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The Bloodline with Blood Cancer United Podcast

A Podcast for Patients and Caregivers

Episode: 'Acute Promyelocytic Leukemia (APL): Advances, Hope, and Healing'

Description:

In this episode of *The Bloodline with Blood Cancer United*, Elissa and guest co-host, Kristen Parker, speak with Dr. Anand Jillella, of Georgia Cancer Center. Together, they explore acute promyelocytic leukemia (APL)—a rare but highly curable subtype of acute myeloid leukemia. Dr. Jillella explains the rapid onset of APL, its hallmark signs and symptoms, and how targeted treatments have transformed outcomes for patients. Kristen, an APL survivor and Blood Cancer United Patient & Community Outreach Manager, also shares her personal perspective. Listeners will gain valuable insight into why APL stands apart as one of the most treatable forms of leukemia today.

Transcript:

Elissa: Welcome to *The Bloodline with Blood Cancer United*. I'm Elissa.

Kristen: And I'm Kristen and thank you so much for joining us on this episode.

Elissa: Today, we are speaking to Dr. Anand Jillella, a hematologist-oncologist and Professor of Medicine at the Georgia Cancer Center at Augusta University in Augusta, Georgia. He is the Founding Director of the Georgia Cancer Center's Adult Stem Cell and Bone Marrow Transplant Program and holds the inaugural J. Harold Harrison, MD, Distinguished Chair of Medical Oncology. Dr. Jillella previously served as the Medical Director of Outreach and Network of the Winship Cancer Center at Emory University in Atlanta.

Dr. Jillella's clinical focus is bone marrow transplantation and the treatment of leukemias, including acute promyelocytic leukemia or APL, for which he has led many clinical trials. We also have a guest cohost today, Kristen Parker. She is a Blood Cancer United Patient & Community Outreach Senior Manager in the Ohio River Valley Region and is also an APL survivor. Thank you for cohosting with me today, Kristen, and welcome Dr. Jillella.

Anand Jillella, MD: Thank you so much. Thank you for having me.

Elissa: Well, thank you for being here. So, our episode today is on acute promyelocytic leukemia, or APL. Can you explain to our listeners what that is?

Dr. Jillella: Acute promyelocytic leukemia is a very aggressive leukemia. The onset is very rapid. For instance, you may not have any symptoms from this disease at Thanksgiving, but by Christmas it could get so aggressive and advanced that it could bring you down to your knees. The main characteristic of this leukemia is it takes your blood counts down; but most importantly, in 100% of these patients, they develop what is called disseminated intravascular coagulation. In short, the blood does not clot right, which is what causes most of the problems.

Elissa: Okay.

Dr. Jillella: So, acute promyelocytic leukemia is a very aggressive leukemia with a very rapid onset of symptoms and is specifically characterized by a condition where the blood does not clot right.

Elissa: Now, APL is a subtype of acute myeloid leukemia, or AML, right, and how does that differ from other AML subtypes?

Dr. Jillella: So, most of the AMLs have certain characteristics like the genetic makeup of the cancer cells, etc. Acute promyelocytic leukemia characteristically has this

translocation called the 15;17 translocation, which is what gives it the proliferation advantage. That is what makes it stronger than the other cells.

So, the difference is that it has the 15;17 translocation. That's one thing. The second thing is virtually all these patients have a tendency to bleed. They have this problem with their coagulation. And then thirdly, the thing which is so different about this leukemia is we have just spectacular therapies where the cure rate for these patients is almost 98 to 100%.

Elissa: Wow.

Dr. Jillella: So, that is actually what separates this leukemia from, from the other type of acute myelogenous leukemias. The therapies have really advanced, so much so that most patients with this condition are cured.

Elissa: Wonderful. That is great to know, and we'll get into the current treatments for this just a little bit later.

Kristen: Yeah. So, what are common signs and symptoms of APL? What might bring someone into the doctor to be diagnosed?

Dr. Jillella: Yeah. So, there are three things that they can have. One is they could be tired because it affects the hemoglobin. The hemoglobin can become low, and that could cause fatigue or shortness of breath. That is one of the things that brings them to the hospital.

The second thing is the white cells could go down, and if your white cells go down, you become vulnerable to infection. So, a third of patients come in with some form of infection. And then when you evaluate the infection, the blood counts are low; and then you evaluate it further, then you diagnose the leukemia.

The third thing is you could bruise. You could have bruising or you could bleed. When you brush your teeth, you're bleeding or you could be bleeding from your bladder or your periods are heavier. Or when you bump into something, you have big bruises on your skin. So, those would be the common symptoms that would bring patients to a physician or to healthcare.

Elissa: Now, I had a friend diagnosed with AML; and she had actually cut herself shaving and required a tourniquet because it just wouldn't stop bleeding. Is that something that would be potentially common of APL patients, that they might cut themselves or do something very simple and just not be able to stop bleeding?

