Making Cancer History®

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Inflammatory Breast Cancer (IBC)

Chasity Yajima MSN, APRN, FNP-C, AOCNP, CBCN

Oncology Nurse Practitioner

MD Anderson Cancer Center

Morgan Welch Inflammatory Breast Cancer Research Program and Clinic

Houston, TX

Email: clidom@mdanderson.org

Disclaimer

- I have no financial interests to disclose
- MDACC photos were obtained with patient signed consent

Learning Objectives

- Identify the presenting symptoms of Inflammatory Breast Cancer.
- Discuss how to differentiate between mastitis and IBC.
- Review case studies which illustrate the aggressiveness and complexities in the management of IBC.

Overview

- Clinical Facts
- Presentation
- Treatment Options
- Local Recurrence Rates
- Komen Scoring System
- Lymphedema
- IBC Pictorial Review
- Recommendations
- Key Points to Remember

How many of you have seen a woman with Inflammatory Breast Cancer?

Making Cancer History®

CLINICAL FACTS

Incidence, Mortality, Risk Factors

- 2%-4% of all breast cancers in the United States
- Commonly affects ages under 40
- Contributes to 7% of breast cancer-caused mortality
- All subtypes, 62-68% 3- year overall survival (OS)
- Race- higher incidence in black women
- High BMI (Overweight/Obesity)

(Menta et al., 2018)

Clinical Facts

- **Commonly missed/delayed diagnosis (e.g. mistaken for mastitis/clogged milk duct)**
- **Progresses in days to weeks**
- **~40% are metastatic on diagnosis**
- **High incidence of brain metastasis**
  - Metastatic Disease: IBC 37% vs Non-IBC 31% HER2+; 32% TNBC; 15% HR+ HER2 -)
  - Non metastatic disease: IBC 15% vs Non-IBC (Widely variable/dependent of stage, biomarker status ~0.22%-5%)
- **No identified association with genetic mutations**

(Kuksis et al., 2021) (Menta et al., 2018) (Warren et al., 2015) (Watase et al., 2021)

Making Cancer History®

PRESENTATION

Clinical, Diagnostic, Histopathologic

Inflammatory Breast Cancer

Presentation- Clinical

Onset

- <6 months and can evolve rapidly over days to weeks
- Likely will involve lymph nodes
- 40% metastatic at diagnosis

Skin Changes

- Pink and mottled
- Hyperpigmented in dark skin tones
- Peau d' orange (enlarged hair follicle pits)
- At least 1/3 of the breast
- Wheals/ridges
- Flattening of the nipple

10 (Menta et al., 2018)

- **Enlargement**
  - May have sensation of heat
  - Visible markings/indentation at bra line
  - Palpable mass not present in 1/3 of patients

(Schairer et al., 2013)

MD ANDERSON CANCER CENTER

Presentation- Diagnostic Imaging

Mammogram

- Skin thickening, global asymmetry, trabecular thickening
- Scattered distribution of tumor emboli throughout the breast may make detection of disease difficult on mammogram
- Diffuse *increased* breast density
- Mass?
- 1/3 may be normal

(Menta et al., 2018)

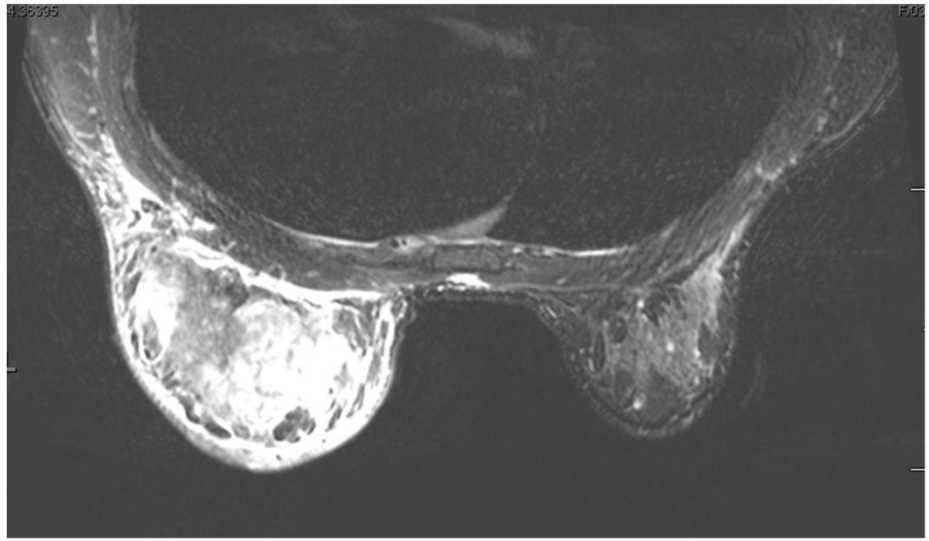
Ultrasound

- Mass?
- Global edema
- Evaluate the regional lymph nodes
  - ~95% will have positive lymph nodes on presentation in the ipsilateral side
  - ~10% will have positive lymph nodes in the contralateral axilla

Presentation- Diagnostic Imaging Cont…

Breast MRI

- Global skin thickening
- Trabecular thickening (secondary to dilated lymphatics)
- Skin enhancement
- Global edema
- ~95% cases with ipsilateral adenopathy



Histopathologic Presentation

Core Biopsy

- Poorly differentiated/Nuclear Grade 3
- Invasive ductal carcinoma
- Invasive lobular carcinoma (less common)
- Triple negative (~30%)
- HER2neu positive (~40%)
- Lymphovascular invasion

Skin Punch Biopsy (NOT Required)

- Tumor emboli
- Dermal lymphatic invasion

(Menta et al., 2018)

Making Cancer History®

TREATMENT OPTIONS

Making Cancer History®

Trimodal therapy

Neoadjuvant Systemic Therapy

- To improve local control
- Treat microscopic disease
- Improve outcomes of surgery/radiation
- Serial monitoring of disease with breast imaging

