



МОСКОВСКИЙ КЛИНИЧЕСКИЙ НАУЧНЫЙ ЦЕНТР ИМЕНИ А.С. ЛОГИНОВА

«Разноликость» тройного негативного рака молочной железы

По материалам устного доклада на 7th Emirates Breast Pathology and Breast Cancer Conference, May 30-31, 2021

Цель демонстрации: представление клинического случая редкой опухоли молочной железы, биологические свойства которой требуют персонализированного подхода к диагностике и лечению



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Конференция «Рак молочной железы»
Мастер-класс по морфологической диагностике опухолей молочной железы

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Adenoid cystic carcinoma of the breast: a case report special triple-negative cancer subtype

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7th Emirates Breast Pathology and Breast Cancer Conference, May 30-31, 2021



Moscow
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History of present complaint (HPC)

- A 55-year-old woman with a left breast mass identified by **mammographic screening** was examined at our center



MCSC Moscow Clinical Scientific Center

LG



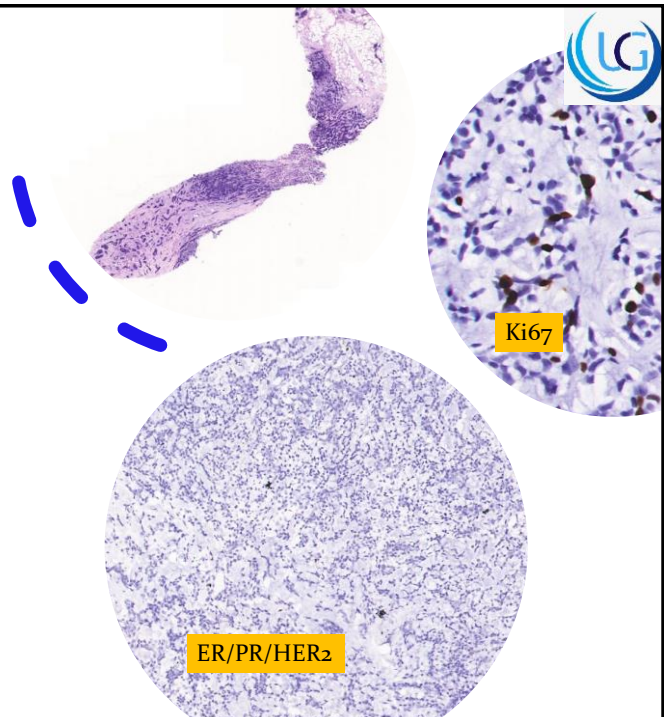
PHYSICAL EXAM

- Breast ultrasound revealed a sharply marginated, hypoechoic mass. $12 \times 0.8 \times 11.2$ mm in size in the upper outer quadrant, and a vacuum assisted biopsy (VAB) was performed at the mass site



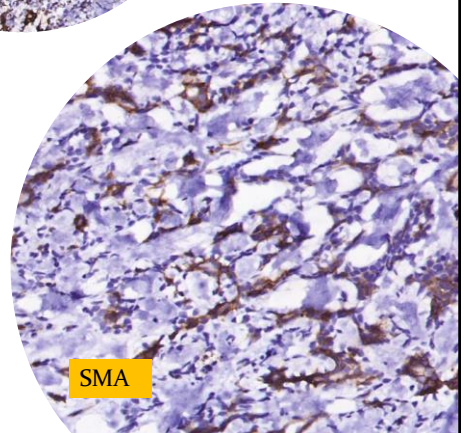
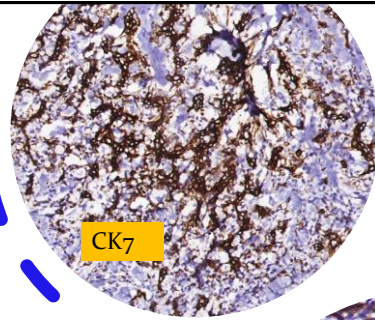
INITIAL INVESTIGATION

- In a pathological examination of the VAB specimen, reaching a pathological diagnosis of **Adenoid cystic carcinoma (AdCC)**
- Were negative for estrogen receptors, progesterone receptors, HER2-negative, ki67 was Low



