



Treatment of Sarcomas

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Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists, who are on the forefront of the battle to fight cancer. This week it is a conversation about the diagnosis and treatments of sarcomas with Dr. Gary Friedlaender. Dr. Friedlaender is the Wayne O. Southwick Professor of Orthopaedics and Rehabilitation and Professor of Pathology at the Yale School of Medicine and Dr. Chagpar is Professor of Surgery at Yale and Assistant Director for Global Oncology at Yale Cancer Center.

Chagpar Tell me a little bit more about sarcomas and musculoskeletal tumors in general.

Friedlaender I appreciate the opportunity. First let me define the subspecialty of musculoskeletal oncology. It is the group of us who are interested in the diagnosis and treatment of people who have tumors of the musculoskeletal system. That system reflects bones, muscles, joints, support ligaments, things of that nature. I am an orthopedic surgeon by training, very early I became interested in tumors in oncology and parenthetically if I jump between the use of the term tumor, lesion, mass, lump, bump, I am really referring to basically the same thing. It is the modification of that term that indicates whether we are talking about something that is relatively harmless or something that is really aggressive. So along the way, reflecting my interest, I took some additional training in both clinical care and research related to oncology and like you, I am a surgeon at heart.

Chagpar When we think about bone cancers, it really seems to me that what you talk about is 2 different kinds of buckets of bone cancers. We talk about cancers that start in bone or start in ligaments and muscles and various other aspects of the musculoskeletal system and then we talk about cancers that go to bone because bone tends to be a place that cancers like to go to.

Friedlaender Absolutely. Primary tumors start in bone are 1 bucket and that tumors that feel welcomed to come to bone as metastasis are another and there are probably 100 times more metastatic tumors to bone than there are primary, so that one person telling another his/her experience with bone cancer immediately makes me wonder if it is primary or metastatic disease because they are very, very different.

Chagpar We hear a lot more about cancers that have metastasized to bone. Let's talk a little bit more about cancers that start in bone because that is really where your expertise lies. Tell us more about what kinds of cancers start in the bone or joints or muscles or ligaments, how common they are, and who is affected?

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Friedlaender Very important distinctions to be made. One is in the field of cancer, lumps, bumps, lesions, tumors happen because cells lose control over themselves in their growth and they cross a line at some point to become malignant and we will leave it at that for the time being. Many of those cells are cells we call epithelioid in nature. They are lining cells. They are the cells on our skin, they are the cells that line our gastrointestinal tract, our glands in the breast, in the thyroid, and other parts of the body and those are called carcinomas. They are nearly 100 times more common than sarcomas, tumors that start in cells of mesenchymal origin, connective tissue or support cells, bone, cartilage, muscle, fat, blood vessels to some degree. Those are the sarcomas. So if it is in the bone, the term is osteo, they are osteosarcomas; if they are of cartilage origin, they are chondro for cartilage, chondrosarcomas, but the sarcomas are about 1% of all cancers.

Chagpar Do they affect certain populations more than others?

Friedlaender They do, as is true of many different lumps, bumps, and cancers in terms of age and in terms of other demographic characteristics. There are some tumors that are relatively very common in kids and relatively uncommon in adults; an example of that would be osteosarcoma or Ewing sarcoma. The predictions are not completely held to but by and large there is something you will see far more often in kids than adults; on the other hand, chondrosarcomas and some of the muscle sarcomas are much more common in adults, multiple myeloma, you could argue is either a primary bone cancer or a cancer that happens to reside in bone.

Chagpar In a lot of cancers, we talk about risk factors. For example, in lung cancer, we say one of the main risk factors is smoking. What are some of the risk factors, or are there really risk factors that cause sarcomas?

Friedlaender There are, but they are getting to be less common in the traditional sense, people who are exposed to radiation for example either on purpose or otherwise are more susceptible to forming certain kinds of cancers and sarcomas in particular that could have been living on top of a source of natural radiation or could have been because they required radiation treatment to remove another form of cancer. There are racial or ethnic biases if you will towards or against certain cancers, Ewing's cancer, Ewing's sarcoma in young children, a primary cancer of bone, primary sarcoma of bone is far more common in European whites than it is in Africans, people of color, but we are also learning the genetics plays a role. Genetics probably plays a role in susceptibility to some degree and it probably plays a very important role in our evolving effects to diagnose and more so to treat cancers. We are learning far more about the genetics of oncology today than ever before, very encouraging.

