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Diagnostic and Treatment Dilemmas in Polymyalgia Rheumatica

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You're listening to *Living Rheum* on ReachMD. This medical industry feature, titled "Diagnostic and Treatment Dilemmas in Polymyalgia Rheumatica (PMR)" is sponsored by Sanofi and Regeneron. Here's your host, Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I'm your host, Dr. Charles Turck.

Today we'll be speaking with Dr William Rigby. He is an expert on polymyalgia rheumatica and is going to tell us about some of the diagnostic and treatment dilemmas physicians may encounter. Dr Rigby is a professor of medicine and of microbiology and immunology at the Geisel School of Medicine at Dartmouth.

Thank you for being here, Dr Rigby.

Dr. Rigby:
Thank you so much for having me. First, I will mention a couple of disclaimers. This program is non-promotional and is sponsored by Sanofi and Regeneron Pharmaceuticals. I am receiving an honorarium in connection with this presentation. The content contained in this presentation was developed by Sanofi and is not eligible for Continuing Medical Education credits.

Dr. Turck:
Let's start with the basics. Can you provide a brief overview of what polymyalgia rheumatica is and its typical clinical presentation?

Dr. Rigby:
Polymyalgia rheumatica, or PMR, is an inflammatory rheumatic condition. Sometimes patients present with classic symptoms, and the diagnosis is very clear and memorable. As rheumatologists, we encounter very few diseases that present so acutely with pain in combination with restricted movement. However, some of the symptoms are nonspecific, which can make a precise diagnosis difficult.

The core diagnostic criteria for PMR include a patient aged 50 years or older, with bilateral shoulder and/or pelvic girdle pain, associated with morning stiffness for 45 minutes or more, over a 2-week period. One patient of mine, an avid soccer player, said that one night she went to bed feeling fine, and then suddenly couldn't get up in the morning. But then, with time, she started to feel better throughout the day. This is typical with PMR. PMR pain is usually acute and intense, but PMR pain also tends to improve with movement or exercise.

Besides pain, other symptoms of PMR may include tenderness in the affected muscles and restricted range of motion. Some patients experience additional physical and mental effects such as fever, fatigue, loss of appetite, and associated weight loss and depression.

Dr. Turck:
What are some of the challenges to diagnosing a patient with PMR?

Dr. Rigby:
Acute shoulder and hip pain with restricted range of motion is often a clear indicator, and PMR should be strongly considered in these cases. PMR is a diagnosis of exclusion, and it can mimic a wide variety of other conditions that need to be ruled out to confirm a PMR diagnosis. These conditions include, but are not limited to, other rheumatologic diseases, inflammatory myopathies, musculoskeletal disorders, occult malignancies, and infectious diseases. In addition to PMR mimicking many other diseases, diagnostic uncertainty may be compounded by atypical presentations of disease and comorbidities.

Overall, about 63% of PMR cases involve overlapping comorbidities, which may result in diagnostic complications. To give you a couple of common examples, PMR overlaps with fibromyalgia in an estimated 6.9% of cases, which can lead to a misinterpretation of patient pain symptoms.

For peripheral arthritis, in a prospective population-based study of PMR patients, 38.5% presented with peripheral arthritis either at the time of diagnosis or during follow-up. In a prospective follow-up study of 177 PMR patients, up to 5.6% of patients presented with atypical PMR with a normal sedimentation rate value at diagnosis. Normally, a baseline workup such as C reactive protein, CRP, and ESR, or erythrocyte sedimentation rate, aids in the diagnosis of PMR and the elimination of other conditions. However, increases in these inflammatory markers are nonspecific and insufficient for diagnostic purposes.

Dr. Turck:
How do providers differentiate between PMR and conditions that mimic PMR?

Dr. Rigby:
Mimicking disorders like giant cell arteritis, rheumatoid arthritis, fibromyalgia, hypothyroidism, and many others, typically have one or more key differentiation features that allow them to be distinguished from PMR. For example, giant cell arteritis, sometimes abbreviated GCA, often presents with headache, jaw claudication, temporal tenderness, and visual disturbances, in contrast to PMR, which has none of these. GCA develops in up to 30% of PMR patients. It may cause permanent damage and should be referred to a rheumatologist for evaluation immediately if suspected.

