Tales from the Clinic: Mucinous BAC
by Dr West - http://cancergrace.org/lung/2009/01/05/ella-a-case-mucinous-bac/

In my last post I outlined the typical clinical scenario for pneumonic bronchioloalveolar carcinoma (BAC), which is typically the mucinous subtype of this unusual disease. In fact, we are still actively learning a great deal about BAC, enough for the lung cancer experts to begin to develop a more sophisticated view that the mucinous and non-mucinous subtypes have different behaviors and respond differently to treatments. Here is a case that illustrates a situation that I would consider to be typical for the mucinous, pneumonic form of BAC.

Ella A. was 74 year-old woman with a very long smoking history of about 50 years, who quit last month in the face of worsening pulmonary and other symptoms. Specifically, she experienced an initial dry cough that became productive of sputum over a six-month period, during which time she also developed increasing shortness of breath and a 20-pound weight loss for a woman who was pretty slender beforehand. This led her to her primary care physician, which showed extensive “consolidation”, shadows in both lungs and particularly extensive on the left. These findings were confirmed on a CT.

As you might suspect, this led to a referral to a pulmonologist for a bronchoscopic biopsy. The pulmonologist needed to start her on oxygen before he could do a thorough bronchoscopy. The biopsy revealed well differentiated BAC, but the pathologist (an expert in lung pathology) didn’t have enough material to specify whether it was mucinous or non-mucinous.
Frankly, at the time when I first met her, in December of 2006, there were only the early inklings that this could be relevant. We don’t have much more information since then, except for the anecdotal experiences of myself and a few others who treatment many patients with BAC, which have corroborated the early impression that the well described effectiveness of oral EGFR inhibitors like iressa (gefitinib) and tarceva (erlotinib) in BAC appeared to be limited to the non-mucinous subtype.

Although these early inklings and her smoking history made me suspect that she wasn’t likely to be one of the tremendous success stories with EGFR inhibitors for BAC. Nevertheless, this was just early speculation that she wouldn’t be a responder, and she had experienced a significant and rapid decline in her lung function and performance status in the weeks before seeing me. I recommended that she start tarceva to check whether she might be a major beneficiary, because the benefits can be so dramatic and long-lasting that I’d have hated to have missed that opportunity if she continued to decline rapidly on an initial approach of chemo. She started tarceva, but I wanted to ensure that I kept a close eye on her, so that we could change plans if it became clear that she wasn’t going to benefit from it.

Although I typically wait 6-8 weeks after starting tarceva (or standard chemo, for that matter) to assess interval response, I thought she had little room to decline while still being a candidate for more treatment. I brought her back two weeks later, at which time she reported no significant rash or other adverse effects from the tarceva, but her shortness of breath and oxygen requirements had increased. I repeated a chest x-ray that also looked modestly worse. Rather than allow her to decline further on what I feared would be futile therapy, we talked about switching treatments, and I started her on carbo/taxol with avastin, although her marginal performance status convinced me that it would be infeasibly aggressive to treat her with the full doses used in the ECOG trial, and instead I decreased the doses of the chemo agents by about 15%. In the first half of January, 2007, she started a slightly dose-reduced regimen of carbo/taxol/avastin. In light of the significant risk for neutropenia and infectious complications, particularly in older patients, I also gave her neulasta on the day after chemo to help boost her white count and minimize the risk.

She tolerated it well, just with some expected fatigue (and the beginning of hair loss), and I scheduled her to again see me two weeks later, when I expected her blood counts to be at their lowest. I wasn’t sure what to expect, thinking that if she experienced another clear decline it may not be valuable to pursue additional treatment if she had already progressed on tarceva, chemo, and avastin and now couldn’t walk across a room without needing to stop because of shortness of breath. But I was gratified to hear her relate that her breathing had improved, along with perhaps some improvement in her cough.

Four weeks later, she had received a second cycle and reported that she sometimes forgot to wear her oxygen around the house but now wasn’t reminded of a need due to immediate shortness of breath. Her family had bought an oxygen saturation monitor, and they noted that her oxygen saturation levels were now in the mid-90s range on just 1-2 liters (previously requiring 4-5 liters). Though her CT scan didn’t show a remarkable improvement, the extensive consolidation looked decidedly less dense and a little less extensive. We continued with more of the same.
After two more cycles, now mid-April of 2007, she had come off of oxygen and was gaining weight. Her scan appeared clearer than the last two.

Unfortunately, the spell was broken after that. Though she gained weight to nearly her prior baseline, she began to experience an increasing cough and shortness of breath again. Corresponding with this, her oxygen saturation levels were now in the high 80% on oxygen 4 liters/minute. Though her repeat CT scan after six cycles wasn't remarkably worse, the right side definitely showed progression. At that point, I wasn’t sure if the benefit she had received was from the chemo, the avastin, or the combination. At that point, in the very end of May, we decided to switch to alimta and continue the avastin, a practice that I haven’t routinely pursued before or since, but I felt that she would need a little more help to control the cancer.

She again continued to tolerate chemo and avastin well, and her scan actually appeared marginally better after her first two cycles. Unfortunately, after a couple of additional cycles, she again experienced clinical and radiographic progression. By that time, she had become frail enough that it wasn’t clear she could tolerate more treatment. Now short of breath with nearly any ambulation, even on 6 liters of oxygen, we discussed the limited options and decided together that palliative care would be the most appropriate and appealing course to pursue. She continued to decline over the next several weeks, ultimately dying peacefully at home in October with hospice care and her loving family caring for her.

Obviously, her case didn’t prove to be a staggering success, but I was happy to have seen her benefit from several months of convincing improvement in her cancer-related symptoms that were probably associated with an improvement in her survival by several months. Although not miraculous, just seeing any meaningful benefit from treatment in what appeared to be mucinous BAC was something positive. I was glad that while we tried tarceva, not wanting to miss whatever chance there might have been to see a terrific response in a person with BAC, but fortunately I was able to follow her closely, and we were able to cut our losses and move on to the next approach after determining that our first approach wasn’t fruitful.

Even though I have about as much experience with BAC as anyone, I still haven’t treated many further patients with the mucinous, pneumonic picture of BAC. I’m still not clear whether many of these patients will respond to a regimen of chemo and avastin, and if so, whether they might do just as well with chemo alone, or whether the avastin is a particularly helpful addition.

I recently met a man from Walla Walla, a few hours from Seattle, who came to Seattle to complete his workup and establish a diagnosis. He has the full blown version of pneumonic, mucinous BAC, including the frothy sputum and extensive consolidation throughout his lungs, with the pathology showing mucinous BAC. I recommended chemo and avastin again, but this was only a few weeks ago, and we don’t yet know how he’s responding.

So with such infrequent cases, this is a clinical situation where we need to learn from everyone who presents a similar case. We need to know what didn’t work as well as what might have, because is a cancer that can’t wait for patients to stay on futile therapy for long. For now, I think it’s important for oncologists to begin to learn about the variability of BAC, so that patients with mucinous, pneumonic BAC aren’t started on an EGFR inhibitor with an
expectation that we'll see a dramatic and long-lasting response. For the patients with non-mucinous BAC, especially in a never-smoker and/or someone with BAC and a known EGFR mutation, you could make a very strong argument for starting with an oral EGFR inhibitor. But for the patients with mucinous BAC, who appear to rarely if ever have an EGFR mutation and if anything are likely to have a K-Ras mutation associated with poor response to EGFR inhibitors, I would say that the very limited evidence thus far suggests that it shouldn’t jump to the head of the queue for these cases, even if it would still be worth a try later, in my opinion.