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Chagpar When we talk about genetics, many people may think about understanding their family history; for example, in breast cancer, we know that if you have a family history of breast cancer or ovarian cancer or prostate cancer or pancreatic cancer that those tend to cluster into forming families that may mutate in particular genes. For example, the BRCA 1 or 2 gene. So are you saying that people should know their family history and that there are particular genes that may be involved in the formation of sarcomas and if so, what is that family history cluster look like. So what should people be aware of in terms of looking at their family history to say "I might be at risk."

Friedlaender I think there are 2 different ways for me to interpret the question and answer it. One is it is always a good idea to know as much as you can about yourself and your family. There are not at the present time very likely genetic clusters in family that predict sarcomas. I will give you one example to the contrary, multiple osteochondromatosis or Ollier disease or multiple enchondromatosis, people generally have one of these tumors and they are benign, cartilage and bone. There are people that by genetics and in a hereditary sense have dozens if not hundreds of these growths, those people are more susceptible to those benign tumors transitioning to aggressive and malignant tumors, but that is unusual. I always had trouble with multiple choice test, I could always think of the exception and so I do not want to over blow this as a concern and there are many people with multiple lesions like this that do extremely well, but we are learning more and more. There are probably some underlying predispositions to forming diseases of all sorts including cancers and sarcomas.

Chagpar Are people with sarcomas, for example let's say you have a child who has Ewing's sarcoma, is it true that his children may also be more likely to develop sarcomas?

Friedlaender It does not tip the balance, these are lightning bolts, they happen, they are unlikely to happen repetitively in the same family; having said that every once in a while you encounter a family that is over represented in a disease.

Chagpar Every so often, you get somebody who is hit by a lightning bolt twice?

Friedlaender That is absolutely true and I still buy lottery tickets, but this is one lottery I do not want to win.

Chagpar Let's talk a little bit about how these sarcomas present. We have talked about the fact that they are incredibly rare. First of all, it is rare to have cancer that starts in bone or cartilage or soft tissue, connective tissue versus having one that has spread to bone from another site and then it is unlikely to have those cancers as opposed to epithelial

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cancers. So how do they present, what symptoms do people show up to your clinic with that make you think, this might be something bad?

Friedlaender First of all, just as at your clinic, most of the people that walk through my clinic door are frightened and anxious about what they are going to learn about themselves. They are generally triggered to come to see me either because they have seen another physician who raised the question or concern, but primarily the answer is a lump or pain. A lump that is increasing, I think, deserves a visit to your healthcare provider, most of those are harmless. Similarly, pain that you cannot explain for other reasons, that does not go away in a reasonable length of time, and finding reasonable is always a little difficult, but I am talking about more than a day or two, deserves attention as well and again, I think one's primary care physician is the right place to start. I do think there is an advantage to relieving one's anxiety and the majority of the time, there is nothing to be concerned about in the field of cancer, but it bothers me to see people harbor that fear for unnecessarily long periods of time and it also bothers me when people ignore symptoms that should be recognized as potential signals of something wrong. Whether it turns out to be a cancer or a gallstone, in our world at this point in time healthcare is important.

Chagpar And so if you feel a lump or bump that does not go away, you have pain that does not go away, these are warning signs that you should go and have it checked out, it might be nothing, but it might be something and it is worth finding out sooner rather than later in having the problem addressed.

Friedlaender That is right. I would like to stress that a lump without pain does not mean that it is not a tumor, that needs attention.

Chagpar Absolutely. Certainly, in my field, lumps in the breast that do not cause pain are actually a little bit more worrisome than the lumps in the breast that do. We are going to take a quick break for medical minute and then when we come back, we are going to learn more about musculoskeletal oncology sarcomas, how these are diagnosed and treated and what the future looks like with my guest, Dr. Gary Friedlaender.

Medical Minute

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This is a medical minute about colorectal cancer. When detected early, colorectal cancer is easily treated and highly curable and as a result it is recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Tumor gene analysis has helped improve management of colorectal cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents resulting in more patient specific treatments. More information is available at yalecancercenter.org. You are listening to Connecticut Public Radio.

