# OCCULT CARCINOMA PRESENTING WITH AXILLARY NODAL METASTASES

# In medicine

- The term "***occult***" generally refers to a disease that is *not accompanied* by clinically discernible *signs or symptoms*.

  is not clinically evident in either breast.

- Most often, the ***occult breast carcinoma*** **(OBC)** presents with *ALN involvement*.

# *Less than 1% of patients*

- who have ***breast carcinoma*** present with an
- ***ALN metastasis*** as the first clinical manifestation of the disease.

# Clinical Presentation

- OBC ***occurs throughout*** the age distribution of breast carcinoma,
- with the **mean and median age** around ***57*** years.

The ***right axilla and breast*** were affected slightly more often **(54%)** than the left in one series, but others have reported left predominance.

# *A positive family history of breast carcinoma*

- in nearly 50% of patients, with about ***25%*** having a maternal ***first-degree*** relative affected.

- One study demonstrated the ***capacity of mammography to detect OBC*** in the presence of a benign, palpable mass.

- To rule out an *extramammary tumor or other metastases*, most women have been studied with a *variety of techniques*.

- However, women with ***false-negative mammography***
- had a *lower frequency of DCIS* and significantly more frequent metastases in ALNs.

- ***If mastectomy is delayed***, **repeat mammograms** of patients who initially had negative studies may reveal *new findings* suggestive of **carcinoma**.

# In one study

- The **interval** until the detection of a breast abnormality clinically or by mammography was **6 to 39 months**, with a mean of

***15 months*** in women who

***did not undergo a mastectomy***.

- The presence of *mammographically*

detectable calcifications in *metastatic carcinoma in ALNs* may be a clue to

the diagnosis of a ***subclinical breast carcinoma.***

- ***MRI*** has proven to be an effective method for detecting OBC that are not evident mammographically.

- The diagnostic yield is low in patients with a *negative mammogram and a negative MRI*, a situation that led the ***European Society of Breast Cancer Specialists*** to recommend that *surgical treatment* be avoided if MRI of the breast is negative.

# *In a high proportion of cases,*

- Lesions *detected by* mammography can be ***localized by sonography***, making them amenable to ***sonographically directed needle core biopsy***.

- Occasionally, nodal enlargement occurs in the ***contralateral axilla*** of a patient *treated previously for mammary carcinoma*.

# In a series of patients

- presenting with axillary metastases from *subclinical breast carcinoma*, about ***8% were previously treated for contralateral breast carcinoma*** or developed ***subsequent carcinoma in the contralateral breast***

- The median interval between treatment of the initial carcinoma and subsequent contralateral axillary metastases was 71 months.

- The frequency with which a primary tumor is detected pathologically in the ipsilateral breast varies from **55% to 82%.** In most series, the proportion with a documented primary was about 75%.

- Although not clinically palpable, most carcinomas were found on gross examination of a mastectomy or excisional biopsy specimen

- Rarely, the breast has contained two separate, grossly evident invasive primary carcinomas, each of which may be accompanied by an *in situ* component.

- The lesions have measured up to 6.5 cm, but most were ***1 to 2 cm*** or less in diameter. In one series, the median size was 1.9 cm and the ***mean 1.5 cm***, with 82% classified as T1, 14% as T2, and 4%

  as T3.

- The occult primary carcinoma has rarely been detected in the axillary tail.

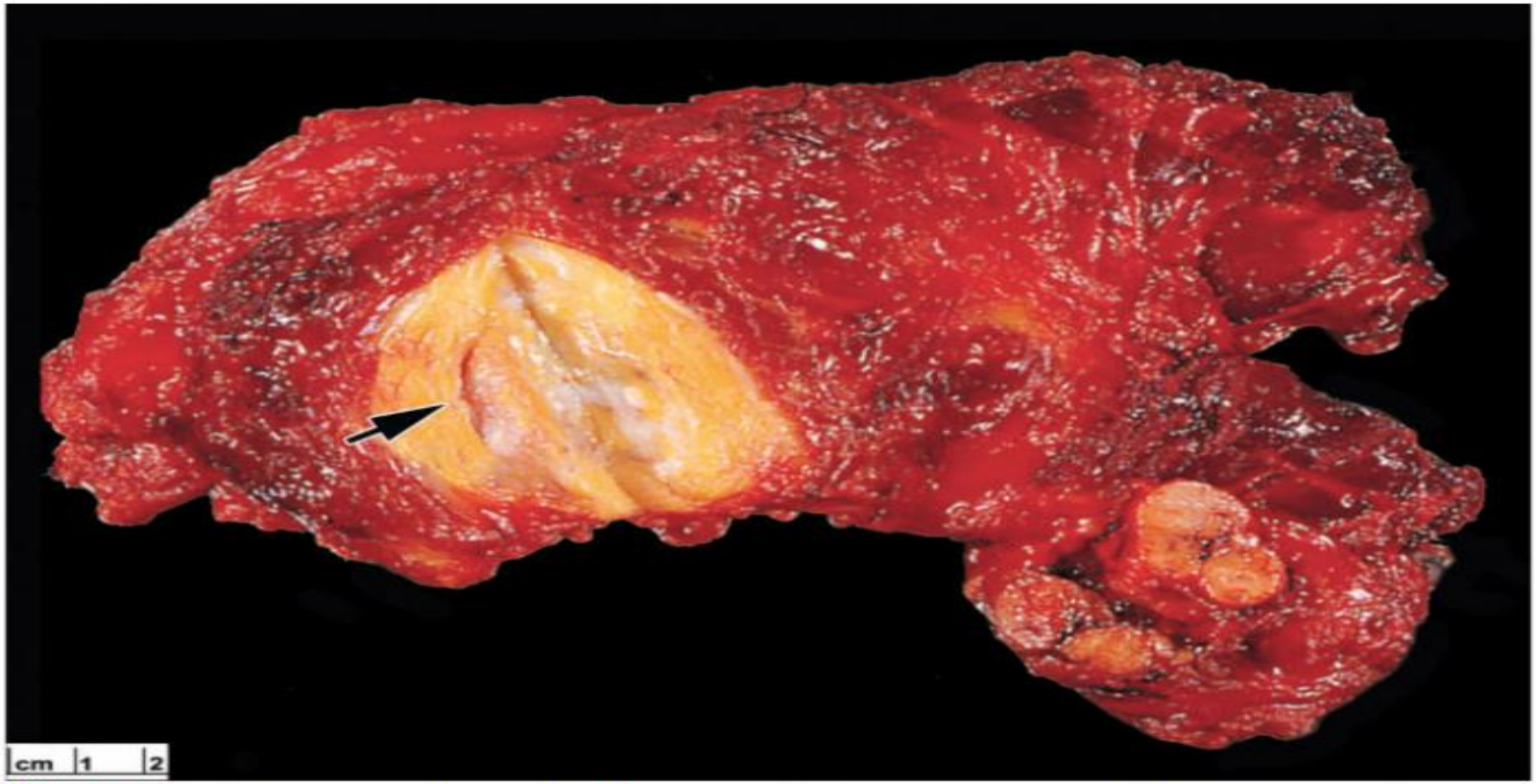



**FIG. 33.10. Occult carcinoma, mastectomy.** The *arrow* indicates a small intraductal carcinoma that was not clinically palpable. A bisected axillary lymph node with metastatic carcinoma is shown in the *lower right* portion of the specimen.

- In a review of eight retrospective studies published in 2010, de Bresser et

al. reported that lesions detected by MRI measured between 5 mm and 3 cm

and that the histopathologically measured size of these lesions ranged from ***1 mm to 5 cm.***

- About 30% of the clinically OBC are not evident when a mastectomy specimen is examined grossly.
- These lesions are found by taking **multiple random sections** of breast tissue that appear grossly unremarkable.

- Consequently, sampling should not be limited to grossly abnormal parenchyma.