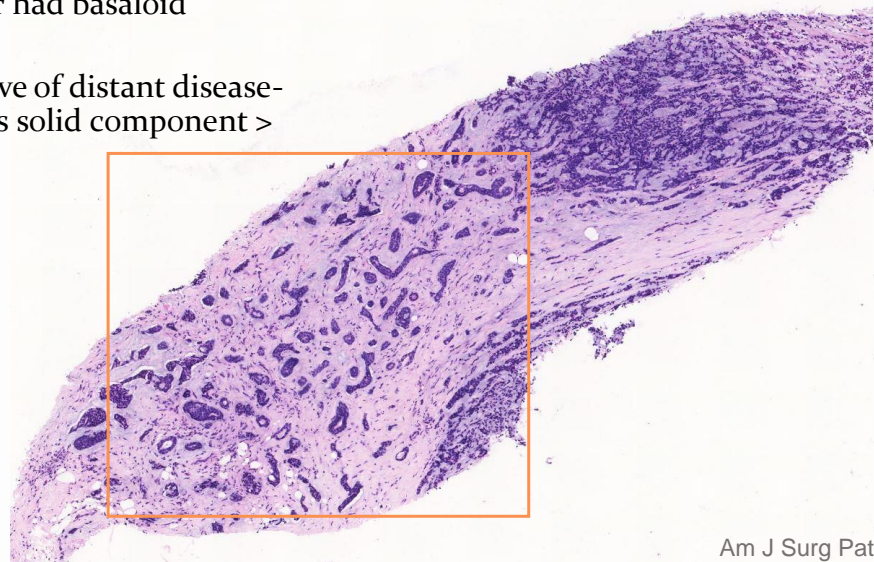
INITIAL INVESTIGATION

- biphasic with ductal and myoepithelial differentiation
- CK7 +
- Myoepithelial markers +



INITIAL INVESTIGATION

- Note, the tumor had basaloid component
- Factors predictive of distant disease-free survival was solid component > 50%



Am J Surg Pathol 2019

