CASE PRESENTATION

Presenter: PGY 陳亭安
Supervisor: 常傳訓 主任
2015/03/22

PATIENT DATA

- OOO 48 y/o F xxxxxxx
- Allergy: no known allergy
- DM (–), HTN (+)
- Operation history: none
- Personal history: non contributory
- Family history: none
- Denied hormonal replacement therapy, OCP or endocrine disease

- Date of admission: 3/13

CHIEF COMPLAINT

- Palpable mass in right breast for 8 years

Present history

- 2008 palpable mass in right lateral breast
  → 1cm, non tender, immobile

- 2014/03 progressive enlargement
  2014/10 went to XX醫院 for survey
  → stage IV breast cancer
  ➔ denial and refused treatment

Present history

- Breast sonography 2014/10/14　　XX醫院

Multicentric invasive carinoma of R' breast over UOQ and upper central region, with R' axillary metastatic lymphpadenopathy
→ BIRAD: 5 ➔ highly suggestive of malignancy

- Mammography 2014/10/14　　XX醫院

multiple microcalcifications
→ suspicious of R' malignant breast tumor with metastatic axillary lymphadenopathy
→ BIRAD: 4c

Present history

- Chest CT 2014/10/15 XX醫院

  Right breast multicentric cancer with right axillarty metastasis lymphadenopathy
  with right lung metastasis and liver metastasis

- Core needle biopsy 2014/10/24 XX醫院

  Invasive ductal carcubinam grade II/III with intraductal carcinoma, ER(+), PR (+), Her2/neu 2+ (IHC), FISH (–)

- Suggest neoadjuvant chemotherapy
  → patient refused and decided to seek Chinese medicine for help

Present history

- Chest CT 2015/02/21 XX醫院

Right breast multicentric cancer with right axillarty metastasis lymphadenopathy
with right lung and liver metastasis
r/o right 7th rib metastasis

Present history

- 2016 1 cm ulcerated wound of right lateral breast→ went back to XX醫院
- Chest CT 2016/02/23

  Right breast multicentric cancer with right axillary metastasis lymphadenopathy and bilateral lung metastasis and liver metastasis

- Whole body one scan 2016/02/24

  Increased radioactivity of sternum, T5, L2, posterior L' 10th rib, lateral L' 6th rib, posterior L' acetabulum

Present history

- Dg: right breast locally advanced cancer $cT_{4c}N_{3a}M_1$, stage4, with bone, liver, lung metastases, ER (+), PR (+), Her2/neu (2+, IHC) , FISH (–)
- 2016/02/24 1# course neoadjuvant chemotherapy with *taxotere* 120mg + *herceptin* 440mg at XX醫院 from peripheral line → chemical cellulitis due to drug leakage
- Patient decided to transfer to our service.

Present history

- 2016/03/02 to Dr. 常傳訓's OPD
- Breast sonography

Compatible with breast cancer (more than 5x5 cm) in right breast with multiple satellite nodules and axillary lymphadenopathy
→ BIRADS: 5 ➔ highly suggestive of malignancy

- ECG: myocardial ischemia
- Cardioecho:

preserved systolic function, dilated ascending aorta root

Present history

- Patient decided to receive treatment in our hospital.
- Arrange admission on 3/13.

right breast locally advanced cancer cT4cN3aM1, stage4, with bone, liver, lung metastases, ER (+), PR (+), Her2/neu (2+, IHC) , FISH (-)

Review of system

- General：Fever(-), Chills(-), Fatigue(-) weight loss(-)
- Skin：Rash(-), Itching(-), Cyanosis(-), Jaundice(-), Hyperpigmentation(-),
- Eyes：vision disturbance(-), Diplopia(-),
- HEENT : Tinnitus(-), Postnasal drip(-), Hoarseness(-), Gum bleeding(-), Chocking(-), Vertigo(-), Cough(-), Sputum(-), Headache(-), Dizziness(-), Rhinorrhea(-), Nasal congestion(-), Sore throat(-),
- Cardio-Respiratory：
  Shortness of breath(-), Hypertension(-), Dyspnea on exertion(+), Palpitation(-), night cough (-), Orthopnea(-), Claudication(-), Chest tightness(-), Chest pain(-), PND(-)

Review of system

- G.I：Poor appetite(-), Vomiting, Tarry stool(-), Abdominal fullness(-), Ascites(-), Dysphagia(-), Abdominal pain(-), Bowel habit change(-), Hemorrhoids(-), Constipation(-), Diarrhea(-),
- G.U：Frequency(-), Urgency(-), Nocturia(-), Dysuria(-), Oliguria(-), Hematuria(-), Tea color urine(-), Retention(-), Incontinence(-), Flank pain(-)
- Limbs：edema (-)　weakness (-)　limited ROM(-)
- Neuro-Psychiatric：