- Neoadjuvant anthracycline and taxane-based regimens
- Addition of immunotherapy if TNBC (e.g. Pembrolizumab)
- Addition of anti HER2 agents if HER2 positive (e.g. Trastuzumab/Pertuzumab)
- Ongoing clinical trials for both upfront and metastatic treatments working towards identifying activating targetable mutations

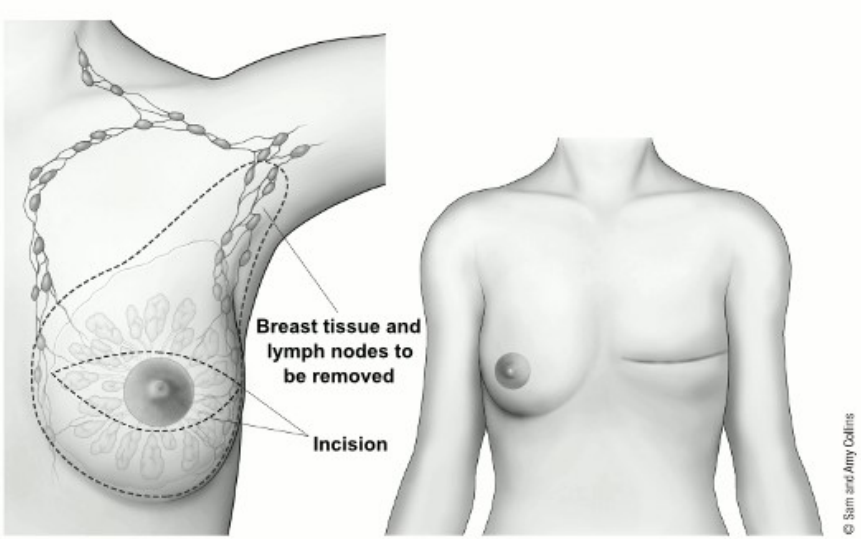
Inflammatory Breast Cancer

Neoadjuvant Systemic Therapy

Molecular Subtype	Standard of Care- FDA Approved	Remarks
TNBC	Keynote-522 (Carboplatin, Paclitaxel, Pembrolizumab, followed by Adriamycin, Cytoxan, Pembrolizumab)	• ***Review for potential clinical trials
ER+	AC DD or AC q3w followed by Weekly Paclitaxel or DD Paclitaxel (Regimen can be flipped)	• ***Review for potential clinical trials
HER2+	THP x 4 cycles followed by AC x 4 or TCHP x 6 cycles **Or start with TCHP x 4 cycles and if sluggish response to TCHP consider switching to AC x 4 cycles. IF responding well to TCHP after 4, can complete total of 6 cycles and omit AC**	• ***Review for potential clinical trials

Surgery

- Total Radical Mastectomy + Axillary Dissection of Lymph Nodes
  - Skin must be removed even if clinically skin has a complete response to systemic therapy to reduce local recurrence rate
- Consider upfront lymphovenous bypass to reduce the risk of lymphedema
- Reconstruction ideally should wait for about 2 years from diagnosis
- Surgery is considered in some metastatic cases to help improve local control



(ACS 2024)

Radiation

- Radiation to chest wall and regional nodal basins
- Completed ~4 weeks post-surgery
- Improves local control rate
- Targets advanced nodal involvement not able to be removed at surgery
- Women ≥45 typically Monday-Friday ~6 weeks
- BID radiation separated by 6 hours Monday-Friday ~4.5 weeks
  - Age <45
  - Residual Cancer Burden
  - Close/ Positive/ Unknown surgical margins
  - Less robust response to systemic therapy

(Stecklein et. al, 2019)

Radiation Cont…

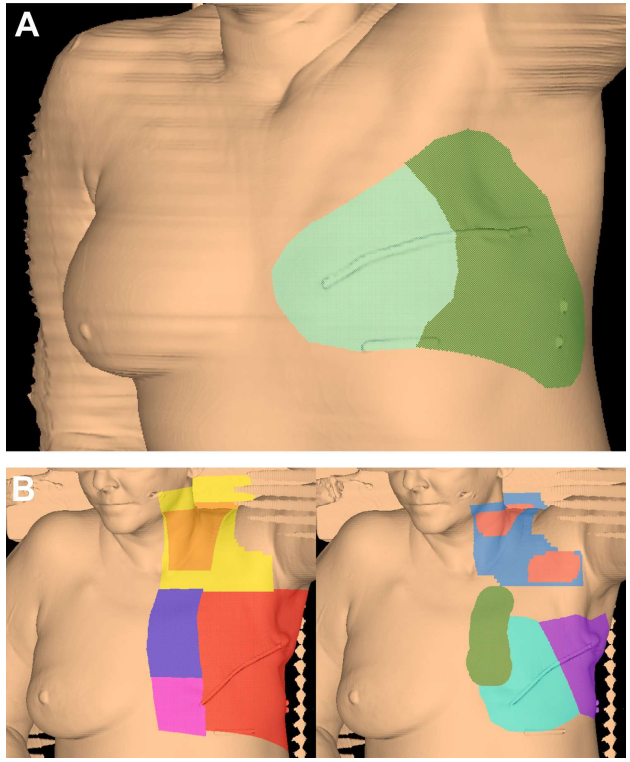
(Fig A)

Sites include mastectomy scar, drain sites, chest wall flaps for the typical electron boost fields

(Fig B)

Patients with undissected or residual nodal disease after systemic therapy, sites include chest wall, regional nodal, and boost fields

(Stecklein et. al, 2019)



Adjuvant Treatment Options

- **Hormone Receptor Positive**
  - CDK4/6 inhibitor + Aromatase Inhibitor +/- ovarian suppression
  - Clinical trial if available
- **HER2 neu positive**
  - Maintenance anti-HER2 therapy
  - Clinical trial if available
- **Triple negative**
  - Immunotherapy
  - Clinical trial if available

