Lessons in Blood Cancer: How Far We Have Come – Multiple Myeloma

TRANSCRIPT

Narrator
Doctors and researchers have been studying cancer for generations. Thanks to pioneers in science and tireless dedication, we have made great strides in diagnosis, treatment, and the quest for a cure.

But we need to understand where we started to learn how to get where we are headed.

Join us as we explore the history of blood cancer and highlight just how far we've come.

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Probably the best achievement is things that happen every day. In working with my patients and seeing them go from being newly diagnosed to being involved in their care and being empowered.

Because cancer can be incredibly unempowering. But when you know about the disease, you know about what to watch, about when to celebrate and when to worry, that empowers you to be able to make decisions and to take control over your life with this disease.

What is Multiple Myeloma?

Multiple myeloma is a cancer of the plasma cells. So, inside our bone marrow (the bone marrow is the blood factory) there are cells called plasma cells. They make blood plasma. Specifically, they make antibodies that help fight infection. And just like any other cell in the body, just like lung cells and colon cells, those plasma cells can become cancerous. And when they become cancerous and mutated, we call that multiple myeloma – malignancy of the plasma cells. And when those plasma cells become malignant, they tend to do four things: 1) they produce lots of antibodies or plasma or protein, which is how we detect myeloma in the first place. [2] And those proteins can get stuck in the kidney causing kidney problems. [3] Those myeloma cells like the bone, and so they can cause holes in the bones and release calcium from the bones. [4] And because it's a cancer inside the bone marrow, the blood factory, when those cells begin to grow, they can make people anemic or have low red blood counts because it begins to push out the normal blood production in the bone marrow.

Discovery of Multiple Myeloma

So, myeloma was first described actually 180 years ago. And how it was first described really speaks to where we are today. A doctor by the name of William McIntyre in London had a patient, Alexander McBean, who was having all these bone fractures and bone breaks. Dr. McIntyre was a family community physician, wasn't a high-powered researcher, but he was committed to Alexander McBean to try and figure out, "Why is this young guy breaking all of his bones?" And so, he examined everything to try and figure out what was wrong with him. And he looked at his urine and saw how unusual his urine was in appearance; he found that there was this protein in his urine. And so, he sent his urine off to a doctor by the name of Henry Bence Jones in London, who we know from the Bence Jones Protein that we do the test for myeloma. And Dr. Jones found that there was this hydroxide of albumin in the urine. Dr. McIntyre did not need to do all these steps. He could have put some leeches on Alexander McBean. He could have done a couple phlebotomies and kind of left it, but he took all the steps to figure out what was wrong with his patient, did his best to try and treat his patient, and wrote it down in a journal that doctors from 1844 moving forward then use as a template to say, this is

that disease, what's causing the bones to dissolve. So that by 1900, when we had X-rays available, then we started seeing that there are holes in the bones. When they discovered plasma cells, and it was found that, yes, this is a cancer of the plasma cells.

The Evolution of Myeloma Treatments

[Let's look at] how the treatments [have] evolved. Back when we first found the protein by the serum protein electrophoresis test, which is used to diagnose myeloma today, that was found in the 1920s, 1930s. People thought that myeloma looked a lot like infectious diseases; so they were treating myeloma with antibiotics. They had these early clinical trials and they said, "Wow, people were at least feeling better." Because the only therapies back in the early 20th century were just radiation and antibiotics.

Then urethane came out. Urethane is a chemical weapon – a plant killer – that they tried with patients with myeloma. For 20 years, urethane was a standard of care for myeloma because it caused such low blood counts, and it was literally, it was a poison.

It wasn't until the 1960s that they did a randomized trial with urethane versus cherry cola. And the response rates and the survival were the same between the two, which meant that urethane wasn't doing anything. But the idea of using these chemicals then were introduced into treating myeloma. And then melphalan, which was also being developed as something to lower blood counts, was then given to patients with myeloma in 1969. It was the first trial that was done that showed a survival benefit in myeloma, which then the survival was only one to two years. All of a sudden people were living longer.

The idea then was, well, if a little bit of melphalan can help, maybe a whole lot of melphalan will help. And we started doing stem cell transplants. [With] stem cell transplants, giving high doses of melphalan, really changed the survival of patients with myeloma.

The question was, "How can we deliver this drug that's so good for myeloma in a safe way?" The way to do that, what was discovered, is that you can grow an entirely new bone marrow by harvesting stem cells. Stem cells are the seed from which the entire bone marrow can grow. You get a few stem cells and you put them in a dish, it'll grow brand new bone marrow.

Treating myeloma these days, we are using targeted therapies. So, it's like using the right punch. You have the bad guy down with that right punch and then the left upper hook that the cancer is not expecting is that single dose of chemotherapy with stem cell support. And that's what we've seen with using stem cell transplant. That left upper hook knocks the disease out. And we've done studies for decades up until recently, showing that people who get stem cell transplant have a longer time in their response and remission than if not.