Chagpar This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Gary Friedlaender. We are talking about sarcomas, musculoskeletal oncology, these cancers that are pretty rare that instead of coming from breasts or lung or thyroid or colon like so many of the cancers that we talk about actually come from connective tissue from bone or cartilage or blood vessels, these happen and we were just talking right before the break about how they present, so if somebody has a lump or a bump or pain that is not explained, that does not go away, they should see their family doctor, but Dr. Friedlaender what happens after they see their doctor, what is the workup entailed, what does that look like?

Friedlaender Let me meld together the workup that might happen in part with the primary care physician and will be complemented or extended when they see me. It involves listening to the patient first and foremost just like everything else we do, a careful history and then a physical examination. In the case of a bone tumor, just focusing on that particular entity, there may be a lump or bump, there may not and there may be some local tenderness or there may not. Some form of imaging and/or laboratory test usually happens next in my field and they're likely to get an x-ray, a plain x-ray does not hurt, it does not take very long and the answer is available almost immediately in today's world and that is very helpful. If that raises a suspicion, the patient may well get a different form of imaging that gives us more information, that might be a CT scan, it might be an MRI, it might be an ultrasound, it might be a PET scan, it might be a variety of those types of tools and if and when we are convinced there is a lesion or tumor or mass, potential change that needs better definition, a biopsy is often required to come to a final conclusion, but not always, there are some things that are so characteristic on plain x-ray, they are of no concern other than understanding them but if we are not in that situation and need more information, the biopsy becomes very crucial. Today, those biopsies are often done with a needle, in our institution, and I literally mean, yours and mine and many other fine institutions that have that ability, they are often done by our radiology colleagues which just reminds me this is a team approach, they sometimes use imaging to make sure they are getting the sample of the right tissue and then the pathologist gives us his or her opinion about what is going on. That is the chain of events that leads to the diagnosis.

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Chagpar We talk a lot on the show about biopsy and I am sure our listeners can understand, a biopsy of breast or a biopsy of colon, even biopsy of muscle, but biopsy of bone, how do you do that exactly, I mean the bone is a hard thing and you are trying to put in a needle into a hard bone?

Friedlaender What you are trying to do and the instrumentation gets better and better all the time, is literally put a drill into the bone and these instruments are sharp enough that they can be done by hand or they can be done motorized if you will. Keep in mind that pain, nerve endings exist in the skin and they can be eliminated as concerns with local anesthetic and in bone, the only nerves are on the outside of the bone and similar to the skin, some Novocain injected in that area could make it completely painless or relatively painless.

Chagpar So these biopsies can be done as an outpatient?

Friedlaender As an outpatient and literally awake and comfortable.

Chagpar Wow, because certainly, I think, for listeners who are thinking about somebody putting a drill into a bone, is reassuring to hear that they can be awake and comfortable because the term drill and bone do not generally sound comfortable.

Friedlaender They do not at all and you are evoking an old memory for me, but in my training days, we used to take care of kids' leg fractures by putting them in traction in bed and in the hospital for days if not weeks or longer and that traction was accomplished by putting a pin in their bone and pulling on that pin and so I have done this to children with Novocain and with great interest in their health and their comfort many many times and they have tolerated it very very well. So it is not the gruesome ordeal that it sounds like and I agree, I do not know about you, but I am a classic hypochondriac and everything I feel, I often imagine the worst and that is why it is so helpful to get somebody else, a healthcare professional to walk through these symptoms with you and explain what they mean, whether it needs more attention or not.

Chagpar And so, the biopsy is really critical for many of these tumors to make a diagnosis, so once a diagnosis is made of a primary bone tumor or a cartilage tumor or a muscle tumor, a sarcoma, what happens then?

