## Transcript Details

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Understanding PMR Pathophysiology: An Expert's Perspective

**ReachMD Announcer**:
Welcome to ReachMD. This medical industry feature, titled “Understanding PMR Pathophysiology: An Expert's Perspective” is sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals. This program is intended for US healthcare professionals.

Here’s Dr. Leonard Calabrese.

**Dr. Calabrese:**
I’m Dr. Len Calabrese. I’m a professor of medicine at the Cleveland Clinic Lerner College of Medicine.

**ReachMD Announcer:**
What are the patterns of inflammation commonly seen in patients with PMR?

**Dr. Calabrese:**
Polymyalgia rheumatica is one of the most common inflammatory syndromes seen in patients after the age of 50. It’s characterized by the acute or subacute onset of pain and stiffness in the neck and shoulders and hip girdle and low back.

This is also exquisitely sensitive to glucocorticoids which are highly effective therapy, but unfortunately are required for prolonged periods of time and mount attendant toxicity.

**ReachMD Announcer**:
Which immune pathways have been linked to PMR disease activity?

**Dr. Calabrese:**
The immunopathogenesis of polymyalgia rheumatica is incompletely understood. But there’s robust evidence that there are perturbations of both innate and adaptive immune responses. There is overexpression of an activation of certain T-cell subsets and at the same time it is mediated primarily by cytokines.

Many of the clinical expressions of PMR such as pain, fatigue, early morning stiffness are believed to be mediated by inflammatory cytokines. These cytokines generate the acute phase response, elevated sed rate and CRP and are also responsible for pain, early morning stiffness. Among these cytokines that have been incriminated in polymyalgia rheumatica include IL-6, IL-1, TNF, IL-17 and others.

**ReachMD Announcer:**
What makes the pathophysiology of PMR different from other rheumatic diseases?

**Dr. Calabrese:**
First of all, it is among if not the most common inflammatory disease associated with aging. It virtually doesn’t occur before the age of 50 and becomes increasingly common after that. We believe that this is linked in some way to immunosenescence of the immune system.

There’s a strong relationship between polymyalgia rheumatica and GCA. Epidemiologically they are tightly linked because many patients may have both conditions. Yet at the same time many patients have either one or the other. We know that cytokines are drivers of both conditions, and that IL-6 plays a prominent role in both of these disorders. Together the links are very strong, but we don’t understand at this time why they are separate and why they overlap.

**ReachMD Announcer:**
What evidence exists for the role of IL-6 in PMR pathophysiology?

**Dr. Calabrese:**
There's a robust body of data supporting the role of IL-6 in the immunopathogenesis of polymyalgia rheumatica. First and foremost is its strong association with giant cell arteritis where we know that IL-6 is an important inflammatory cytokine. In polymyalgia rheumatica IL-6 can drive pain, early morning stiffness, is associated with intercurrent mood disorders and fatigability. Experimental evidence has demonstrated that IL-6 increases as disease activity increases in polymyalgia rheumatica and finally and most recently IL-6 has been found by in situ immunohistochemistry within the inflamed tissues of patients with PMR. Collectively, IL-6 is a very prominent part of the pathogenesis of polymyalgia rheumatica.

**ReachMD Announcer:**
How does IL-6 contribute to disease progression?

**Dr. Calabrese:**
The role of IL-6 in polymyalgia rheumatica has broad implications. Not only is it a driver of the acute phase response but it's responsible for many of the attendant symptoms. We know that it is directly related to pain where IL-6 has nociceptive properties. We also know that IL-6 is a highly efficient biomarker for intercurrent mood disorders, which are often seen in patients with chronic inflammatory diseases. IL-6 is also probably the most reproducible circadian cytokine during sleep and disturbances of sleep and painful and inflammatory conditions cause intrusion of IL-6 in the early morning hours contributing to early morning stiffness. Finally, IL-6 has been directly linked to many fatigue-like states which are very common polymyalgia rheumatica.

**ReachMD Announcer:**

For More Information on PMR, Visit www.PMRandIL6.com

This program was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals. If you missed any part of this discussion, visit ReachMD.com/industry-feature. This is ReachMD. Be Part of the Knowledge.

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