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(همراه با امتیاز بازآموزی)

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(موضوع سخنرانی:
ماستیت گرانولوماتوز)

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وبینار چالشهای تشخیصی – درمانی
ماستیت گرانولوماتوز
تومور فیلودس

پژوهشکده سرطان معتمد

1400/6/2

Idiopathic Granulomatous Mastitis (IGM)

Etiology

- hypersensitivity to extravasated lactation Products
- local breast trauma
- Infection
- Hyperprolactinemia
- Autoimmune processes

Common characteristics

- IGM affects women of childbearing age.
- Most of the patients had a history of pregnancy and breastfeeding.
- A correlation between tobacco use, hormone therapy, number of pregnancies, duration of lactation, DM and the severity of the disease
- Rheumatologic findings were more common among moderate to severe cases

Common presentations

- Breast mass
- Pain
- Skin thickening, Erythema, Edema
- Abscess
- Fistula and sinus tract
- Deformity and nipple retraction
- Ulcer
- Fever
- Systemic disorder eg Erythema Nodosum
- Lymphadenopathy

Diagnosis

- Imaging studies, including ultrasonography, mammography, and magnetic resonance imaging, are nonspecific and these imaging techniques are used primarily to exclude other breast diseases, especially carcinoma.
- Core needle biopsy may be the diagnostic method of choice because of less morbidity and acceptable accuracy in demonstrating the tissue architecture

Classification of severity

- Mild: size <2 cm in ultrasonography, no ulcer or fistula and occasional mild pain;
- Moderate: size 2-5 cm, collection needing aspiration drainage, one fistula and small amount of discharge;
- Severe: size more than 5 cm, severe pain and multiple fistulas and ulcers with discharge more than 20 cc daily.

Treatment options

- Observation only (for non-symptomatic patients with palpable mass and pathology of IGM)
- Supportive care including aspiration
- Non-Steroidal Anti-Inflammatory Drugs
- Corticosteroids
- Antibiotics
- Immuno-suppressors(Methotrexate, AZA)
- Surgical interventions.

Breast Phyllodes Tumor

Dr. Shiva Moghadam
Radiation Oncologist, Motamed Cancer Institute

Overview

- Phyllodes tumors are uncommon fibroepithelial breast tumors that are capable of a diverse range of biologic behaviors
- The term "phyllodes," which means leaf-like, describes the typical papillary projections that are seen on pathologic examination. It includes a group of lesions of varying malignant potential, ranging from completely benign tumors to fully malignant ones.

Benign ……Borderline……Malignant

EPIDEMIOLOGY

- less than 1 percent of all breast neoplasms
- The vast majority of phyllodes tumors occur in women, with a median age of presentation of 42 to 45 years
- Higher-grade tumors are more common in older patients
- In men, phyllodes tumors usually occur in association with gynecomastia

CLINICAL PRESENTATION

- The average age at diagnosis is in the fourth decade
- usually identified as a breast mass.
- smooth, rounded, usually painless multinodular lesions that may be indistinguishable from fibroadenomas.
- size is variable
- Shiny, stretched, and attenuated skin may be seen overlying a large tumor.
- Skin ulceration may be seen with large tumors, but this is usually due to pressure necrosis rather than invasion of the skin by malignant cells.

- Although palpable axillary lymphadenopathy can be identified in up to 20 percent of patients, most are reactive; metastatic involvement of lymph nodes with phyllodes tumor is rare

