

Round Table with Drs. Anne Tsao and Alex Farivar, Case 2: Mesothelioma

Dr. West: I'd like to welcome everyone, thanks for coming out to our lunch with experts. The faculty today are great people in the thoracic world coming from all different angles.

I'd like to introduce Dr. Ann Tsao who is an assistant professor at M.D. Anderson Cancer Center. She works in Thoracic, Head and Neck Cancer and has particular expertise in lung cancer as well as mesothelioma. She has grown up in Chicago and has trained and been living in Houston at M.D. Anderson for several years now.

Also joining us is Dr. Alex Farivar who had done his surgical training. He's a thoracic surgeon at Swedish Cancer Institute; had done training at the University of Washington and then went to the Harvard system working at Brigham & Women's Hospital for additional thoracic surgical training before coming back to Seattle to join the Thoracic Surgery group here.

Dr. West: We're going to shift gears to another corner of the thoracic surgery arena, and both Dr. Tsao and Dr. Farivar have a particular expertise in mesothelioma, which we haven't talked much about on the GRACE website previously. So I wanted to present a case that may have some converging or differing perspectives from the experts.

This is a 68-year old male, never smoker, who had prior asbestos exposure working in the coal mines in Germany in the 1950s. He had some right chest discomfort for several months that he mentioned to his primary care physician and that led to a chest x-ray that showed a large right pleural effusion, a collection of fluid outside of the right lung and he had no lung masses or other findings. The fluid was removed by sticking a needle in that space and that actually did not show cancer cells. They tested for infection and for TB and that did not show any evidence of infection. He was followed again and the fluid came back, at that point he was referred to a pulmonologist, a lung specialist. The CT scan again showed an effusion with no other findings. A repeat tap showed negative cytology. At that point he was referred to a thoracic surgeon for what's called pleuroscopy. Alex can you tell us about that procedure?

Dr. Farivar: Sure. A pleuroscopy in the surgical literature, people use pleuroscopy in a very nebulous fashion. It generally means that you use one port, so one access into the chest with an incision about this large, use a camera and its utilized to be able to evaluate the pleural space, take biopsies and

personally if this situation came up and I was the surgeon, I would also put talc there once a diagnose is established because it makes a potential subsequent operation easier. A pleuroscopy is generally an evaluation via one port of the pleural space.

Dr. West: This is what his CT scan looked like and you can see that gravity-dependent fluid collection on the right side. Again, these slices are having a patient basically lying on their back with their feet coming towards you and their head behind the wall.

These are the lung windows, which are a different way of looking at the images that can show with better resolution what's happening in the lungs and answer is not much there to see.

So he had his pleuroscopy and at that time, pleural studding was seen and biopsies were obtained that showed mesothelioma. He had what's called pleurodesis and Dr. Farivar alluded to that. He recovered well from that and had a good performance status.

Here are some of the images of what we're seeing through the camera.

This is what the pathology showed under the microscope. This is what's called epithelioid pleural mesothelioma, epithelioid being the more common subtype with a relatively better prognosis, although it maybe more appropriate to say that sarcomatoid, the less common has quite a poor prognosis rather than this being so favorable.

I'd like ask about your feelings about a pleurodesis, how helpful or problematic is that for subsequent management and outcomes? Maybe we should actually backup and say what is a pleurodesis and what's it for.

Dr. Farivar: A pleurodesis is during that procedure of pleuroscopy most oftentimes talc is instilled into the pleural space and the attempt is to get the two pleural layers which line both the lung and the chest wall to oppose. That's done with the fusions from a malignant source from whatever cancer it may be, oftentimes talc is used and that's an attempt to decrease a reaccumulation of pleural fluid subsequently.

Oftentimes, surgeons see that there is fluid, drain it, make a diagnosis of cancer and then put talc into the area, even if they don't know exactly what type of cancer it is, that's what's done. I think that's fine. I think its good care. I personally think it makes a subsequent operation for mesothelioma easier. I, personally, have absolutely zero problems if a surgeon out in the community sees this patient and does this operation and does a pleurodesis.

Dr. West: How common is it to see negative cytologies where you draw off the fluid from a thoracentesis and can't find cancer cells there, but have that still be from cancer?

Dr. Farivar: I think that it's exceedingly common with mesothelioma. If you suspect mesothelioma, you shouldn't even bother taking the fluid off and looking on cytology. Oftentimes, when we see patients when they arrive to us, even if they carry a diagnosis of mesothelioma just on small tissue samples, we'll repeat that, obtain more tissue on larger biopsy samples so that we can be sure what type of mesothelioma it actually is so that we can help direct what their subsequent care will be. I think it's exceedingly common, not only with mesothelioma, but other malignancies as well.