  Unconsciousness(-), Syncope(-), paralysis (-) Sensation change(-), Convulsion(-), Memory loss(-), Coordination(-), Depression(-)

Physical examination

- Height/weight: 167 cm/83 kg
- Vital signs: 36.6/64/18 BP: 147/96 mmHg
- General appearance: fair, no acute discomfort, no cyanosis appearance
- HEENT: no visual acuity deformity, no palpable LAP
- Chest: symmetrical and normal expansion; normal breathing sounds.
- Breast: right palpable mass, stiff, non tender, immobile, 9’ ulcerated skin wound, 1cm, no nipple retraction, no discharge
- Heart: Regular heart beats, no murmur audible, no carotid bruits or thrills; PMI over left 5th MCL
- Abdomen: Flat and soft; non tender non distended; normal active bowel sounds
- Back: lower back tenderness(-),
- Extremities: left forearm dry darkened skin, no limited ROM

Lab

CBC		
WBC	1.6	10^3/uL
RBC	4.94	10^6/uL
HGB	13.7	g/dL
HCT	40.8	%
MCV	82.6	fL
MCH	27.7	pg
MCHC	33.6	g/dL
PLT	244	10^3/uL
DIFF		
NEUT%	27.8	%
BAND	8.3	%
LYMPH%	42.6	%
MONO%	17.6	%
EO%	1.9	%
BASO%	0.0	%
ATYPICAL LYMPH	1.9	%
Gaint Platelet	Positive	

BUN	16.8	mg/dL
Creatinine	0.63	mg/dL
eGFR	100	
AST	42	IU/L
ALT	42	IU/L
Na	135	mmol/L
K	4.8	mmol/L
Cl	100	mmol/L

HBsAg	0.040	IU/mL
Anti-HBs	0.0	mIU/mL
Anti-HBc	0.11	S/CO
Anti-HCV	0.13	S/CO

CEA	13.5	ng/mL
CA125	15.0	U/mL
CA153	124.3	U/mL
CA199	18.7	U/mL

Diagnosis

- Metastatic breast cancer with progression (2014/10/15- 2016/2/23), cT4N3aM1, stage 4
- Initial right breast upper outer & central 9'-12' locally advanced, multicentric, invasive ductal carcinoma, cT3aN1M1, stage 4, ER (+), PR (+), Her2/neu (2+, IHC) , FISH (-) with bone, liver and lung metastases
- left forearm chemical cellulites post chemotherapy extravasation

Plan to do

- Port-A implantation
- Consult PS for left forearm extravasation
- Thorough explanation to patient and family.
- Consult hospice, R/T, dentist