DIAGNOSTIC EVALUATION

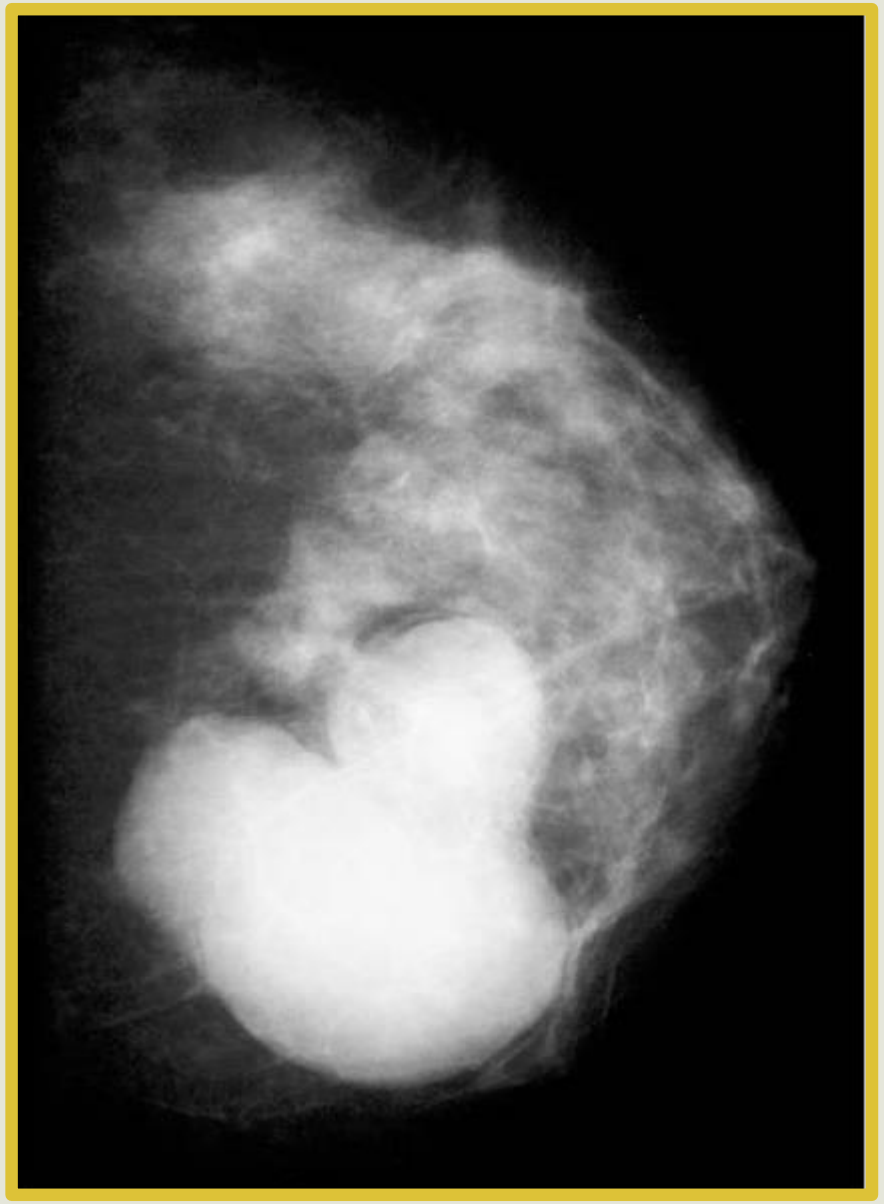
- Phyllodes tumors should be suspected when a patient presents with a large (>3 cm), rapidly growing breast mass that is usually palpable. Although imaging features of a phyllodes tumor can be suggestive of fibroadenoma, the large size and history of rapid growth indicate otherwise.