WORKING DIAGNOSIS AND TREATMENT



The preoperative clinical diagnosis was stage I (cT₁N₀M₀) triple-negative left breast cancer

Surgery consisted of breast segmental resection with axillary contents

The patient received one course of adjuvant chemotherapy

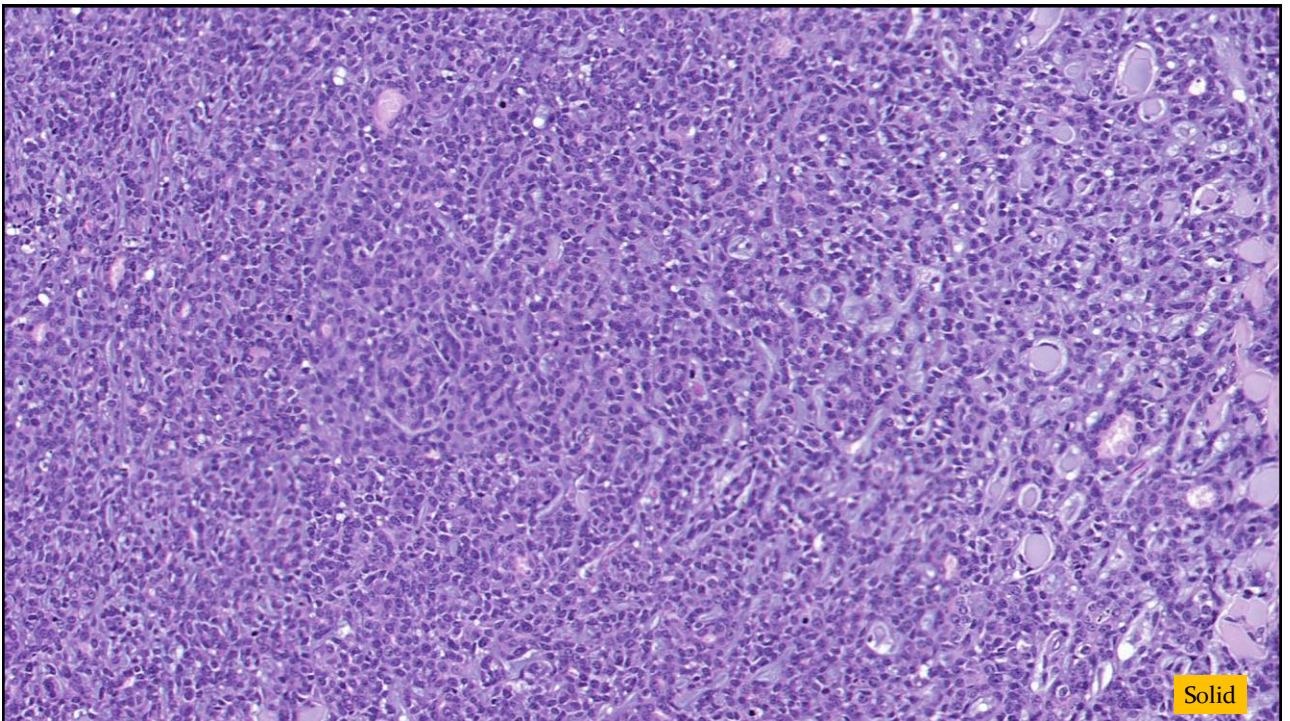
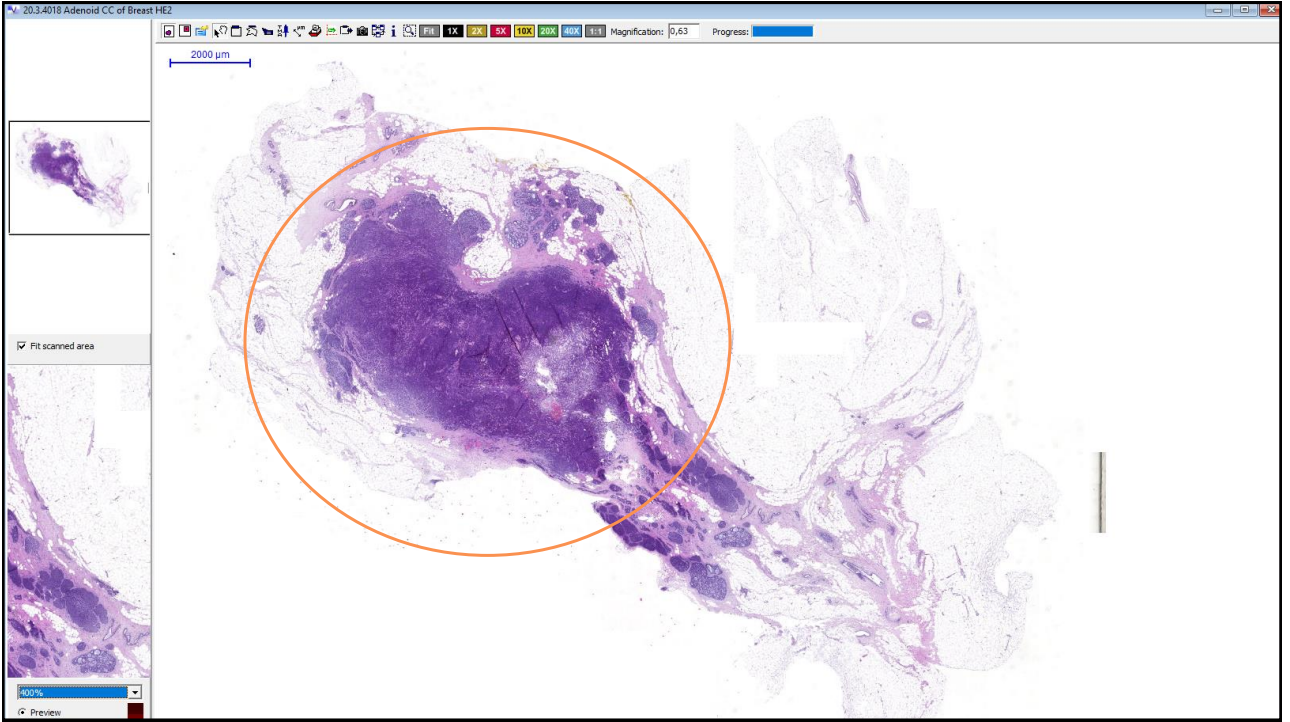