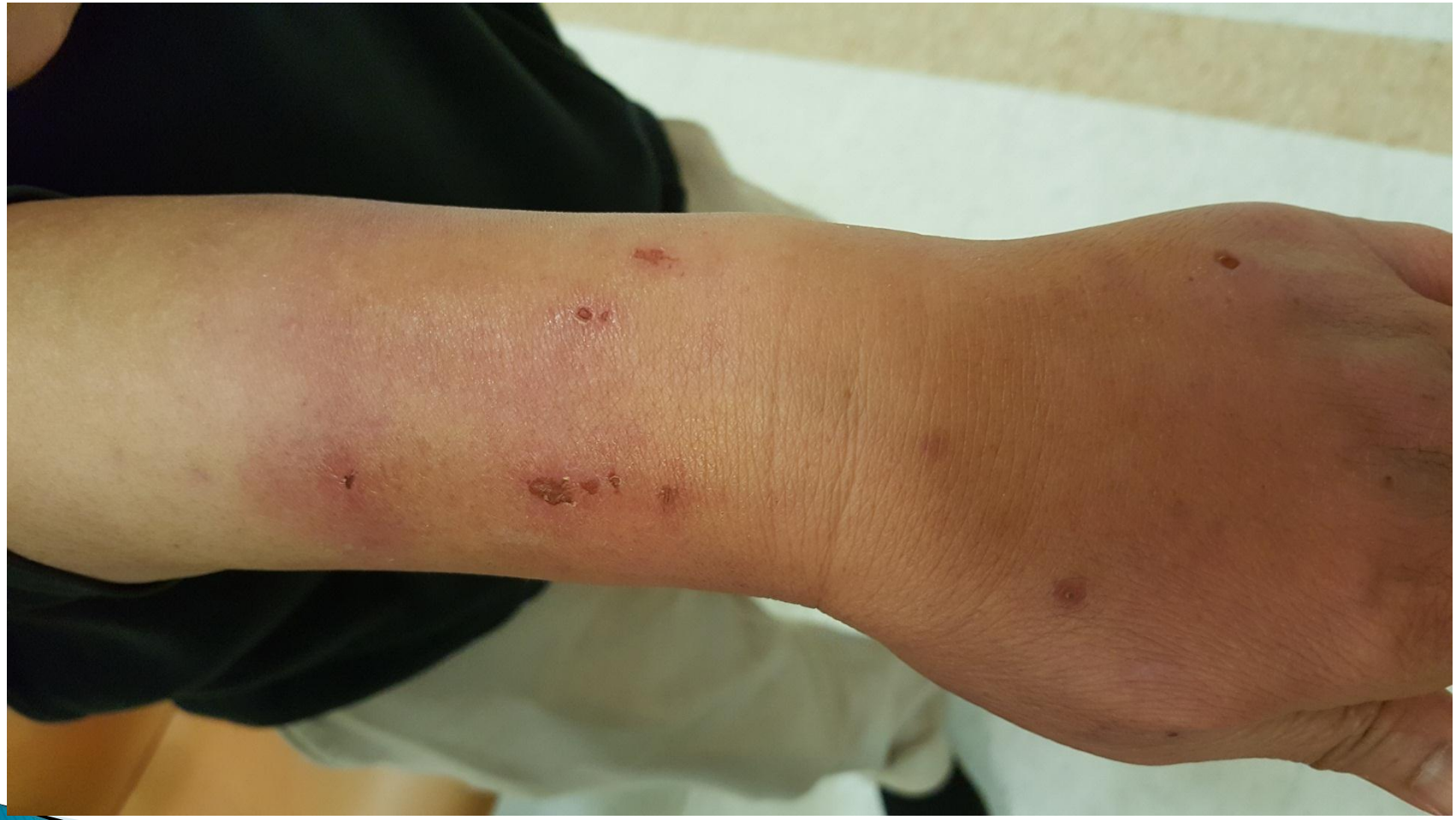
Hospital course

- 2016/03/13 admission
- 2016/03/14 am port-A implantation
- 2016/03/14 pm disease explanation to patient and family
  → consult hospice, R/T, dentist
  → consult PS for left arm: Neomycin Oint 0.5% 28gm wound care
- 2016/03/15 initiate hormonal therapy with *Femara* 2.5mg 1# QDPC
- 2016/03/17 discharge with continuation of *Femara* medications