***Adjuvant therapy recommendations will largely depend on residual cancer burden (RCB) and any available clinical trials when the patient is seen for post operative discussion

Metastatic Disease Management

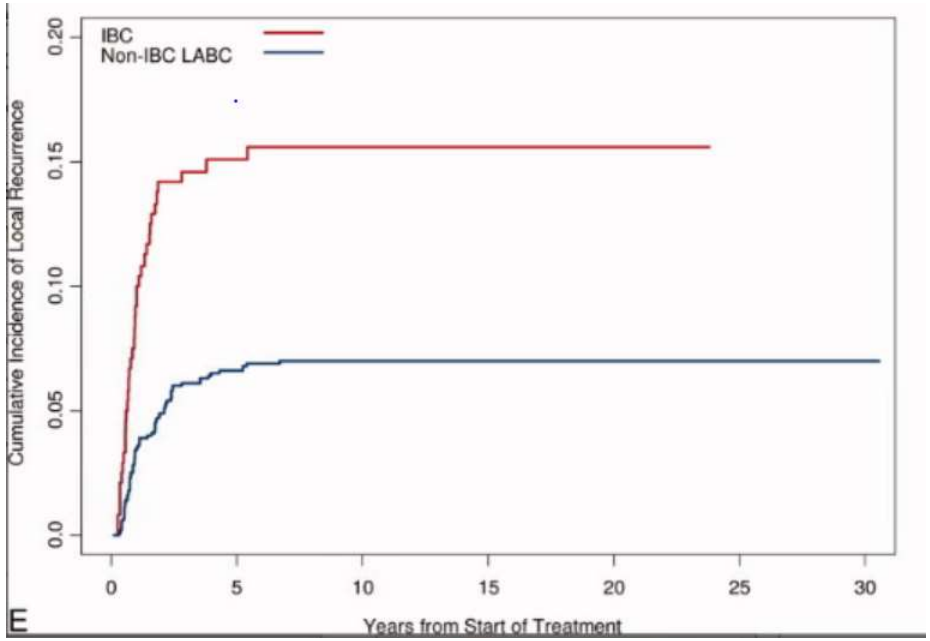
- Systemic chemotherapy (May be similar as neo-adjuvant approach if intention is to still include local/regional therapies)
- Clinical trial first line if available
- Consider local regional therapy (surgery/radiation) if there is a sustained response to initial systemic therapy
- If unable to complete local regional therapy due to extensive metastatic disease, then standard is systemic therapy and often times can consider palliative radiation to the breast

Making Cancer History®

LOCAL RECURRENCE RATES

Hx of Soft Tissue Recurrence- Data 2007

- Risk of local soft tissue recurrence in locally advanced breast cancer over 5–10-year estimate is around 6.6-7% versus 15.1-15.6 % in IBC as of data from 2007



(Cristofanilli et. al, 2007)

Local Regional Recurrence

MDACC Study Stecklein et. al 2019

- 5.7% LRR probability at 4 years
- Rate observed when utilizing trimodally approach
- Much lower than older studies
- Largely due to advancements in systemic treatment, surgical and radiation techniques

(Whelan et al., 2006)

Making Cancer History®

KOMEN SCORING SYSTEM

Inflammatory Breast Cancer

Komen Scoring System

Priority Factor	Characteristic	Score		
		3	2	1
3	Timing of signs/symptoms	≤ 3 months	3-6 months	>6 months
3	Skin changes	Any peau d'orange	Skin edema/thickening over ≥ 1/3 of the breast	Focal skin edema/thickening (< 1/3 of the breast)
3	Swelling/engorgement of the breast	Clinically apparent enlargement of the breast or new asymmetry in breast size		Breast edema identified on imaging but not clinically detectable
2	Erythema or other skin discoloration: pink, red, darkened, bruising/purplish or serpiginous in character (2)	Complete or near complete involvement of the breast	Not nearly complete but greater than minimal involvement of the breast	Minimal involvement or ambiguous color change
2	Nipple abnormalities (2)	New nipple inversion	New nipple flattening or other asymmetry	Crusting of the nipple/areola without other nipple changes
2	Lymphatic emboli (2)	Dermal lymphatic emboli present without evidence of direct involvement of the dermis or epidermis	Non-dermal lymphatic emboli present in breast parenchyma or stoma	
1	Breast imaging	Diffuse involvement of breast parenchyma, with or without dominant mass		Enlargement of non-axillary nodes (internal mammary, supraclavicular, subpectoral, etc)

27 (Jagsi et al, 2022)

Scoring rubric/multipliers determine score and likelihood of IBC

Score:
≥42: Definitely IBC
25-41: Strong possibility of IBC
14-24: Weak possibility of IBC
<14: Not IBC

*Skin thickening may be assessed on clinical examination or observed on breast imaging

MD ANDERSON CANCER CENTER

Making Cancer History®

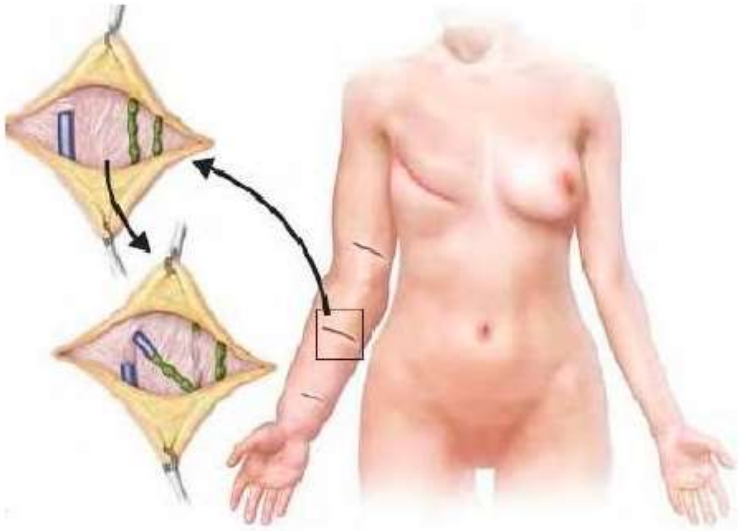
LYMPHEDEMA

MDACC Study of Lymphedema in IBC

- N=83 treated with trimodal therapy between 2016-2019
- Median follow up 33 months
- Incidence of lymphedema = 50.6% (n=42)
- Treatments received:
  - 95.2% received treatment
  - 42.9% received surgical treatment