Dr. Jillella: Absolutely, absolutely that can happen. And they might come with other symptoms, such as an infection or not feeling well, like tired. But when you ask them were you bleeding more often, were you bruising more often, they always say, "Yes," in the last few weeks those were symptoms that they had.

So, it's not like a disease which goes for a long period of time. The onset is very abrupt, like three weeks ago they were completely fine, and now they're having all these symptoms that brings them to a physician or to a healthcare facility.

Elissa: Now, Kristen, I'm curious. Did you have any of those signs and symptoms that he just mentioned when you were diagnosed?

Kristen: I actually had all three. So, initially, I had the unusual bruising and extreme fatigue. But eventually it actually ended up being severe abdominal pain that ultimately made me go to urgent care, thinking it was kidney stones, anemic, whatever it might be. And it was actually an infection. They originally thought it was appendicitis, so that's really what sparked it. So, I checked all three of those boxes when it came to the signs and symptoms that were mentioned.

Elissa: Wow. Okay, so let's discuss treatment. What are the current treatments for APL?

Dr. Jillella: Yeah, so this is the disease for which we now call it targeted therapy, was probably one of the first diseases for which targeted therapy has been developed where you know what the problem is. What is the problem, which is causing APL, and then you design something that would actually reverse that problem or eliminate that problem. And this is probably one of the first diseases for which something like that has been developed.

It's actually very unconventional cancer treatment that is applied in these patients. One is what is called all-trans retinoic acid which is a type of vitamin A; and the other one is arsenic, which is also very unconventional medication to treat this. So, we now use mostly a combination of all-trans retinoic acid or a form of vitamin A along with arsenic trioxide to treat these patients.

Kristen: You know, I always get that-

Elissa: Wow.

Kristen: -reaction as well when people ask how I was treated, and I said one of my main chemotherapies was arsenic. It always raises some eyebrows there, but it's one that I took for ten months and was actually one that was approved by the FDA that LLS helped advance. That's the drug that saved my life, so I'm forever grateful for arsenic.

Dr. Jillella: Yeah. I mean we give enough arsenic to make it toxic to the cancer cells, but not enough to cause problems to the patient. But it's super effective. I mean they're so effective that the likelihood of relapse is virtually negligible.

We just concluded a trial of about 201 patients, in whom we had a handful of patients who relapsed. And four out of those five did not want any more treatment. They were older patients. They were from rural areas. They came to the hospital. We got them into remission, and once they went back, they said, "No. This is fine, and we don't want any more treatment." And then they relapsed and died.

But there was actually only one patient out of these 201 patients who we think had what I would call a relapse. But generally, the relapse rates with the combination of arsenic and all-trans retinoic acid is virtually negligible. At the most, it might be 1%. 2% is probably a stretch.

Elissa: Wow, yeah. I mean, you really do have to think about that balance with a lot of cancer treatments, including chemotherapy. the balance of effective enough to kill the cancer but not killing the patient. And so, I'm sure people listening are probably a little shocked with the arsenic. I'm curious how does that actually work to affect the cancer? How is the arsenic working?

Dr. Jillella: What happened in APL is, I think, investigators were able to figure out what causes the leukemia. It is the 15;17 translocation, which actually makes a type of protein. And that protein actually gives these cells what we call the proliferative advantage. Actually, it makes them stronger so they can grow. And what arsenic does is it actually reverses that protein or gets rid of the protein that actually causes that problem.

Elissa: Okay.

Dr. Jillella: So, the treatment is actually super intelligent, meaning it focuses on just the problem that causes it; and there are side effects, but not substantial. And the interesting thing about APL is you could treat these patients, you could cure them, and look at Kristen. She's mainstream back. She goes back to whatever it she was doing

before. So, it does not leave them with a host of side effects like some of the older chemotherapy drugs like we have used.

Elissa: That's great. Yeah, it does sound like these treatments are very, very successful; and, obviously, the prognosis is wonderful. So, what happens with those few patients that do relapse or may not respond to that treatment? Are there options available for them?

Dr. Jillella: There are options available, but the relapses are so few that there aren't any systematic studies that are looking at it. I mean, you have to have enough patients to do anything, I guess, from a research point of view.

I think if they relapse, you could re-treat them, get them back into remission. Some of them have a transplant, and you can get them back into remission again. But I have been taking care of APL patients in a very large way for the last 15 years. And I can count on my fingers the number of patients who relapsed after the initial treatment that we give-

Elissa: Wow.

Dr. Jillella: -for whom we had to do something else.

But, the biggest problem, I tell you, in treatment that everybody needs to know, especially providers in the community and academic centers as well, the 98, 99% cure rates are in clinical trials. So, it's usually younger patients who are placed on a clinical trial. If you look at the average age of a patient in a clinical trial, it's about 40 to 45 years.

