

Yale CANCER
CENTER
answers

WNPR Connecticut Public Radio



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Understanding Sarcoma

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Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Francine Foss, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and he is an internationally recognized expert on colorectal cancer. Dr. Foss is a Professor of Medical Oncology and Dermatology and she is an expert in the treatment of lymphomas. If you would like to join the discussion, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This evening Ed and Francine welcome Dr. Gary Friedlaender. Dr. Friedlaender is the Wayne O. Southwick Professor of Orthopedics at Yale School of Medicine and an expert in the treatment of sarcoma.

- Chu Why don't we start off by discussing what sarcoma is because I suspect many people out there listening may not have a real good sense of what type of cancer that refers to.
- Friedlaender It is a type of cancer, and cancers in general are broken down into two broad categories. One are the carcinomas, malignancies of epithelial cells, surfaces of organs and organ systems in the skin, but what we are talking about are sarcomas, cancers of support tissues, such as connective tissues, bone, cartilage, muscle and some of the tissues that are in the support organs or tissues like blood vessels and nerves.
- Chu There is also soft tissue sarcomas and non-soft tissue sarcomas, how do you break down those two groupings?
- Friedlaender We usually refer to bone and softer tissues, cartilage gets caught in between a little, but there is bone on one end of that spectrum and then there are tissues like fat and muscle, the softer tissues, on the other end, and we call those soft tissue sarcomas.
- Foss Gary, can you tell us a little bit about how common these types of sarcomas are?
- Friedlaender I'd be glad to Francine. They are uncommon in general, about 1% of the overall cancer population. For me, it is something that I deal with everyday, and that's what happens when you become a sub-specialist and part of a team like we have here at Yale. These are things that I see all the time, but really are only about 1% of the pool of cancers in general.
- Foss What ages do they occur in? Are they common in children, and do they occur in older adults as well?
- Friedlaender That's an important question. They are tumors that occur at all ages, but the specific kind of sarcoma one finds in children is different than the kinds of sarcomas of older individuals. As an example, retinoblastomas are more common in very young children.

3:12 into mp3 file http://www.yalecancercenter.org/podcast/Answers_May-24-09.mp3

Ewing sarcoma and osteosarcomas occurs in later childhood, young adulthood, and then we see fibrosarcomas and chondrosarcomas that more commonly appear in older age.

Chu And there are also sarcomas that can involve the GI tract as well, is that correct?

Friedlaender I am an orthoped, an orthopedic surgeon, so I am aware of that, but I don't take care of them as much, but indeed they are the most common sarcomas. There are less than 10,000 sarcomas occurring each year in the United States, of which a third are GI tract.

Foss We talk about low grade and high grade sarcomas, I wonder if you could tell us if there are sarcomas that are not truly malignant tumors? Is there a spectrum in terms of the behaviors of these tumors?

Friedlaender It's a very important question and the answer is yes, there is a spectrum. The spectrum starts on one end with benign, and on the other end with what we term high grade. There are intermediate stops between those two extremes that are generally termed low grade and intermediate grade. Treatment, on the other hand, tends to be either focused on benign and low grade or on the higher grades, and so when you find tumors in between, intermediate, you have to choose whether to, if you will, over-treat or under-treat and by convention we over-treat, if you will, we lump them with the high grade. And the treatment is different for benign and a low-grade cancer, and intermediate or high-grade cancer.

Foss It seems funny to use the terms benign and tumors, or benign and cancer in the same breath. These benign sarcomas or lesions, are they really tumors, or are they cancer?

Friedlaender Let me back up for a moment. The word tumor to me represents a lump, and you can have a benign tumor or a malignant tumor. In common parlance, when you begin to use the word tumor, it often conjures up the notion of something nasty, and it's important that as we talk to each other and as we talk to patients, to define the terms. I find myself doing this regularly with patients, and almost apologizing sometimes for using the word tumor, when I mean, potentially benign. Your point is well taken, and we should start out with the definitions. If I use the word tumor, I should let you know if I am talking about a benign tumor or a malignant tumor. There are no benign malignant tumors; that's incongruence. What makes a tumor malignant is its ability to metastasize, and once it gains that potential it is a malignancy. That potential may be low or high, and consequently, our classification of low grade malignancies, but still able to metastasize, versus high-grade malignancies. We are sometimes caught in the dilemma of conventions that have classified a tumor as a low-grade malignancy, despite its inability to metastasize, so the terms get fuzzy

6:56 into mp3 file http://www.yalecancercenter.org/podcast/Answers_May-24-09.mp3

sometimes. Trying to keep things relatively simplistic, malignant means it can spread, benign means it can't.

