Polymyalgia Rheumatica: Steroids and Beyond

BY BRUCE JANCIN
FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

ROME — Polymyalgia rheumatica may be the presenting manifestation of silent giant cell arteritis, and therein lies a diagnostic dilemma: Which patients need a temporal artery biopsy?

Dr. Miguel A. Gonzalez-Gay, one of the investigators.

Polymyalgia rheumatica (PMR) is the most common inflammatory rheumatologic disease among the elderly. It would be inappropriate to subject everyone who has symptoms consistent with PMR to temporal artery biopsy. Yet giant cell arteritis is a diagnosis that physicians cannot afford to miss because of the risk of irreversible blindness when the vasculitis isn’t promptly recognized.

The rationale for the study lies in what Dr. Cimmino calls the adrenal insufficiency theory of PMR, which holds that a viral antigen or other exogenous trigger stimulates host defenses in genetically predisposed aging individuals. This results in a proinflammatory state with increased interleukin-6 levels.

If the patient cannot produce sufficient endogenous glucocorticoids to curb this systemic inflammation as a consequence of impaired hypothalamic-pituitary-adrenal axis function, the result is PMR.

If the adrenal insufficiency theory is correct, then 10 mg/day or even less might well be sufficient to abolish the chronic proinflammatory state while avoiding some steroid side effects.

If the adrenal insufficiency theory is incorrect, 10 mg/day of prednisone or even less might be enough to abolish the chronic proinflammatory state, said Dr. Cimmino, professor of medicine at the University of Genova (Italy).

“PMR is still very much an open field for research, including treatment studies,” the rheumatologist observed.

Long-term prednisone is considered the standard therapy for PMR. Yet this practice is surprisingly lacking in supporting evidence from controlled trials.

Nonetheless, PMR is generally well controlled by steroid therapy, albeit with a high incidence of side effects.

Because of the lack of controlled studies, the optimal dose of prednisone for PMR is unclear. Most experts recommend using 15-20 mg/day, although studies show that in clinical practice many physicians use considerably higher doses, with a corresponding increase in side effects and no evidence of added benefit.

Another unsettled issue involves treatment duration. Most physicians keep their PMR patients on prednisone for a period of 6-18 months. Dr. Cimmino recommended tapering the medication with the goal of stopping it at the 6-month mark in order to minimize side effects. He noted, however, that he and his colleagues found in a long-term follow-up study that 30%-39% of PMR patients needed to stay on prednisone for more than 6 years.

The take-home message is that PMR is often a less benign disease over the long term than generally supposed (Clin. Exp. Rheumatol. 2008;26:395-400).

With regard to combination therapy with methotrexate and prednisone, Dr. Cimmino was coauthor of a multicenter double-blind clinical trial in which 72 newly diagnosed PMR patients were randomized to prednisone plus either oral methotrexate at 10 mg once weekly or placebo. Prednisone was started at the relatively high dose of 25 mg/day and tapered to zero within 6 months, with dosing adjustments for flares.

At 76 weeks of follow-up, significantly more patients in the methotrexate arm were off prednisone. Indeed, the mean duration of prednisone was 30 weeks in the combination treatment arm, compared to 59 months with prednisone alone. The combined therapy group also had significantly fewer relapses (Ann. Intern. Med. 2004;141:493-500).

The one ray of hope that biologic therapy might be beneficial in PMR comes from a recent case report by rheumatologists at Osaka (Japan) University detailing a dramatic response to tocilizumab (Actemra) in a 65-year-old woman with long-standing steroid-refractory PMR complicated by diabetes, osteoporosis, and hypertension. After her first injection of tocilizumab her C-reactive protein and serum amyloid A levels normalized and the pain in her shoulders and pelvic girdle improved, but her morning stiffness continued. After her fifth injection at a dose of 8 mg/kg every 4 weeks, her morning stiffness was gone and she was in remission (J. Rheumatol. 2010;37:1075-6).

While this is merely a first case report, it’s particularly exciting because interleukin-6 levels are consistently high in patients with PMR, and tocilizumab is a humanized monoclonal antibody directed against the IL-6 receptor. Thus, this initial report opens the door to IL-6 inhibition as a novel potential treatment strategy in PMR. “Tocilizumab for PMR is a rheumatologist’s dream,” Dr. Cimmino declared.

For now, methotrexate is the only medication of proven efficacy as a steroid-sparing agent in patients with PMR—and it’s considerably underutilized for this purpose.

Randomized trial data show that combining methotrexate with prednisone not only is steroid sparing, it also reduces the relapse rate, compared with steroids alone, Dr. Cimmino said.

Combining methotrexate and prednisone “makes a lot of sense” in patients with PMR who are at high risk for steroid side effects or who are resistant to oral prednisone at up to 20 mg/day, he said.

In contrast, antitumor necrosis factor therapy using etanercept or infliximab has compiled an unimpressive record overall for PMR in case reports and pilot studies.

“At present, I think there is no role for antitumor necrosis factor therapy in PMR,” he said.

Disclosures: Dr. Cimmino disclosed having received research grants from numerous pharmaceutical companies, including Roche, Schering Plough, Abbott, and Pfizer.

Lower doses of prednisone and a greater use of biologics are on the PMR treatment horizon.

Lack of Steroid Response Flags Biopsy Candidates in PMR

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ROME — Temporal artery biopsy may be a extension of silent giant cell arteritis, and therein lies a diagnostic dilemma: Which patients need a temporal artery biopsy?

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