Elissa: Okay.

Dr. Jillella: So, the drugs have been approved in patients who are young and patients who are healthy get enrolled in clinical trials. If you have heart failure or your kidneys are not working or you're 80 years old, you're automatically eliminated. But the thing is, in real life, not every APL patient is 40 years old with no health problems.

Elissa: Right.

Dr. Jillella: So, you can have a 70-year-old who might have kidney failure or you might have a 65-year-old whose liver is not working or you might have a 50-year-old who had a heart attack. So, what do you do with these patients? And if you apply the same treatments that have been approved in clinical trials, those patients don't do well. They actually die from complications of the treatments because the drugs are complicated.

Elissa: Yeah.

Dr. Jillella: And once you apply the drugs, you can actually give them side effects that can cause the demise of the patient. It's not the APL, but it's the side effects of the drugs.

So, if you look at all-comers, and you take 100 patients in the community, about 30% don't leave the hospital, meaning they die during the first month. But the thing is, if you get them through the first month, it's a home run. They don't relapse.

We were actually one of the first groups in the world to recognize this as a problem way back in 2006, 2007. We figured out at that point why these patients were getting into trouble during the first month and what should we do to prevent this.

So, the last two trials that we conducted was from 2013 to 2017, where we decreased the induction mortality or the mortality in the first month from an estimated 35% to 8.5%. And in the most recent trial that we concluded, which was sponsored by the

National Cancer Institute (NCI), we decreased the first month mortality from an estimated 35% to 3%. So, there was a whole program that we developed in how to treat these patients during the first month to keep them alive.

Kristen: So, are there any complications early in treatment that patients or even doctors may need to be aware of?

Dr. Jillella: Yes, I think one of the main complications, like I told you, is bleeding is a problem because it causes problems with the clotting mechanism. So, the standard of care is to keep the platelets, which actually help the blood to clot, higher. You actually keep them at 30,000 to 50,000. So, you have to check the labs at least two times a day; and if the platelets fall below that number, you transfuse them.

The second thing is a protein called fibrinogen, which also helps in clotting. And in APL, the fibrinogen is either low to begin with, or it actually goes down as you initiate treatment. So, that is something that has to be measured two times a day. And if it goes down, you have to give them a transfusion to fix it. One complication is infection. So, we would use prophylactic antibiotics to make sure that patients don't get this infection.

The biggest complication, I think now, especially in older patients and patients who have other health issues, is what is called differentiation syndrome. It's a complication of the drugs. Both ATRA (all-trans retinoic acid) and arsenic can cause this problem.

So, there are ways in which you can prevent it. One is we routinely use steroids to prevent that complication. We check their weight, and this is something that we learned from our own experience by trial and error. If they gain too much weight, then they're more likely to develop this complication. So, what we do is the day they come in, we take their weight; and let's say they are 75 kilos (165 lbs), we check it every day. And if they're gaining any weight, we give them diuretics to take the weight off.

And then the other complications that you can have from the drugs, this very unusual complication called differentiation syndrome. If they catch a fever or if they develop body aches, etc., that's another manifestation of differentiation syndrome. So, you have to watch for that very meticulously. And if you have any of those symptoms, then you hold the drugs till those symptoms go away; and then you restart them once those symptoms go away.

The key is it's a rare disease. There are probably 3,000 cases per year. When we started this program, there were 15,000 oncologists who treat this. Now I think there are about 27,000 to 30,000. So, that means you'll have one patient for every ten oncologists per year. That means an oncologist would see one today and may not see one for the next ten years.

The sad part with APL is all you have to do is make one mistake. You're not going to cause a complication. You're actually going to cause death of the patient. So, there are two things to it. One is using an algorithm and following the guidelines that the algorithm says and, number two, which is part of the guidelines in treating this patient now, is to talk to somebody who has more experience in taking care of these patients.

Elissa: Okay, so it is very important that they find a specialist?

Dr. Jillella: Yeah, absolutely. Operative inexperience, which is what I have termed it, I think is a problem and can actually result in early deaths in these patients.

Elissa: Okay.

Dr. Jillella: Which is what we showed in both the trials that we conducted.

Elissa: So, you mentioned some particular side effects with the differentiation syndrome. Are there any other common side effects of the treatment that patients might have, and can they be managed?

Dr. Jillella: Yeah, I think there are others. These are the main side effects which can actually cause death during the first month. Other things would be, it can take your white count up. There are ways in which you can manage it. It can actually cause problems with the liver tests. Those are manageable too. Basically, you withhold the drugs till those symptoms go away, and then you restart them.

So, during the first month, this is my editorial based on my experience, is you have to keep the patient alive. The biggest problem with APL is death during the first month which we still have not really fixed. We have shown a method to fix it. The question is how do you scale this? How do you implement this nationwide?