- Chu Gary, what do we know about the risk factors that are commonly associated with the development of neurosarcoma? Is there any genetic component to the risk factors?
- Friedlaender Absolutely, and if I were to point to an area of progress it's our understanding of why these tumors happen under a certain circumstances. It used to be very easy to say, "I don't know, we just haven't figured it out yet," and for a large number of tumors we don't know, but we do have increasing information about risk factors. For example, radiation, something we use to treat tumors, can, at higher doses, cause new tumors to happen years later. We know that certain chemicals, chemicals in our work place and chemicals in our homes can cause cancers. Certain pesticides, certain herbicides, certain chemicals like arsenic that are used in industry and in preparing fabrics; we know now can cause cancer. Chronic lymphedema, a circumstance that happens when we interrupt the lymph drainage, a classic example being in mastectomies, seems to lend itself towards the formation of some cancers. We know there are individuals, families, that genetically seem predisposed to have multiple malignancies, so there is a genetic or hereditary component. There are malignancies associated with HIV infection, Kaposi sarcomas. It's not a simple answer, but what we are finding is there are multiple pathways to get to the same endpoint of cancer.
- Foss There are a lot of patients out there now that have been treated with radiation, patient's with prostate cancer, breast cancer, and Hodgkin's disease for instance, that are long term survivors. To what degree do these people have to worry about sarcomas, and how frequently do sarcomas occur in patient's who are long term survivors of radiation, therapeutic radiation?
- Friedlaender It's a small but important number, and not cause for great alarm in individuals. What it does tell me, these small numbers, is that people just need to remain vigilant, they need to remain under the care of people that can help monitor whether or not one of these late sarcomas is developing.
- Chu Are there any symptoms that you would typically look for that might suggest that a lump or bump in the arms or legs might be something more serious?
- Friedlaender Yes, the symptoms of a sarcoma are pain, a lump, or both. Malignancies tend to grow and they tend to be deeper in the body rather than just underneath the skin. The most common lump is a harmless fatty tumor underneath the skin, and if it's less than 2 inches it almost

10:47 into mp3 file http://www.yalecancercenter.org/podcast/Answers_May-24-09.mp3

never is malignant. I have given up saying always and never, but there are some guidelines, and a lump that is growing deserves some additional attention and a healthcare professional should be able to guide you as to whether further studies are important to clarify what's going on.

Foss When we are talking about imaging studies, we have PET scans, MRIs and CAT scans, can you tell us a little bit about how each one of those is used in the diagnosis and follow-up of patient's with sarcomas?

Friedlaender Yes Francine, and I would like to just back up a half step, because those are part of the tools that their physician is going to use to help clarify what is going on, beginning with a good discussion, history, and a physical examination, which often can clarify whether or not something is in need of more evaluation. Then you get into plain x-rays, which are very helpful for bone, and are not as helpful for things that happen in the soft tissues. CAT scans and MRIs are extremely valuable imaging opportunities that help us see the inside of the body very clearly and see the soft tissues. CT scans see bone very well and MRI does not see bone at all, but it sees the things around bone, so they are complementary. An MRI also helps us know a little bit about the biology more than a CAT scan. An MRI does not involve any radiation while a CAT scan is based on radiation. With an MRI you put yourself in a tube that is surrounded by a magnet, that magnet gets turned on and makes a huge amount of racket, but what it is doing is pulling the electrons in each molecule a little bit, they turn off that magnet and everything goes back where it belongs, but sends out a little blip of energy that the computer then picks up in three dimension. We then ask the computer to pretend we are looking at a person from the front, from the side, or literally making slices through them and by assigning some arbitrary colors to different tissues types, we can sort out both anatomy and biology or physiology; very-very powerful. PET scans are also very special, along with bone scans, and there are a number of tools that are worth mentioning, but the PET scan in particular helps us look at the metabolism of individual cells and the metabolism of cancer is often different than the metabolism of normal cells. It is a study that looks at us from head to toe. An MRI is a study that has to be focused on a small area.

Chu If there is a suspicious lesion that's identified on either CT scan or MRI, what would be the next step in terms of the workup process?

