



Current Concepts & Controversies in Locally Advanced NSCLC, Part 2: Ambiguous Imaging Findings after Chemo/Radiation, with Drs. George Blumenschein and Wally Curran

Dr. West: Hello, my name is Jack West, I'm a Medical Oncologist in Seattle, Washington and the President and CEO of GRACE, The Global Resource for Advancing Cancer Education.

I'm here today with a couple of very excellent guests, true experts in the field of lung cancer management and in particular within that spectrum of managing locally advanced non small cell lung cancer. One is Dr. George Blumenschein, Medical Oncologist and Associate Professor in Thoracic and Head and Neck Oncology at the MD Anderson Cancer Center in Houston, TX.

And also we have Dr. Wally Curran, who is a Radiation Oncologist and Executive Director at Winship Cancer Center at Emory University in Atlanta, GA

Dr. West: Our program this evening is made possible through support from an educational grant from OSI Pharmaceuticals, and they had no input in the development of the content.

Both of the guest faculty had offered their conflicts of interest and didn't have any relevant conflicts of interest to disclose this evening.

Our second case: a 39-year-old woman who was referred with a pancoast tumor, however she has staging consistent with 3B disease again based on clinical findings in the mediastinum. She's a teacher who had smoked a couple of packs per day for 25 years and has known emphysema, COPD, and pretty dramatic findings on her imaging for that.

And she had lost 25 pounds over the preceding three months and in that setting had a decreasing appetite increasing fatigue and non-exertional chest pain in the right upper chest anteriorly. Also a bit of a dry cough with no hemoptysis -- not coughing up blood. And she had seen her local physician, who had a chest x-ray done that showed a large right upper lobe pulmonary mass that we will see, the chest CT demonstrated an eight by six centimeter right apical medial mass and some emphysematous changes on the left more than the right.

She was referred to a pulmonologist who did a bronchoscopy that was non diagnostic and then underwent a CT guided biopsy that revealed a squamous cell, non small cell lung cancer with an immunohistochemistry profile consistent with a squamous histology.

Her PET CT showed a maximum SUV of 9.5 in the primary right apical mass abutting the pleural surface in the first rib, but no increased activity in her rib or chest wall. And she had mildly increased SUV in the pre carinal nodes and various other areas in her mediastinum where her maximum SUV was in the two to three ranges. Her pulmonary function test showed an FEV1 of 1.8 liters and a DLCO 47% of predicted.

So here her CT image is showing a very impressive right apical and also these large bullae in her apices on the left more than the right.

We actually decided to treat her with concurrent chemo and radiation and maybe I can start by asking: Wally for somebody who presents with a Pancoast tumor, do you consider someone with mediastinal involvement to be outside the range of surgery categorically? Is there a major distinction between N0, or N1 even, and a higher stage?

Dr. Curran: N1 I'm not so sure about, but N2 disease the historic literature would clearly show that for those patients who had documented N2 disease, the survival in surgical series is drastically inferior to those who are either N0 or N1. So once mediastinal nodal involvement is documented, I think the appropriate approach for most patients is going to be an optimized chemo/radiation approach without surgery.

Dr. West: And George, is that what you would pursue also at MD Anderson for a Pancoast tumor a real distinction between N0/ N1 versus mediastinal involvement?

Dr. Blumenschein: Yes, it would be.

Dr. West: So she received radiation to 66 Gray with cisplatin and etoposide, three cycles actually on an every three week basis, and she tolerated it pretty well -- did have some mild nausea and fatigue, but she was able to eat and even despite the challenges of concurrent cisplatin/etoposide and radiation, was gaining some weight because she was having some presumable positive effects against the cancer.

So I'll turn to the question of the challenge in assessing patients after they undergo chemo and radiation. How do you do it, and when do you do it to get a sense and provide some feedback for patients about how effective the treatment was? George, can you start with that?