29 (Farley et al., 2022)

Surgical Treatment of Lymphedema



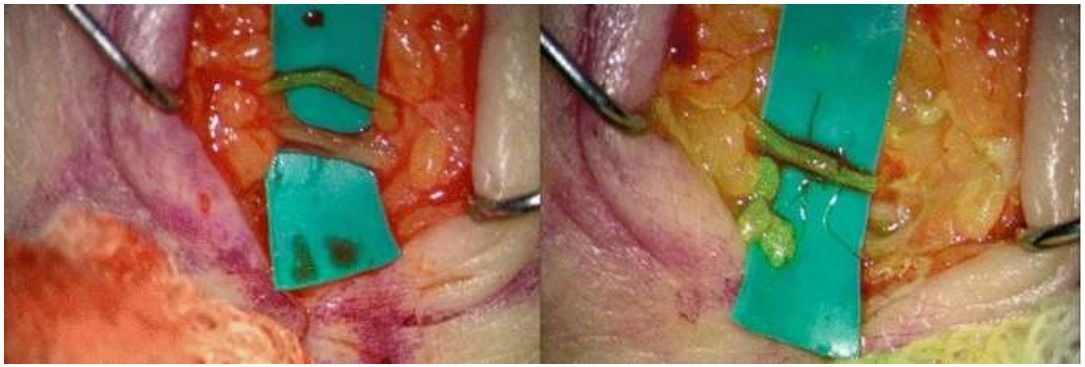
(Sakra World Hospital, 2024)

Therapeutic Lymphovenous Bypass (LVB)

(Wendling, 2016)

Prophylactic Lymphovenous Bypass

- Purpose is to PREVENT lymphedema
- Performed during MRM
- Axillary reverse mapping allows for identification of arm lymphatic channels
- Arm lymphatic channels preserved during axillary dissection and anastomosed to branches of axillary vein



(Park et al., 2022)

Making Cancer History®

I AM IBC

IBC Pictorial Review

I AM IBC

"Not Classic"

A

- Not swollen
- No nipple asymmetric
+ Diffuse redness (but not uniform)

"Classic"

B

+ Swollen
+ Flattened Nipple
+ Diffuse skin change

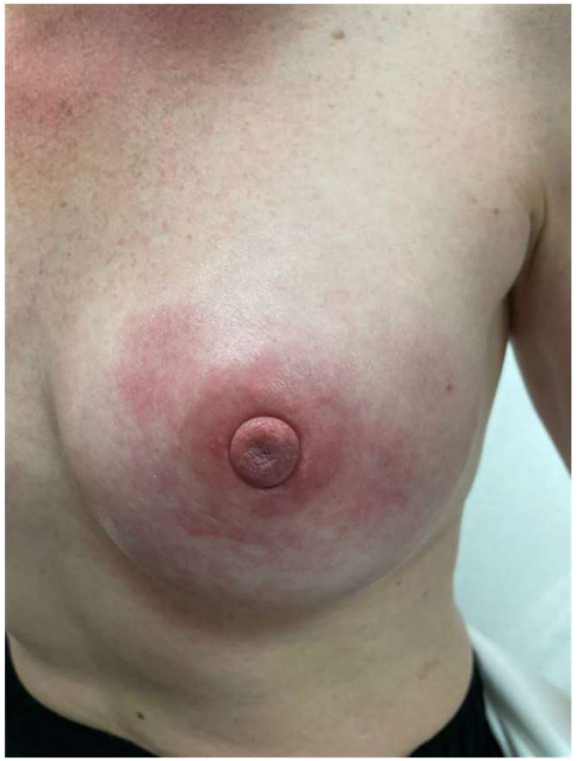
(Balema et al., 2021)

