六大核心能力 – Medical knowledge & Patient care

2016.09.10
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Patient’s Profile

- Chart no./ Name: xxxxxxxx/ OOO
- Age/ Gender: 65/ Female
Chief complaint

- Painful while coughing on right lower chest wall for 1 month.
- Chronic cough for 6 months, voice hoarseness since 2016/4.
• 1998.7.28 : Infiltrating ductal carcinoma of left breast s/p MRM on, pT2N20 stage IIIA, ER:14.30, PR: (-), LN:6/19, FECx6, Tamoxifen x5Y

• 2000.2.3 : hysterectomy and BSO.

• 2004.7.16 : excision of thyroglossal duct cyst

• Hypertensive cardiovascular disease

• GERD
present illness

- She was under regular f/u at xxxx 醫院 annually, which 2015/9/23 breast sono showed negative findings.(routine f/u)

- This time she complained about chronic cough for 6 months, hoarseness of voice since this April, and pain on right lower chest wall for 1 month. Nausea and vomiting were noticed in June 2016.

- PE showed right chest wall tenderness, no left chest wall recurrence, no mass over right breast, no axillary LNs.

- Lab data in normal range(including CEA and CA153), no leukocytosis, normal liver and renal function, normal electrolytes.
2016/8/12 xxxx 醫院 Chest CT (2016.8.12): expansile soft tissue lesion noted at right 5th, 9th and 10th rib, and osteolytic nodules at C7 and T10 vertebral body, bone metastases is compatible, suggest bone scan correlation.

Subsegmental atelectasis over right apical lung, paramediasitnum region, cause to be determined. Focal thickening and increased pleural infiltration over RLL of lung.

No enlarged lymph node within the mediastinum.
8/31  Chest x ray:
Impression:
1. Atherosclerosis of thoracic aorta.
2. Normal heart size.
5. Scoliosis of thoracolumbar spine.
6. Expansive bony mass over 5th rib, right R/I metastasis.
7. S/P MRM, left.
Admission course

- 8/30 Admission
  - CT-guide biopsy (check origin)
  - port-A implantation
  - zometa
- 9/2 bone scan
  - bronchoscopy: pleural wash for cytology (-)
  - consult ENT for laryngoscopy
  - consult RT for palliative radiotherapy
- 9/5 radiotherapy
  - neck sono
An expansile bone lesion (3.28x1.3cm) was noted in the posterior aspect of right 10th rib.
PATHOLOGICAL DIAGNOSIS:
Bone, rib, ?site, CT guided biopsy, carcinoma, metastatic.

MICRO:
Sections show a metastatic carcinoma with neoplastic cells arranged in single files and small clusters, consistent with metastasis from breast carcinoma.

IMMUNOHISTOLOGY:
ER: + (60%)
PR: - (0%)
Her-2: 0+
MIB-1: 15%
GATA3: +

Left vocal cord palsy with big closure gap
9/5 Neck sono

- No identified enlarged LAPs.
- A few small L-N(<6mm) over left supraclavicular region, suggest f/u.
Current diagnosis

- Metastatic breast carcinoma with multiple bony metastasis, ER: + (60%), PR(-), Her-2: 0+
  MIB-1: 15%
  GATA3: +

- Infiltrating ductal carcinoma of left breast s/p MRM, pT2N20 stage IIIA, ER: 14.30, PR: (-), LN: 6/19, FECx6, Tamoxifen x5Y
Treatment plans

- Major treatment: Hormone therapy
- For bone destruction: Zometa + radiotherapy
- Pain control
6 Core Competencies

Patient Care
What You Do to the patient?

Medical Knowledge
What You Know?

Interpersonal and
Communication
Skill
How You Interact with Others?

System-Based
Practice
How You Work Within the System?

Professionalism
How You Act?

Practice-Based
Learning and
Improvement
How You Get Better?
Hormone receptor(+) Metastatic breast cancer

2016 treatment guideline
Endocrine Therapy for Hormone Receptor–Positive Metastatic Breast Cancer: American Society of Clinical Oncology Guideline


2016 by American Society of Clinical Oncology

Methods
The ASCO Expert Panel was convened to conduct a systematic review of evidence from 2008 through 2015 to create recommendations informed by that evidence. Outcomes of interest included sequencing of hormonal agents, hormonal agents compared with chemotherapy, targeted biologic therapy, and treatment of premenopausal women.
Hormone therapy should be offered to patients whose tumors express any level of ER/PR receptors.

Endocrine therapy should be recommended as initial treatment for patients with HR-positive MBC, except for patients with immediately life-threatening disease or rapid visceral recurrence during adjuvant endocrine therapy.(and HER2 +)

=> consider adding chemotherapy
Treatment should be administered until there is unequivocal evidence of disease progression as documented by imaging, clinical examination, or disease-related symptoms.