Dr. Blumenschein: Certainly. Generally after concurrent chemo radiation, I'll see the patient in a follow up in approximately six weeks and obtain a repeat CT scan. That's the earliest that I would repeat imaging. And if a patient's getting consolidation treatment as is standardly done with RTOG regimen -- concurrent chemo radiation with carboplatin/paclitaxel followed by two cycles of consolidation treatment, I wouldn't get my imaging until I completed all therapy. So on the inside, it'd be six weeks after concurrent if I wasn't planning on any additional therapy afterwards: otherwise I'd do it after completion of consolidation.

Dr. West: And if you do the consolidation approach, is that uninterrupted three weeks after their second cycle, they'll get their third and then their fourth? There's no break after the radiation portion?

Dr. Blumenschein: Well, they would finish the radiation, we'd give them a three week break, and then give them two more systemic doses of chemotherapy; and so approximately nine weeks after finishing radiation we'd get an image.

Dr. West: There's certainly a lot of variability in whether people will pursue a PET or a CT. If a patient asks about getting a PET scan, what do you tell them in terms of either your policy or how things are done at MD Anderson?

Dr. Blumenschein: We do get PET scans periodically. My sense is it's difficult to interpret the data, at least with what my radiology colleagues have noted, that sometimes it's hard to differentiate between residual disease, inflammation, healing if you get a PET scan too soon after treatment. I know that it can be an indicator of the success and potential success of a therapy if you don't see any residual activity.

But in general they've made the point that it's sometime difficult to interpret, but I think it is something that's gaining traction and is being studied in a prospective fashion. But currently it's not a standard thing that's done, but it is being done more frequently.

Dr. West: Wally what's your approach? Do you have any clear standard at Emory, or in Philadelphia when you were there?

Dr. Curran: Our approach is we do find it useful to get a PET scan approximately three months after completion of radiation. We would just get CT prior to that, and it's a snapshot of really both responses to therapy in the chest as well as looking for the risk of potential new metastatic sites. You have to be careful in looking in the chest because inflammation that follows a radiation field pattern can show inflammation that can mimic residual disease. But at least it's a scan against which future scans could be compared with.

Dr. West: I must say that we were largely thinking along the lines of the University of Alabama and other centers' experience in considering her for a tri-modality approach, really from the beginning even.

And she underwent a PET/CT a few weeks after she completed the chemo and radiation, and it showed that her tumor was smaller with slightly less, but not much less metabolic uptake. But clearly smaller, at least and her mediastinum was now at background levels.

So that was what we'd found, and the real question is if this was done whether weeks later or months later, would this be a setting in which you would, say, continue to watch her because she could still be

improving, or would you say that this is a trigger to pursue additional systemic therapy?

Would you consider more local therapy along the lines of surgery and would that depend on doing staging her mediastinum? George?

Dr. Blumenschein: Well, she got definitive chemo/radiation with full doses of chemo and completed her intended course of radiation, so I would consider that she's gotten definitive treatment and I would consider observing her. There's not really any proven utility for additional systemic therapy in this setting, speaking to the HOG trial, which looked at chemo radiation with etoposide/cisplatin versus chemo/radiation with etoposide/cisplatin followed by consolidation with docetaxel: no difference in outcomes *per se* in terms of improvement in overall survival.

And I don't think I would consider surgery: again, she's had definitive treatment to over 60 Gray, so my take on this would be to observe and follow with serial scans.

Dr. West: In the RTOG approach there is consolidation, but we don't have data that supports a benefit for consolidation at least with docetaxel (Taxotere), so how are you thinking about the benefit of additional systemic therapy after the concurrent chemo and radiation?

Dr. Blumenschein: Well, for me it really depends on how much chemotherapy a patient got during a concurrent portion of treatment. For example, with the SWOG regimen which she received, they are essentially getting systemic doses of treatment. And as I mentioned before, the HOG trial demonstrated a good outcome with just concurrent chemo/radiation. But you're right, though: we haven't really settled the question of whether consolidation adds anything to concurrent.