Inflammatory Breast Cancer

I AM IBC

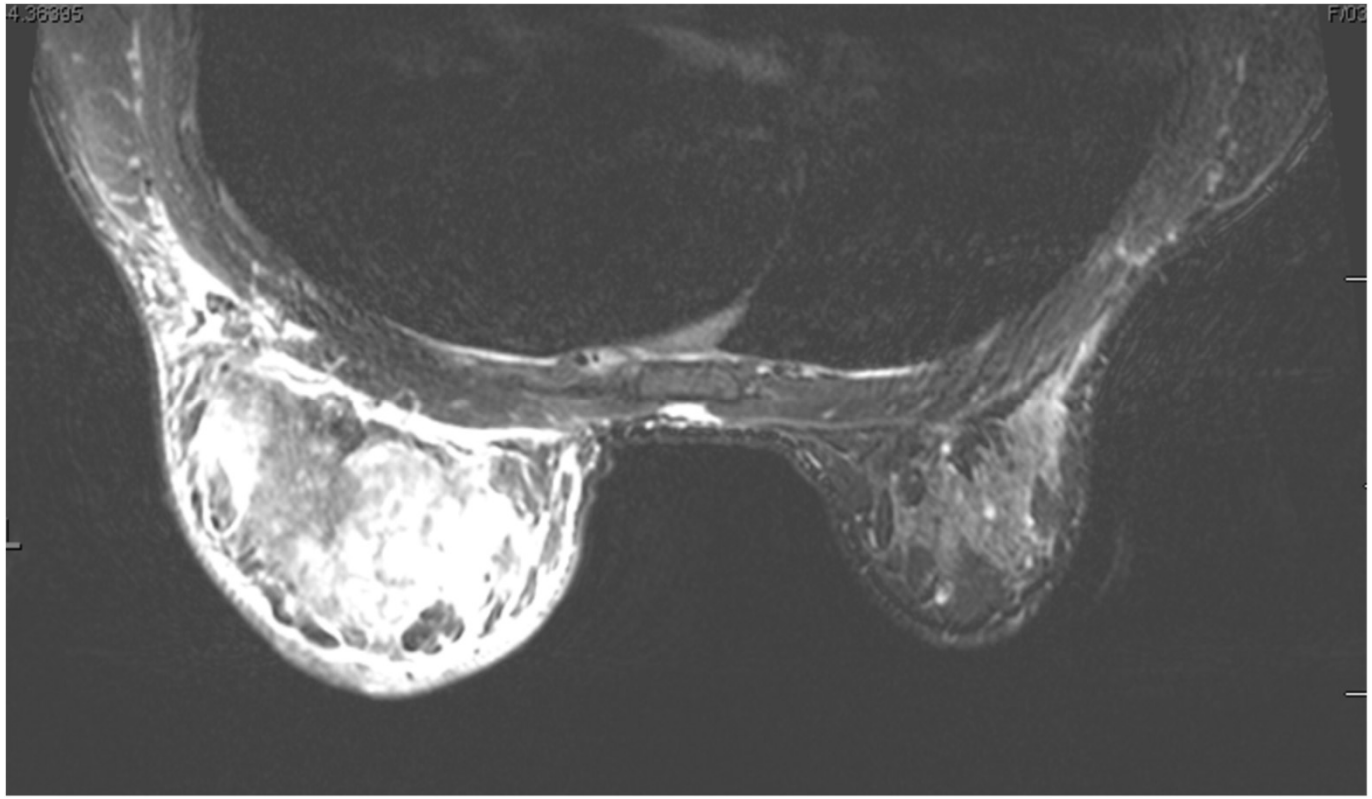
Inflammatory Breast Cancer

I AM IBC



Inflammatory Breast Cancer

I AM IBC

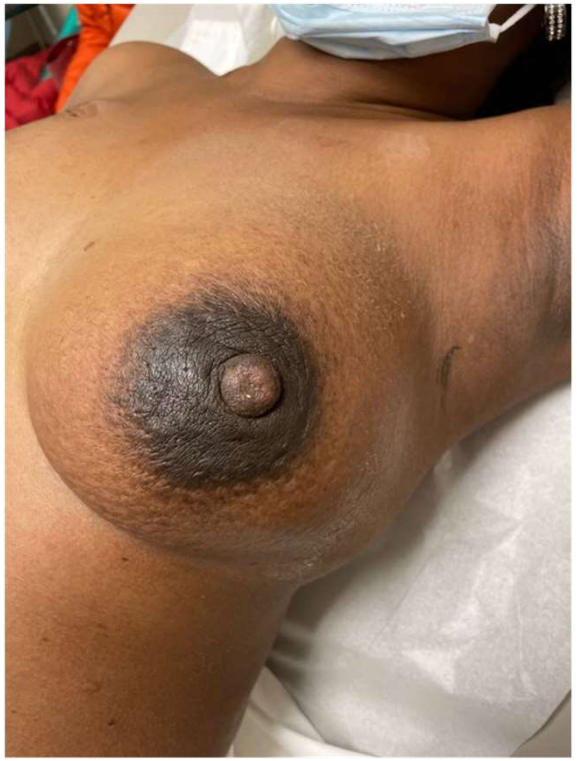


37

MD ANDERSON CANCER CENTER

Inflammatory Breast Cancer

I AM IBC

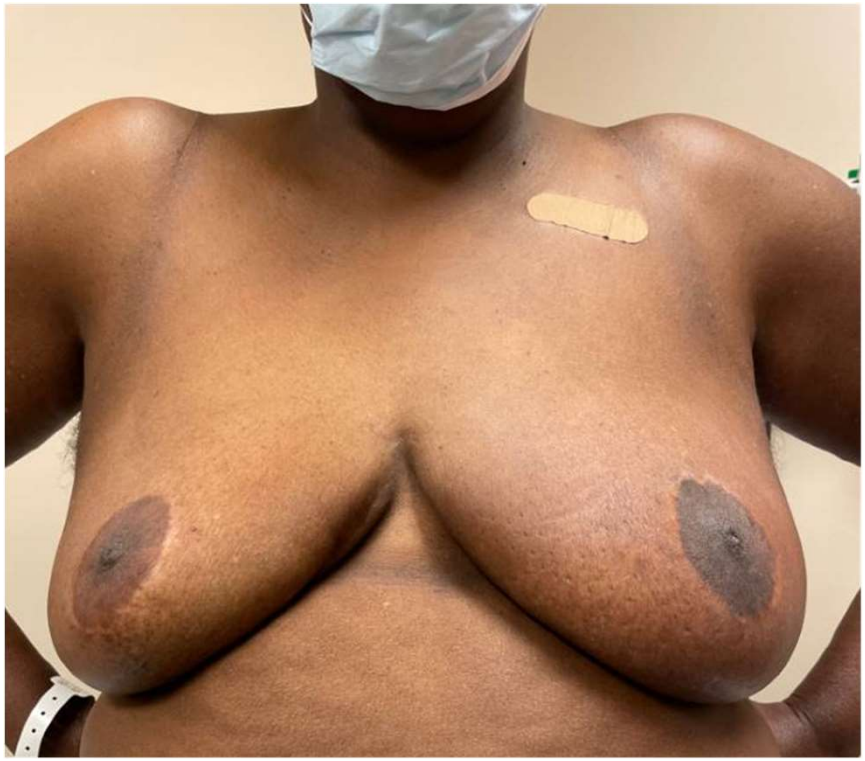


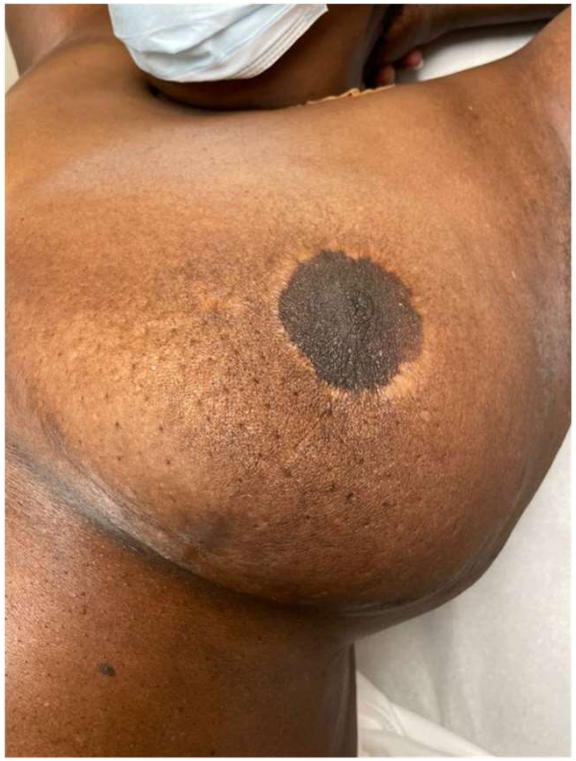
Inflammatory Breast Cancer

I AM IBC

Inflammatory Breast Cancer

I AM IBC



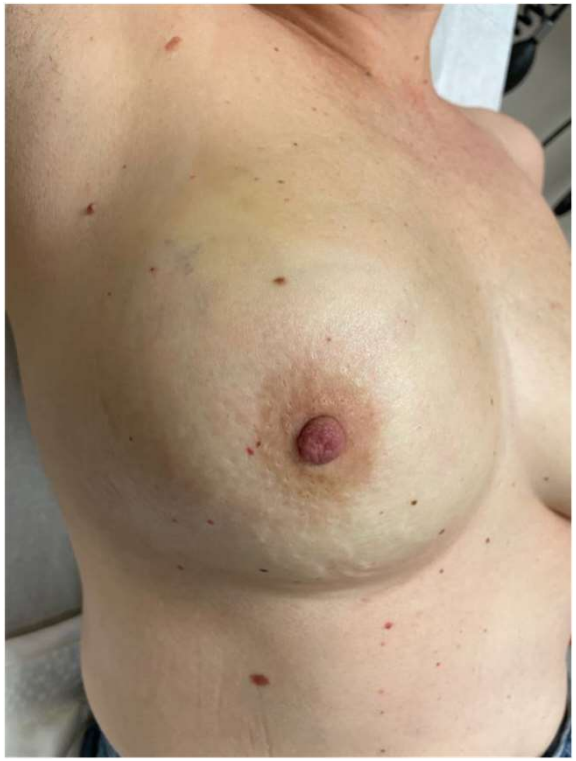


40

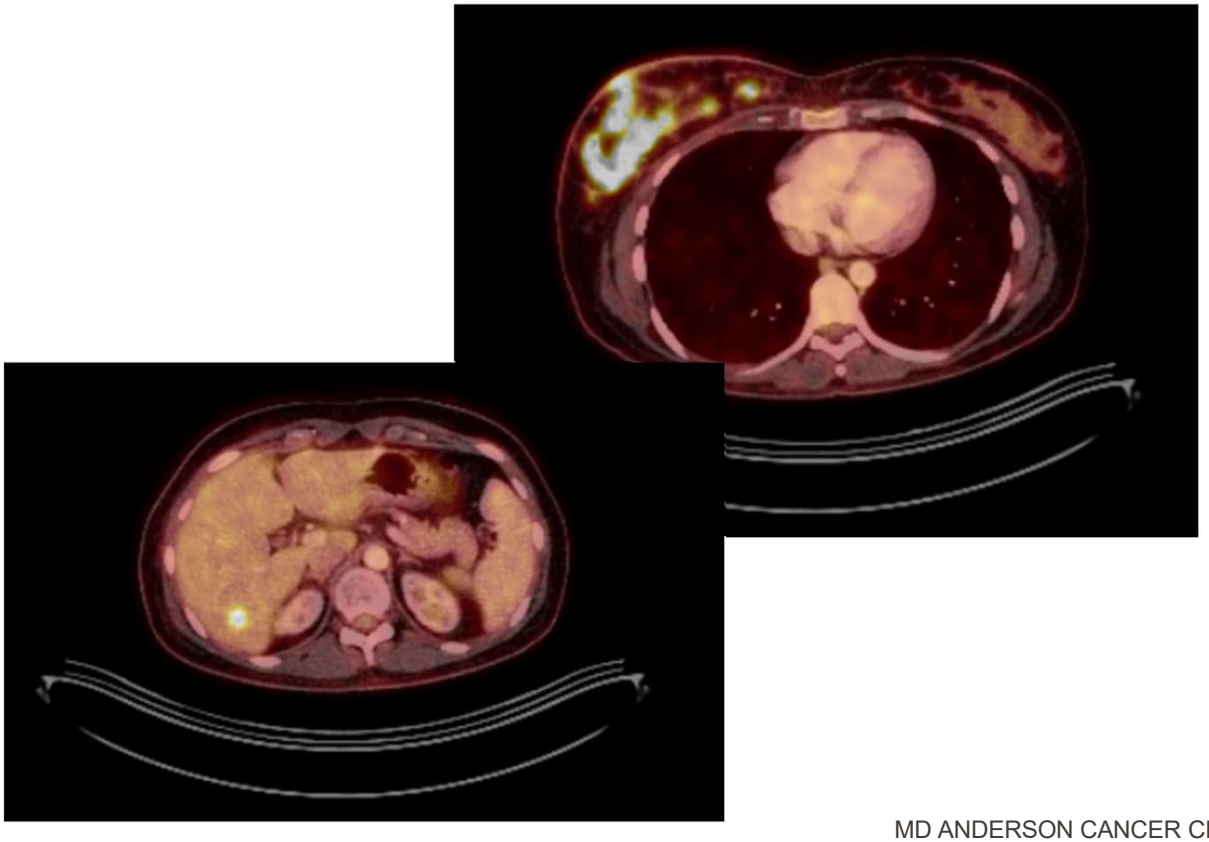
MD ANDERSON CANCER CENTER

Inflammatory Breast Cancer

I AM IBC

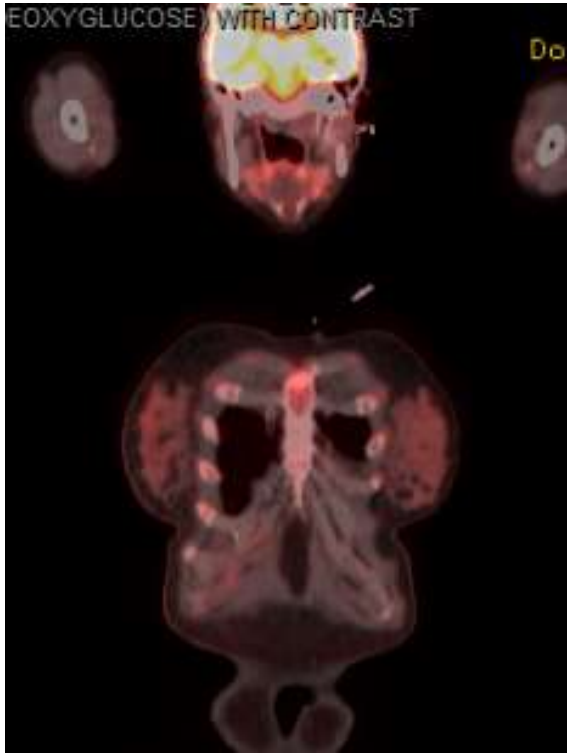


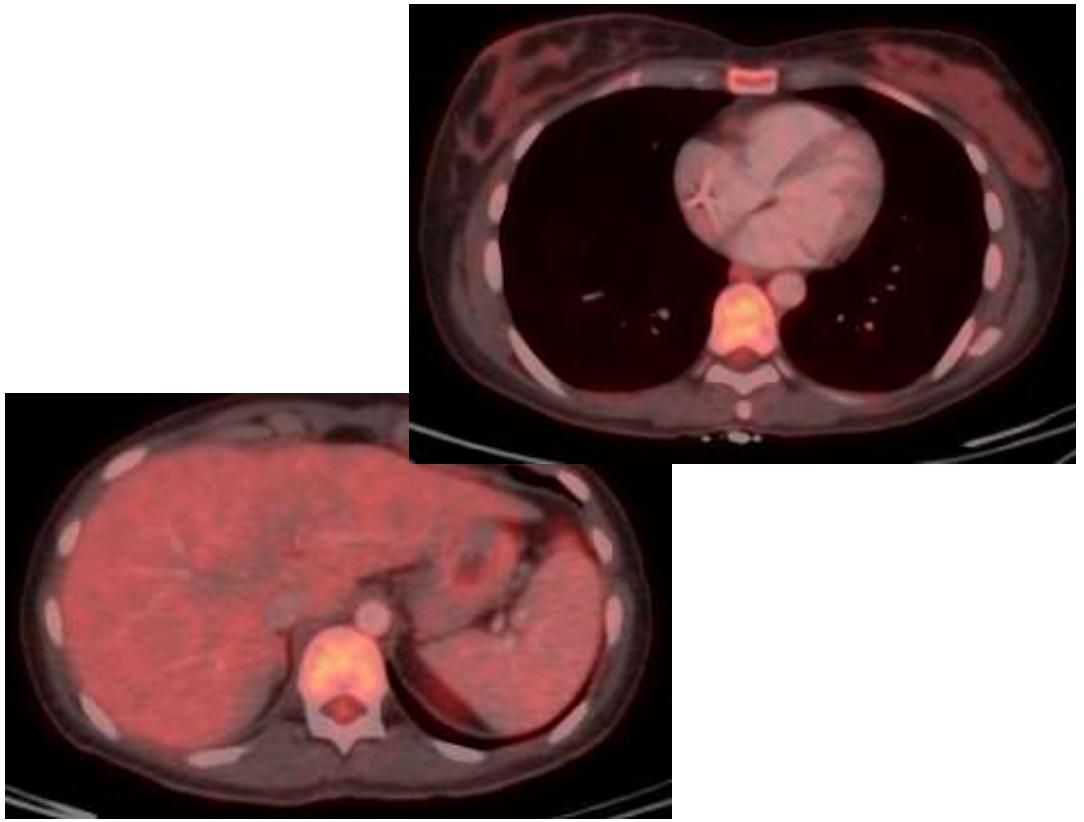
I AM IBC Patient Case Cont…



MD ANDERSON CANCER CENTER

Patient Case Cont… 3-month FU Scans





Making Cancer History®

RECOMMENDATIONS

Advice to Providers and Patients

- Newly developed skin lesion? Biopsy!
- New breast redness workup:
  - Obtain imaging: MMG/US, review carefully for skin change
  - If negative: 1-2 weeks of conservative management with follow up
  - IBC has been diagnosed in pregnant and lactating women
  - If unresolved: MRI (non pregnant pt) +/- skin punch biopsy. If pregnant, MMG with fetal shielding + US +/- skin punch biopsy.
    - If negative: 3 month follow up with advice to return and re-image
      - ➢ If progresses, consult dermatology

Making Cancer History®

KEY POINTS

Key Points To Remember

- Atypical breast cancer presentation/Can have breast cancer with NO mass
- A presumed breast infection is not always an infection!
- Skin change presentation is different in different skin tones
- Breast swelling and nipple inversion are common
- Short follow up, good RTC instructions when treating suspected mastitis without fever
- Don't hesitate to get imaging; MRI is very sensitive
- Biopsy if symptoms don't resolve and clear diagnosis isn't made
- Direct and efficient referral system can facilitate the process of accurate and timely diagnosis and treatment