Dr. West: Anne, what are your thoughts on the question of pleurodesis?

Dr. Tsao: Without a doubt, our surgeons tell us that it makes a subsequent surgery much easier. I do disagree with the idea that we like our surgeons out on the outside to do it. The only reason is that, as you know, M.D. Anderson is a research facility. We know that mesothelioma has several different histologic subgroups, meaning that there are three main types: epithelioid, biphasic and sarcomatoid. Sarcomatoid has a worse prognosis. The biology of that cancer is very aggressive. There are a lot of patients who have mixed phenotypes. If you take one core biopsy from a patient, you can't tell necessarily; you just know in that particular area that they have this specific phenotype. Usually it's going to come back epithelioid.

So, what we like to do is take multiple biopsies from different areas of that big tumor. And that helps us also because we've learned that the different biopsies have different genetic abnormalities. Whenever people on the outside have had a talc pleurodesis, that becomes almost impossible for us to do that. So we usually recommend that the docs outside just send them directly to M.D. Anderson so, we end up repeating a lot of the VATS thoracotomies anyway as well, but instead of having the patient go through several procedures, if there is a suspicion of mesothelioma, just send them directly to us and we will basically go through and get the diagnosis. We'll be able to do the multiple biopsies and then do the talc pleurodesis.

Dr. Farivar: Why does doing a talc pleurodesis preclude you from being able to obtain more biopsies?

Dr. Tsao: Multiple biopsies -- because our surgeons want to go through one port and they can't the camera up to the multiple areas because of the adherence of the tissues makes it impossible.

Dr. Farivar: In that scenario, though, you don't necessarily need to go back into the pleural space to get multiple biopsies. So you can make your incision in the

area of where your subsequent thoracotomy will be and then take multiple biopsies of the pleura. You're not getting visceral pleura, but you are getting parietal pleura.

Dr. Tsao: Our surgeons seem to find it's more complicated, so I don't know.

Dr. Farivar: What you're doing in that scenario is you're reentering the pleural space multiple times, which I would venture to say is probably not optimal.

Dr. Tsao: Right.

Dr. West: One of the things that they're discussing is that mesothelioma is a kind of cancer that tends to track through the wound sites. So we do see in the channels from prior surgery that the cancer will grow through there more commonly than you'll see that, which is quite unusual to see in lung cancer or others. That is something to be mindful of with this particular type of cancer.

Let's go to the big question: to start with is this somebody whom you think is approached with curative intent or are you trying to palliate and improve survival but not thinking that you can cure? Alex?

Dr. Farivar: I think of this operation as a palliative operative.

Dr. West: Not so much this operation, but in this person in terms of treating, your treatment goal from this point forward would be the palliative or curative?

Dr. Farivar: In general, I hope to palliate them well, such that whatever time they may have going forward is as comfortable and high in quality as possible. There are some people I think that you can achieve some longer term remission and I've certainly seen patients out greater than 5, 6, 7 years. So there are people that have I think cures, but in general I think of it as palliation.

Dr. West: Anne?

Dr. Tsao: I have to agree. This is a very, very tough disease to have. Oftentimes currently because there is not a lot of research that has gone into this disease type as compared to other solid tumors. This is something that doesn't have any specific agents that are well targeted to this cancer. It also tends to be more rare so it's harder to do clinical trials with a rare population.

We highly encourage patients to go onto clinical trials with new novel targeted agents. Even with our current treatments, we're not curing these patients.

Dr. West: What would you consider to be an optimal approach for this patient in terms of whether to offer chemo, surgery, radiation, and the sequencing of them?

Dr. Tsao: So I think he still needs to get his full staging. We have to make sure the disease hasn't spread to the abdomen that it hasn't spread to the lymph nodes in the center of the chest or the other side of the chest. If he truly does have contained disease, our optimal therapy at M.D. Anderson would be to put him on an neoadjuvant clinical trial.

Dr. West: Neoadjuvant meaning...

Dr. Tsao: Neoadjuvant meaning systemic treatment before definitive surgery. We have a few targeted therapies that we're investigating that we can offer the patients and we're able to personalize the medicine because we look specifically at their molecular profile and we see whether or not they respond to these drugs based on their molecular profile and then we're able to provide them with two years of the drugs after surgery and after radiation and potentially chemo.