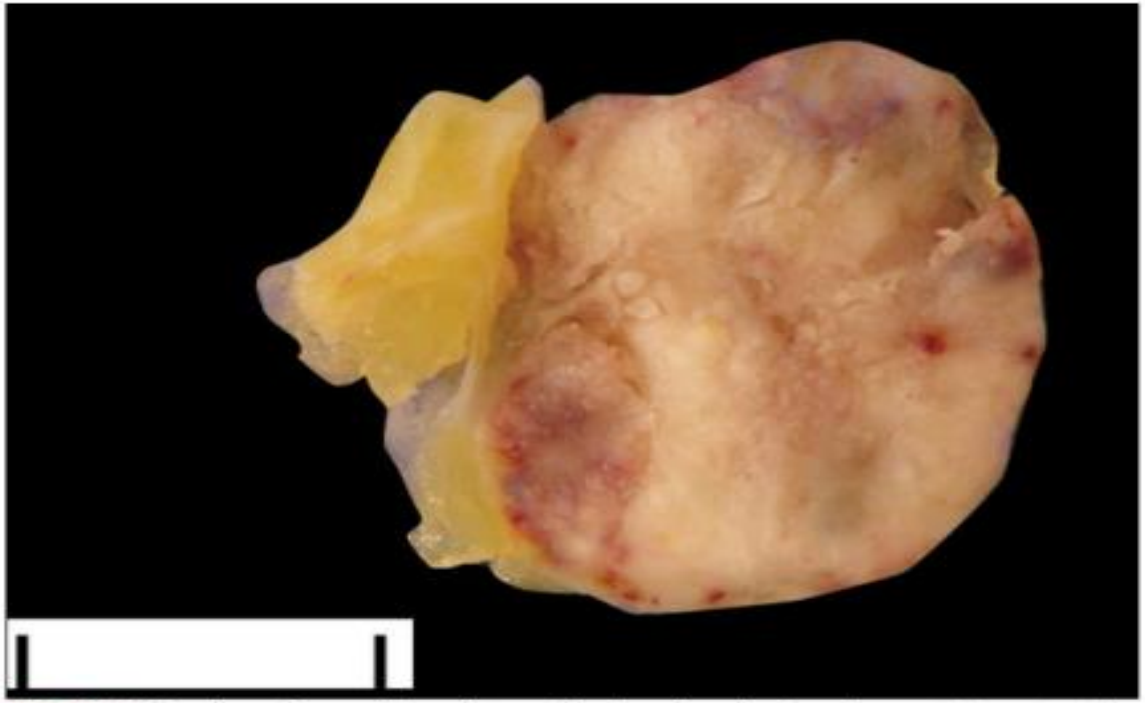


FIG. 33.11. **Occult carcinoma.** This solitary enlarged axillary lymph node containing metastatic papillary carcinoma is greater than 2 cm in diameter. No primary tumor was detected in either breast by clinical palpation or on radiologic evaluation. The metastatic carcinoma in the lymph node wasestrogen receptor positive, cytokeratin 7 positive, cytokeratin 20 negative, Wilms tumor 1 positive, and paired box gene 8 positive. A 3.0-cm ovarian papillary serous carcinoma was subsequently resected.

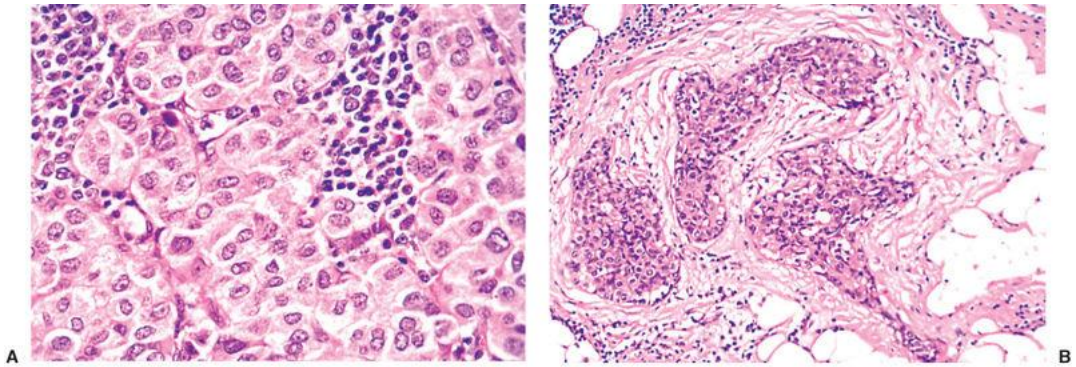



**FIG. 33.12. Occult carcinoma. A:** Metastatic adenocarcinoma in an axillary lymph node. The tumor cells have apocrine features consisting of abundant, finely granular eosinophilic cytoplasm, large nuclei, and prominent nucleoli. **B:** This minute focus of intraductal carcinoma with periductal fibrosis and lymphocytic reaction was the only parenchymal lesion in the mastectomy.

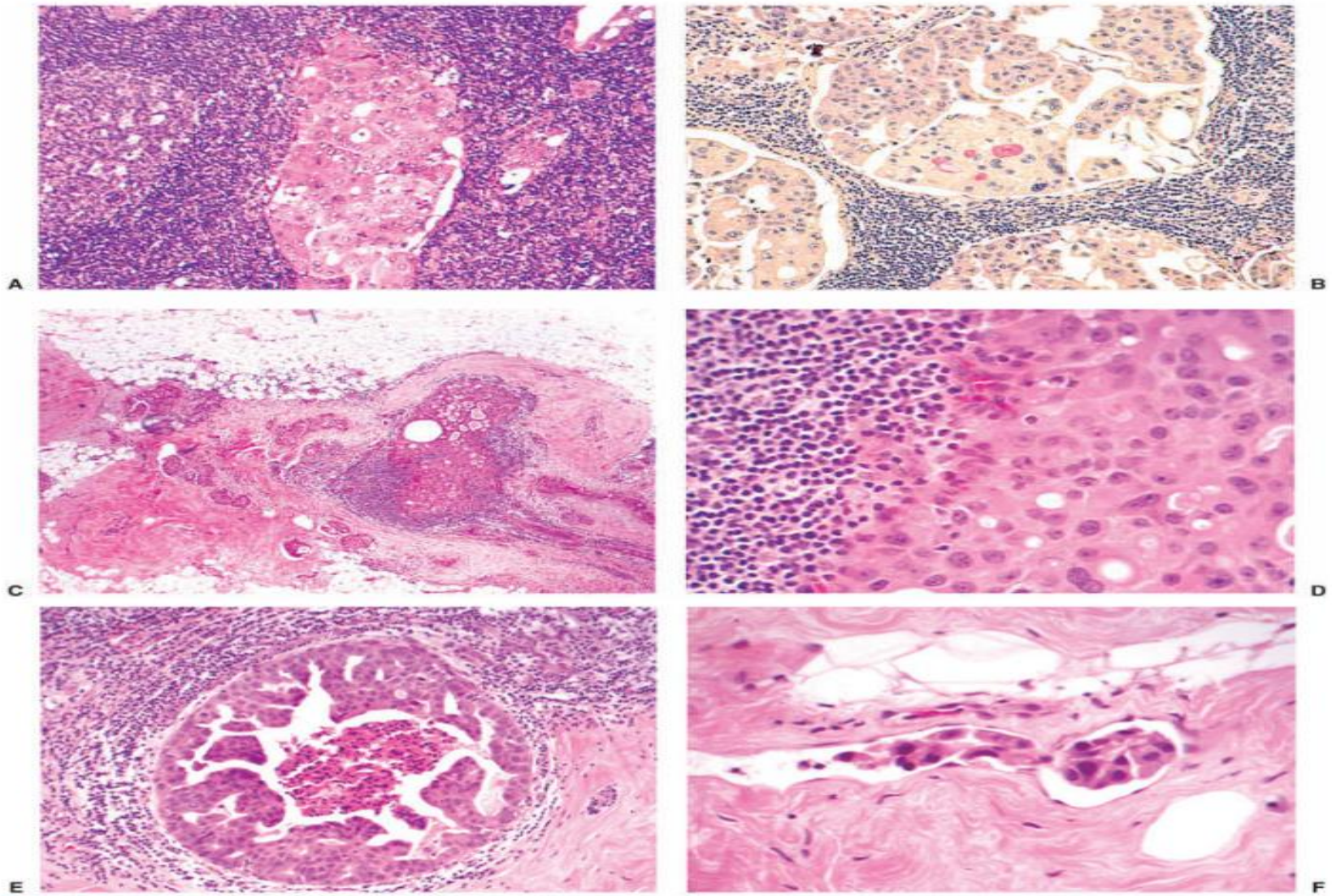



**FIG. 33.13. Occult carcinoma, apocrine. A:** Metastatic carcinoma, apocrine type, in a sinusoidal space of an axillary lymph node. **B:** Intracytoplasmic mucin is demonstrated with the mucicarmine stain. **C:** The nonpalpable intraductal and invasive primary ductal carcinoma in the breast has focal lymphocytic infiltrates. **D:** Apocrine differentiation in the primary carcinoma. **E:** Intraductal carcinoma, papillary, with necrosis. **F:** Lymphatic tumor emboli in the primary carcinoma. All images are from the same case.