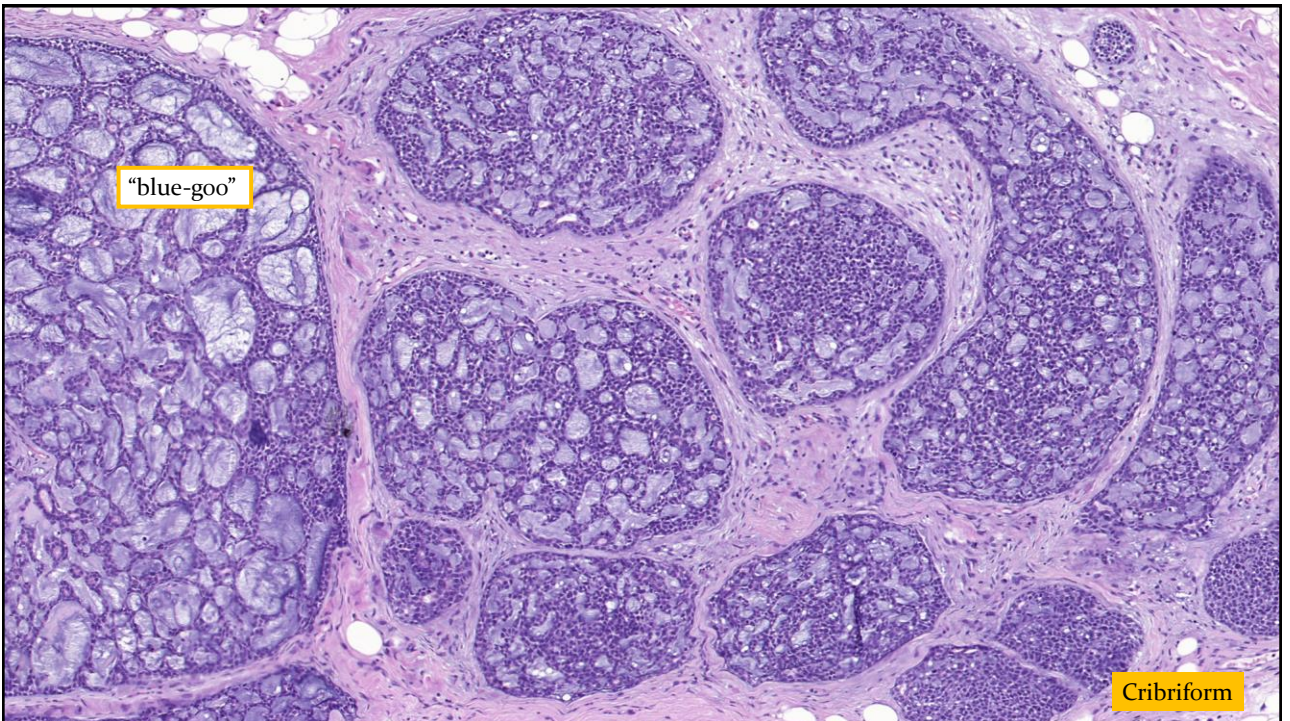
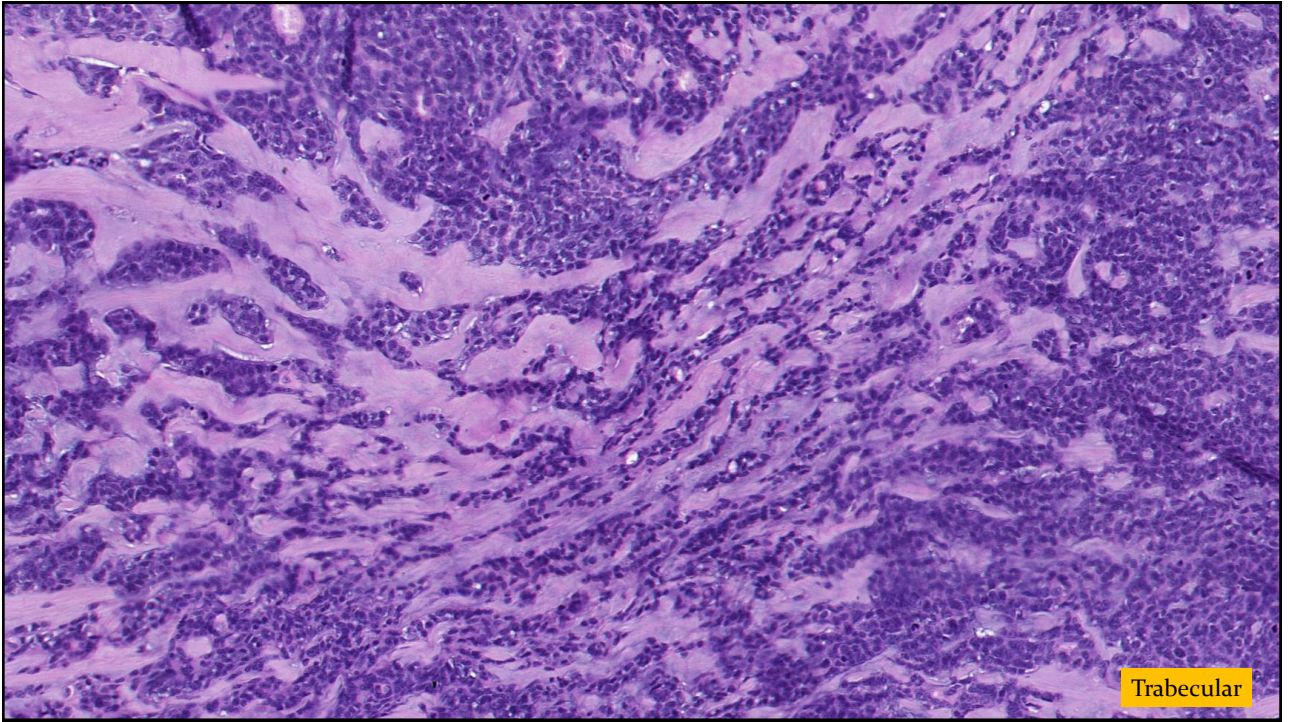
PATHOLOGICAL EXAMINATION