Now, obviously though, not every place has access to clinical trials and drugs. Out in the community, a very common practice to do for these patients is to give chemotherapy with cisplatin/pemetrexed followed by surgery.

Dr. West: Pemetrexed being Alimta.

Dr. Tsao: Yes, cisplatin/Alimta.

Dr. West: That combination is approved by the FDA for mesothelioma in general.

Dr. Tsao: Yes, it is approved for the metastatic setting of mesothelioma or the unresectable setting and it has shown survival benefit over cisplatin chemotherapy alone. There are other options such cisplatin/gemcitabine that could be considered as well. In general, we do recommend that mesothelioma patients specifically are treated at a cancer center that is familiar with treating this disease because it is such a rare tumor type. You want to get the input of a surgeon that is familiar with treating this disease as well as a medical oncologist.

Dr. West: Alex, what are your thoughts about optimal treatment if the guy saw you before he had even embarked on any further treatment?

Dr. Farivar: I have to agree with Anne, I think it's a difficult disease to take care of. We don't have clearly a standard moving forward as to what is the optimal

treatment. I think Ann raises some great points with respect to delivering chemotherapy, thinking about surgery and then some treatment afterwards. I will say that where I came from where we took care of a lot of patients with mesothelioma, there was clearly a bias to move towards surgery after we knew a couple of things: 1) that the mesothelioma was indeed in one chest, the chest that we thought and was not anywhere else; and 2) that the patient could tolerate an operation – one of the operations is a big operation moving forward. There is no consensus. There are places here in fact some of our busier mesothelioma surgeons believe this is a disease where you need everybody working together to try to cure the patient, so chemotherapy is given ahead of time.

I do think if you're going to operate you should make sure that there's no disease anywhere else and that includes the lymph nodes in the mediastinum. You have to make sure of that at the very least before you operate. I would also argue you need to be absolutely sure of the histology that you're dealing with. If it is sarcomatoid mesothelioma, it should be a relatively rare circumstance that you're moving forward with a big operation.

Dr. West: Alex alluded to the fact that it's a big surgery and a lot of times patients are somewhat debilitated, in fact a lot of times patients are older with this. If you have a patient who is over 70, more marginal performance status, do you advocate strongly for cisplatin and Alimta or do you feel comfortable substituting carboplatin or giving single agent Alimta, Anne?

Dr. Tsao: The data right now that we have is that carboplatin/pemetrexed doesn't give you as good a response rate as cisplatin/pemetrexed in the metastatic setting. If you extrapolate that into the neoadjuvant setting, if you're trying to go for potential curative treatment, you really need to try to go forward with cisplatin.

Dr. West: Particularly in a palliative setting if someone was unresected.

Dr. Tsao: If it's somebody who can't get surgery, then absolutely you could just use carboplatin/pemetrexed. You'd get similar survival results and your quality of life maybe better for each particular person.

Dr. West: I'd like to bring up a case that is a little different, but all too common that is someone who presents with what is considered unresectable mesothelioma after being seen by a surgeon who does a lot of mesothelioma surgery and he receives cisplatin/Alimta. He actually showed progression of his disease. Clinically, he was having more pain; radiographically his scan showed progression. He also had worse shortness of breath.

So, what do you suggest in this situation? Is this someone for whom we have any treatments either off the shelf or investigational that you would be inclined to recommend somebody for? Or are you going to focus on symptom management?

Dr. Tsao: Absolutely, there are treatment options for this patient. Certain clinical trials are the ones that I favor with these new novel targeted agents. There is a whole spectrum of treatments available now. But if for whatever reason they did not wish to go onto a clinical trial, there are standard of care chemotherapies that could be used here such as single-agent gemcitabine or even single-agent Navelbine. Those are all potential options for this patient.

Dr. West: Alex, do you ever offer palliative surgeries here?

Dr. Farivar: We do sometimes. It's the exception and not the rule. We recently had an older patient with mesothelioma who had been treated in the past. He was close to 80 years old, came from very far away, showed up at the clinic one day late in the afternoon. He was very short of breath and that was his problem. He had a large recurrent effusions oftentimes had to be tapped. People weren't very excited about that. So we offered him the catheter that we can leave more permanently called the PleurX which worked very well for him for a long time.

I think there could be a role for debulking, but it's the exception and I would need a lot more information than is presented in this scenario.

Dr. West: Thank you very much for taking the time.