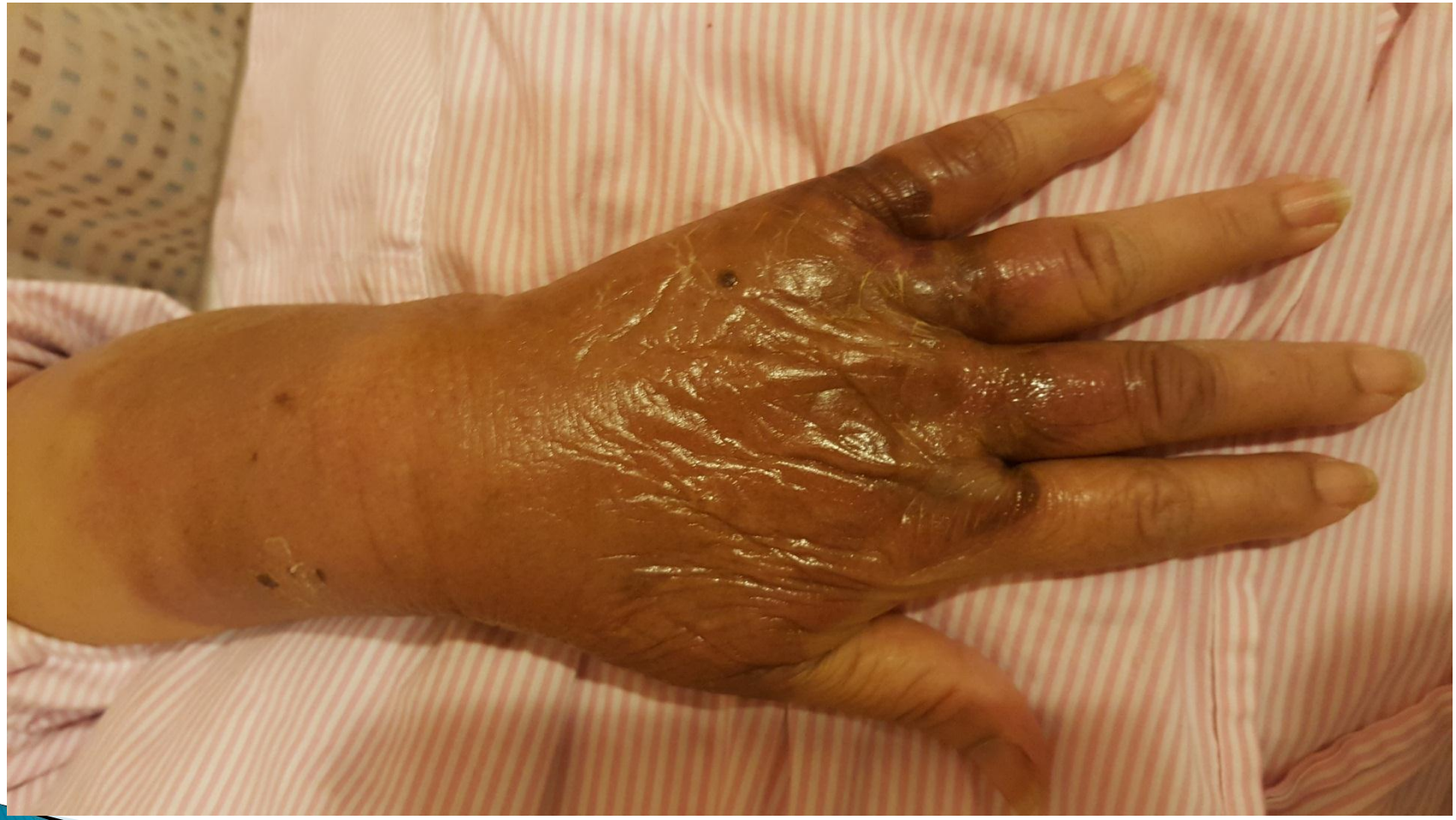
Discussion

- Chemotherapy extravasation skin reaction

PATIENT'S HAND



PATIENT'S HAND



Cytotixic drug extravasation

- local skin reactions that occur when the drug escapes from the veins or IV catheter into the skin (extravasation).

- divided into 2 types:
  irritants
  vesicants

Irritants

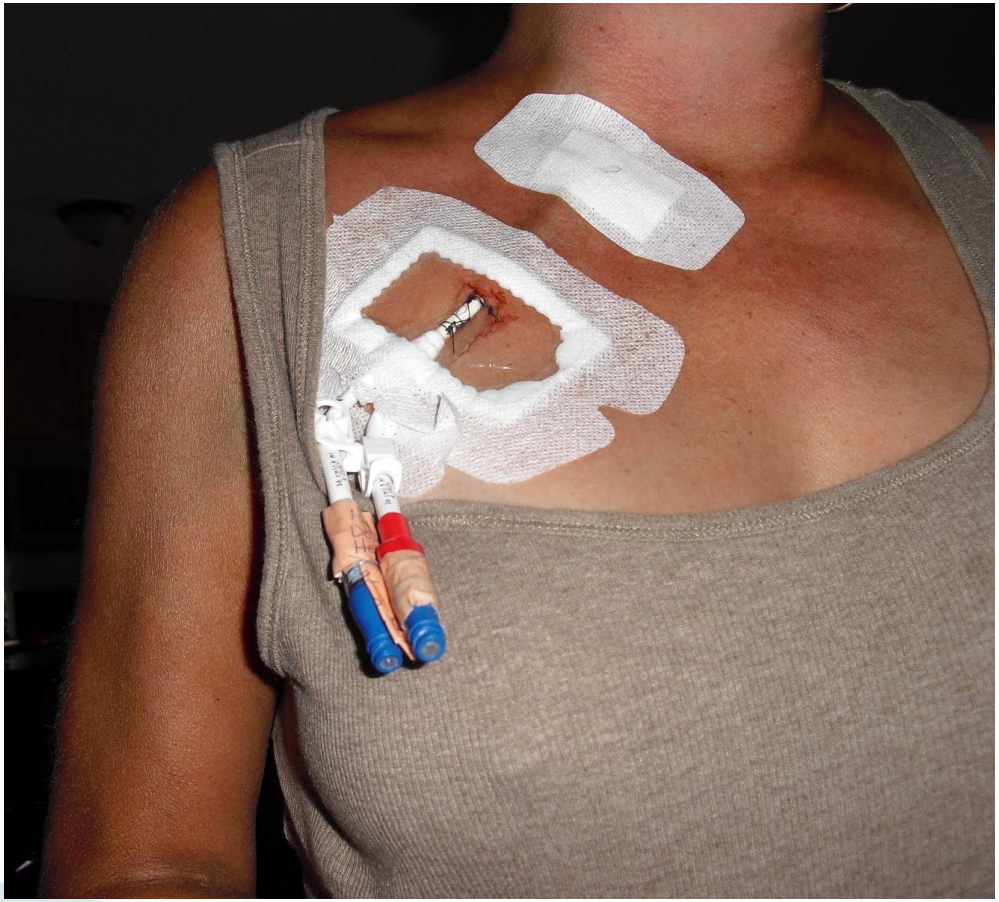
- cause a short-lived and limited irritation to the vein
- Symptoms: tenderness, warmth, itchness or redness along the vein or at the injection site
- A variation to this is a hypersensitivity "flare reaction" at the injection site
- agents include: bleomycin, carboplatin, cisplatin, dacarbazine, denileukin difitox, doxorubicin, doxorubicin liposome, etoposide, streptozocin, teniposide, thiotepa, vinorelbine.