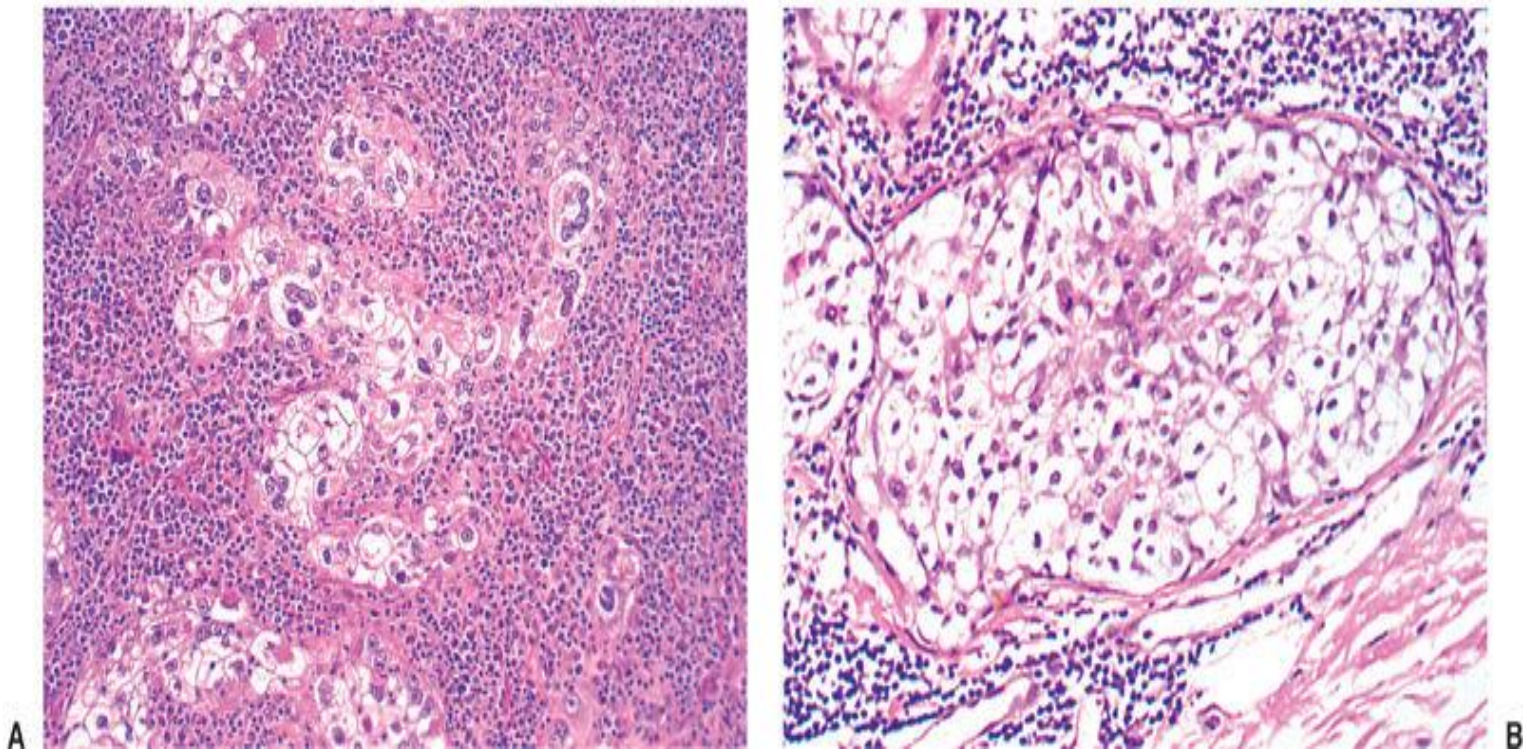



**FIG. 33.14. Occult carcinoma, clear cell. A:** This metastatic carcinoma in an axillary lymph node was the initial manifestation of breast carcinoma in this patient. **B:** A clinically inapparent focus of intraductal carcinoma, clear cell type, with a surrounding lymphocytic reaction was found in the breast.

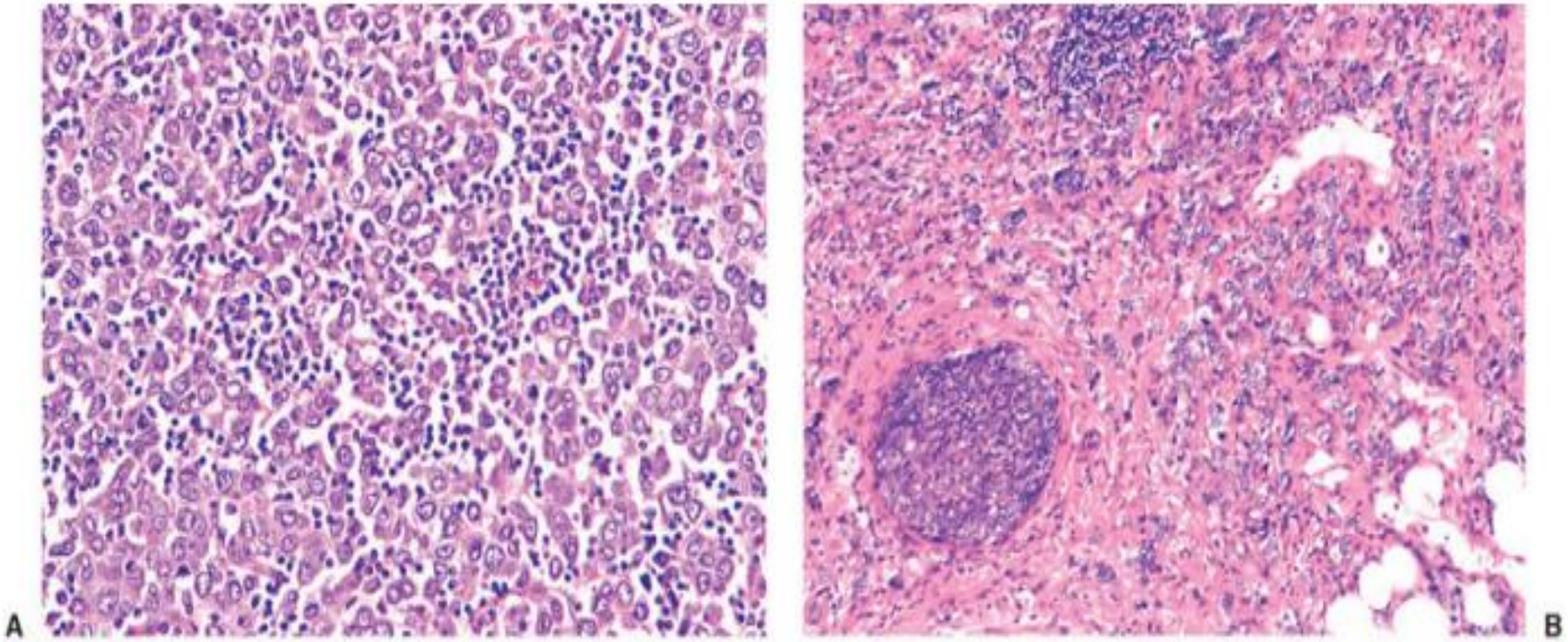



**FIG. 33.15. Occult carcinoma, diffuse. A:** The patient presented with this enlarged axillary lymph node found to contain malignant cells diffusely involving the lymphoid tissue. The tumor cells were immunoreactive for cytokeratin (*not shown here* ). **B:** Poorly differentiated invasive ductal carcinoma found in the breast.

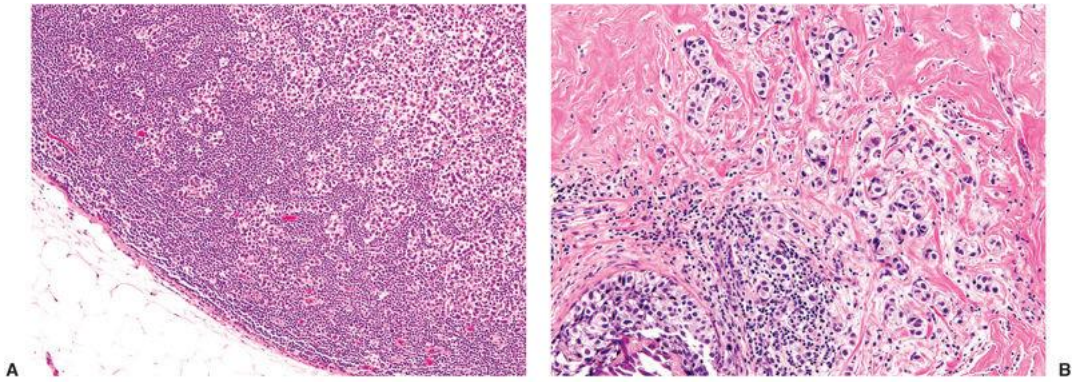



**FIG. 33.16. Occult carcinoma, diffuse. A:** An enlarged axillary lymph node in which poorly differentiated malignant cells, most prominent in the *upper right corner* , mingle with lymphocytes. The differential diagnosis for this pattern includes metastatic carcinoma, malignant lymphoma, and metastatic melanoma. The tumor cells in this case were immunoreactive for cytokeratin. **B:** An ipsilateral breast biopsy, targeting a minute focus of calcification, showed a focus of ductal carcinoma *in situ* with calcification (*lower left* ) and microinvasive ductal carcinoma.

