

The Japanese group’s future projects, in addition to a controlled trial of minocycline, include investigating the possibility that Takayasu’s arteritis patients with normal MMP-2 do not develop arterial stenoses.