- Phyllodes tumors can only be diagnosed histologically

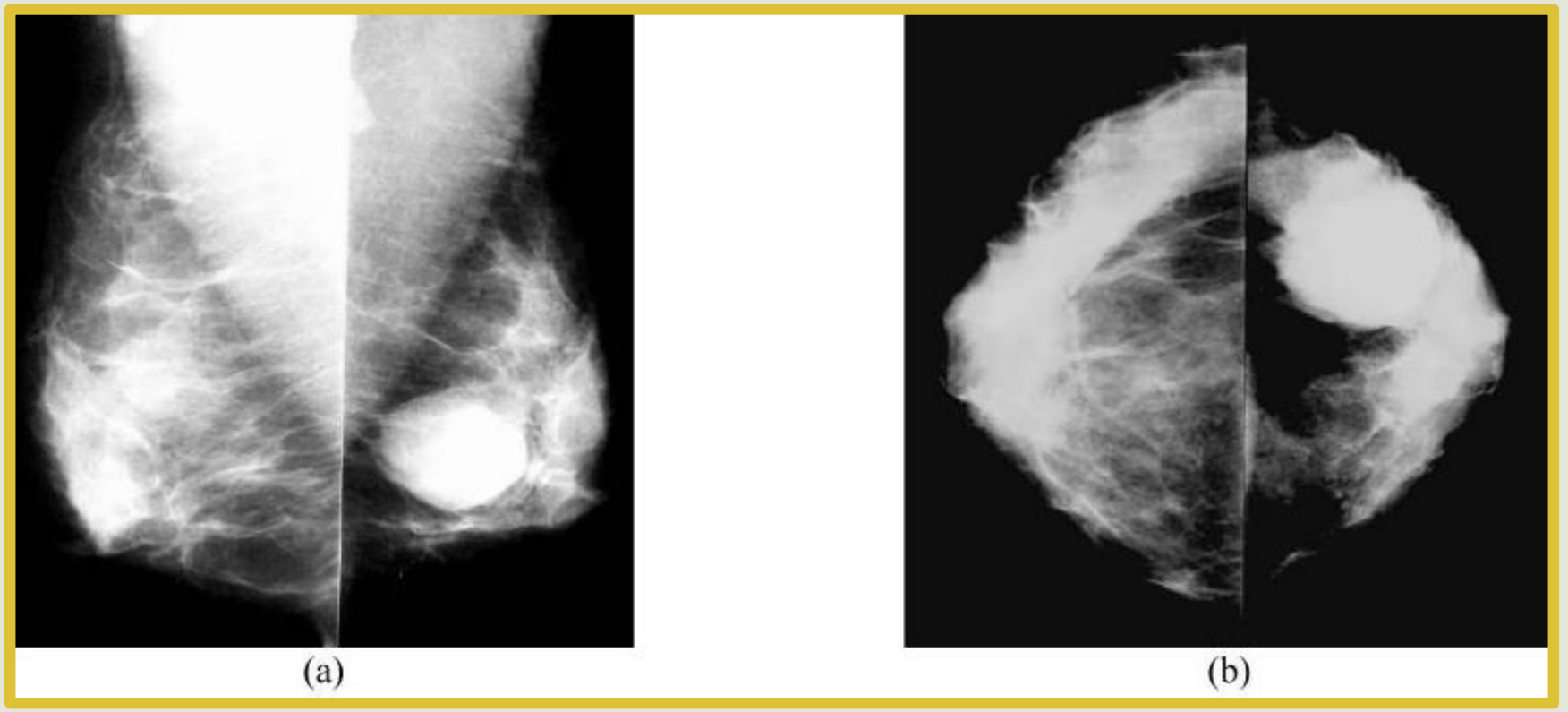
Imaging

Mammography

- Approximately 20 percent of phyllodes tumors present as a nonpalpable mass identified on screening mammography
- The typical appearance of a phyllodes tumor on mammography is a smooth, polylobulated mass resembling a fibroadenoma



Benign phyllodes tumour in a 48-year-old woman. Left craniocaudal mammogram shows a 6-cm lobulated, circumscribed mass in the inner quadrant



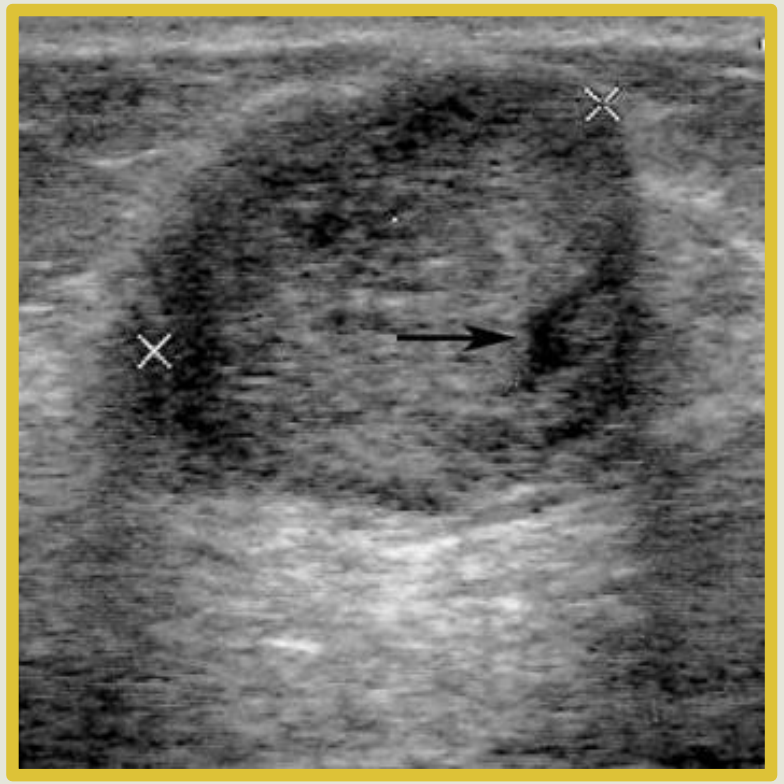
(A) Mediolateral oblique and (B) craniocaudal mammograms show a heterogeneously-dense breast with a round, well-circumscribed, 4.5-cm mass at 3 o'clock in the left breast