Vesicants

- chemical cellulitis
- initially similar to irritation→ may worsens over days
- Symptoms: redness , blistering, itchness without pain → symptoms may be delayed for up to 6-12 hours
- Severity depends on the drug, the amount and concentration of the exposure, and the immediate measures taken once the extravasation occurs
- agents include: daunorubicin, doxorubicin, epirubicin, idarubicin, mitomycin, mitoxantrone, paclitaxel, tenoposide, vinblastine, vincristine.

Managements

- **Prevention** is the key!
- Proper selection of venous access device
  - PICC
  - tunnel catheter
  - port-A



Managements

- Discontinue injection and remove as much of as possible from the injection site

- Ice (or heat) compression to injection site
  → heat compression if vincristine, vinblastine.

- Various antidotes available based on the drug and the amount of drug infused.
  → Hyaluronidase: *controversial*

Managements

- Chemical cellulitis
  → prevent secondary infections
  → topical care

- Keep IV hydration and supportive care

- Careful observation and explanation to patient.

Discussion

- Treatment choices for stage IV breast cancer

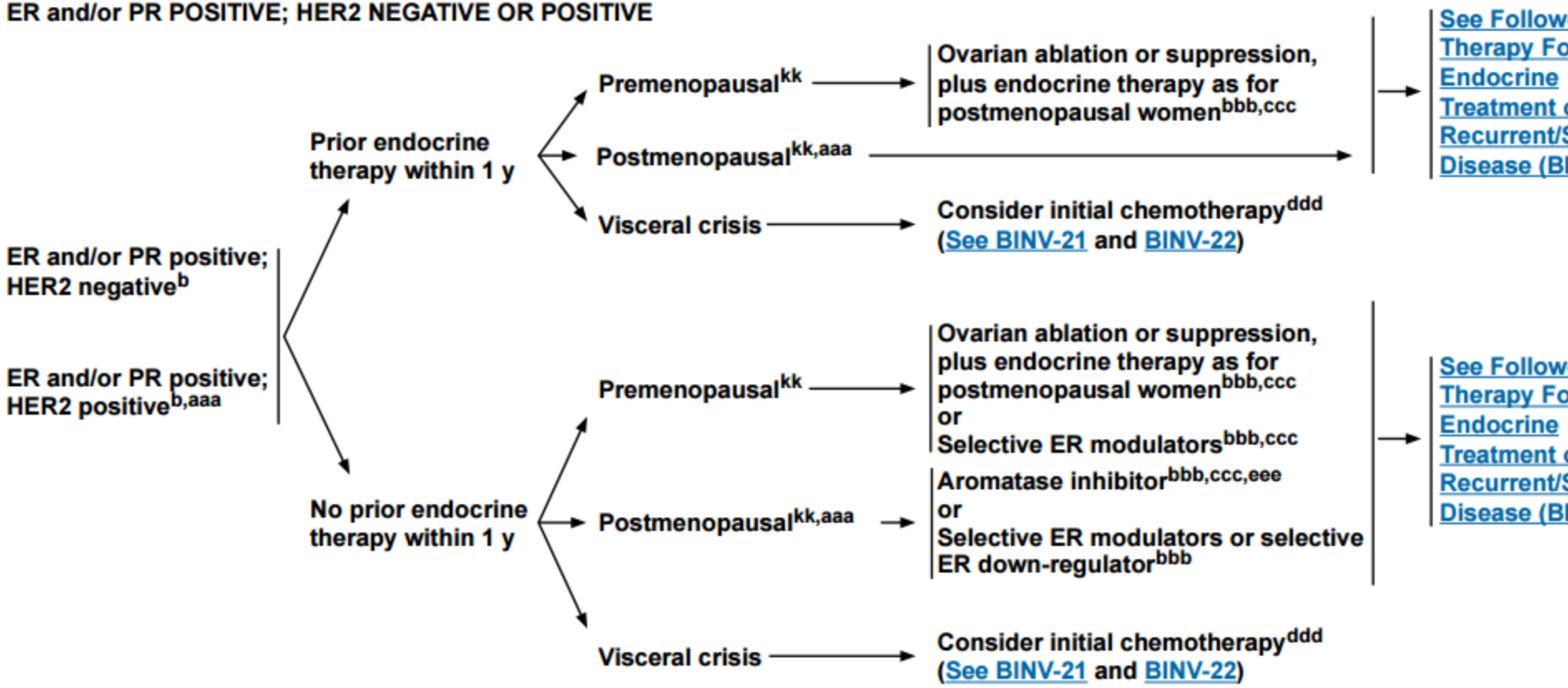
NCCN guideline for stage IV disease ER and/or PR (+); HER2 (–)