Another example is that fibromyalgia pain is general, widespread pain that is sensitive to touch, whereas PMR pain is localized in the hips and shoulders. The patient population is also different between PMR and fibromyalgia. Patients with fibromyalgia may be younger in age, as opposed to PMR patients who are more typically or commonly over the age of 50.

Telling peripheral or rheumatoid arthritis apart from PMR is a little bit more straightforward. Peripheral and rheumatoid arthritis involve the small joints of the hands and/or feet, in contrast to PMR. Most rheumatoid arthritis patients are also autoantibody positive.

A couple more examples include paraneoplastic syndromes, which also do not respond to glucocorticoid treatment. Patients with systemic lupus erythematosus present with multiple organ system involvement and antinuclear antibodies, being ANA and double-stranded DNA antibody positive, which is not typically seen in PMR. Patients with inflammatory myopathies typically have elevated CPKs and/or aldolase. They may also present with muscle weakness, rather than the muscle tenderness that is more characteristic of PMR. Hypothyroidism can be differentiated from PMR using thyroid function tests. Bursitis or tendinitis may resemble some symptoms of PMR; however, these usually do not have systemic symptoms, an elevated sedimentation rate, or bilateral shoulder involvement.

Dr. Turck:
What kind of treatment is recommended for PMR?

Dr. Rigby:
Patients with PMR typically show a marked response to glucocorticoid treatment, sometimes as soon as 1 day after initiation. The European Alliance of Associations for Rheumatology and the American College of Rheumatology recommend glucocorticoid therapy at the lowest effective dose, with gradually tailored tapering. A recommended starting dose for PMR is 12.5 to 25 mg of prednisone equivalent daily for 2 to 4 weeks. For patients whose symptoms respond to glucocorticoid therapy, dosing should be tapered to 10 mg per day by 4 to 8 weeks after treatment initiation. Then for patients in remission, daily doses of prednisone can be tapered by 1 mg every 4 weeks until discontinuation.

Physicians may vary their tapering strategy dependent on patient's symptoms. But in case of relapse, the European Alliance of Association for Rheumatology and the American College of Rheumatology recommend an increase to the pre-relapse effective dose, and then to resume tapering within 4 to 8 weeks to the dose at which the relapse occurred. A faster taper may be warranted in some patients at risk for glucocorticoid toxicity.

Dr. Turck:
Are there any potential complications associated with the use of glucocorticoid, or GC, therapy used to treat PMR?

Dr. Rigby:
Glucocorticoid therapy may be very effective with a rapid initial response. However, many patients are either unable to taper or may experience toxicity. Literature reports indicate 1/3 of patients showed persistent features of active PMR after 3 weeks of treatment initiation; 43% of patients with PMR relapsed within 1 year, and only 19% of PMR patients are able to discontinue glucocorticoids 1 year after treatment onset. Approximately 60% of patients remain on glucocorticoids for over 2 years due to relapses, which generally occur within 2 weeks of reducing the steroid dose. This inability to taper can lead to chronic glucocorticoid use for many patients. In one study,

patients still being treated with glucocorticoids for over 2 years, reported an average prednisone dose of 19 mg daily.

Dr. Turck:
Are there side effects associated with chronic GC use?

Dr. Rigby:
In some patients, yes. In another study, 65% of patients with PMR treated with an average dose of 9.6 mg daily for 2.4 years, experienced severe glucocorticoid toxicity. That included diabetes, fracture, aseptic necrosis, infection, cataracts, GI bleeding, hypertension, and myopathy. Glucocorticoid toxicity effects are both dose and duration dependent. And while many adverse events were more common at higher doses and with chronic use, they are not limited to these cases. Depending on the duration of treatment and patient susceptibility, even low-dose glucocorticoid treatment can cause toxicity. Glucocorticoid toxicity has been reported in multiple organ systems at prednisolone equivalent doses of less than or equal to 2.5 mg a day after glucocorticoid exposure for an average of 31 days. Some toxicities at these low doses, including fractures, may even occur as soon as 1 month treatment duration.

Dr. Turck:
In light of these reports, are there certain risk factors that may inform how susceptible a patient is to GC toxicity?