Friedlaender First of all and I try to make sure people understand this, it is far better to know what is going on than to ignore it and the reason is that when we know, you and I, when we know what is going on, we have a pretty good idea of what is available to make that person better, it does not happen every time, I wish it did, but the outcomes, the

success of the things that we have to work with today are enormously better than ever before and so knowing what is going on is critical and matching the treatment to the right problem is critical, it never hurts to know what is wrong before you treat it, that is what the biopsy does for us. If the needle biopsy does not work, a small incision in the operating room under anesthesia one way or another you need to know what is going on. Depending on what it is, the way it is treated includes generally and we are talking about, just for this example, that it is malignant, that it is aggressive, most things are not actually, but if it is malignant or aggressive the tools we have to work with are systemic drugs, some of them chemotherapy, some of them are immunotherapy, a wide variety of systemic treatments. These treatments go everywhere in the body, whether we know there is a tumor there or not, compared to what you and I do every day which is targeted surgery, targeted on the lump or bump or irradiation which is targeted to the lump or the bump or both. Excising a tumor requires an envelope of normal tissue around it, that envelope needs to be thicker as things get more aggressive. I would love to talk a little bit more about what the implications are in terms of whether that leads us to an amputation or a limb sparing resection but for now, the diagnosis triggers the team getting together and deciding which modalities, in which order are likely to provide the best outcome for that particular individual patient.

Chagpar So frequently this will involve more than one specialty, systemic therapy and local therapy. So tell us about the local therapy and surgery because I am certain that people when they think about bone cancer and then they come to see an orthopedic surgeon, they likely are very worried about losing a limb.

Friedlaender Absolutely. Let's use osteosarcoma as an example, that is a primary tumor that starts in bone, very often in children or young adults. Through careful clinical trials in the past, we found out that the outcomes are better if the next thing you do is treat them with chemotherapy, systemic treatment, it treats the primary tumor and it also treats those small numbers of cells that are roaming around the body looking for a place to metastasize. When that neoadjuvant treatment is done, I as a surgical member of the team, need to decide whether I can remove the tumor successfully without removing the limb and I must say 90% to 95% of the time that is possible, or whether an amputation is the safest best way to get rid of that problem and get somebody back to their activities in life and there are times when that is very important. What I am trying to do is understand the relationship of the actual tumor to the surrounding functional tissues, nerves, arteries, veins, to a lesser degree muscles, muscles are very redundant, we have lots of muscle in our body we can actually move muscles around a bit, they tend not to be the limiting factor. It is really the nerves in particular because we are not very good at reconstructing nerves that have to be removed to get rid of the

tumor, we are much better at replacing arteries that may be too close to the tumor and in that envelope of normal tissue that we need to get rid of the tumor. Job #1 is to get rid of the tumor. Job #2 is put things back together in the most functional and pleasing way we can.

Chagpar After the patient has had this systemic therapy and you look at things and you decide, yes I can spare the limb as you can in most cases, do they then need radiation? For example, in breast cancer, if you have a partial mastectomy or you have a lumpectomy instead of a mastectomy, you need radiation as another modality of local control. Does it work the same way in musculoskeletal oncology?

Friedlaender Similar thought process, but usually irradiation for bone tumors is not part of the usual way of treating them, in part because they are not as sensitive to the radiation as we might otherwise like, conceptually is making that envelope bigger, thicker, wider. When we talk about tumors that start in muscle for example, radiation is often a very important component to the treatment. Tumors that start in bone are not as important and cartilage tumors, in particular are not sensitive to radiation as many other tumors. So the tumor is in the bottom part of the thigh bone, what we call the distal end of the femur. We take out the distal half of the thigh bone and we can do that and it can very very affectively include all of the tumor that we know about.

Chagpar And can the patient then have a part of the distal femur reconstructed so that one leg is not shorter than the other?

Friedlaender I was hoping you would ask that. Of course, there was a time when we would replace that distal femur with someone else's distal femur, the way we use kidney transplants, heart transplants, lung transplants. There were generous families and individuals who donate parts of their skeleton, these went to places called bone banks, they are carefully screened and thoughtfully taken care of these anatomical gifts and made them available to surgeons like me to replace the distal femur of a child that needed it after their tumor resection. Today, however, much more commonly we have metals and plastics that we can use, just like we replace hips and knees and shoulders with plastics, we do the same with the defects of these children.

Dr. Gary Friedlaender is the Wayne O. Southwick Professor of Orthopaedics and Rehabilitation and Professor of Pathology at the Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against the cancer. You are listening to Connecticut Public Radio.