The gestalt, though, is that if someone receives weekly doses of chemotherapy as per the RTOG regimen with weekly carboplatin and paclitaxel, most of my colleagues gestalt, and mine certainly, is give them some systemic therapy at some point; which is what we generally do with the consolidation portion of therapy.

Dr. West: So a distinction between cisplatin and etoposide, which we think has a meaningful systemic effect, and weekly carbo and taxane, usually carbo and paclitaxel, not necessarily having enough of an impact on micrometastatic disease distantly: is that fair to say?

Dr. Blumenschein: That's fair to say.

Dr. West: Wally, what's your thoughts about a situation like this, where the imaging if not definitive is concerning for residual disease, but localized?

Dr. Curran: I agree with George that there's no data to prove that giving additional chemo is going to benefit the patient. I would probably be comfortable if

this patient was to receive additional platinum/etoposide. The scan has improved it's not progressing, but it's still there.

But I agree with George that as part of a standard of practice it's far more important to consider post chemo/radiation chemotherapy in the setting of the low dose weekly carboplatin/paclitaxel rather than this type of regimen.

Dr. West:

Well, she ended up going to surgery, and I would say that part of this was the uncertainty about the findings, and also partly that she was a 39-year-old who we thought it would be better to err on the side of doing a lobectomy. She did have that, and the pathology demonstrated extensive necrosis and no viable tumors and no viable tumor tissue.

So I guess through the "retrospectroscope" it might represent over-treatment. And this could have been something that if we had sat tight longer it might have just resolved over time.

So I welcome your thoughts on that, and also just the question of, what does this tell us about doing imaging within a month or six weeks of chemo and radiation? Can we use that to reliably say anything? Wally what's your thoughts?

Dr. Blumenschein:

As I mentioned earlier, we know that CT scans are notoriously unreliable as an early indicator. We've had mixed results when we've looked at PET. There are some series, Jack, which have shown that a PET scan done after a couple of cycles of chemo and prior to surgery, the extent of PET response was a very good predictor of ultimate survival.

This is a great result for this woman, and it just shows you as you say that perhaps the PET response would have taken longer. Having radiation may have confused it, or it might have been just as confusing with chemo alone, but it does show us that it's tough to make that decision about a surgical procedure in that very short time zone between when you want to give induction therapy and when you want to do the surgery. Fortunately for this woman, there was a good result.

Dr. West:

And I would say that that was one of the things that we were thinking about was the group at University of Alabama Birmingham with Dr. Cerfolio also has published on the utility of post chemo/radiation scans, PET scans, in predicting pathologic complete responses and good outcomes, and suggests that if you have a significant drop in the standard uptake value, it's definitely associated with a much more favorable outcome.

She did not, which made us more concerned that this would not be the favorable pathologic result we saw. Maybe it was an issue of timing, but that was certainly one of the factors. As was the concern that there may be a window of time to do a surgery, and that if you go too long, it can make it extremely difficult after the chemo and radiation to actually do an effective surgery. So there's a potential down side to watch and

wait, and by the time something may declare itself as an increasing SUV in a localized area, you may not be able to do the surgery. It's just a lot of uncertainty here.

George, what are your thoughts here?

Dr. Blumenschein: I think this wasn't standard care, but the rationale behind it makes sense. This young woman looking for every option to make things go well for her, I think it's an understandable decision to go forward for her.

Dr. West: That's something that I must say: it's always difficult when we go through these exercises' through slides and discussion. It's never the same thing as having the patient in front of you, and it's hard to really say what you would do, because it's a lot easier to make an impartial judgment of the standard of care -- and I'm not trying to be defensive, but to say that we all deviate, I think, a lot, from any proven standards more in our own case series just because reality is messier than the data.

Dr. Blumenschein: It is, and that's why it's an art and not a science. You take into account patients, in terms of what their comorbidities are, and especially younger patients who are heartier and can tolerate a more aggressive approach. I think we all tend to lean toward doing something that you would say is outside the box, trying to be more aggressive in order to facilitate a better outcome.