When we had the trial, it was opened in 291 centers, and people were calling us. Now that the trial is over, how do we translate this into a sustainable model? I think that's the next question.

Kristen: And so, thinking about the future, what does the future of APL treatment look like, and are there any emerging therapies? Are those in clinical trials that you're particularly excited about?

Dr. Jillella: Yeah. So, the thing is everything is done in APL. There's really not much research left. I think the only trials that were open in the last 15 years were the two trials that we conducted. There are no other trials, honestly. Everything is done, and nobody supports APL trials anymore because this is a home run. So, arsenic is actually being developed as an oral agent. I think there are trials that are looking at it. I don't think it's open yet. So, that is one possible thing where you don't have to go to the doctor's office like you did for eight months or ten months or whatever to get it. That's an option.

But the therapies are spectacular. I think we need to focus on preventing early deaths in these patients. If I told you that in clinical trials, 98, 99% of patients are cured, if you

look at populations, like the SEER data (Surveillance, Epidemiology and End Results), shows that the one-year survival is not 90%. It's actually 70%, which means 30% of the patients have not even left the hospital. I think that's where we need to focus. How do we fix this problem? In my opinion, that's probably the most frustrating and the biggest cause of treatment failure in this disease.

Elissa: Yeah. And then you also mentioned earlier about patients with comorbidities or those with ages that are, older patients or maybe younger patients than what we see in clinical trials. Is that something that's being addressed to make sure that they're getting the treatments that are successful for them?

Dr. Jillella: Yes, so we answered those questions in the trials that we did. So, as we went along, if I told you that, with the first 19 patients that we treated, 7 patients died, which is actually 37%.

Elissa: Okay.

Dr. Jillella: And with the subsequent trial, we treated 120 patients, and 11 patients died. And what we did with that is with every patient who died, we quickly analyzed the patient. We didn't say, "Oh, this patient was 80 years old and had kidney failure and had APL and was destined to die, etc." That was not the approach that we took. Actually, one of my coinvestigators, Dr. [Vamsi] Kota, he's really the brain behind all this. He is the one who came up with all the brilliant ideas.

Every time a patient died, the two of us would sit together and we would try to figure out what did we do and what did we not do that resulted in the demise of the patient, and how were we going to prevent this? And the key was don't make the same mistake twice. You already did that once before, and it didn't work.

So, as we went along, we streamlined the treatment and actually changed treatments. So, your question, "How do you treat an older patient?", if I'm using this dose in a patient who's 45 years old and it's working, I can't use the same dose on an 80-year-old who has heart failure. I have to do something different.

So, what we showed was in those patients, you need to turn the dose down and treat them with a smaller dose. We are actually looking at publishing that experience now, and the next trial that we are looking at is treating older patients above the age of 60 and how do you do that and keep them alive during the first month? That's a trial that we are proposing to the National Cancer Institute.

Elissa: Okay, wonderful. So, our final question today, on our patient podcast home page, we have a quote that says, "After diagnosis comes hope." What would you say to patients and their loved ones to give them hope after a diagnosis of APL?

Dr. Jillella: So, for us, if you see a patient with APL, no matter how old they are, what other health problems they have, we actually encourage them very much to participate in the treatment because nine out of ten times, they are cured of their problem; and we can send them back to wherever they came from.

So, the positive thing about this is all oncologists would agree that once a patient is diagnosed with APL, the likelihood of curing that patient is very, very high, regardless of what their other health issues are and regardless of what their age is.

Elissa: And you want to make sure that they're not afraid of the arsenic.

Dr. Jillella: Right, absolutely. I think people do get flustered when you mention it.

Elissa: Yeah.

Dr. Jillella: But the way we present it is we say, "We just give enough to cause problems with the cancer cells, not enough to give you any problems." That's the thing. I think one of the first patients who I treated, young guy, he used to put cable lines on telephone poles.

Elissa: Okay.

Dr. Jillella: And I treated him for eight months or so, and then he went back to doing whatever he used to do before.

Elissa: That is wonderful.

Dr. Jillella: So, that's the thing. They're cured, and you send them back and they're mainstream to doing what they used to do before.

Elissa: That's great. Wonderful news. Well, thank you so much, Dr. Jillella, for joining us today and talking all about APL. And again, thank you, Kristen, for cohosting with me. We love to have you on here today.

But I think this was a great discussion, and it's so encouraging to hear about a blood cancer that has such a successful cure rate and successful treatments. So, wonderful to hear; and again, thank you so very much for joining us.

Dr. Jillella: Thank you so much for having me. Thank you. It's been a pleasure.

Elissa: And thank you to everyone listening today. *The Bloodline* with Blood Cancer United is one part of our mission to improve the quality of lives of patients and their families.

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