Ultrasonography

- Patients with a palpable breast mass or suspicious lesion on mammography should have an ultrasound examination. Phyllodes lesions are primarily solid, hypoechoic, and well circumscribed on ultrasonography

- Suspicion for a phyllodes tumor, rather than a fibroadenoma, is based on clinical features such as large tumor size at presentation and rapid growth

- Although not always present, cystic areas within the mass on ultrasonography may increase the level of suspicion for phyllodes tumors



Benign phyllodes tumour in a 35-year-old woman. Transverse US image shows a circumscribed heterogenous echo with a small cystic space (arrow) and a slight posterior acoustic enhancement.

Role of MRI?

- Phyllodes tumors and fibroadenomas cannot be reliably differentiated by breast MRI
- However, when a phyllodes tumor has been diagnosed on core biopsy, breast MRI may help determine the extent of disease and resectability in selected cases

✓However, the **routine use** of breast MRI in surgical planning for phyllodes tumors is **controversial and not supported by data**

BIOPSY

- Breast lesions suspicious for phyllodes tumors should undergo **core biopsy**, which is typically diagnostic.
- Compared with core biopsy, fine needle aspiration (FNA) is less accurate.
- If the core biopsy results are indeterminate or if there is clinical-pathologic discordance, an excisional biopsy should be performed.

BIOPSY

- A core biopsy diagnosis of "cellular fibroadenoma," "cellular fibroepithelial lesion," or "fibroepithelial lesion with cellular stroma" should prompt surgical excision of the lesion, regardless of its appearance on imaging studies.

- Core biopsy has a 25 to 30 percent false negative rate when used to diagnose phyllodes tumors. Thus, if a solid mass has a benign core biopsy but subsequently grows rapidly or becomes symptomatic, an excisional biopsy is also indicated.

Histopathology

- like fibroadenoma, is composed of epithelial elements and a connective tissue stroma.
- Phyllodes tumors are classified as benign, borderline, or malignant on the basis of the nature of :

  ★The tumor margins (pushing or infiltrative)

  ★Presence of cellular atypia

  ★Mitotic activity

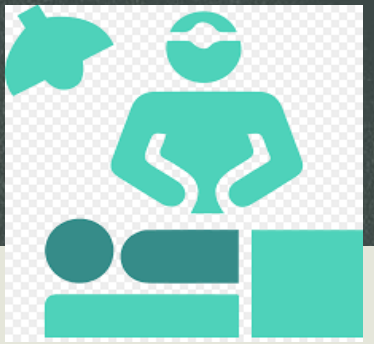
  ★Overgrowth in the stroma

There is disagreement about which of these criteria is most important, although **most experts favor stromal overgrowth**.

TREATMENT

- Given the rarity of the disease, treatment principles are based mainly on retrospective series and case reports.

Surgical resection



- **Breast surgery** — A complete surgical excision is the standard of care for phyllodes tumors.
- Current NCCN guidelines recommend excisional biopsy for benign phyllodes tumors and wide excision with intention of obtaining surgical margins of 1 cm or more for borderline and malignant phyllodes tumors.

(with a statement that a narrow margin is not an absolute indication for mastectomy when partial mastectomy fails to achieve a margin width of >=1 cm)

- **However, the minimal acceptable margin beyond "clear" is controversial and depends on tumor grade**
- **For benign phyllodes tumors, we aim for a clear margin but do not require a wide (eg, 1 cm) margin**.

- A 2019 meta-analysis of 54 observational studies also found that narrow or positive margin only correlated with a higher local recurrence risk for malignant, but not for benign and borderline, phyllodes tumors. Consequently, it has become controversial whether a negative margin should be strictly obtained for a benign phyllodes tumor
- . Some authors advocate only a "grossly complete excision," arguing that it would make re-excision of benign phyllodes tumors unnecessary when they are mistaken for fibroadenomas on core biopsy and excised with narrow margins or enucleated, as long as no gross tumor is left behind and regardless of microscopic margin status
- **Despite the controversy, however, it appears safe to accept a clear margin for benign phyllodes tumors without mandating re-excision for margins narrower than 1 cm**

- For borderline or malignant phyllodes tumors, we also aim for a 1 cm margin.
- However, for patients with a clear but narrower than 1 cm margin, we determine the need for re-excision on a case-by-case basis.