The use of combined endocrine therapy and chemotherapy is not recommended.
Figure 2. Mechanism of action of the aromatase inhibitors.

Androstenedione  Testosterone

Peripheral tissues (subcutaneous fat, liver, muscle, or brain)

Aromatase  Aromatase inhibitors  Aromatase

Estrone

Estradiol

Estradiol

Tamoxifen

Breast cancer cell

Estrogen receptor

regimen

- **AI (non steroidal):** such as **anastrozole** (Arimidex) and **letrozole** (Femara), inhibit the synthesis of estrogen via reversible competition for the aromatase enzyme.
- **Fulvestrant** (Faslodex): a **complete estrogen receptor antagonist** with no agonist effects, which in addition, accelerates the proteasomal degradation of the estrogen receptor.[1] The drug has poor oral bioavailability, and is administered monthly via intramuscular injection.
- **Palbociclib** (Ibrance, 125mg capsule): a selective inhibitor of the cyclin-dependent kinases **CDK4 and CDK6**
- **Tamoxifen** (Nolvadex): **selective estrogen-receptor modulator** (SERM)
- **Everolimus:** an inhibitor of **mammalian target of rapamycin** (mTOR).
Fig 1. Hormone therapy for postmenopausal women with hormone receptor-positive metastatic breast cancer by line of therapy and adjuvant treatment. NOTE. Use of palbociclib should be reserved for patients without prior exposure to cyclin-dependent kinase 4/6 inhibitors. Fulvestrant should be administered at 500 mg every 2 weeks for three cycles, then once per month as an intramuscular injection. Withdrawal of tamoxifen or progestins was reported to result in short-term disease responses in older literature. Steroidal indicates exemestane; nonsteroidal indicates anastrozole or letrozole. AI, aromatase inhibitor.
Endocrine therapy
Single agent

- AI (anastrozole)
- Fulvestrant
- Tamoxifen

anastrozole (Arimidex) v.s. fulvestrant
Endocrine therapy combined agents

- anastrozole (Arimidex) + Fulvestrant v.s. anastrozole (Arimidex) alone
  -> 1. FACT (most s/p hormone therapy) +/-
  -> 2. SWOG0226 trial (never s/p hormone therapy) combined 效果較好

Letrozole (AI) + palociclib v.s. letrozole alone
  -> PALOMA I trial combined 效果較好
Endocrine Therapy Guideline for Metastatic Breast Cancer

**Fig 1.** Hormone therapy for postmenopausal women with hormone receptor-positive metastatic breast cancer by line of therapy and adjuvant treatment. NOTE. Use of palbociclib should be reserved for patients without prior exposure to cyclin-dependent kinase 4/6 inhibitors. Fulvestrant should be administered at 500 mg every 2 weeks for three cycles, then once per month as an intramuscular injection. Withdrawal of tamoxifen or progestins was reported to result in short-term disease responses in older literature. Steroidal indicates exemestane; nonsteroidal indicates anastrozole or letrozole. Al, aromatase inhibitor.
First-Line Therapy for MBC patient

- **Postmenopausal** women with HR-positive MBC should be offered **aromatase inhibitors (AIs)** as part of first-line endocrine therapy.

- Combination hormone therapy with a **nonsteroidal AI and fulvestrant** may be offered for patients with MBC **without prior exposure to adjuvant endocrine therapy**.

- When fulvestrant is administered, it should be administered using the **500-mg dose** and with a **loading schedule** (treatment start, day 15, day 28, then once per month).

- **Premenopausal** women with HR-positive MBC should be offered **ovarian suppression** or ablation and hormone therapy.
Second-Line Therapy

- Everolimus + steroidal AI (Exemestane)

  Prominent side effects (Oral ulcer, infection, fatigue, rash)

Fulvestrant + palbociclib -> PALOMA III
Endocrine Therapy Guideline for Metastatic Breast Cancer

No prior adjuvant endocrine therapy

Prior adjuvant endocrine therapy

Prior treatment with tamoxifen

Early relapse (≤ 12 months since adjuvant therapy)

AI, nonsteroidal preferred
AI + fulvestrant

Fulvestrant ± palbociclib
AI + everolimus
AI (steroidal)
Tamoxifen

Sequential therapy based on prior exposure and response to hormone therapy

Estradiol (2 mg three times per day)
Megestrol acetate
Flucytmesterone
Reintroduction of prior therapy

Prior treatment with an AI

Early relapse (≤ 12 months since adjuvant therapy)

Fulvestrant ± palbociclib
AI (steroidal)
Tamoxifen

Late relapse (> 12 months since adjuvant therapy)

