Hello, and welcome to The University of Texas MD Anderson Cancer Center lecture series on Inflammatory Breast Cancer. In this section we’ll discuss the clinical diagnosis of IBC. My name is Wendy Woodward and I am a Radiation Oncologist in the Breast Section here at MD Anderson.

Our goals over the course of this discussion are to be sure that we can recognize the clinical presentation of inflammatory breast cancer; understand the clinical definition; and identify common features.

We'll begin with who is at risk. Demographic studies of women who have inflammatory breast cancer have demonstrated that this is largely a disease of younger women, compared to non-inflammatory breast cancer. In addition, demographic studies have demonstrated an increase in the risk among women from the Mediterranean area and North Africa. Some of the limitations of studying a rare disease like inflammatory breast cancer, however, are that it’s difficult to validate risk factors and thus far, there are indeed no validated risk factors that could be used for screening. There is, however, evidence that there is an increasing incidence in inflammatory breast cancer and these are areas of active research.

This is an age density histogram showing the age distributions of patients with inflammatory and non-inflammatory breast cancer. You can appreciate in Panel A, looking at non-T4 breast cancer patients, patients who have no disease involving the skin or the chest wall, that there are two peaks in the age density with the largest peak amongst older women at 69 years of age. Amongst locally advanced breast cancer patients, independent of their T4 status, again, two peaks with a larger peak amongst older women 74 years of age. This stands in contrast to the distribution for inflammatory breast cancer patients where the largest peak here is at 50 years of age and really no second peak is demonstrated.

Looking in this population, the same authors, Hance et al., were able to demonstrate that, in fact, the incidence of inflammatory breast cancer is increasing. Here, looking from the early 1980s up through 2000, you can see an increase in the number of women per 100,000 woman/years. And inflammatory breast cancer is going up at the same time that the incidence of locally advanced breast cancer is going down, likely through the benefits of increased early screening. Interestingly, while there has always been an increased incidence amongst African-American women, particularly beginning in the early 1980s and extending up through 2000, we begin to see that white women are catching up in terms of incidence with an increased incidence over this time period.

So “is this a new disease?” It certainly is not. The clinical presentation of inflammatory breast cancer was first described in 1814 by Sir Charles Bell, “A purple color on the skin over the tumor accompanied by shooting pains.” It was later then identified as inflammatory breast cancer based on this visual description, the symptoms that could be seen on the breast. This is an important distinction because “inflammatory” indicates to many that this is in fact a response to an infection, but that’s a misnomer. There is no
clear evidence of the signs and symptoms of infection, simply a breast cancer that looks like infection.

Here's an example of the signs and symptoms of inflammatory breast cancer. In particular there's erythema and breast edema that develops in a previously normal breast. This can happen rapidly, even overnight. Typically it will advance to involve approximately two-thirds of the breast. The breast can be tender; can have induration or warmth, or peau d'orange, literally the skin of an orange. Depicted here, you can appreciate that fluid and swelling in the skin itself has caused the hair follicles to stand out, making the skin appear orange-like. This is a classic symptom of inflammatory breast cancer. Because of the swelling and redness, this is often diagnosed --- misdiagnosed as infection. It is often not detected by mammogram, which adds to this misdiagnosis.

An important distinction about inflammatory breast cancer from non-inflammatory breast cancer is that it is a clinical diagnosis. It's not based on any specific pathologic finding. So in the presence of the clinical features we've just described and a biopsy proving invasive breast cancer, the diagnosis of inflammatory breast cancer can be made. In 2008, at the first International Inflammatory Breast Cancer Conference which was held here at MD Anderson Cancer Center, a consensus panel of experts came together to try and clarify the specific clinical symptoms and signs which should lead to a diagnosis of inflammatory breast cancer. Specifically, a number of challenges were identified. This is a relatively subjective diagnosis. “What is the difference between one-third coverage of the breast or two-thirds coverage of the breast?” “Is there clear data exactly where this threshold should lie?” The answer is “no”. Nevertheless, the authors and participants of the Consensus Conference decided that one-third of the breast would be the defining characteristic over a time span of less than six months. This indicates the rapid progression of inflammatory breast cancer as we understand it as well as the skin involvement. It is hallmark in inflammatory breast cancer to find invasion of the dermal lymphatics by tumor cells pathologically. That’s depicted here. This, however, is not required for the diagnosis of inflammatory breast cancer. You must have a diagnosis of invasive disease but in the absence of dermal lymphatic invasion but the presence of clinical symptoms, this is still inflammatory breast cancer.

Another pathologic feature of this disease, however, is the thickened skin that can be appreciated as a result of blocking of the dermal lymphatics by the tumor emboli within these structures. You can appreciate that here on the gross specimen where the skin is highlighted and on the pathologic specimen.

Since the opening of the Morgan Welch Inflammatory Breast Cancer Clinic all consenting patients have been treated on a clinical registry and have provided information regarding their presentation of disease as well as other demographic information. In our experience the vast majority of patients have self-detected symptoms, over 80%. In addition, over 80% of our patients have a body mass index of over 25, while nearly 50% of them had sometime had a history of smoking. The degree of patients with any first degree relative with breast cancer was just over 15% and the
rate of breastfeeding, any breastfeeding, was 47%. Looking at self-exam observations amongst 192 patients, you can appreciate that erythema is the most prominent finding in 63% of patients but not all patients. Edema followed at 59%, followed by growth, warmth, dimpling of the skin, pain, inversion of the nipple, and in some cases, a lump.