- In a retrospective review of 48 women with high-grade malignant phyllodes tumors, 10 patients were treated with local excision (margins <1 cm), 14 with wide local excision (margins ≥1 cm), and 24 with mastectomy. At a median follow-up of nine years, the local recurrence rate was higher after local excision with narrow margins than after wide local excision (60 versus 28 percent).
- Surgical margins of ≥1 cm have been associated with a lower local recurrence rate in borderline and malignant phyllodes

Breast-conserving surgery versus mastectomy

- In a study of 821 women with malignant phyllodes tumors from the Surveillance, Epidemiology, and End Results (SEER) database, mastectomy and wide local excision were performed in 52 and 48 percent, respectively. Compared with mastectomy, breast-conserving surgery was associated with equivalent or improved cause-specific survival regardless of tumor size

- Mastectomy is generally not indicated for benign phyllodes unless the tumor is so large that breast-conserving surgery would result in suboptimal cosmetic outcomes

Axillary surgery

- **Axillary surgery** — Axillary lymph node involvement by phyllodes tumors is rarely reported, even when tumors are malignant
- In the SEER database study cited above, only 8 of 498 women with known lymph node status had involved nodes.

- Thus, axillary surgery is rarely indicated in patients diagnosed with phyllodes tumors.

Radiation therapy

- When adequate surgical margins cannot be achieved because of tumor location, adjuvant radiation therapy (RT) should be administered, even after mastectomy.
- However, when adequate surgical margins can be achieved, there is less agreement about the need for adjuvant RT. We base our decision about adjuvant RT on tumor grade:

➢ We do not suggest adjuvant RT for patients with benign phyllodes tumors that have been completely excised.

➢ We suggest adjuvant RT for all patients undergoing BCS for a borderline or malignant phyllodes tumor as it substantially reduces local recurrence rates

Radiation therapy

- In a meta-analysis of eight observational studies, adjuvant RT reduced local recurrences of borderline or malignant phyllodes tumors after breast-conserving surgery (HR 0.31, 95% CI -0.10 to 0.72). The effect of adjuvant RT on local recurrences after mastectomy was less pronounced (HR 0.68, 95% CI -0.28 to 1.64).
- Another meta-analysis of 17 studies concluded that radiation is effective in decreasing local recurrence over surgery alone

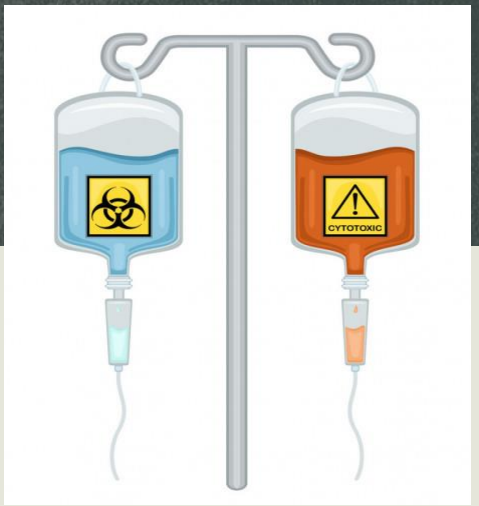
Radiation therapy

- Adjuvant RT has not been shown to improve survival compared with surgery alone.
- In a retrospective analysis of 3080 patients analyzed using the National Cancer Database, radiation did not improve overall survival
- In a retrospective analysis using the SEER database, although there was no benefit in terms of overall survival for the group as a whole, there was a trend toward a survival benefit with the addition of adjuvant radiation in the subgroup of patients with tumors larger than 5 cm

Radiation therapy

- In clinical practice, the utilization of adjuvant RT for phyllodes tumors appears to be modest. In a retrospective review of the National Cancer Database that included 3120 patients with phyllodes tumors, only 14 percent received adjuvant RT . Patients were more likely to receive radiation therapy if they were diagnosed later in the study, were 50 to 59 years old, had tumors >10 cm, high grades or had lymph nodes removed.
- adjusted models, adjuvant radiation reduced local recurrence but did not impact survival after a median follow-up of 53 months

Chemotherapy



- the role of systemic chemotherapy in phyllodes tumors is limited

- Patients with benign or borderline phyllodes tumors are usually cured with surgery and should not be offered chemotherapy

- chemotherapy in malignant phyllodes tumor is controversial and should not be routinely offered.