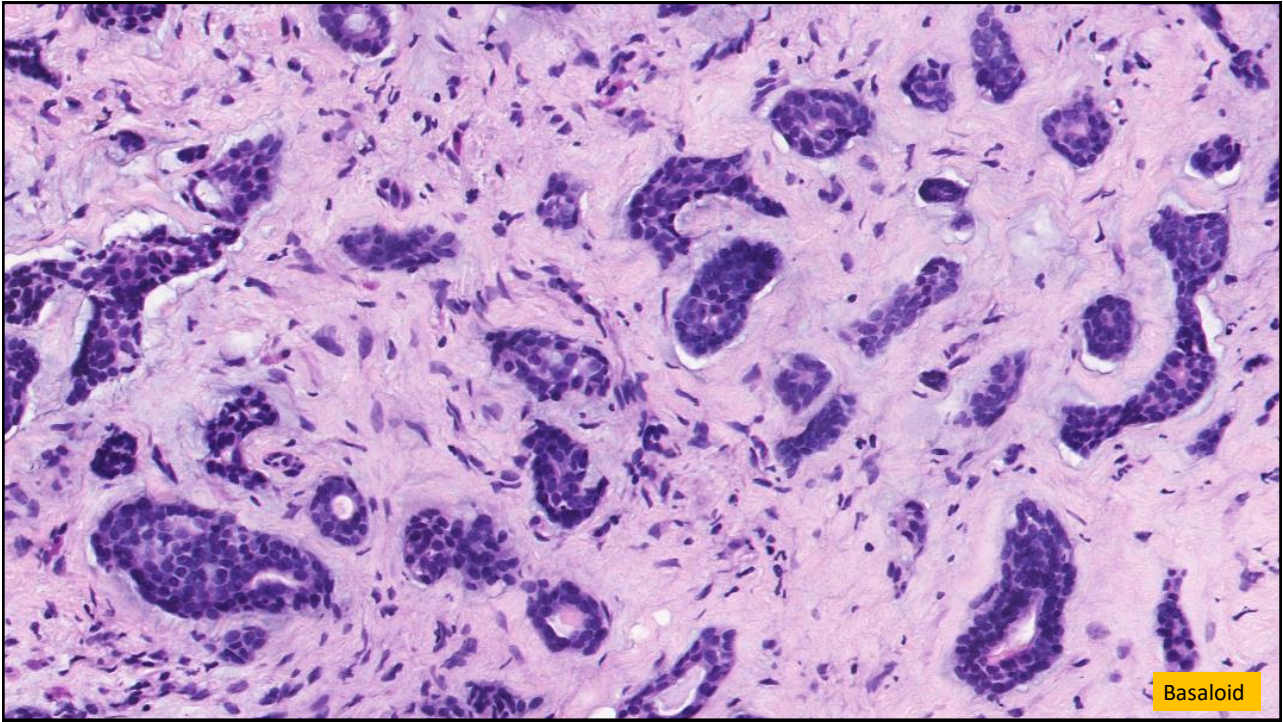


- The specimen of lumpectomy was sent within an hour to a pathology laboratory
- Used multiple ink colors
- Size of the tumor: 1.3x0.8x1 cm
- Distance to near margins: 5 mm
- 12 lymph nodes founded

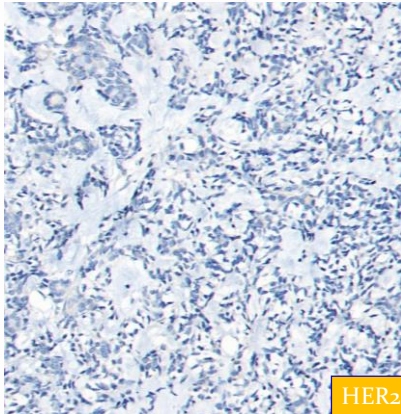
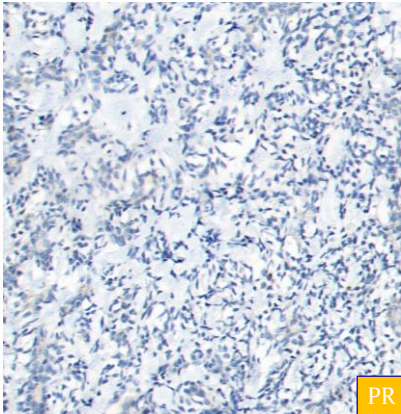
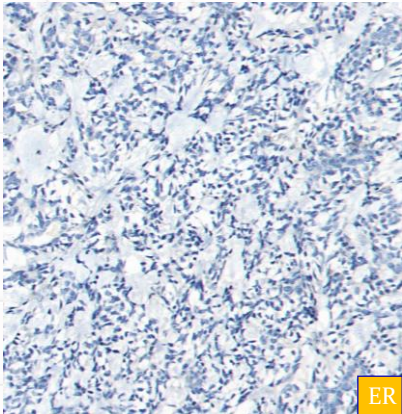