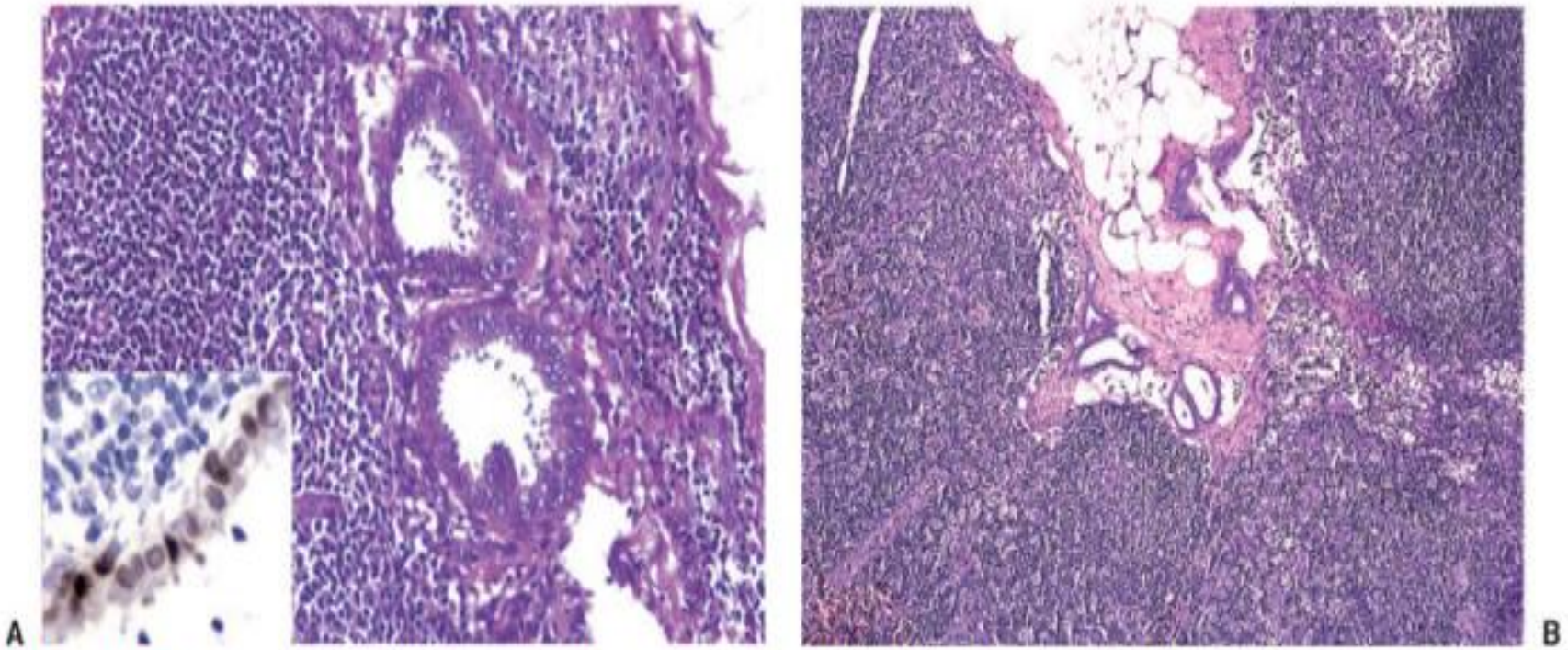



**FIG. 33.17. Occult carcinoma, tubular type** . **A:** Two glands of metastatic tubular carcinoma in lymph node tissue. *Inset* shows nuclear immunoreactivity for estrogen receptor in one of the glands from **(A) . B:** Metastatic tubular carcinoma in subcapsular sinus of a lymph node.

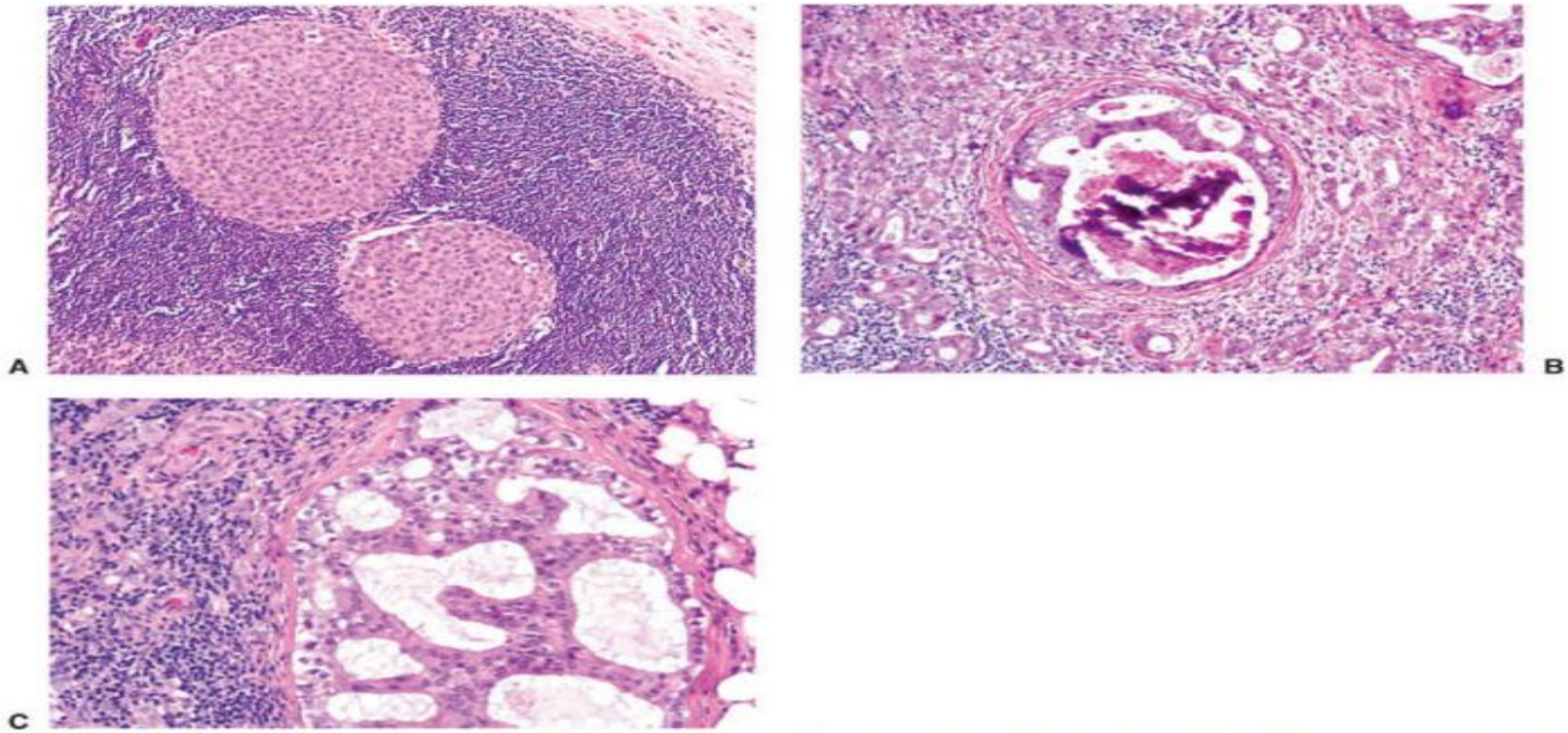



**FIG. 33.18. Axillary nodal metastases that resemble intraductal carcinoma.** All images are from cases of occult carcinoma presenting as axillary nodal metastases. **A:** Round, solid aggregates of metastatic ductal carcinoma. **B:** Necrosis and calcification in intraductal-like metastatic carcinoma. **C:** Metastatic apocrine cribriform carcinoma with peritumoral linear fibrosis that resembles basement membrane.

