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# The Feverish Case of the Fatigued and Fibrotic

**Announcer:**
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

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**Dr. Casper:**
This is CME on ReachMD, and I'm Dr. Corey Casper. Here with me today is Dr. Sudipto Mukherjee.

Let's discuss the relapsing and remitting symptoms that our patients have with Castleman's disease. So, Dr. Mukherjee, what can you tell us about the systemic symptoms? How can we prepare our patients for what's in store for them over the course of their disease?

**Dr. Mukherjee:**
Thank you, Dr. Casper, for this very interesting question. And I think it all begins with a diagnosis of iMCD [idiopathic multicentric Castleman disease]. And before launching into any treatment, that is one of the key times when the provider and the patient needs to sit down and have a very broad and a frank discussion about what are we getting into. iMCD is a chronic disease; none of the therapies are curative. And when the treatment is started, the current recommendation is to continue the treatment indefinitely or lifelong until disease progression or unacceptable toxicities. So we may be talking about in some patients for a few years, in some patients up to a decade or more of treatment. That's the most data we have on siltuximab-responding patients as of now.

So in these patients, we have to counsel them that because this is a chronic disease, even on treatment there can be instances where there might be acute flare-ups, acute exacerbations that may require the patient to be hospitalized or may end up in the ICU on life support. Why it happens, we do not know. There are many hypotheses, and one of them that has been shown has been differential levels of interleukin-6 in different body compartments. For example, in patients who have a pulmonary failure, interleukin-6 levels in the pleural fluid would be sometimes as high as 6- or 8-fold than the levels in the circulating plasma. There are other factors in play, which we do not really know about. And we even don't know who are the patients who will relapse and remit, and who are the ones who will not. But typically, in these patients who relapse, in most of the cases, there is an underlying driver, and it still remains that the common biological underpinning is overproduction of interleukin-6.

How we best manage these patients is through best supportive care. Sometimes it may require the use of high-dose steroids to calm down the cytokine storm, and in several instances mostly reported either in personal clinical experience, including my experience, and in some case reports, is more frequent use of interleukin-6 [inhibitor] from once every 3 weeks to even once weekly. These have not been rigorously tested or validated, but there are some reports that these have been used to manage these significant adverse outcomes in the clinical journey of these patients when they relapse.

And clearly, for a patient to be on a lifelong journey with these therapies, especially knowing that these therapies, when they work, they do have improved the survival of these patients, it is critically important to get some buy-in from the patient and the caregivers who take care of these patients. And letting them know about the anticipated difficulties or complications through their clinical journey, and setting up realistic goals is critically important in shared decision-making, because that will allow adherence to the treatment and better

compliance, and which hopefully will turn into better clinical outcomes.

**Dr. Casper:**
Thank you, Dr. Mukherjee, for sharing your extensive clinical experience with us.

The most important thing in this chronic disease that has its ups and downs is that close partnership between the patient and the provider for that therapeutic relationship that allows that close partnership to select and to adhere to the most effective therapies. I think patients need to know that there are multiple treatment options, that there are lots of different ways of dealing with the ups and downs of Castleman's disease, but that it's a journey, and it's one that, together, the patient and the provider and maybe even the greater community of Castleman's providers and patients can support and can be again a long and healthy life.

So with that, I want to end our brief but great discussion. Unfortunately, our time is up. Thank you all for tuning in.

**Announcer:**
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