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Invasive Breast Cancer

NCCN Guideline
Breast Cancer Table of C
Dis

SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE
ER and/or PR POSITIVE; HER2 NEGATIVE OR POSITIVE



Letrozole (*Femara)*

- oral non-steroidal aromatase inhibitor
- In postmenopausal women, production of estrogen by the conversion of androgens through aromatase enzyme.
  → inhibition of enzyme decrease estrogen production.
- most common side effects: hypoestrogenism, sweating, hot flashes, arthralgia, fatique, osteoporosis

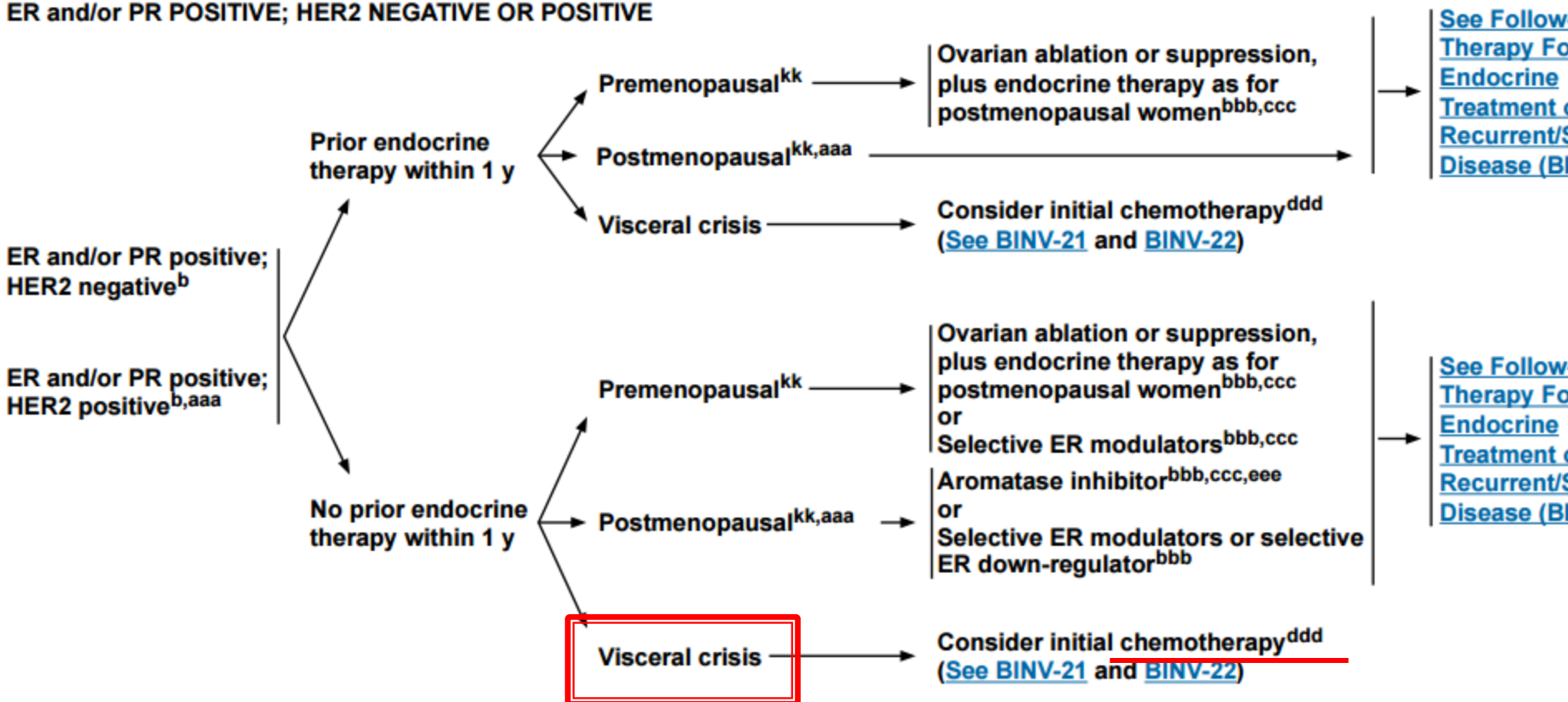
NCCN guideline for stage IV disease ER and/or PR (+); HER2 (+)