IMMUNOHISTOCHEMISTRY

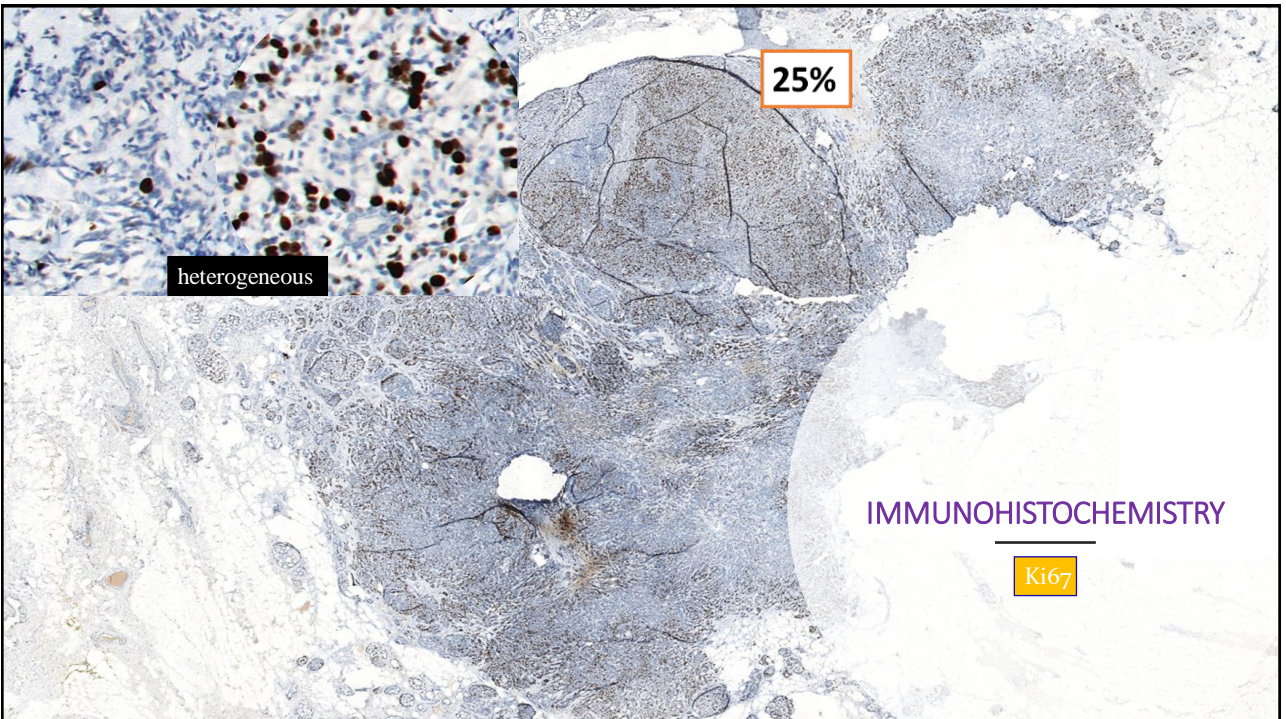
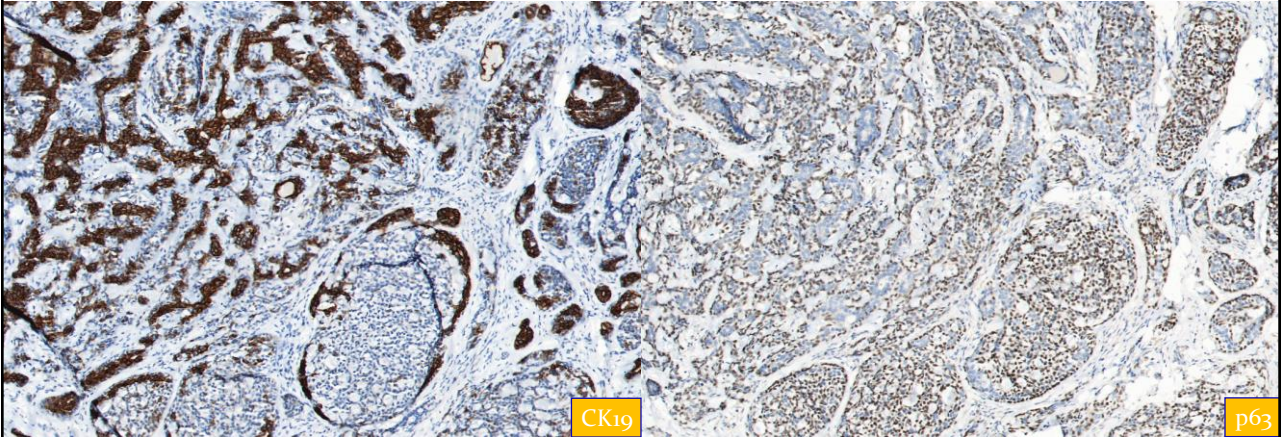


triple negative breast cancer

IMMUNOHISTOCHEMISTRY



Epithelial-myoepithelial carcinoma "dual cell composition"



FINAL DIAGNOSIS



- Pathological examination of the excised specimen revealed a so-called **adenoid cystic carcinoma without high-grade transformation (special triple-negative Low grade cancer)**
- ICD-O code 8200/3, LVo, Pno, Ro, pT1cNo (TNM AJCC 8th)