(Malignant phyllodes tumors are pathologically and clinically most similar to soft tissue sarcomas; however, localized malignant phyllodes tumors have a better prognosis than most high-grade sarcomas of similar stage. Thus, systemic chemotherapy should be considered for malignant phyllodes tumors with even more caution.)

Chemotherapy

- Based on experience and limited data, we recommend adjuvant chemotherapy only to a small minority of patients with high-risk (>10 cm) or recurrent malignant phyllodes tumors who have excellent functional status and minimal comorbidities, and only after a thorough discussion about the risks, benefits, and controversial nature of such treatment

Hormone therapy

- **Hormone therapy** — Hormone therapy is **not** effective against phyllodes tumors.
- Despite the presence of hormone receptors in the epithelial component of some phyllodes tumors, the stromal component is the principle neoplastic cell population responsible for the metastatic behavior.

POST-TREATMENT SURVEILLANCE

- Since most recurrences occur in the first two years after treatment, perform a history and physical examination every six months for the first two years, then annually.

- Patients who have not had mastectomy should resume surveillance with mammography annually. If suspicious lesions are found on mammography or breast examination, further imaging and/or biopsy may be required.
- Patients with large (≥5 cm) or malignant phyllodes tumors are at higher risk of developing metastatic disease. For such patients, surveillance may be performed more frequently and with chest radiograph or chest computed tomography (CT)

RECURRENT AND METASTATIC DISEASES

- When phyllodes tumors recur, they typically recur locally within two years of the initial excision

- Some series have found that the time to local recurrence was shorter for malignant than for benign or borderline tumors

RECURRENT AND METASTATIC DISEASES

- Although recurrences typically have the same grade as the original tumors, there have been several case reports of benign tumors transforming into malignant ones upon recurrence

- A systematic review of 54 retrospective studies reported some 26 percent (range 13 to 38) of benign and 21 percent (8 to 33 percent) of borderline tumors that recurred underwent upgrade.

RECURRENT AND METASTATIC DISEASES

Treatments for LR:

- Resectable recurrent disease is treated with either re-excision with wide margins or mastectomy, followed by radiation therapy (RT).

- Unresectable recurrences are treated with palliative radiation alone.

RECURRENT AND METASTATIC DISEASES

- Phyllodes tumors metastasize most often to the lungs. Tumors that metastasize are typically large (≥5 cm) or have malignant histologic features.
- For patients with metastatic disease, chemotherapy may be administered with palliative intent based upon treatment guidelines for soft tissue sarcomas.
- Most regimens have limited or short-lived benefit, with the highest levels of efficacy seen in doxorubicin and alkylating-based therapies .
- Similar to metastatic soft tissue sarcoma, there may be a role for metastasectomy in select cases with oligometastatic disease when technically feasible.

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NCCN Guidelines Version 5.2021
Phyllodes Tumor