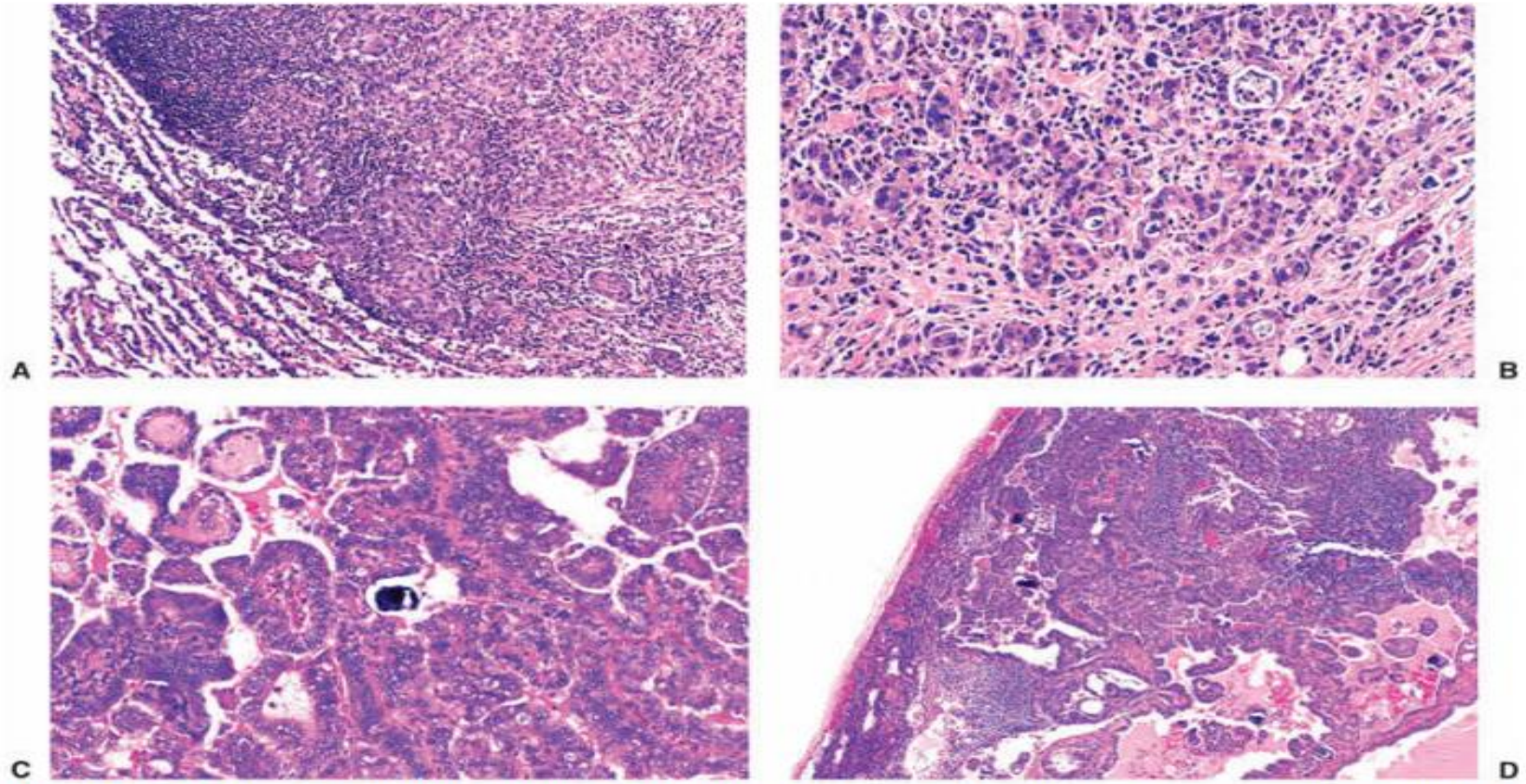



**FIG. 33.19. Metastatic nonmammary carcinoma. A:** Poorly differentiated adenocarcinoma of the lung. **B:** Metastatic pulmonary carcinoma in an axillary lymph node. **C,D:** Serous ovarian carcinoma **(C)** metastatic in an axillary lymph node **(D)** .

# Immunohistochemical studies

- ***for GATA3, ER, PR, cytokeratin 7 (CK7), CK20, thyroid transcription factor 1***, lymphoid markers, and other markers usually resolve the differential diagnosis

# *Mammary carcinoma*

- is typically ***immunoreactive for CK7*** but not for CK20.
- ***Absence*** of reactivity for ***E-cadherin*** is helpful for identifying metastatic ***lobular carcinoma***.

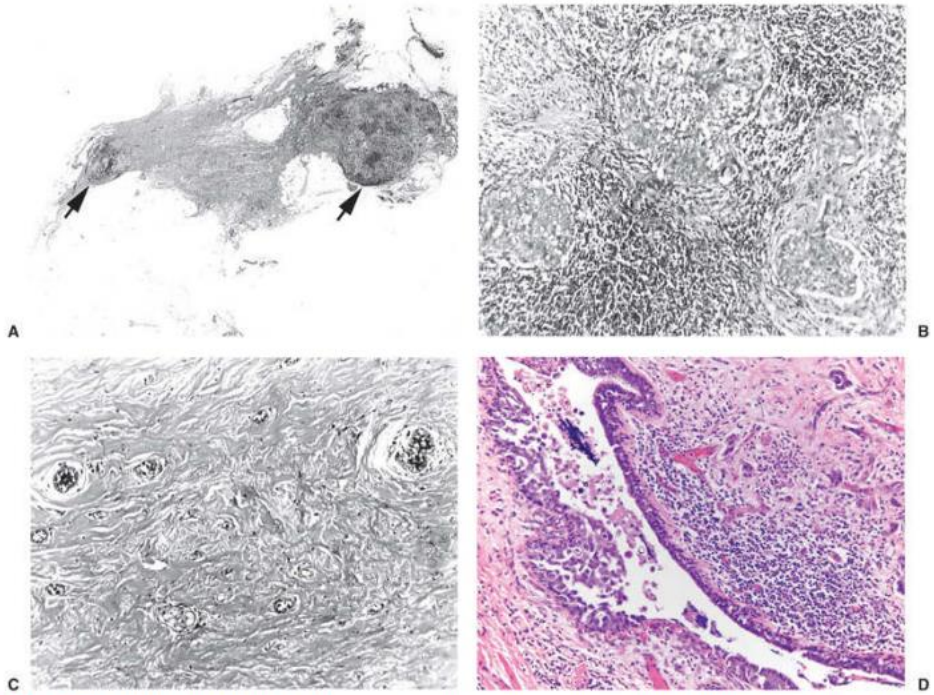



**FIG. 33.20. Occult carcinoma. A:** The entire occult carcinoma represented in this illustration consists of two nodular foci of intraductal carcinoma with lymphocytic reaction (*arrows* ) and in intervening zone of fibrosis. **B:** Focus of intraductal carcinoma in the *right-hand* nodule. **C:** Dense collagenous tissue in the center of the lesion could be the site of "healed" invasive carcinoma. **D:** Nearly the entire "occult" microinvasive and intraductal carcinoma in this case is represented in this figure. The patient presented with an enlarged lymph node. The metastatic poorly differentiated carcinoma therein was estrogen receptor negative and human epithelial growth factor receptor positive. More than 200 sections were prepared from the mastectomy specimen before this focus was detected. Ductal carcinoma *in situ* partially involved one duct. The invasive and *in situ* carcinoma cells were human epithelial growth factor receptor positive (not shown).

- An exceptionally high proportion of the occult primary ductal carcinomas have *apocrine cytology*, and there is a tendency for *cytoplasmic clearing* in the primary lesions as well as in the metastases.

- The invasive carcinomas tend to be poorly differentiated. The data presented in show some cases in which the only carcinoma detected in the breast appeared to be DCIS

# This phenomenon has been described

- in several studies.
- It is thought that metastases in these cases arose from invasive carcinoma that was inapparent **amid the *in situ* carcinoma** or from foci of ***"healed" invasive carcinoma***

**TABLE 33.2**

## Primary Carcinomas Found in Breast

| | No. (%) [a] |
|---|---|
| **Invasive** | 22 (79) |
| Invasive duct | (65) |
| Invasive lobular | (6) |
| Medullary | (6) |
| Colloid | (3) |
| **Noninvasive** | 7 (21) |
| Intraductal | (12) |
| *In situ* lobular | (6) |
| Intraductal and *in situ* lobular | (3) |

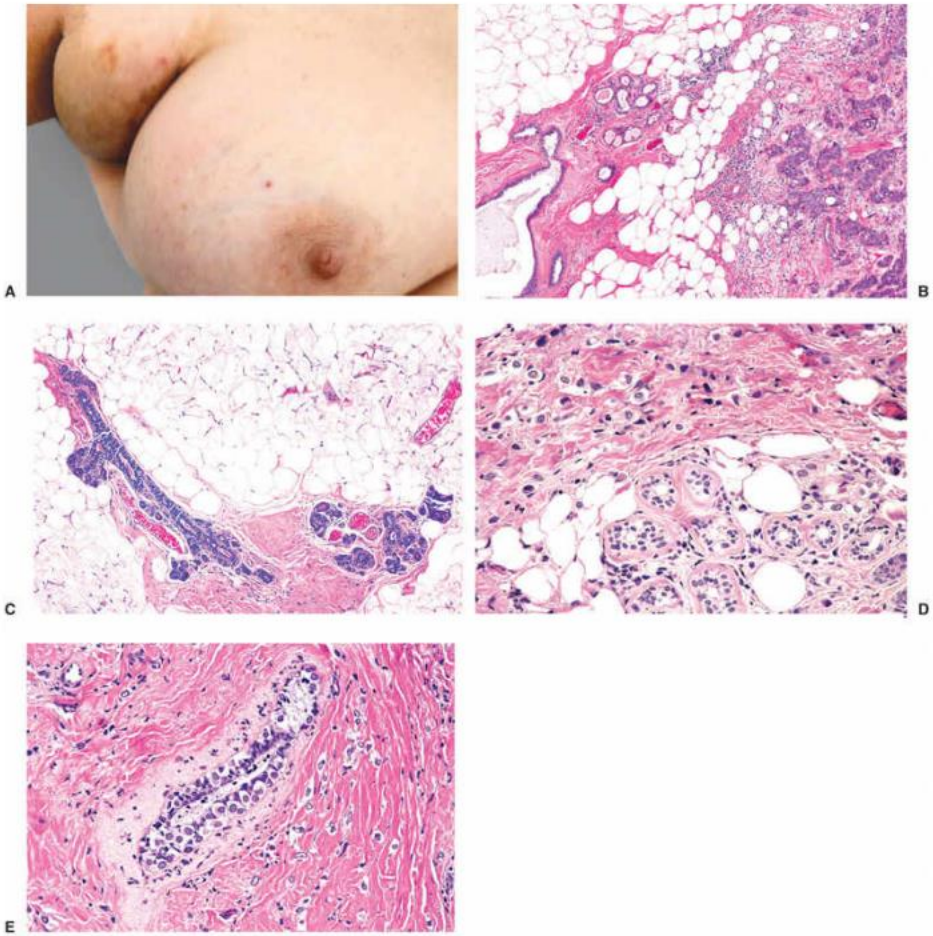



**FIG. 33.24. Ectopic breast tissue in axilla with invasive carcinoma. A,B:** Invasive carcinoma presenting as a distinct axillary mass (Courtesy: Dr. Alexander Swistel). **B:** Poorly differentiated ductal carcinoma in ectopic breast tissue in the axilla. **C–E:** These images are from a single axillary tumor. **C:** A normal lobule in axillary breast tissue. **D:** Invasive lobular carcinoma (ILC) in axillary tissue above benign glands. **E:** Pagetoid lobular carcinoma *in situ* (LCIS) in a duct surrounded by ILC.