Friedlaender Putting all the information together is very important, but ultimately the decision or the answer often will come from a biopsy. Deciding when to do a biopsy and how to do a biopsy is critical, and that's part of a team decision very often, but the surgeon and the radiologist play the central roles. For example, there are needle biopsies where with some

14:33 into mp3 file http://www.yalecancercenter.org/podcast/Answers_May-24-09.mp3

Novocain and a very special needle you can get a small piece of a lump or bump, even if it's deep within the body, using a CAT scan machine to guide you or an ultrasound machine to specifically target even a small lump. The advantage is it's not an operation, the disadvantage is it gets a very small amount of tissue and you need a very skilled pathologist, the people who look at these samples, to help interpret them. About 90% of the time a needle biopsy is sufficient. The other alternative is termed, an open biopsy, where you are in the operating room more often than not, although they do it in some offices, but you make a modest incision and take a representative portion of the lump to look at under the microscope and that generally gives us the answer in 99 point something percent of the time.

Foss Thank you Gary, we would like to talk more about the treatment for sarcomas when we come back after this break. You are listening to Yale Cancer Center Answers and we are here today with Dr. Gary Friedlaender.

Medical Minute

Over 170,000 Americans will be diagnosed with lung cancer this year and more than 85% of these diagnoses are related to smoking. The important thing to understand is that quitting even after decades of use can significantly reduce your risk of developing lung cancer. Now, everyday patients with lung cancer are surviving thanks to increased access to advance therapies and specialized care and new treatment options giving lung cancer survivors new hope. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale, to test innovative new treatments for lung cancer and patients enrolled in these trials are given access to medicines not yet approved by the Food and Drug Administration. This has been a medical minute and you will find more information at yalecancercenter.org. You are listening to the WNPR Health Forum from Connecticut Public Radio.

Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am here with Dr. Ed Chu and Dr. Gary Friedlaender discussing sarcomas. Gary, we talked a little bit about the diagnosis of sarcoma, can you tell us what happens next after you have a definitive diagnosis?

Friedlaender Yes, and I can't help but reminisce a little bit. When I first became involved with bone tumors as a resident, and you can't see me on the radio but that was a while ago, the success rate was rather oblique, and indeed for an osteosarcoma, the survival rate for two years was about 10% to 15%; very miserable. Today, the survival rate, the cure rate, not just the two years survival rate, but the cure rate, is around 80%, and the difference is a reflection of the

17:35 into mp3 file http://www.yalecancercenter.org/podcast/Answers_May-24-09.mp3

team that gets pulled together to take care of these individuals and the tools that each of those members has to make a difference. Some parts of those are diagnostic with the radiologist and pathologist, some of them are interventional by surgeons, sometimes radiation and often chemotherapy.

Foss Do all patients require an amputation?

Friedlaender Not at all, and in fact, one of the very gratifying changes over these years has been our opportunities as surgeons, parenthetically, because you as chemotherapists have been able to deal with systemic disease better, but we can now isolate the part of the body that has a tumor, be that bone or muscle, and remove just the part that has the tumor and then use some very creative opportunities to reconstruct the skeleton.

Chu At Yale you lead the multidisciplinary team that focuses on sarcoma. Can you tell us a little bit more about the specific players who make-up that team, that team-based approach?

Friedlaender Absolutely, and with our new Smilow Center Hospital and our additional leadership this is a very exciting time to bring these people together in a more formal way and perhaps even a bit more efficient. I can tell you that as of right now, it is superb, and it involves a patient seeking out help, sometimes me as a surgeon, sometimes you as a medical oncologist, but most often going to their primary care physician and saying it hurts, I feel a lump, and then they get referred into our system. It's each of our jobs to call the team together, depending on what we think the patient's needs might be. Early on, again the radiologist is absolutely critical, the radiologist I work with sits 15 feet away from me while I am seeing patients and the partnership is enormously important and effective. They help me interpret what I see, help me decide what additional tests to get. Then a biopsy is done if necessary, and the pathologist becomes the center of attention and it is always important to know what you are dealing with, because that determines what the alternatives are and there are always choices. That's when I as a surgeon, you two as medical oncologists, and our colleagues in radiation therapy get together as we do formally and informally. We see each other in the hallways, we see each other in conferences, whatever it takes to make sure this patient has the benefit of all those opinions, and we come to a consensus and the consensus may include, again, surgery, radiation, chemotherapy, one of them, all of them, sequencing those. There are also all of the other support people that go along with the social aspects or the psychological aspects of people that have these disorders, and the pain management that they deserve. They rehabilitate people by body, by mind, occupational therapists, physical therapists, psychologists, pain management specialists, all are part of the team.