Fulvestrant ± palbociclib
AI + everolimus
AI (steroidal)
Tamoxifen

Late relapse (> 12 months since adjuvant therapy)

Fulvestrant ± palbociclib
AI + everolimus
AI (steroidal)
Tamoxifen

First line

Second line

Third line or greater

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Treatment for bone destruction
雙磷酸鹽 (Bisphosphonate) 化合物，作用在降低噬骨細胞的活力，活化造骨細胞的活動力：減少骨質流失，骨折、骨疼痛、高鈣血症。

適應症: 惡性腫瘤之蝕骨性骨頭轉移之病患，在使用嗎啡、可待因等止痛劑後仍不易控制者。惡性腫瘤之高血鈣症。

預防性: 更年期後接受AI治療之病患若骨密度檢查T Score小於-2.0、年齡大於65歲、BMI值小於20kg/m2、有家族股骨頭骨折史，個人在50歲後曾發生骨折或類固醇使用超過六個月以上時，考慮接受雙磷酸鹽治療。

Zometa的使用，對乳癌病人復發率的降低，具有統計上的差異，可是在死亡率及骨轉移率方面，使用Zometa與否在統計上並沒有意義的差異。

有腎臟功能受損的可能副作用。滴注時間30分鐘。建議在每一次投予Zometa前監控血中之creatinine，注意有無低血Ca,Mg情形。

• Zometa(Zoledronic acid) •
癌症病人骨轉移後發生病理性骨折的機率約為10%，至於在脊椎轉移後所引起脊椎不穩定的背痛約佔所有癌症病人的10%。因此，一旦癌症轉移到病人的骨骼後，將會引起病人背痛、高血鈣、病理性骨折及脊隨壓迫等症，而降低病人生活品質和增加死亡率。

骨轉移之處理原則若骨轉移之部位涵蓋身體承重之肢體骨骼及軀幹骨骼（如脊椎及骨盆腔），或骨轉移疼痛無法控制時則應優先局部放射治療以預防病理性骨折導致癱瘓及長期臥床。
Pain control

免於疼痛是一種基本人權 (WHO 1990)。
疼痛治療應在最少的藥物副作用下，控制在疼痛量表的分數小於3的程度。

WHO 三階段式的疼痛治療方案

1. Pain
   - Non-opioid ± Adjuvant

2. Pain persisting or increasing
   - Opioid for mild to moderate pain ± Non-opioid ± Adjuvant

3. Freedom from cancer pain
   - Opioid for moderate to severe pain ± Non-opioid ± Adjuvant

疼痛分級量表

- 0: No hurt
- 1-3: Hurts little bit
- 4: Hurts little more
- 5-6: Hurts even more
- 7: Hurts whole lot
- 8-10: Worst pain
第一階段: Acetaminophen 或者 NSAIDs) 做為起始治療，同時考慮併用輔助藥物。

第二階段，使用弱效的鴉片類藥物，同時考慮併用輔助藥物。

第三階段，使用強效的鴉片類藥物，如 Morphine、Fentanyl、Oxycodone 等，同時考慮併用非鴉片類的止痛藥以及輔助藥物。
輔助藥物例如抗憂鬱藥物、抗癲癇藥物、類固醇、局部麻醉劑、肌肉鬆弛劑等，可增加疼痛控制的效果，也可以減低止痛藥的副作用及耐受性的發生，尤其是用於神經性疼痛。

於2012年Cochrane Database發表「組合藥物用於治療成人神經性疼痛」的整合分析報告中，證實多種藥物併用可得到更好的止痛效果，多重機轉的疼痛控制策略已廣為被各學會所接受。
6 Core Competencies

- **Patient Care**
  What You Do to the Patient?

- **Medical Knowledge**
  What You Know?

- **Professionalism**
  How You Act?

- **Interpersonal and Communication Skill**
  How You Interact with Others?

- **System-Based Practice**
  How You Work Within the System?

- **Practice-Based Learning and Improvement**
  How You Get Better?
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REFERENCE


- 肺癌醫療暨衛教網頁


THANK YOU!
Fig 2. Hormone therapy for premenopausal women with hormone receptor-positive metastatic breast cancer by line of therapy and adjuvant treatment. NOTE. Use of palbociclib should be reserved for patients without prior exposure to cyclin-dependent kinase 4/6 inhibitors. Fulvestrant should be administered at 500 mg every 2 weeks for three cycles, then monthly as an intramuscular injection. Withdrawal of tamoxifen or progestins was reported to result in short-term disease responses in older literature. Steroidal indicates exemestane; nonsteroidal indicates anastrozole or letrozole. Al, aromatase inhibitor.