Dr. Rigby:
Yes. Many factors such as older age, dose, and duration of glucocorticoid therapy, underlying comorbid conditions, and concomitant use of other medications, which may alter glucocorticoid metabolism, contribute to the risk of glucocorticoid toxicity.

Dr. Turck:
Is there any way to prevent or manage GC toxicity?

Dr. Rigby:
Rheumatologists utilize a combination of baseline assessments, routine monitoring, and patient education for the early recognition and prevention of glucocorticoid toxicity. Baseline assessments typically include a physical exam, a comorbidity evaluation taking into consideration, medical history, a baseline blood workup, and a bone density test. Patients should also be up to date on necessary vaccines before beginning glucocorticoid therapy to mitigate the risk of infection.

Guidelines suggest routine monitoring for glucocorticoid toxicity, particularly for patients who have risk factors for glucocorticoid toxicity or who may be taking long-term maintenance glucocorticoids. The panel strongly recommends individualizing dose-tapering schedules based on regular monitoring of patient disease activity, laboratory markers, and adverse events. Repeat scans such as a DEXA or x-ray of the lateral spine may be utilized 1 year post glucocorticoid therapy initiation to determine changes in bone density for a fracture risk assessment. Retesting is recommended again every 2 to 3 years if bone density is stable, or annually if a decrease is observed. I also assess lipids 1 month after glucocorticoid initiation and again every 6 to 12 months thereafter. Blood glucose should be assessed for 48 hours after glucocorticoid therapy initiation, then again every 3 to 6 months for the first year, and annually thereafter.

Dr. Turck:
And you mentioned patient education?

Dr. Rigby:
Yes. Rheumatologists can inform patients of which potential symptoms may be related to glucocorticoid use and the importance of discussing these symptoms with their healthcare providers. In my practice, I also recommend lifestyle modifications, such as smoking cessation, alcohol reduction, and avoidance of live vaccines as well as weight-bearing exercise and weight reduction. All of these may help manage glucocorticoid toxicity effects. Dietary changes, including sodium and saturated fat restriction with supplemental calcium and vitamin D may also mitigate these toxicities.

Dr. Turck:
What is the appropriate course of action when faced with complicated clinical scenarios?

Dr. Rigby:
Complex clinical scenarios during diagnosis or treatment are common in PMR, and referral to a rheumatologist is recommended. Examples of diagnostic complications include when a patient presents with normal sedimentation rate values, has overlapping comorbidities, or overlapping giant cell arteritis. GCA may cause permanent damage, so if a patient has symptoms of GCA, immediate referral to a rheumatologist is recommended.

Examples of treatment complications include when a patient has an inadequate response to glucocorticoids after 3 weeks, experiences repeated flares during glucocorticoid tapering that would result in chronic glucocorticoid use over 5 mg a day, as well as relapses at 1 year, or experience other side effects or glucocorticoid toxicity.

Early referral is recommended, as the median wait time to see a rheumatologist for systemic rheumatic inflammatory disease in the United States is 66 days post referral. Rheumatologists will be aware of newly available technologies and alternative treatments and may recommend these options for certain patients. Both biologic and synthetic alternative treatment options are either available or currently under investigation. Additionally, imaging technology including PET scans is emerging as a diagnostic tool with the potential to further define the full character of PMR.

Dr. Turck:
This is all very interesting. Since we're almost out of time, could you give us a quick summary?

Dr. Rigby:
I'd be happy to. Getting to a PMR diagnosis can be difficult, but there are certain things healthcare providers can do to ensure they are able to differentiate PMR from other mimicking conditions. Classic symptoms of PMR are acute intense pain of the hips and shoulders with restricted mobility and a rapid improvement in these symptoms upon treatment with glucocorticoids. However, some cases of PMR may be complicated, which is why it's crucial to refer patients to a rheumatologist as early as possible to ensure optimal outcomes.

Dr. Turck:
It was great to speak with you today. Thank you for being here.

Dr. Rigby:
Well, thank you so much. It was a pleasure to be here today.

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This medical industry feature was sponsored by Sanofi and Regeneron. To revisit any part of this discussion or to find others in this series, visit *Living Rheum* on ReachMD.com, where you can Be Part of the Knowledge.

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