Further investigation of features that are specific to the receptor subtypes of inflammatory breast cancer reveal differences. Interestingly, several studies, including our own, have revealed a higher than typical incidence of triple negative breast cancer amongst the inflammatory breast cancer cohort. Here at the time of this analysis, at 30%. Amongst the triple negative breast cancer cohort, for inflammatory breast cancer, we observed a reduced incidence of ever breastfeeding and the total time of breastfeeding. An additional study will go into understanding how these factors contribute, if at all, to the development of inflammatory breast cancer. At this point, I’d like to go over several examples of patients who present with relatively common features of inflammatory breast cancer. Now, of course, some of these examples are very dramatic. And I want to highlight that many women still are cured of their inflammatory breast cancer in spite of its difficult disease and prognosis. And these are relatively dramatic images.

This is not a typical presentation of inflammatory breast cancer because of the masses that are present in the breast. The timing of it, however, was very typical, swelling and redness in a short period of time, a matter of weeks, clearly a dramatic asymmetry between the involved breast and the opposite breast. But most importantly, as is typical of 70% of inflammatory breast cancer patients,…

…this patient, in spite of that dramatic disease, presented with no evidence of metastasis. And again as I mentioned, 70% of the time patients will present with disease which, in spite of its dramatic symptomatology, is confined to the breast or regional lymph nodes.

Here is an example of a more typical presentation, of a patient with a swollen breast, with peau d’orange of the skin, with erythema of the skin, the nipple is inverted. This is a very classic presentation of inflammatory breast cancer. Interestingly, in this patient, she actually presented with bilateral cancer. There is a non-inflammatory breast cancer in the opposite breast.

And by MRI you can appreciate some of the distinguishing features including, importantly, the thickened skin by MRI. Another important issue to note, that although many of these cancers can be mammographically occult, MRI can detect abnormalities in the involved breast the majority of the time. So “what should a patient do who has symptoms of inflammatory breast cancer, has been given antibiotics, is not responding, and has a negative mammogram?” Go back and request for additional imaging, ultrasound or MRI, and a biopsy of the affected area to truly rule out inflammatory breast cancer without delay.
This patient ultimately was not surgically resectable. She progressed on chemotherapy and went on to have preoperative chemo and radiation. One demonstration here, using PET CT, is that the disease in the skin itself is actually quite resistant to treatment, and as can be demonstrated here, the residual disease, FDG avid in the skin, remains in spite of aggressive therapy.

This patient went on to develop metastatic disease including cutaneous spread throughout the skin into the shoulder.

This is an example of a bilateral inflammatory breast cancer. Again, a surprisingly common presentation for inflammatory breast cancer which does migrate throughout the skin of the breast and can move beyond the clinical breast mound. You can appreciate on both sides; the patient has involvement of the breast mound proper with progressing disease in the superior aspect of the breast.

This is an example of contralateral inflammatory breast cancer. This is a patient who, has had a previous mastectomy for a non-inflammatory breast cancer, that has gone on to develop inflammatory disease in the opposite breast.

Similarly, a secondary inflammatory breast cancer presenting after a non-inflammatory cancer, then to demonstrating the typical skin findings, now spreading without --- in the absence of the clinical breast mound into the disease --- into the skin of the chest all the way onto the opposite side. This obviously is a very difficult clinical scenario, very difficult to treat.

Lastly, inflammatory breast cancer, as you could see in the previous slide, can become a very significant local skin problem, expanding from beyond the breast mound proper into the skin of the thorax, the neck. We've seen this up through the side of the head into the scalp. Here in the abdomen this disease curves around to the back. In some unique situations we are able to target these local spread with radiation therapy.

And here’s an example after radiation therapy and chemotherapy of regression of that disease with aggressive locoregional management.

Importantly, I think it will become clear, and hopefully as clear throughout the course of this series, that multidisciplinary management is critical. Inflammatory breast cancer treatment typically requires chemotherapy, surgery, and radiation therapy from a coordinated team staying in step throughout the care to really change course when needed, and do what is needed in order to get control of this disease. We’re pleased to see that since the initiation of our Inflammatory Breast Cancer Clinic, we are able to report better outcomes than prior --- than amongst patients treated prior to the organization of our clinic. While there are many, many factors that contribute to this including new treatments, the organization of the multidisciplinary clinic really helps to make sure that things move forward in a timely fashion. And we’re doing absolutely the best, most coordinated care that can be done to take care of this difficult disease.
In summary, inflammatory breast cancer is an aggressive form of breast cancer. It can develop in weeks. It’s frequently self-detected and misdiagnosed. There’s often no clinically apparent mass. A negative mammogram and ultrasound in the presence of suspicious symptoms should lead to further imaging and a biopsy. And coordinated multidisciplinary care and experience are likely very important in the treatment of this difficult and unusual subtype of breast cancer. I’d like to thank you for your attention and we welcome your feedback.