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Invasive Breast Cancer

NCCN Guideline
Breast Cancer Table of C
Dis

SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE
ER and/or PR POSITIVE; HER2 NEGATIVE OR POSITIVE



Visceral crisis

- defined as severe organ dysfunction
  → assessed by signs and symptoms, laboratory studies, and rapid progression of disease.

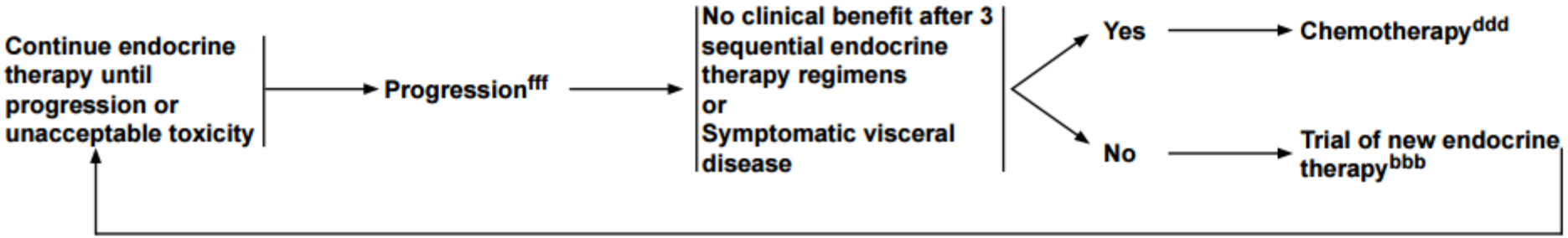
- NOT just visceral metastases→ clinical indication for rapid efficacious therapy

- lymphangitic lung metastases, bone marrow replacement, carcinomatous meningitis, or significant liver metastases.

- It is recommended that patients with symptomatic visceral metastases receive chemotherapy, whereas patients with asymptomatic visceral disease receive endocrine therapy.

- In visceral crisis, current guidelines recommend chemotherapy to achieve rapid symptom control.

FOLLOW-UP THERAPY FOR ENDOCRINE TREATMENT OF RECURRENT OR STAGE IV DISEASE

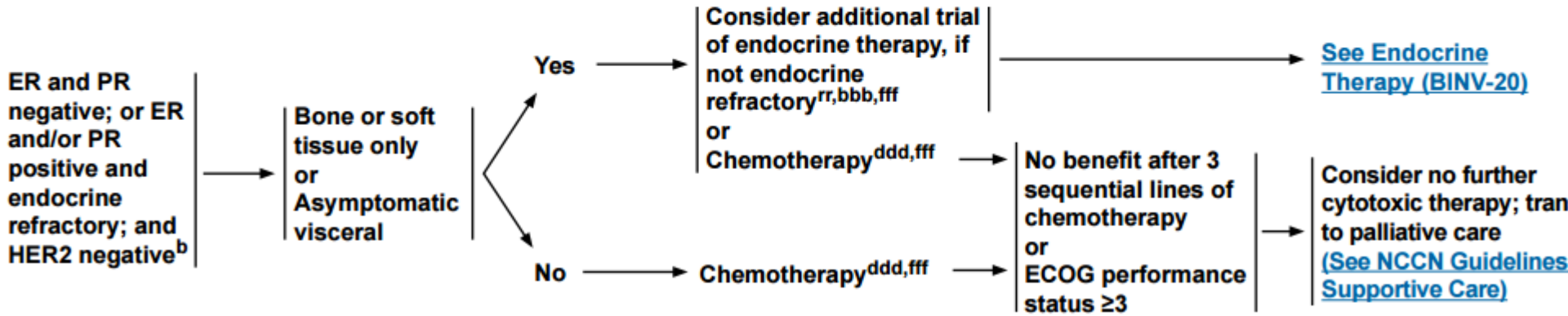


National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Invasive Breast Cancer

