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Chronic Lymphocytic Leukemia: Insights into the Epidemiology and Patient Care

Dr. Caudle:
Welcome to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me to explore the epidemiology of chronic lymphocytic leukemia, or CLL for short, and ways to better manage this cancer, is Dr. Adam Kittai. Dr. Kittai is an Associate Professor at the Icahn School of Medicine at Mount Sinai New York, where he's also the Assistant Director of Lymphoma Clinical Research and CLL Clinical Research Leader. Dr. Kittai, thank you so much for being here today.

Dr. Kittai:
Great to be here. Thanks for having me.

Dr. Caudle:
Well, we're excited to have you, so let's dive right in. How common is CLL?

Dr. Kittai:
CLL is a relatively rare disease, and I actually looked up today what the chance of someone developing CLL is, and the lifetime risk of anybody developing CLL is 0.57 percent. It's really hard to think about that percentage in context, so I'm going to give you some other statistics as well to think about your chance of developing CLL and how common it is in society. So about one in 175 people will get CLL. About 20,000 cases of CLL are diagnosed per year in the United States; worldwide, it's 191,000 cases. But in terms of the commonality of CLL in the world of leukemia, is that it actually is the most common leukemia. And when we think about leukemias in general, those include things like AML and ALL, the acute leukemias, whereas this is a chronic leukemia and is the most common leukemia, and really represents about 25 to 35 percent of all leukemia in the United States.

Dr. Caudle:
Thank you so much for that. And along those lines, are there any populations who are at a higher risk of CLL?

Dr. Kittai:
CLL is mainly a disease of older patients. And so the median age that people get CLL is 70, and it's more common in men. However, we do see it in younger patients, but not typically children or teenagers. So I have had some patients who are in their 30s, but those tend to be the minority of patients with CLL.

Additionally, in the U.S., patients with CLL are more likely to be White, and the incidence is actually lower in Asian countries, whereas in Asian countries, it occurs at about 10 percent less of a rate than the United States. And the reason why this is all the case is likely due to genetics where there probably is a higher risk of CLL in patients who are Eastern European lineage. On that note, it can run in families. So if you do have CLL and you have multiple family members who have CLL, specifically first or second-degree family members, you should consider talking to a genetic counselor to get a better idea of how risky CLL might be for you and your children. But that being said, even though it can run in families, that is also extremely rare and not usually the case. Just like other diseases, like heart disease and lung disease, if you have CLL, it is more likely that somebody in your family might also get CLL.

In addition, there is some increased risk of CLL if you had exposure to weed killers or Agent Orange. But as opposed to other data that is more strongly correlated with this exposure, it's not as strong with CLL. The Association of Non-Hodgkin's Lymphoma was recently reported with exposure to weed killers, and technically, CLL is a type of non-Hodgkin lymphoma.

Dr. Caudle:

Could these patients be at risk for any other cancers or comorbidities?

Dr. Kittai:
The answer is yes. Actually, the risk of secondary cancers or comorbidities is actually one of the number one things I think about for patients with CLL because not only is the risk for secondary cancers prevalent for patients who require treatment for their CLL, but it is also prevalent in patients who are not currently on treatment. And there's a distinct reason for this. Patients with CLL have a compromised immune system, and we might think to ourselves that a compromised immune system might increase the risk of infection, but it also increases the risk of secondary cancers. And the reason that is, is because our immune system is responsible for surveilling our bodies for cancers before they become a problem.

So in general, for my patients with CLL, I recommend that they get age-appropriate cancer screening. So for women, they should make sure that they are getting their mammograms on time. For men, they should make sure that they're getting their prostate cancer screening and discussing it with their primary care doctors. And for both patients, both men and women, they should definitely make sure that they are getting their colonoscopies as scheduled as well. In addition, there's a high risk for secondary skin cancers for patients with CLL. And so I recommend that everybody see a dermatologist at least once per year.

Additionally, another comorbidity, which I mentioned, was risk of infection. So patients with CLL might notice that they get recurrent viral infections; think pneumonia, upper respiratory tract infections, those are the two big ones that I've seen with my patients with CLL. So anyone who reports multiple infections within one year, I often check IgG levels. IgG is immunoglobulin G and can be low in patients with CLL. Just to clarify, IgG, or immunoglobulin G, is just a type of antibody, and patients who have low antibodies are more prone to getting viral infections. Luckily, the reason why I test it is because there's something we can actually do about it. So patients who have multiple infections with a low IgG level can really benefit from receiving something called IVIG, which is intravenous immunoglobulin, which may decrease the risk and severity of infections.

Dr. Caudle:
For those of you who are just tuning in, you're listening to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Adam Kittai about the prevalence and risks of chronic lymphocytic leukemia.

So with those risk factors in mind, Dr. Kittai, what challenges exist when it comes to diagnosing patients with CLL?

Dr. Kittai:
In my opinion, there are four main challenges to the diagnosis of CLL. The first challenge I think about is access to care. So if patients don't have access to a hematologist or oncologist to diagnose their CLL, that can really lend itself to be a barrier to actually getting the diagnosis and getting the care that our patients need. So that is number one to me, making sure that patients who are suspected to have a leukemia or lymphoma or CLL need to have good access to a hematologist and oncologist.

