Highlights from the IG Living Teleconference, May 23, 2018

Topic: Autoimmune Disorders Treated with Immune Globulin Therapy

[This is an edited version of a live teleconference presentation.]

Guest Speaker: Sue Romanick, MD, Rheumatology Specialist, Bellevue, Wash.

During this talk, instead of boring you with statistics and lists, I will use a conceptual approach and metaphors. Hopefully, by the end of this talk, you will have a comfort level with some autoimmune conditions, basics of immunology and immune globulin (IG) therapy and, maybe, you will have an idea of how doctors think through a problem.

What Is a Rheumatologist?

First, I want to provide a quick explanation of what rheumatologists are and are not. We are internists who need to have an understanding of the whole body — even though we are specialists. I often get sent cases other doctors can't figure out. I have to know about other specialties and understand how patients can overlap.

Rheumatology often covers minutiae in different parts of the body at the same time. As such, rheumatology requires detective work. As a detective, I'm not looking at the patient in front of me as if he or she is a photograph of one thing happening now and then making a diagnosis. Lab tests can be highly detailed and specialized. But, I am also looking into the past of each patient. I will often ask: "Did you ever have something?"

Understanding the Complexity of the Body

So, where do you come in? Dear listener, why would you even care about my field if none of you have ever heard of a rheumatologist? To answer this, consider for a moment what you take for granted. Do you take walking for granted? How about picking up a chair or a fork? How about simply thinking and using your brain? Do you take for granted that your skin is going to heal after a cut? These are things that, when taken for granted, can impact the conditions in my field.

Your bones are neither concrete nor plastic. Bones are made up of living cells. At this very time in your body and mind, certain cells are breaking down bone somewhere in your body, and there are other pathways and cells building up your bones. So, there's a lot of stuff we take for granted.

Our bodies have a very complex immune system with a primitive original system called innate immunity. Rather than bore you, let's start off with a metaphor. I bet most of you know what a grenade is. Pull the pin, and boom! Well, in innate immunity, let's use the example of gout, which has been known to cause pain worse than childbirth and can develop over hours. Gout likes to go to the big toe, and it is activated by a tiny crystal of uric acid that can suddenly lead to inflammation, which leads to excruciating pain.

In rheumatology, there are conditions other than gout that are not so simplistic but still involve this innate immunity. These can include adult-onset Still's disease, familial Mediterranean fever and periodic syndromes, which can frequently lead to intermittent fevers and other syndromes.

Today, instead of the grenade-type of mechanism, we are more concerned with adaptive immunity, which involves different levels of complex and intricate communications between cells of all types.

Blood is comprised of solid cells that are visible under a microscope, and the liquid portion is, quite frankly, a miraculous juice. I wish I could use an alphabet soup analogy, but that would be too simplistic. I was hoping to reference a soup I grew up with, but in this case, instead of looking for letters of the alphabet, an improved metaphor is that the letters come from different characters of different languages floating in a broth containing an overwhelming number of types of molecules that cannot be seen under the microscope without some kind of labels or alterations of the microscope. The incredible miracle is that these noncellular components can function as bullets, sponges for mopping up other molecules, glue to hold cells together or to glue a foreign protein onto a cell, flags to attract attention, snipers with long memories, traffic signs, and chemicals to speed up and others to slow down certain immune pathways. And, you thought you were just sitting in a chair? There's a lot more going on in your body than you know

The cellular component of the immune system contains attack cells that act like they are presenting invaders on a silver platter to another cell. That's called antigen presentation. There are also cells intimately cooperating with other cells. And, there are my favorite, what I call roving garbage cans. Those are your macrophages.

Autoimmunity and IG Therapy

Today, adaptive immunity often results in autoimmune disorders that are treated with IG therapy. And, there are lists and lists of conditions being treated with IG therapy, and it's growing. It's exciting. It's a new area even though it started a while back when someone immunized an animal and realized that by taking some of that animal's fluid part of its blood, certain diseases could be prevented in human beings. That was pretty amazing at the time.

There are different uses for IG therapy. On the one hand, if you don't have enough of certain antibodies, you might need IG therapy as a supplement to replace what you don't have. But other conditions can also benefit from IG therapy such as in neurology (nerve conditions), hematology (blood conditions), dermatology (skin conditions), nephrology (kidney conditions), rheumatology (all types of conditions), and even ophthalmology (eye inflammation conditions).

Why Are People Affected by Autoimmune Disorders?

So, when is autoimmunity going to factor into this presentation? Now. Within 10 minutes, I'd like you to know how to answer the question that is on the mind of every patient in my office who has an autoimmune condition: Why me?

Essentially, our bodies need to heal or fix things without thinking about it. Otherwise, we would be sitting around licking our wounds. And that is not compatible with survival of the human species. But, imagine yourself in a situation in which the healing process cannot turn off. This is what happens in autoimmunity, and there are some specific conditions that often share similarities.