- Among the tools available to pathologists in approaching these lesions, ***immunohistochemistry*** is a reliable, inexpensive, and widely available resource.

**TABLE 1.** Most Frequent CK7 and CK20 Profiles of Various Primary Carcinomas

| | |
|---|---|
| $CK7^{+}/CK20^{-}$ | Breast |
| | Ovarian |
| | Pulmonary (adenocarcinoma) |
| | Endometrial |
| | Thyroid |
| $CK7^{+}/CK20^{+}$ | Upper gastrointestinal (adenocarcinoma) |
| | Pancreatic (ductal) |
| | Urothelial |
| $CK7^{-}/CK20^{+}$ | Colorectal |
| | Merkel cell |
| $CK7^{-}/CK20^{-}$ | Prostatic |
| | Hepatocellular |
| | Renal cell |
| | Adrenal cortical |

- Two cytoplasmic markers used to identify breast carcinoma, ***mammaglobin*** (SCGB2A2) and
- **gross-cystic disease fluid protein-15** (GCDFP-15; prolactin-inducible protein),

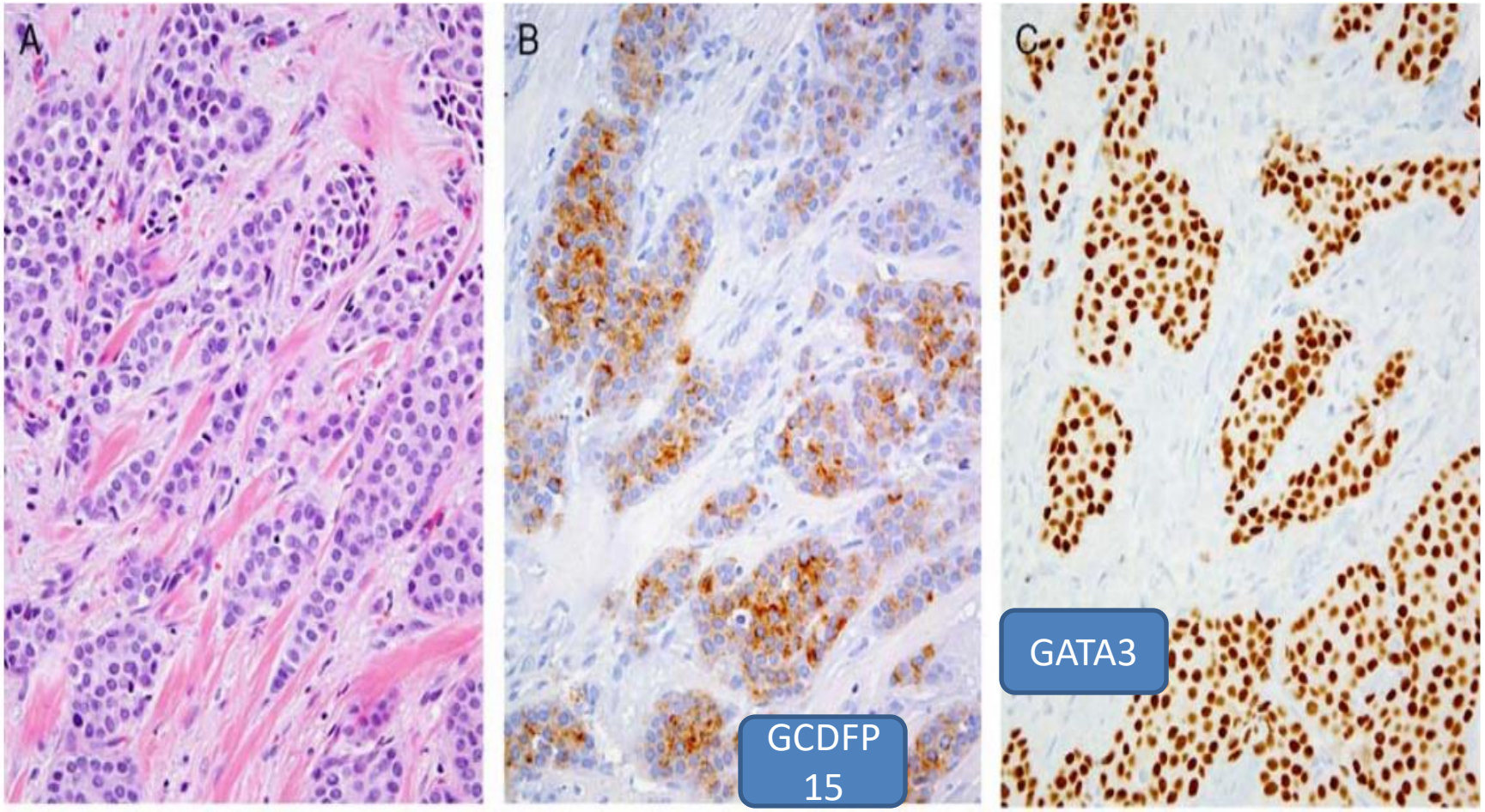
# Napsin A

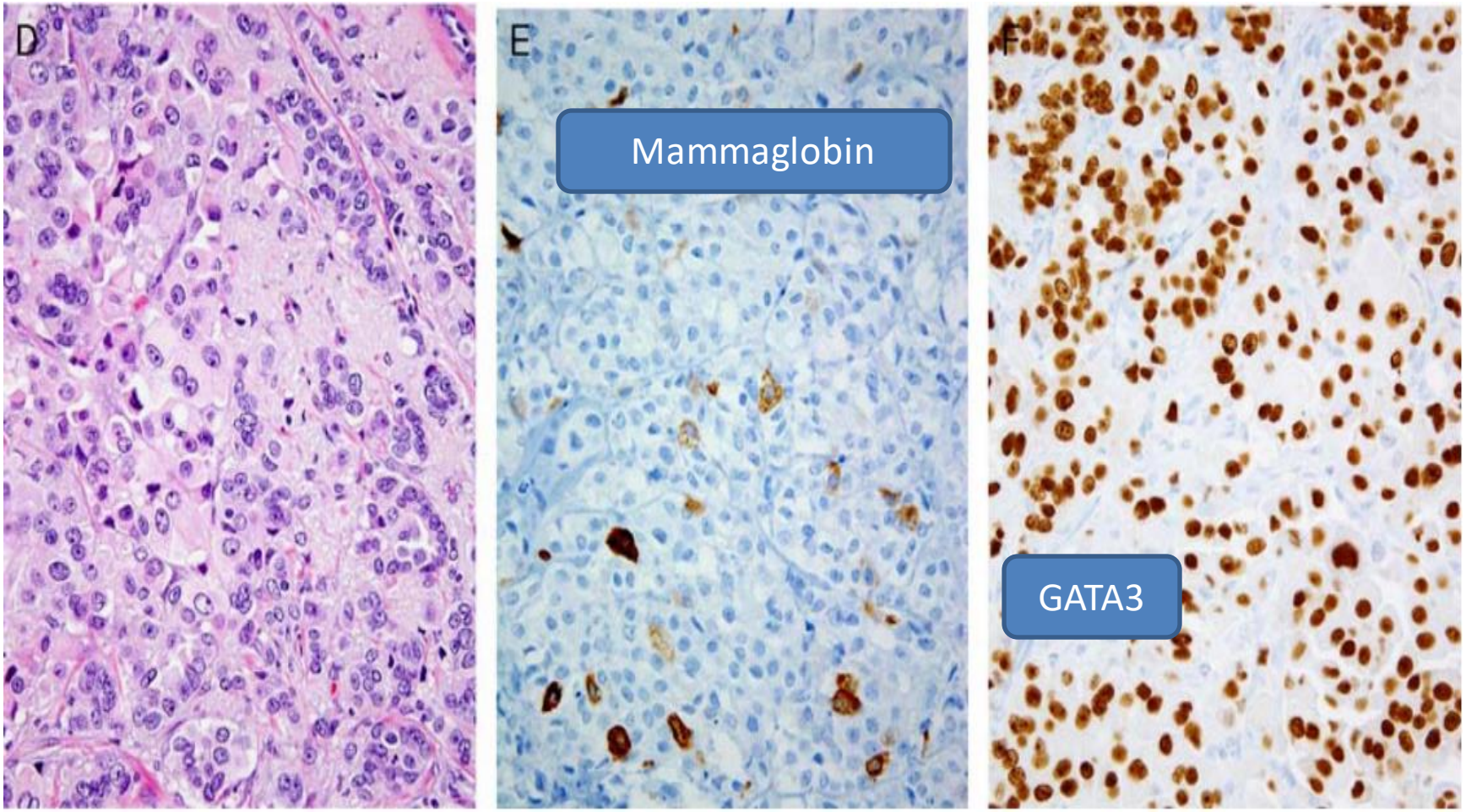
- is a relatively sensitive cytoplasmic marker of lung primary origin .
- It is expressed in *60% to 80% of*