The next thing is, is that CLL often presents with B symptoms. B symptoms are fevers, chills, weight loss, and fatigue. And specifically with the fatigue, there's a lot of things that can cause fatigue. And so when you have a patient coming in with fatigue, CLL might not be number one or number 10 on your diagnosis list. And so really, these symptoms are universal to most diseases, which can make diagnosing CLL a little bit tricky.

Next is lymphocytosis. So lymphocytosis is high white blood cell count, specifically high lymphocytes. And with CLL, we usually see high lymphocytes. Sometimes patients will have not high lymphocytes but have big lymph nodes, and that's SLL. But having high lymphocytes can be caused by a lot of different things, including medications or a viral infection or other infections. And so that can get a little tricky. And for patients with CLL, what we're looking for is sustained lymphocytosis, high lymphocytes on multiple different counts.

Last but not least, the fourth challenge with diagnosing CLL is that CLL can be misdiagnosed for other lymphomas. So when we think about non-Hodgkin's lymphoma, there's a lot of different types of lymphomas that fall underneath it, and CLL sometimes can look like other lymphomas, but can actually be CLL that may require advanced testing to actually say this is CLL. Specifically, one of the other non-Hodgkin's lymphomas that oftentimes we debate as to whether it's CLL or something else is mantle cell lymphoma, which can look very similar underneath the microscope and using some of our advanced testings to CLL.

So overall, I think there are four main challenges. One is access to diagnostic care and treatment with a hematologist/oncologist; B symptoms mimicking other diseases; high white count, which can be induced by various infections and medications, so really we want to see sustained high lymphocytosis or high white count; and also difficulties with telling the difference between CLL and other types of non-Hodgkin's lymphoma.

Dr. Caudle:
Thank you for that. And turning now to treatment, what barriers often prevent optimal care for these patients? And how would

overcoming these barriers improve a patient's quality of life?

Dr. Kittai:
So as we started transitioning from using chemoimmunotherapy to oral therapies and novel therapies, cost of care has become a real issue. And ultimately, it is rare, in actuality, that I find somebody who has to pay the full cost of these new drugs. Usually, we're able to find various different coupons and programs through either the drug company or through other nonprofit agencies, like the Leukemia Lymphoma Society and the Lymphoma Research Foundation and the CLL Society, to help cover the cost.

But as more and more people are being treated on these medications, I worry that more and more people are going to have limitations in terms of affordability for the cost of some of these medications. That may be balanced out by generic forms of some of these medications eventually being produced once the patent runs out, but that still will take time. But ultimately, if cost becomes an increasing issue, one could easily imagine where people who can't afford the drugs don't get treated the way they should get treated. And if they can't get treated with our new therapies, they'll have worse outcomes and probably have worse toxicity when treated with chemoimmunotherapy.

Another thing that often happens and is difficult with oral medications is making sure that our patients are compliant in taking the medication. And I think that how I view compliance is that it really comes out to an issue in communication, which is both an issue from the patient perspective of not taking the drug and also the physician's perspective of not finding out about whether or not their patient is taking the drug that they expect they're taking at home by mouth.

And so one of the ways to overcome this barrier is to make sure that you have strong communication with your treating physician. I want to encourage all of the patients that are listening to this to please have an open line with your hematologist and oncologist, let them know how you're feeling, let them know if you're experiencing any toxicity because ultimately, it's important to continue on your treatment to get the best outcomes. But there are different tactics that we can use to make sure that our patients are the most successful at taking these oral medications.

So the last barrier that I think prevents optimal care is the time required of our patients to receive therapy. Time is a limited benefit that we all have, and ultimately, when we are requiring our patients to come in weekly to get their labs checked or get an infusion, that time spent in our clinic is time away from work, is time away from family. And ultimately, we need to do a better job of creating treatment regimens that improve our patient's quality of life, where they can do most of it at home or at work.

So to summarize barriers that prevent optimal care, in my opinion, include cost of the drug itself; potential issues with communication between the patient and physician that might lead to compliance with decreasing the amount of oral meds that our patients take; and the time requirement that we make our patients do in order to get the therapy in terms of coming into our clinic. And we are working on all four of these things to make it better for patients, to improve their quality of life, to make treatment not so impactful on how they experience life and enjoy life.

Dr. Caudle:
Thank you so much for that. And finally, do you have anything else you'd like to add?

Dr. Kittai:
I want to conclude by saying that we've made drastic improvements in the outcomes of patients with CLL over the last 10 years, so much so that recent data shows that patients with CLL are living as long as age-matched controls. This is really exciting. But ultimately, we still have room to improve by making sure that our new therapies are available to everybody, and that our new therapies do not come with increased toxicity that could impact patients' quality of life. But overall, patients with CLL are living longer, more fruitful lives, with low rates of toxicity, which I'm so excited about. And this is why I love treating patients with chronic lymphocytic leukemia.

Dr. Caudle:
I love that. And with those final thoughts in mind, I'd like to thank my guest, Dr. Adam Kittai, for joining me to discuss the barriers to effective CLL management. Dr. Kittai, it was great having you on the program today.

Dr. Kittai:
Thanks for having me.

Dr. Caudle:
For ReachMD, I'm your host, Dr. Jennifer Caudle. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.