47

Inflammatory Breast Cancer

References

American Cancer Society 2024. Mastectomy. Retrieved from https://www.cancer.org/cancer/types/breast-cancer/treatment/surgery-for-breast-cancer/mastectomy.html

Balema, W., Liu, D., Shen, Y., El-Zein, R., Debeb, B. G., Kai, M., Overmoyer, B., Miller, K. D., Le-Petross, H. T., Ueno, N. T., & Woodward, W. A. (2021). Inflammatory breast cancer appearance at presentation is associated with overall survival. Cancer medicine, 10(18), 6261–6272. https://doi.org/10.1002/cam4.4170

Cristofanilli, M., Valero, V., Buzdar, A.U., Kau, S.-W., Broglio, K.R., Gonzalez-Angulo, A.M., Sneige, N., Islam, R., Ueno, N.T., Buchholz, T.A., Singletary, S.E. and Hortobagyi, G.N. (2007), Inflammatory breast cancer (IBC) and patterns of recurrence. Cancer, 110: 1436-1444. https://doi.org/10.1002/cncr.22927

Farley, C. R., Irwin, S., Adesoye, T., Sun, S. X., DeSnyder, S. M., Lucci, A., Shaitelman, S. F., Chang, E. I., Ueno, N. T., Woodward, W. A., & Teshome, M. (2022). Lymphedema in Inflammatory Breast Cancer Patients Following Trimodal Treatment. Annals of surgical oncology, 29(10), 6370–6378. https://doi.org/10.1245/s10434-022-12142-7

Hosomi K, Banda CH, Shiraishi M, Mitsui K, Ishiura R, Danno K, Narushima M. (2023). Vascularized lymph node transfer with efferent lymphatico-lymphatic anastomosis for treatment of upper extremity lymphedema. Plastic and Aesthetic Research, 10(60), http://dx.doi.org/10.20517/2347-9264.2023.77

Jagsi, R., Mason, G., Overmoyer, B.A. et al. Inflammatory breast cancer defined: proposed common diagnostic criteria to guide treatment and research. Breast Cancer Res Treat 192, 235–243 (2022). https://doi.org/10.1007/s10549-021-06434-x

Kuksis, M., Gao, Y., Tran, W., Hoey, C., Kiss, A., Komorowski, A. S., Dhaliwal, A. J., Sahgal, A., Das, S., Chan, K. K., & Jerzak, K. J. (2021). The incidence of brain metastases among patients with metastatic breast cancer: a systematic review and meta-analysis. Neuro-oncology, 23(6), 894–904. https://doi.org/10.1093/neuonc/noaa285

Menta, A., Fouad, T. M., Lucci, A., Le-Petross, H., Stauder, M. C., Woodward, W. A., Ueno, N. T., & Lim, B. (2018). Inflammatory Breast Cancer: What to Know About This Unique, Aggressive Breast Cancer. The Surgical clinics of North America, 98(4), 787–800. https://doi.org/10.1016/j.suc.2018.03.009

Inflammatory Breast Cancer

References cont..

Park, J.Kh., Seo, J., Yang, E.J. *et al.* Association of lymphatic flow velocity with surgical outcomes in patients undergoing lymphovenous anastomosis for breast cancer-related lymphedema. *Breast Cancer* 29, 835–843 (2022). https://doi.org/10.1007/s12282-022-01363-z

Schairer, C., Soliman, A. S., Omar, S., Khaled, H., Eissa, S., Ayed, F. B., Khalafallah, S., Ayoub, W. B., Kantor, E. D., Merajver, S., Swain, S. M., Gail, M., & Brown, L. M. (2013). Assessment of diagnosis of inflammatory breast cancer cases at two cancer centers in Egypt and Tunisia. Cancer medicine, 2(2), 178–184. https://doi.org/10.1002/cam4.48

Stecklein, S. R., Rosso, K. J., Nuanjing, J., Tadros, A. B., Weiss, A., DeSnyder, S. M., Kuerer, H. M., Teshome, M., Buchholz, T. A., Stauder, M. C., Ueno, N. T., Lucci, A., Woodward, W. A. (2019). Excellent Locoregional Control in Inflammatory Breast Cancer With a Personalized Radiation Therapy Approach. Practical Radiation Oncology, 9(6), 402-409. https://doi.org/10.1016/j.prro.2019.05.011

Warren, L. E., Guo, H., Regan, M. M., Nakhlis, F., Yeh, E. D., Jacene, H. A., Hirshfield-Bartek, J., Overmoyer, B. A., & Bellon, J. R. (2015). Inflammatory breast cancer and development of brain metastases: risk factors and outcomes. Breast cancer research and treatment, 151(1), 225–232. https://doi.org/10.1007/s10549-015-3381-8

Watase, C., Shiino, S., Shimoi, T., Noguchi, E., Kaneda, T., Yamamoto, Y., Yonemori, K., Takayama, S., & Suto, A. (2021). Breast Cancer Brain Metastasis-Overview of Disease State, Treatment Options and Future Perspectives. Cancers, 13(5), 1078. https://doi.org/10.3390/cancers13051078

Wendling, P. 2016. Lymphedema microsurgery gaining momentum. Retrieved from https://www.mdedge.com/surgery/article/105865/general-surgery/lymphedema-microsurgery-gaining-momentum

Whelan, M., Larkin, J., Collins, C., Cashman, J., Breathnach, O., Soden, D., & O'Sullivan, G. (2006). Effective treatment of an extensive recurrent breast cancer which was refractory to multimodal therapy by multiple applications of electrochemotherapy. Ejc Supplements - EJC SUPPL. 4. 32-34. 10.1016/j.ejcsup.2006.07.006


MD Anderson Cancer Center

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®