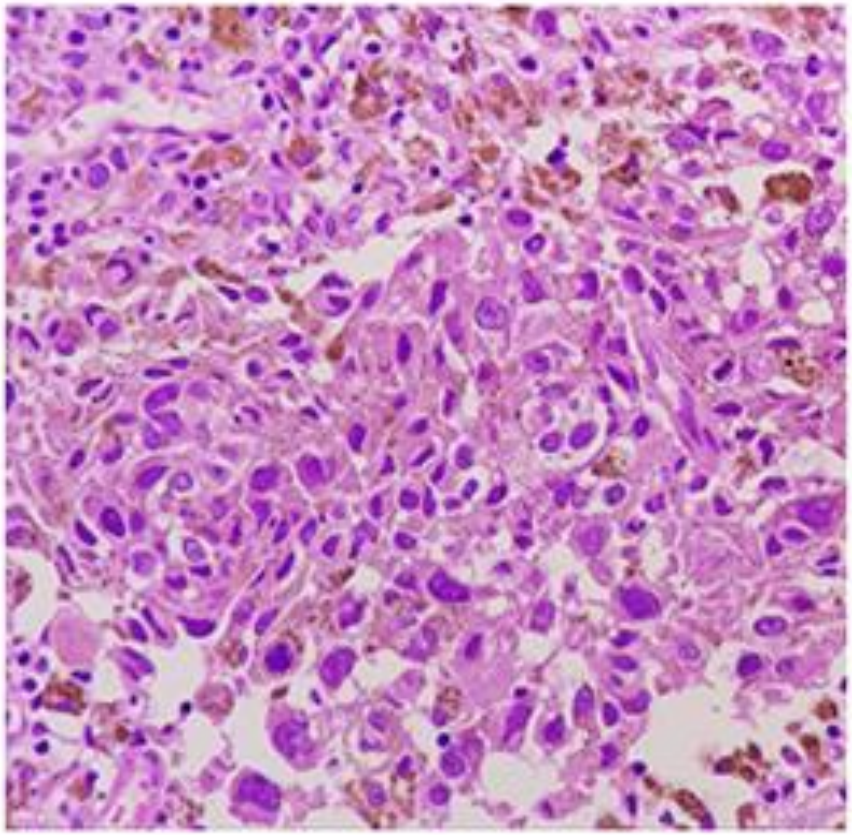
*lung adenocarcinomas* and is ***only slightly less sensitive*** than the nuclear marker

TTF-1 (NKX2-1), which is positive in 70% to 90% of these tumors.

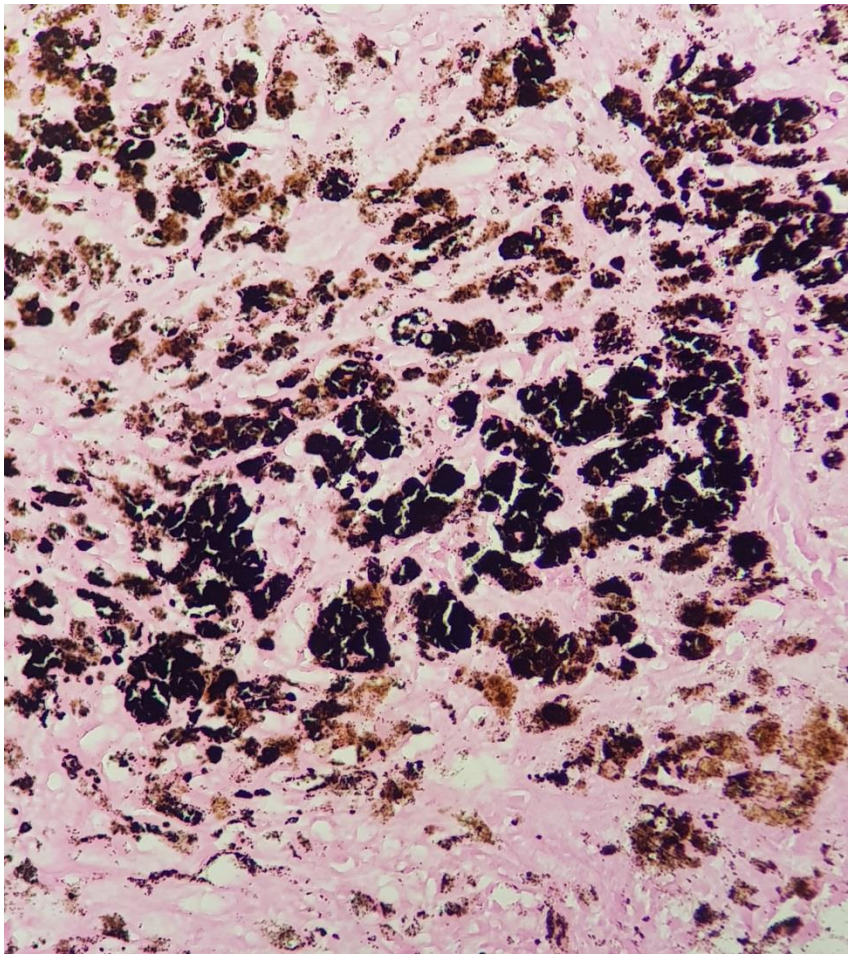
- Renal cell carcinoma marker (RCC), also known as
- GP200 (podocalyxin-like), is the most *widely utilized cytoplasmic marker of tumors of renal origin* in the metastatic setting.