NCCN Guidelines
Breast Cancer Table of Co
Discu

SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE
ER and PR NEGATIVE; or ER and/or PR POSITIVE and ENDOCRINE REFRACTORY; HER2 NEGATIVE



Current treatment plan

- Hormonal therapy first
- Combine radiotherapy→ palliative care

- Consider target therapy with everolimus (*afinitor)*→ mTOR inhibitor

- Visceral crisis→ consider chemotherapy

Back to the patient

WHAT WERE YOU THINKING!?!?!?

Back to the patient

- Denial attitude
- Fear of the truth
- Inadequate resources?
- Mistrust of physician

Back to the patient

- Denial attitude
- Fear of the truth
- Inadequate resources?
- Mistrust of physician
- Supportive system
- Power of religion
- Finally a trustworthy doctor!
- Acceptance of disease

ACGME 六大核心能力

Medical Knowledge

Professionalism

Interpersonal & communication

Patient care

System based practice

Practice based learning

Reference

- NCCN guideline for breast cancer treatment 2016
- Extravasation: a dreaded complication of chemotherapy- D. L. Schrijvers, *Annals of Oncology 14 (Supplement 3), 2003*
- ESO-ESMO 2nd international consensus guidelines for advancedbreast cancer (ABC2) – F. Cardoso, *The Breast 23 (2014)*
- Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up- E. Senkus, Annals of Oncology 26 (Supplement 5), 2015
- Management of patients with hormone receptor-positive breast cancer with visceral disease: challenges and treatment options- Wael A Harb, Cancer Management and Research, 21/Jan/2015

Thank you for listening

DOSING SCHEDULES FOR CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER

Chemotherapy combinations:

CAF chemotherapy[20]
- Cyclophosphamide 100 mg/m² PO days 1–14
- Doxorubicin 30 mg/m² IV days 1 & 8
- 5-fluorouracil 500 mg/m² IV days 1 & 8

Cycled every 28 days.

FAC chemotherapy[21]
- 5-fluorouracil 500 mg/m² IV days 1 & 8 or days 1 & 4
- Doxorubicin 50 mg/m² IV day 1 (or by 72-h continuous infusion)
- Cyclophosphamide 500 mg/m² IV day 1

Cycled every 21 days.

FEC chemotherapy[22]
- Cyclophosphamide 400 mg/m² IV days 1 & 8
- Epirubicin 50 mg/m² IV days 1 & 8
- 5-fluorouracil 500 mg/m² IV days 1 & 8

Cycled every 28 days.

AC chemotherapy[23]
- Doxorubicin 60 mg/m² IV day 1
- Cyclophosphamide 600 mg/m² IV day 1

Cycled every 21 days.

EC chemotherapy[24]
- Epirubicin 75 mg/m² IV day 1
- Cyclophosphamide 600 mg/m² IV day 1

Cycled every 21 days.

CMF chemotherapy[25]
- Cyclophosphamide 100 mg/m² PO days 1–14
- Methotrexate 40 mg/m² IV days 1 & 8
- 5-fluorouracil 600 mg/m² IV days 1 & 8

Cycled every 28 days.

Docetaxel/capecitabine chemotherapy[26]
- Docetaxel 75 mg/m² IV day 1
- Capecitabine 950 mg/m² PO twice daily days 1–14

Cycled every 21 days.

GT chemotherapy[27]
- Paclitaxel 175 mg/m² IV day 1
- Gemcitabine 1250 mg/m² IV days 1 & 8 (following paclitaxel on c

Cycled every 21 days.

Gemcitabine/carboplatin[28]
- Gemcitabine 1000 mg/m² on days 1 & 8
- Carboplatin AUC 2 IV on days 1 & 8

Cycled every 21 days.

Paclitaxel plus bevacizumab[29]
- Paclitaxel 90 mg/m² by 1 h IV days 1, 8, & 15
- Bevacizumab 10 mg/kg IV days 1 & 15

Cycled every 28 days.