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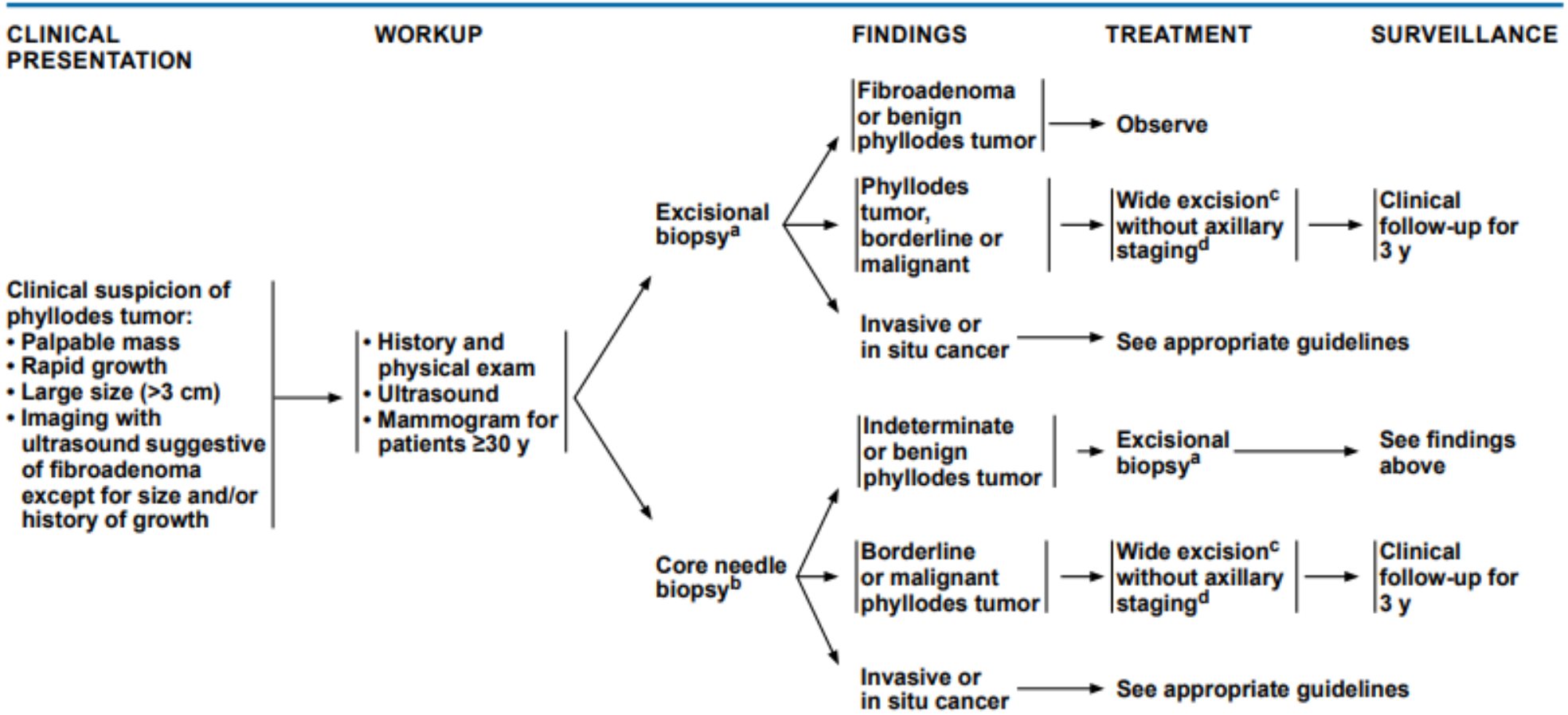

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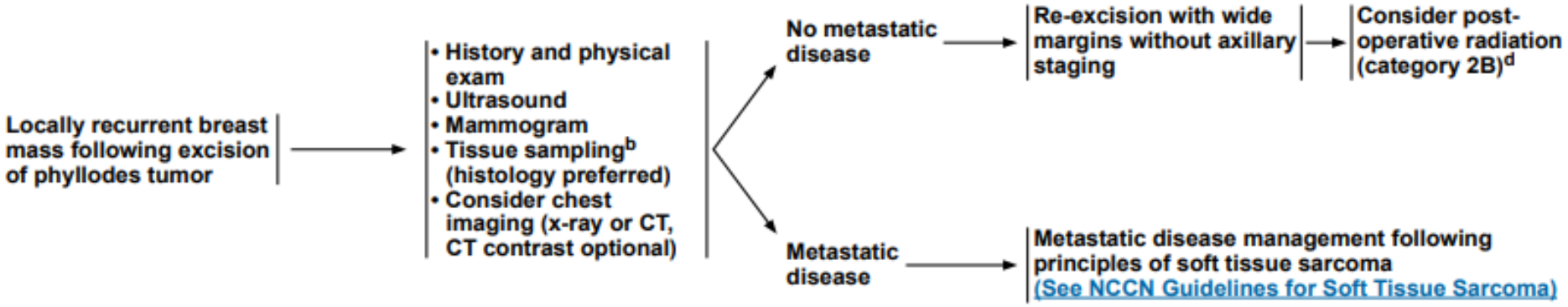
PHYLLODES TUMOR RECURRENCE



Phyllodes Tumors:

- ✓ Should be completely excised;
- ✓ Axillary lymph node dissection is not necessary.
- ✓ Adjuvant radiation therapy may benefit borderline or malignant, but not benign, tumors.
- ✓ Chemotherapy is reserved for highly selected patients with large, high-risk, or recurrent malignant phyllodes tumors.
- ✓ Hormonal therapy is not used to treat phyllodes tumors.

Given the rarity of the disease, treatment principles are based mainly on retrospective series and case reports


THANK YOU :)