In autoimmunity, a symptom sometimes occurs after a trigger. This trigger is perhaps not what your thinking. Triggers can be an infection as simple as a cough, cold or traveler's diarrhea. They can be caused by a certain medication like an antibiotic or a vaccine (even those vaccines adults commonly get), pregnancy, surgery, and even gum disease. There is a link between gum disease and autoimmunity, including rheumatoid arthritis. So, something, somehow, is introduced into the body, and the body says to itself: It's time to attack. But, as I said, certain cells are attack cells and certain bullets like molecules can also attack. But, there are also suppressor cells in other parts of the immune system that inhibit pathways. It is very complex. And the problem is when activation overpowers inhibition and control is lost. When that happens, welcome to autoimmunity. And this can happen almost anywhere in the body.

How Do Doctors Think About Autoimmunity?

Someone sent in an interesting question that I'm going to try to summarize:
I have an immunodeficiency, small fiber neuropathy, Reynaud's disease, polymyositis, fibromyalgia, DISH (bony spurs up and down the spine), insomnia, anxiety and depression. How can I find a doctor who understands my complicated medical conditions? Do you have any suggestions for pain management?

This very complex patient is very much the bread-and-butter of my practice. In evaluating a patient like this, I look at the individual, but I also look at all the conditions. Because we're talking about an intricate immune system, the reason for different kinds of pain does not always stem from that immune system. Pain can happen for other reasons as well. And certainly one could have other conditions that are causing pain. A condition not associated with the immune system is one I come across very frequently: fibromyalgia. Fibromyalgia is a chronic pain syndrome. Generally, symptoms have been going on for at least three months, but often for years. They are worse with stress and with little sleep, and there can be a history of past abuse, severe trauma and psychological trauma. When I see these patients, it is my job to figure out if the pain is coming from an inflammatory area, maybe from a joint or an organ internally not getting enough blood supply. And, that drops over into the area of blood vessel inflammation that in the world of rheumatology is known as vasculitis. Or, could that pain be coming from something with a totally different mechanism — that of chronic pain syndromes that include fibromyalgia.

I'm never happy to say to a patient: Yep, that's what you've got, because we're not that simple. Our immune systems are not that simple, and we are certainly not limited to only one diagnosis. So I start making a list that helps me understand whether several conditions are clustering, which in itself can be very common in the field of rheumatology and autoimmunity.

Let me give you a few examples. I'm sure you've heard of arthritis, of which there are many types. You've heard of rheumatism, which is an archaic term. And that should not be substituted from rheumatoid arthritis (RA), which can affect joints in the body, and can lead to stiffness in the morning from 30 minutes to 60 minutes upon wakening. RA patients often say they feel better after they get a warm or hot shower. Those patients truly have inflammation. But, then, I find out about dry eye or dry mouth, or I find out they have breathing problems and maybe something has popped up in the kidneys, and all of a sudden, I'm asking myself what other conditions can be present? This idea of clustering means something like Sjogren's syndrome. Sjogren's has to do with dryness, but not always, and like RA, is not limited to one area. So, you can imagine just how tough my job can be. Sjogren's and RA can both affect lungs and lead to chronic problems. When other symptoms pop up, I never feel the discussion is finite with a patient. That's why I have to monitor them over time to see what symptoms develop and how they react to medications.

Another caller asked a question that has to do with clustering with immunodeficiency. Absolutely! Autoimmune conditions can cluster in patients or be present in patients who also have an immune deficiency. And, certainly, a combined diagnosis of Sjogren's syndrome and CVID is not unusual.

In autoimmunity, doctors don't use a cookie-cutter approach. I cannot overemphasize how important that is. To that end, I will tell you that given we have different triggers and different genetic makeup, unfortunately, we generally try medications to see if they work. And if they don't work after an appropriate amount of time, we move on to the next option. So, whereas if you have an immunodeficiency, you can supplement that by adding back the antibody if that's what you need, it's different in the field of autoimmunity.

Hopefully, at this point, you respect how complex the immune system is and you understand that when we try different medications, often their underlying mechanisms differ a fair amount, and it's up to the individual and how they respond to those medications whether or not we have to move on to other medications.

I'm not talking about a step-care approach. And I'll interject a political comment here: I think doctors are in a better situation than health insurance companies to decide on medications that are appropriate for patients. And while insurance companies are often trying to force doctors into a step-care approach that starts with the cheapest medications, you are listening to a specialist who differs with that approach.

Is IG Therapy Right for Autoimmune Disorders?

A number of callers have asked if IG therapy is appropriate for certain conditions. Certainly, there are some conditions treated with IG therapy after first being treated with other medications that were not sufficient to control the disorders. There are also conditions that require immediate treatment with IG therapy to prevent further damage later on.

With autoimmune conditions, we're balancing the safest medications. We have many choices, so we need to look at the risk-benefit ratio. This is where we really stress that the primary care or specialty provider (whoever is prescribing medications) take time to discuss potential side effects with patients. You really do want to have a team approach.