21:23 into mp3 file http://www.yalecancercenter.org/podcast/Answers_May-24-09.mp3

Foss Can you talk about some of the advances with respect to helping you rebuild say a bone or muscle or tissue that you have to excise?

Friedlaender Certainly, let me focus on bone for a moment, and picture if you will that the tumor is in the lower half of the thigh bone, just above the knee. The first step is to remove the lower half of the thigh bone or femur, and then there are choices about how to reconstruct it and they fall into two general categories. One is a bone from another person, a donor, someone who has passed away, some generous person or family. Just as we have the ability to transplant hearts, lungs, livers, kidneys, and corneas, we also have the availability of large segments of the skeleton in a similar way to replace a similar part of our anatomy. And there are some advantages and disadvantages to that approach. The other option is the metals and plastics that we are so familiar with joint replacements, total hip replacements, and total knee replacements, that have allowed us to build upon those concepts and replace large portions of the skeleton with metal and plastic.

Chu Are there any long-term complications with using these metal prosthesis or joint replacements?

Friedlaender There are sometimes issues in the short run, but most commonly in the longer run. In that you have to bind them or bond them to the skeleton. You have to insert a stem or some other mechanism to bind these, often by bone cement, to the skeleton, and over a long period of time that bond can deteriorate. In a regular total hip replacement or total knee replacement, we think in terms of 15, 20, 25 years of good outcome, excellent bond, no need to change. In these larger, we call them megaprosthesis, that bond also breaks down overtime, but probably doesn't last quite as long. The good news, if you will, is that when these bonds wear, they can be replaced. And I can tell you that 2009 model has been better than the 1999 model and I have every reason to believe in the future we are going to get better and better.

Chu Is there any way in terms of imaging or some other kind of test where you can figure out who is going to have trouble with the bonds breaking down, or is it just a matter of the patient comes back for followup and says there is pain, discomfort, and just can't do the same kinds of things they were able to do previously?

Friedlaender These patient's become very important to us as physicians, as you know, and we windup seeing each other over a very long period of time, a part of the practice I enjoy. Most of these patient's we can help dramatically and we get to know them as they go through life, but periodically, its our responsibility to make sure they are healthy and they come back for their 1000-mile checkups. Part of that evaluation includes making sure that their prosthetic

25:14 into mp3 file http://www.yalecancercenter.org/podcast/Answers_May-24-09.mp3

device is in good shape and it's a combination of x-ray, plain x-ray generally, and symptoms, that is pain, that allows us to determine how healthy that bond is and if it deteriorates you come to mutual decisions about how to address it, which is usually to replace it. And that starts the clock all over again, so they can enjoy school, play, work, and enjoy their life as usual.

Foss We talked a little bit about the use of chemotherapy in the management of sarcomas and I wonder if you could comment on some more investigational approaches such as isolated limb perfusion or hyperthermia, and whether these actually play a role nowadays in our treatment algorithm for patients?

Friedlaender Yes, thank you for the question. In terms of context, cancer has two parts to it. One is where it begins, we call that the primary tumor. As the surgeon, I and the radiation therapist usually have responsibility for the primary, but what makes cancer dangerous as we talked about earlier, is its ability to spread, and until we found ways to deal with the rest of the body and the potential spread through chemotherapy, and in particular multidrug chemotherapy, we didn't make the dramatic success rates that we enjoy today and set the stage for even better tomorrow. Now, the way we give the chemotherapy can be targeted at the primary tumor as well, and we can deliver some of these drugs directly into the tumor, the primary tumor, by inducing or putting the catheter into a blood vessel that feeds them; limb perfusion techniques. And we find in certain types of tumors it has been extremely helpful.

Chu Any new developments from your program in terms of bone research? I know that's been an area of your specific interest.

Friedlaender Absolutely, we have found in our parallel lives, thinking about the skeleton, many ways to control the way bone repair itself, bone regenerates. To me its marvelous, whether you are just sitting there, have fractured your bone, or have a bone graft, there is a process of cells that get together and replace old bone with new bone. We now have isolated many of the molecules that turn on the process of making new bone and this I believe is going to play a very important role in improving the reconstructions that we are already doing.

Chu We look forward to hearing more about what's going on in that area of research from you on a future show. You have been listening to Yale Cancer Center Answers and we would like to thank our guest expert for this evening's show, Dr. Gary Friedlaender, for joining us. Until next time, I am Ed Chu from the Yale Cancer Center wishing you a safe and healthy week.

28:36 into mp3 file http://www.yalecancercenter.org/podcast/Answers_May-24-09.mp3

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