A
B
C
GCDFP 15
GATA3

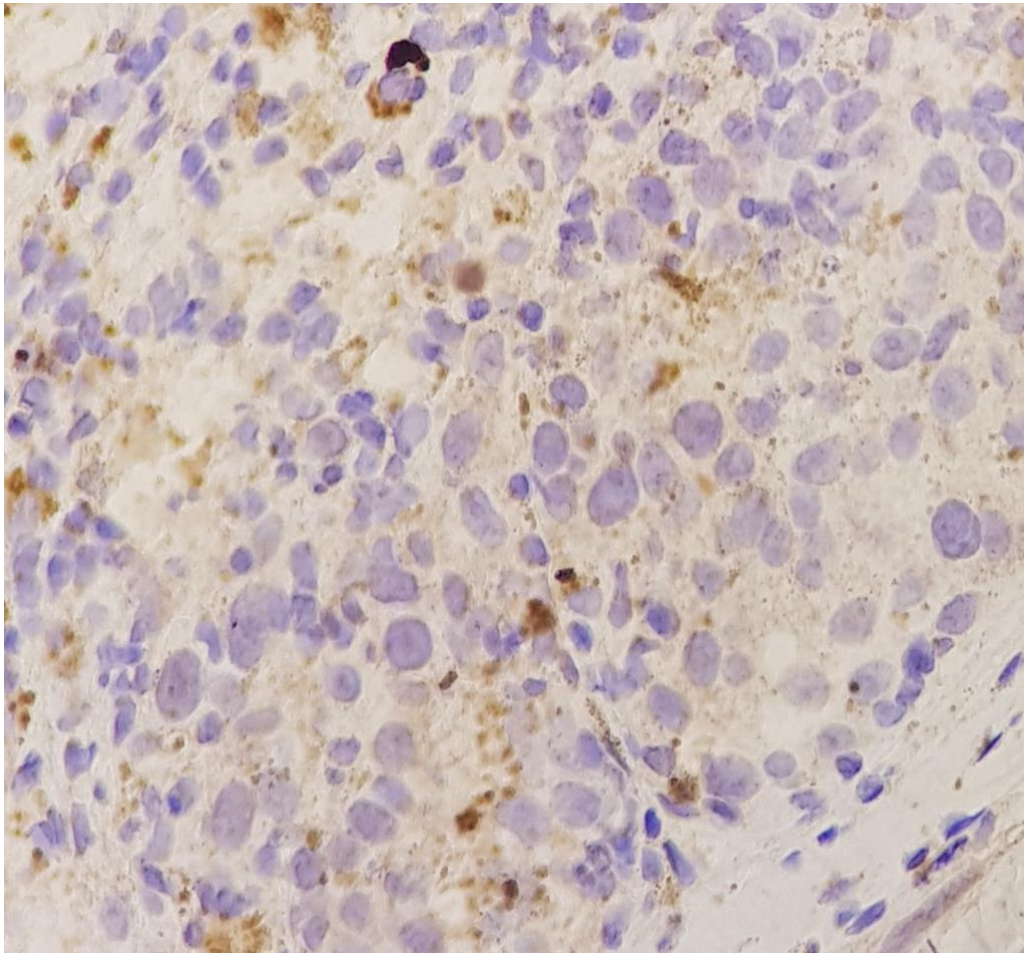

D
E
Mammaglobin
F
GATA3



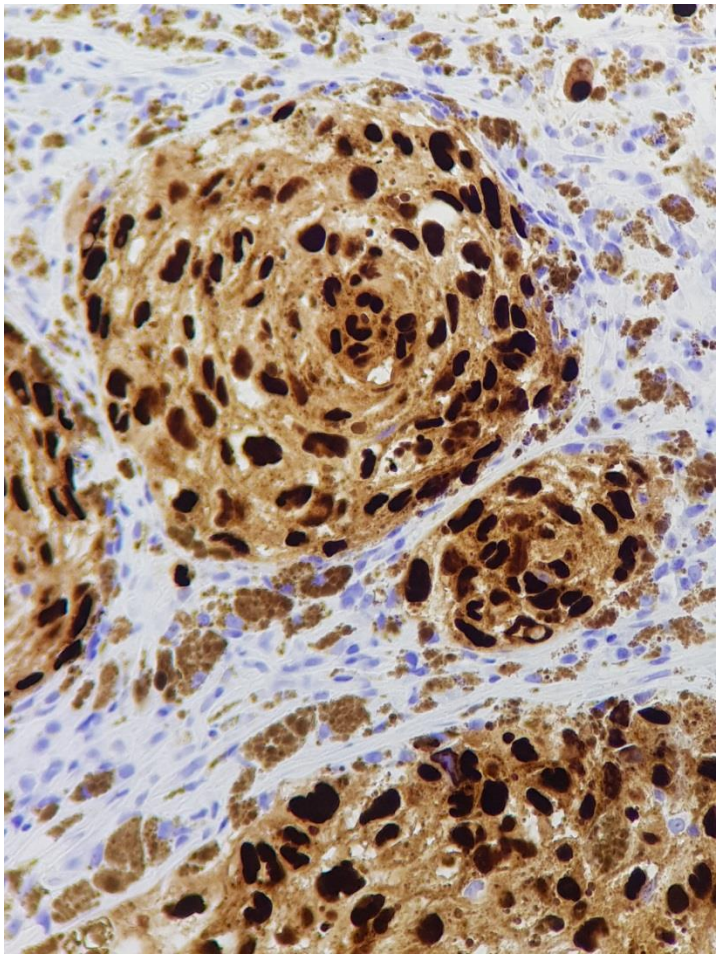
# FONTANA-MASSON



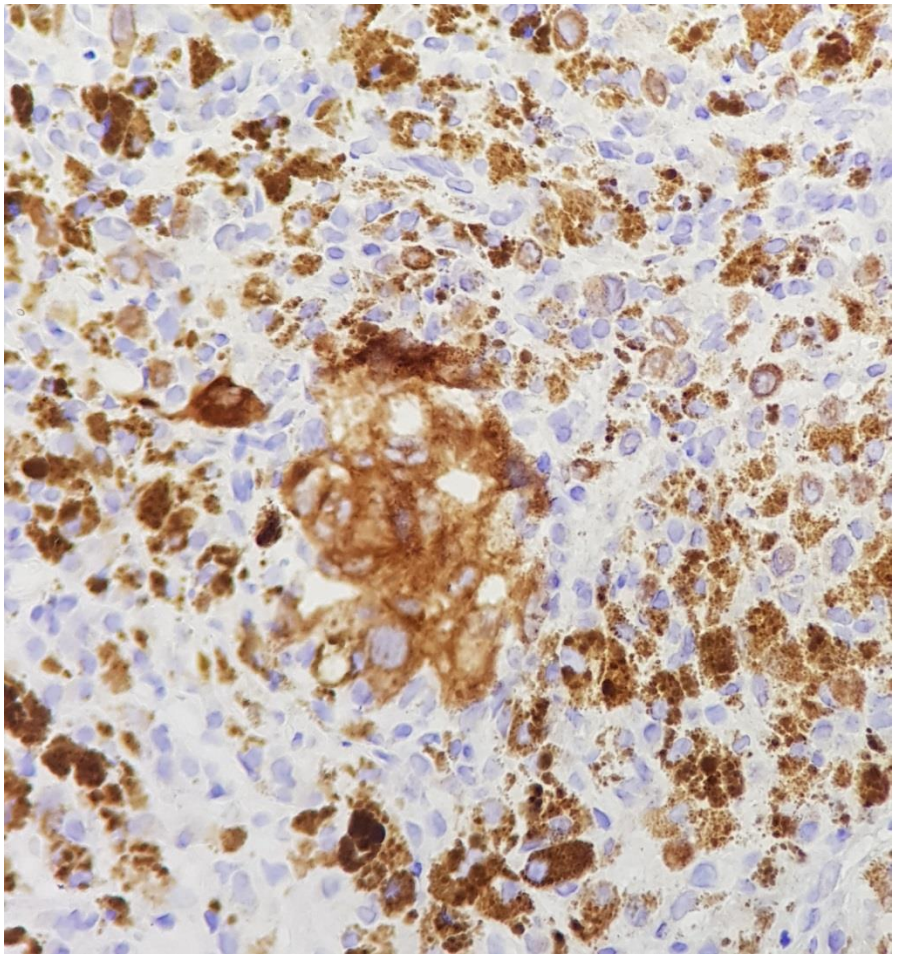
# CK AE1/3



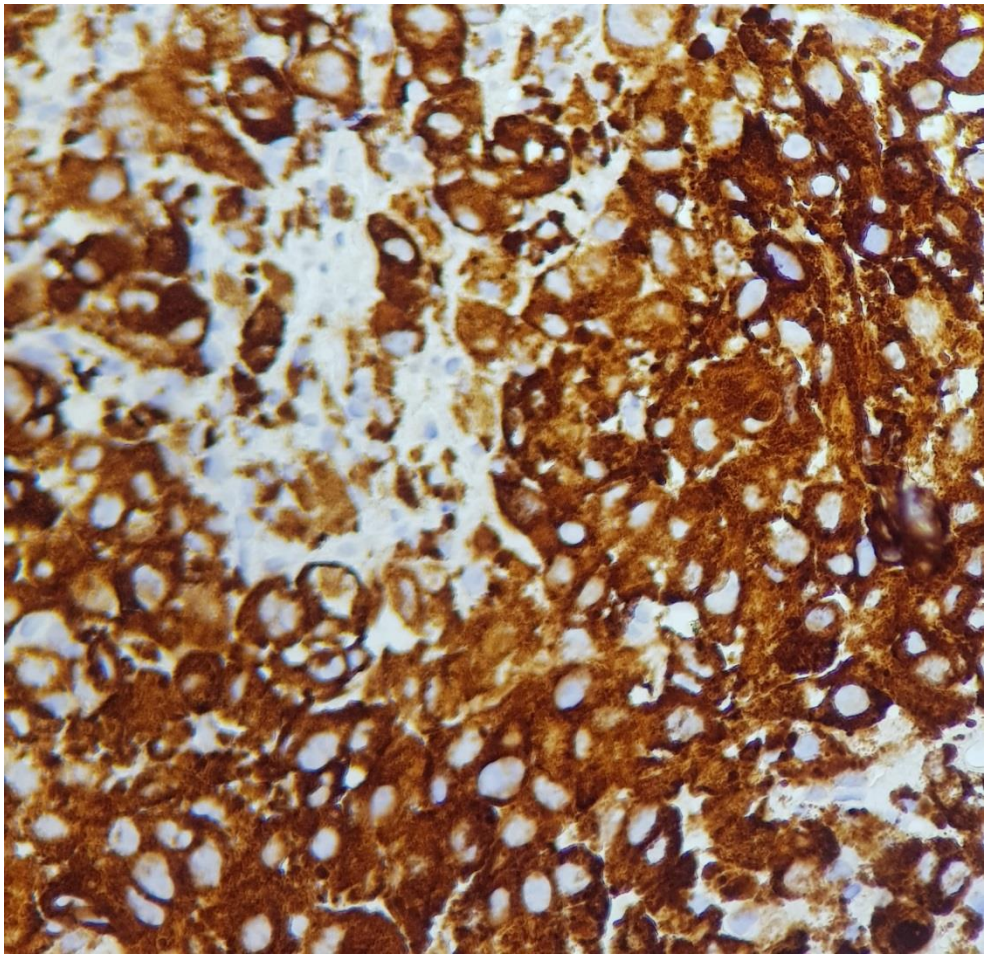
# SOX10



# Melan A



# HMB45



# S100