SPECIAL TRIPLE NEGATIVE BREAST CANCER



WHO classification of epithelial tumours of the breast

| | | | |
|---|--|---|---|
| Benign epithelial proliferations and precursors | | Invasive breast carcinoma | |
| Usual ductal hyperplasia | | 8500/3 | Infiltrating duct carcinoma NOS |
| Columnar cell lesions, including flat epithelial atypia | | 8290/3 | Oncocytic carcinoma |
| Atypical ductal hyperplasia | | 8314/3 | Lipid-rich carcinoma |
| Adenosis and benign sclerosing lesions | | 8315/3 | Glycogen-rich carcinoma |
| Sclerosing adenosis | | 8410/3 | Sebaceous carcinoma |
| 8401/0 | Apocrine adenoma | 8520/3 | Lobular carcinoma NOS |
| | Microglandular adenosis | 8211/3 | Tubular carcinoma |
| | Radial scar / complex sclerosing lesion | 8201/3 | Cribiform carcinoma NOS |
| Adenomas | | 8480/3 | Mucinous adenocarcinoma |
| 8211/0 | Tubular adenoma NOS | 8470/3 | Mucinous cystadenocarcinoma NOS |
| 8204/0 | Lactating adenoma | 8507/3 | Invasive micropapillary carcinoma of breast |
| 8503/0 | Duct adenoma NOS | 8401/3 | Apocrine adenocarcinoma |
| | | 8575/3 | Metaplastic carcinoma NOS |
| Epithelial-myoepithelial tumours | | Rare and salivary gland-type tumours | |
| 8940/0 | Pleomorphic adenoma | 8550/3 | Acinar cell carcinoma |
| 9983/0 | Adenomyoepithelioma NOS | 8200/3 | Adenoid cystic carcinoma |
| 9983/3 | Adenomyoepithelioma with carcinoma | | Classic adenoid cystic carcinoma |
| 8562/3 | Epithelial-myoepithelial carcinoma | | Solid-basaloid adenoid cystic carcinoma |
| | | | Adenoid cystic carcinoma with high-grade transformation |
| Papillary neoplasms | | 8502/3 | Secretory carcinoma |
| 8503/0 | Intraductal papilloma | 8430/3 | Mucoepidermoid carcinoma |
| 8503/2 | Ductal carcinoma in situ, papillary | 8529/3 | Polymorphous adenocarcinoma |
| 8504/2 | Encapsulated papillary carcinoma | 8509/3 | Tall cell carcinoma with reversed polarity |
| 8504/3 | Encapsulated papillary carcinoma with invasion | | |
| 8509/2 | Solid papillary carcinoma in situ | Neuroendocrine neoplasms | |
| 8509/3 | Solid papillary carcinoma with invasion | 8240/3 | Neuroendocrine tumour NOS |
| 8503/3 | Intraductal papillary adenocarcinoma with invasion | 8240/3 | Neuroendocrine tumour, grade 1 |
| | | 8249/3 | Neuroendocrine tumour, grade 2 |
| Non-invasive lobular neoplasia | | 8246/3 | Neuroendocrine carcinoma NOS |
| | Atypical lobular hyperplasia | 8041/3 | Neuroendocrine carcinoma, small cell |
| 8520/2 | Lobular carcinoma in situ NOS | 8013/3 | Neuroendocrine carcinoma, large cell |
| | Classic lobular carcinoma in situ | | |
| | Floreal lobular carcinoma in situ | | |
| 8519/2 | Lobular carcinoma in situ, pleomorphic | | |
| Ductal carcinoma in situ (DCIS) | | | |
| 8500/2 | Intraductal carcinoma, non-infiltrating, NOS | | |
| | DCIS of low nuclear grade | | |
| | DCIS of intermediate nuclear grade | | |
| | DCIS of high nuclear grade | | |

WHO Classification of epithelial tumours of the breast, 5th Edition



DISCUSSION



- Adenoid cystic carcinoma (AdCC) of the breast is rare, accounting for less than 0.1% of all breast cancers
- Unlike counterpart in the salivary gland, AdCC of the breast is associated with an excellent prognosis paradoxical to its unfavorable, triple-negative hormonal receptor profile

Table 1 Summary of rare triple negative breast cancers

| Variables/population | Adenoid cystic carcinoma | Secretory carcinoma | Acinic cell carcinoma | Carcinoma with apocrine differentiation | Carcinoma arising in microglandular adenosis |
|---------------------------------|------------------------------|--|------------------------|---|--|
| ER | Negative | Negative | Negative | Negative | Negative |
| PR | Negative | Negative | Negative | Negative | Negative |
| HER2 | Negative | Negative | Negative | Positive/Negative | Negative |
| AR | – | – | Negative | Positive | – |
| Mean age (range) | 64 years | 25 years (3–87 years) | 56 years (35–80 years) | – | 50–60 years |
| Location (percentage) | Subareolar (50%) | Near the areola | – | – | – |
| Tumor size (average) | 0.5–12 cm (3 cm) | 0.5–12 cm (3 cm) | 1–5 cm | – | Typically a microscopic lesion |
| Chromosomal translocation | t (6; 9) (q22-23; p23-24) | t (12; 15) | – | Gain of 1p, 1q, 2q, loss of 1p, 12q, 16q, 17q | Gain of 8q, loss of 5q |
| Fusion/mutation genes | MYB, NFIB | ETV6-NTRK3 | TP53, MLL3, FOXA1 | AR | – |
| Malignant biological properties | Low-grade malignant | Low-grade malignant | Low-grade malignant | – | Uncertain |
| Prognosis | 10-year survival rates > 90% | Favorable prognosis in young patients (< 20 years) | Favorable prognosis | Relatively poor prognosis | Uncertain |



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CANCER, 2002 Apr 15;94(8):2119-27. doi: 10.1002/cncr.10455
Cancer Biol Med 2020. doi: 10.20892/cbm.2019.0465

DISCUSSION

Is adjuvant chemotherapy **necessary**?



