Trimodality Therapy for Pancoast Tumors

In a very recent post I provided an introduction to the special case in NSCLC known as a Pancoast tumor, including a historical perspective of how it has evolved from being perceived initially as an untreatable, uniformly fatal diagnosis to a cancer that could be cured with radiation and then surgery in a significant minority of patients (35% in one large series). Here we'll focus on the new era of managing Pancoast tumors, which often now incorporates chemotherapy into the mix.

In some other prior posts (here and here, for instance) I described the debate about whether patients on the outer limits of resectability, such as many with stage IIIA N2 NSCLC are better served by undergoing chemotherapy and radiation without surgery or radiation alone. One approach that was shown to be feasible for patients with stage III NSCLC was to give chemo with cisplatin/etoposide for two cycles along with concurrent radiation to an “induction” (not full strength) dose of 45 Gray (Gy) over about 5 weeks (a full, potentially curative dose of radiation for locally advanced NSCLC is usually considered to be in the 60-67 Gy range, given over 6-7 weeks). The Southwest Oncology Group (SWOG) had pioneered this approach for initial therapy to be followed by surgery to remove all evidence of cancer and leave negative surgical margins for cancer (a so-called R0 (zero) resection), if possible (abstract here). Additional chemo with cisplatin/etoposide and more radiation up to 60 Gy was given to patients who were unable to have surgery or who were found to have positive surgical margins for cancer (called an R1 resection) or with visible tumor left behind at surgery (an R2 resection). We know that patients who have any tumor left behind, either visible or even microscopically at the tumor margins, are very unlikely to do well long-term without further treatment. And unfortunately, we also know from renowned thoracic surgeon Valerie Rusch’s report (abstract here) describing Memorial Sloan Kettering’s extensive surgical experience from 1974 to 1998 that even with modern imaging it is very difficult for even expert surgeons to predict who will be able to achieve an R0 resection vs. R1 or R2, particularly for those tumors that look like they may involve important anatomic structures around them. In those patients with T4 N0 lung tumors based on imaging, and for whom surgery was attempted, only 38% were able to achieve an R0 resection, with no evidence of microscopic or gross evidence of cancer left behind.

In contrast to all of the preceding work on Pancoast tumors that reported on patients from a single center, there is just one reported multicenter prospective trial (where treatment was planned to be the same for everyone moving forward) and one more that has just completed enrollment and is not yet reported. The first actual “trial” done for patients with Pancoast tumors was conducted by SWOG, with other cancer cooperative groups throughout North America joining in (an “Inter-group” study). This was SWOG trial 9416, led by Dr. Rusch and published just this past year (abstract here). There was no randomization, just one study arm: patients received cisplatin/etoposide for two cycles along with radiation to 45 Gy, then surgery, and finally two additional cycles of cisplatin and etoposide (at least planned). A total of 110 eligible patients (2/3 men) were enrolled, and 95% received all of their pre-operative chemo and radiation as intended. Repeat clinic visits and radiation were performed 2-4 weeks after radiation was completed, showing that 46 patients (42%) had a partial response by imaging (no complete responses seen, 36% with stable disease). Patients who didn’t have distant
Disease or local progression near their primary cancer went on to surgery. Of the 95 patients eligible for surgery, 88 (80% of the total enrolled) underwent thoracotomy, with 2 patients dying post-operatively (within the first 30 days). Quite encouragingly, 83 patients (76% of the full starting group) had a complete (R0) resection. Despite the fact that no complete responses were seen on imaging, 61 patients (56%) were found to have either NO viable cancer or just microscopic areas of viable cancer cells in the resected tumor specimen after induction chemotherapy and radiation.

Sixty patients (55% of total study population) were registered for the post-operative chemo, of whom 49 hardy souls (45% completed it).

The trial results were the best we’ve ever seen in patients with a Pancoast tumor. With a median follow-up of nearly seven years, the median survival for all patients was 33 months, and for those who achieved an R0 resection, it was 94 months, meaning that half of these patients were still alive nearly 8 years after starting the study. The trial corroborated that patients who had no evidence of viable cancer at the time of surgery, called a pathologic complete response (pCR), did better than everyone else, and in fact did considerably better even than those with microscopic areas of living cancer removed by surgery:

So there are a few take-home messages here, I think. One, chemo and radiation do a good job and can cure Pancoast tumors without surgery. The folks with a pathologic complete response may have had some viable cancer that was missed when reviewing the specimen under the microscope, but a pCR means that the chemo and radiation (even less radiation than would be ideal for curative therapy) can kill ALL of the cancer in some patients (32 of 88 who underwent surgery). However, there is a plateau on the right side of the curves also for the patients who had residual viable cancer, on a graph that goes out to approach 10 years. This means that
several of the 56 others who had viable cancer at the time of surgery are alive 5-10 years later, almost certainly because of the surgery.

The more recent study by the Southwest Oncology Group, S0220, was very similar in design but substituted three cycles of single agent taxotere for the two additional cycles of cisplatin/etoposide post-operative. This is based largely on the very favorable results of the SWOG 9504 trial that used consolidation taxotere (see prior post) with “consolidation” taxotere after chemo and radiation for locally advanced NSCLC. However, the benefit of consolidation taxotere has been shown to be very questionable based on recent work (see prior post). Regardless, the S0029 trial was also an Intergroup trial throughout North America that enrolled 45 patients over the past several years and just closed in the last few weeks. We haven’t seen any results from that trial, but now we need to figure out the next important question to ask in terms of how to improve outcomes for patients with Pancoast tumors, perhaps increasing the radiation and/or including a newer targeted therapy for maintenance therapy. We still have a ways to go, but with a 5-year survival of 44% on the S9916 trial and perhaps even better results with the more recent study (we’ll see…), we’ve come a long, long way for what was once a “hopeless neoplasm”.

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