In the 1990s, there was all this talk about angiogenesis and anti-angiogenesis, and if you could destroy blood vessels that feed cancer, you could treat and cure cancer. The hunt was on to find anti-angiogenesis agents, and one of those anti-angiogenesis agents was thalidomide. Thalidomide was thought to be an anti-angiogenesis agent because the birth defects that it caused in the 1960s and 1950s were thought to be due to decreased blood vessel growth in fetuses, which is why they had thalidomide babies. And so, if we could use that in patients who had myeloma, it could starve the cancer of blood vessels and therefore treat myeloma. So, the first trials were with the intention [of] the targeted therapy using thalidomide as an anti-angiogenesis agent. It actually didn't inhibit the blood vessels, but it starved the myeloma cells of the most important thing that it needs, which is the microenvironment inside the bone marrow. And when it did that, that completely changed the narrative of how we treat the disease.

Groundbreaking Therapies

In using the successors to thalidomide, the immunomodulatory drugs in treating myeloma, and using the proteasome inhibitors to treat myeloma, these drugs did incredible things because they were targeted towards the biology of the disease, not just blanket giving chemotherapy to treat the disease. And then we were using these targeted agents. We started combining them, the IMiDs (the immunomodulatory drugs) and the proteasome inhibitors with steroids, and the response rates were incredible. We started combining these drugs together and response rates went up.

Then developing new drugs, developing and using the targets for myeloma, having the immune system clear out the disease, did fantastic for relapsed myeloma. But when we combined that, we added the antibodies plus the immunomodulatory drugs, plus the proteasome inhibitors, and dexamethasone. It changed everything. The response rates were then moving to 99%, which is something that 15 years ago I would have never, ever imagined.

The Search for a Cure

What can we do to cure this disease? What can we do? What science do we have to push it even further? Because the one thing about myeloma in its history is no one said, “We're done.” Ever. And they saw that the T cells, which should clear our bodies of cancer cells, when people have myeloma, their myeloma cells or their T cells can't find each other. The T cells can't destroy the myeloma cells. So, the idea was to use science to redirect those T cells to kill the cancer cells, and that was revolutionary.

If you would have asked me when I first started doing this, “Would you see responses of 99%, you know 98%?” I would say, “No.” Because I grew up in an era with this disease where the response rates were 30% and 40%. Now the standard is that if you don't have a therapy that's performing at a very high level, then it's not going to see the light of day, and that's kind of an incredible place to be.

Relapsed/Refractory Multiple Myeloma

Myeloma comes back in large part because of the biology of how myeloma works – that myeloma is very good at finding additional mutations to keep itself alive and to evade drugs that are being used on it.

So, there are lots of ways you can describe multiple myelomas, that multiple myelomas can mean that everybody [who] has myeloma has a different flavor of the disease. That's a very unique disease; I don't have two patients on the same therapy. But also, inside an individual patient, the studies that have been done show that a newly diagnosed patient will actually have three different clones of myeloma, and that those different clones compete and they vie for superiority inside the body. And when you give one therapy that may be effective against two of the clones, the third clone then grows back in and becomes the dominant clone. We used to call that and still call it clonal tiding. That you're able to treat one clone and another clone then pops up, and then a new clone will find a mutation that will find its way to be superior. And the reason that four drugs are superior to three drugs, are superior to two drugs, are superior to one drug is because you're trying to control all those different clones and trying to find a way to keep these multiple myelomas from coming back.

The trick in this disease is finding the common denominator between those different clones that keep playing whack-a-mole – where you pushed on one and one comes up – to find the common denominator between those clones to try and kill and get all of them. And things like the CAR Ts, and the bispecifics, and using T cells to recognize myeloma cells is really the beginning of that process of finding ways to find common denominators to kill all the clones, not just one or two at a time.

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Quality of Life

The quality of life for myeloma patients has had an incredible transformation. My grandfather-in-law had myeloma back in the 1970s before the bone strengtheners, when we just started using chemotherapy. And patients with myeloma had terrible quality of life because of breaking bones and breaking bones. The reason that people died of myeloma for the past 180 years was because of broken bones. With the introduction of the bone strengtheners, it has been transformative in alleviating, and most importantly, preventing pain with patients with myeloma.

Also, the quality of life has changed for patients because of the drugs that we use. We're no longer using these blanket chemotherapy drugs to treat the disease, but targeted therapies to treat the disease. It's very rare for patients with myeloma to have nausea or hair loss. It's very rare for them to have the side effects that traditional chemotherapy would have. So, the day-to-day lives have changed away from the hair loss and all the complications of chemotherapy, and now using targeted therapy.

And now something unique about myeloma is that you can follow and monitor the disease by doing blood tests, which I think can give patients peace of mind and empower them. That empowerment and knowing what is happening with this disease then gives, I believe, quality of life and strength to patients that they can have informed conversations with their doctors and their family.

A Hopeful Future

In my opinion, you haven't cured anyone with myeloma until you have cured everybody with myeloma. And my true hope and what I pray that happens with this disease is that we will find ways to treat this disease that can treat the 95-year-old lady who is in a rural area, that we can treat the person who doesn't have insurance, that we can find and detect this disease and countries that don't have access to the same drugs that we have; that we can bring the good news of how we're able to treat this disease, not just to a few people that go to academic centers, but around the world.

Narrator
For more information about multiple myeloma and other blood cancers, please contact an Information Specialist at 1-800-955-4572 or visit www.LLS.org/InformationSpecialists.

We welcome your feedback!
Please complete the evaluation for this program at
www.cancereducation.com/HowFarMyeloma.