- Conclusion of retrospective study in China: AdCCs all patients (N=16) were not responsive to chemotherapy

Original Article

The effect of first line chemotherapy on adenoid cystic carcinoma of breast

Yang Yang, Zhaoqing Fan, Yingjian He, Yiqiang Liu, Tao Ouyang

Table 1. Characteristics of ACCs and matched IDCs

| Characteristics | ACCs (N=16) | 1:4 matched IDCs (N=64) |
|--|---------------|-------------------------|
| Age (years) | 54.6 (35-77) | 58.2 (40-78) |
| <50 | 7 (43.7%) | 28 (43.7%) |
| ≥50 | 9 (56.3%) | 36 (56.3%) |
| Tumor size | 2.3 (1.2-5.7) | 2.5 (1.5-5.4) |
| T1 | 7 (43.7%) | 28 (43.7%) |
| T2 | 8 (50%) | 32 (50%) |
| T3 | 1 (6.3%) | 4 (6.3%) |
| ER | | |
| Negative | 16 (100%) | 64 (100%) |
| PR | | |
| Negative | 16 (100%) | 64 (100%) |
| HER2 | | |
| Negative | 16 (100%) | 64 (100%) |
| LN | | |
| Positive | 2 (12.5%) | 8 (12.5%) |
| Negative | 14 (87.5%) | 56 (87.5%) |
| Chemotherapy regimen | | |
| 4 cycles CEF3w followed by 4 cycles Tq1w | 16 (100%) | 64 (100%) |

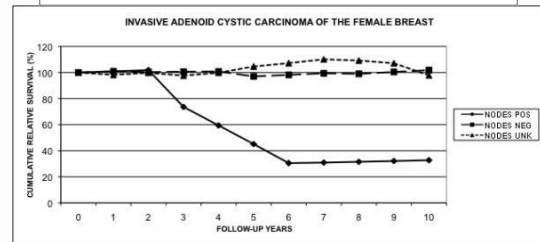
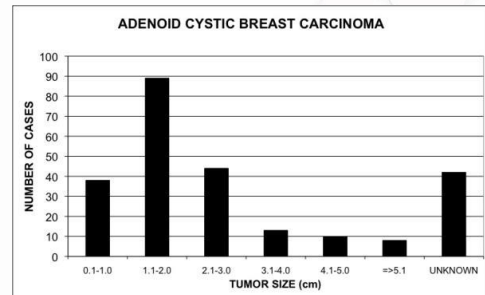
Int J Clin Exp Med 2019;12(12):13700-13705

DISCUSSION

Is Axillary Staging **Necessary** in All Cases?



- At the time of diagnosis, 92% (n = 225) of patients had localized disease
- 5% (n = 12) of patients had regional disease, and even fewer (n = 7) had either distant or unknown staged disease
- Lymph node involvement was not present in any tumors smaller than 1.4 cm



Breast J. 2011 ; 17(5): 485-489. doi:10.1111/j.1524-4741.2011.01117.x.



DISCUSSION

May ACC of the breast has an **aggressive** potential?



CASE REPORT

Open Access



Adenoid cystic carcinoma of the breast – an aggressive presentation with pulmonary, kidney, and brain metastases: a case report

Hasnae Alaoui Mhamdi^{1*}, Hampig Raphael Kourie², Christiane Jungels³, Philippe Aftimos³, Rhizlane Belbaraka¹ and Martine Piccart-Gebhart³

- The tumor measured: was **8 cm (T₃)**
- Distant metastasis: was in brain, lung, kidney
- Time to relapse: **5 years**

There is not enough data about pathological examination!



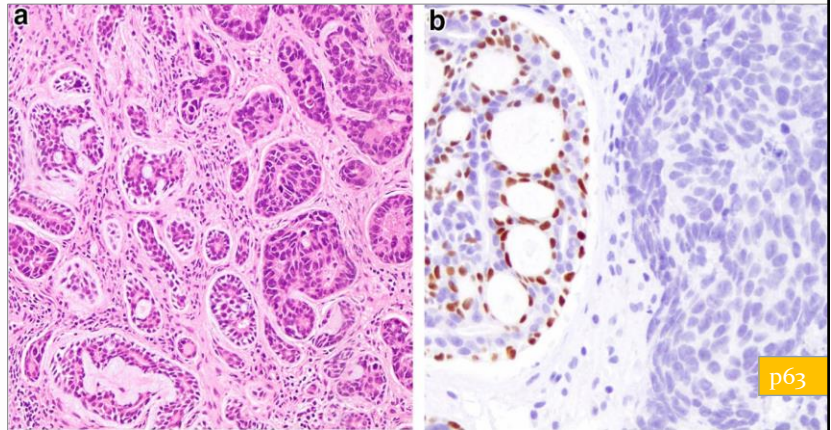
Mhamdi et al. Journal of Medical Case Reports (2017) 11:303, DOI 10.1186/s13256-017-1459-0

DISCUSSION

May ACC of the breast has an **aggressive** potential?

High-Grade Transformation

- HGT is the preferred terminology (over dedifferentiation) for progression of a (usually) lower grade carcinoma with conventional morphology into a pleomorphic high-grade carcinoma
- Tumors for which this phenomenon is well characterized include AdCC
- **The same phenomenon can occur in AdCC of the breast**



Head and Neck Pathol DOI 10.1007/s12105-017-0795-0
Am J Surg Pathol, 2007 Nov;31(11):1683-94.

CONCLUSION

- Pathologist should examine the tumor totally to exclude HGT
- More effective therapies for patients with special types of breast cancer require tailored investigations through international cooperation. It should not rely on information predominantly contributed from small retrospective analyses



Thank you for your attention!

as diverse as our life

works by Dimitr Taushanskiy