Other callers had questions about combining IG therapy with other medications. Yes, there are cases in which IG therapy is combined when there is an immune suppressant already on board. From my standpoint, I truly have a comfort level combining immune suppressants. If, for example, I'm treating a patient with lupus that is not very far progressed (if there are not a lot of organ-threatening issues), I'm going to choose a simpler medication, changing it only after I've given it an adequate trial.

I say that because IG therapy is a complex soup of a lot of molecules and portions of the immune system already introduced in the body. And, in some cases, it is not totally understood what mechanisms are causing patients to get better. So, there is not a universal mechanism for all conditions treated with IG therapy. Therefore, I want to stress there is a great need to finance research so we can get to the bottom of this and to be better armed with the evidence for which part of the IG therapy we feel will be best used for some of these very complex autoimmune disorders.

How Is It Known if It's an Autoimmune Disorder?

Autoimmune disorders can attack any part of the body. Many patients want to know whether their symptoms are actually an autoimmune disorder, but it's not always that easy. I really enjoy being a detective and going back to see if something has been missed. There are symptoms that could be associated with autoimmune conditions such as fatigue, but fatigue doesn't mean you have an autoimmune condition. However, fatigue can be common in autoimmune disorders, as can pain in joints, swelling, rashes, irritated eyes and dry mouth — even worrisome things such as inflammation around the heart, lungs or kidneys, liver failure, thyroid involvement or brain involvement. All of these represent a wide spectrum that can be ways that autoimmune conditions can start expressing themselves. It can be very indolent or it can be an emergency. This is where I come in as a detective to determine if you have a condition that needs treatment.

In autoimmune conditions, triggers are often not sufficient to start the battle with swings out of control. It can have started with an infection or traveler's diarrhea. But it also takes something else: susceptibility. Genetics, genetic makeup, stress, medications or even on-the-job exposure such as military personnel who can get infectious gastroenteritis and end up with nerve problems could result in autoimmune disorders.

With autoimmune disease, everyone is unique, and if it sounds like a given condition, remember you may be misled by someone on the Internet who claims to have the same thing and confidently suggests a miraculous query for you, but be weary.

Types of Autoimmune Conditions Treated with IG Therapy

This is a good time to segway to a sampling of autoimmune conditions, starting with Guillain Barré syndrome (GBS). I don't like the name GBS because it's really a number of subgroups that can respond differently. Simply, GBS is the most common cause of flaccid paralysis (meaning you have a very dangerous paralysis). It often starts ascending upward from the feet and, in some cases, can paralyze muscles needed to breathe. Our equivalent of WD-40 or go-to medications for inflammatory disorders is corticosteroids (prednisone). But, for GBS, they're not very effective. Instead, intravenous IG (IVIG) or plasma exchange are very effective and are best introduced in the first few weeks of disease.

Another condition best treated with IVIG is Kawasaki disease (KD). KD occurs in young children usually between 6 months and 5 years of age. Symptoms include high fever lasting from four to five days and rashes, which are quite different. If you've ever seen a snake molt, that's how the fingers and feet look in these children. Others have a strawberry (very red) tongue, and there can be peeling of the lips. I would say not all children have all the symptoms. But the most serious symptom of KD is heart disease. The goal of IVIG is to prevent serious heart disease.

A new autoimmune syndrome is called systemic capillary leak syndrome. In some cases, the leak is going into the gut, and patients present in shock. When patients are in shock, their heart can't maintain good blood pressure. With the complexity of the immune system, this condition can be compared to having a shower of all the body's cytokines. Some of these patients end up requiring IVIG monthly to prevent it from recurring.

Other conditions are a lot less dramatic, one of which is eosinophilic granulomatosis polyangiitis. I had a patient two days ago who previously had a cold and some calf pain, and now he has bilateral foot numbness so when he walks, he can't lift up his foot properly. That's called foot drop. Do you see the pattern with infection first? But why is he worried? With this type of problem, he could have involvement in his lungs, gut, kidneys or tissue that becomes permanent and chronic. A paper I looked at recently showed a singular course of IG therapy allowed a patient with this condition to go into remission. I'm not saying that just one course is going to work in my patient because his symptoms have been going on for a while, and unfortunately, it took him a while to get to me. Generally, in the field of autoimmune conditions, we like to see people early if possible, but we get people in later stages.

There are many other conditions that can be treated with IVIG. I have a patient who got breast cancer who responded well to therapy but then she got rashes on her face and trunk, swelling and discoloration around her eyes, and weakness in her muscles. The weakness in her muscles is an example of what we call myositis (inflammation of the muscles). There are many reasons for muscles not working, including nerves, toxins, hormones, thyroid, medication side effects, cocaine, and the list gets longer and longer. But with myositis, I used to perform certain tests because there's generally a pattern with clusters around autoimmune conditions. So in this case, the lungs had to be looked at and the skin was involved. We diagnosed her with dermatomyositis, which can be treated with IVIG.