

## Evaluation of Tru-Cut biopsy in differential diagnosis and challenges in breast adenoid cystic carcinoma on a case basis

Ilyas Sayar <sup>A,C,F</sup>, Ufuk Memiş <sup>B,C,D</sup>, Sami Bilici <sup>B,C,D</sup>, Nurten Arslan Isik <sup>\*B,C,E</sup>

Erzincan Binali Yıldırım University, Turkey

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

### Key words:

adenoid cystic carcinoma, breast carcinoma, Tru-Cut biopsy.

### Pathologia

2022; 19 (2), 142-145

### \*E-mail:

nurtenarslanisik1@gmail.com

Adenoid cystic carcinoma (AdCC) is a very rare low-grade invasive carcinoma primarily in the breast. The fact that similar patterns can be observed in invasive breast carcinomas (IBC) such as AdCC and breast ductal carcinoma in situ (DCIS) in Tru-Cut biopsies creates difficulties in the differential diagnosis.

**Case presentation.** A 70-year-old female patient was admitted to our outpatient clinic with the complaint of a palpable mass in the left breast subareolar region. In the light microscopy examination of 3 tissue samples with a size of 3 measurements, IBC-like tubular structures, some of which were formed by tiny uniform cells with narrow cytoplasm, and some with eosinophilic material, and solid nest structures suggesting DCIS in focal areas were observed.

Immunohistochemical examination showed continuity of myoepithelial cells with p63 and calponin, and epithelial cells, staining with Cd117 and CK7. No staining was observed with progesterone, estrogen, and Cerbb2. The staining rate of Ki-67 was determined as 2 percent. A diagnosis of AdCC was made with these findings.

**Conclusions.** It is important to search for different patterns in addition to double cell population and pay attention to the material in the lumens in breast Tru-Cut biopsies that contain AdCC patterns that may cause the diagnosis of IBC and DCIS in error.

### Ключові слова:

аденоїдно-кістозна карцинома, карцинома молочної залози, черезшкірна біопсія.

### Патологія. 2022.

Т. 19, № 2(55).  
С. 142-145

## Проблеми оцінювання та диференційної діагностики аденоїдно-кістозної карциноми молочної залози в черезшкірній біопсії на основі окремого випадку

Ільяс Саяр, Уфук Меміш, Самі Білічі, Нуртен Арслан Ісік

Аденоїдно-кістозна карцинома (AdCC) – дуже рідкісна низькодиференційована інвазивна карцинома переважно молочної залози. Те, що у черезшкірних біоптатах подібні з AdCC патерни можна спостерігати в інвазивній карциномі молочної залози (IBC) та в карциномі in situ (DCIS), спричиняє труднощі їхньої диференційної діагностики.

**Клінічний випадок.** Хвора, 70 років надійшла до нашої клініки зі скаргами на пальпаторне утворення в субареоларній ділянці лівої молочної залози. Під час мікроскопічного дослідження в 3 зразках тканини черезшкірного біоптату пухлини молочної залози виявили IBC-подібні трубчасті структури, деякі з яких були утворені дрібними уніформними клітинами з вузькою цитоплазмою, інші містили еозинофільний матеріал у просвітах, а також гнізда солідноклітинних структур, що вказувало на DCIS у фокальних зонах.

Під час імуногістохімічного дослідження визначили р63-позитивні і кальпонін-позитивні міоепітеліальні клітини, Cd117-позитивні та CK7-позитивні епітеліальні клітини. Експресію прогестерону, естрогену і Cerbb2 не спостерігали. Експресія Ki-67 виявлена у 2 % клітин. За цими результатами встановили діагноз AdCC.

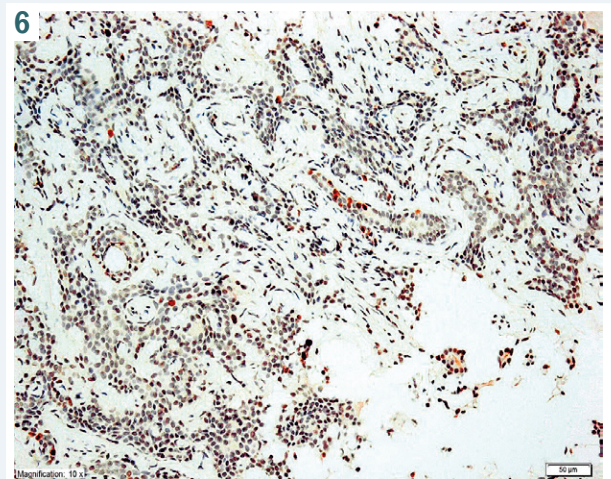
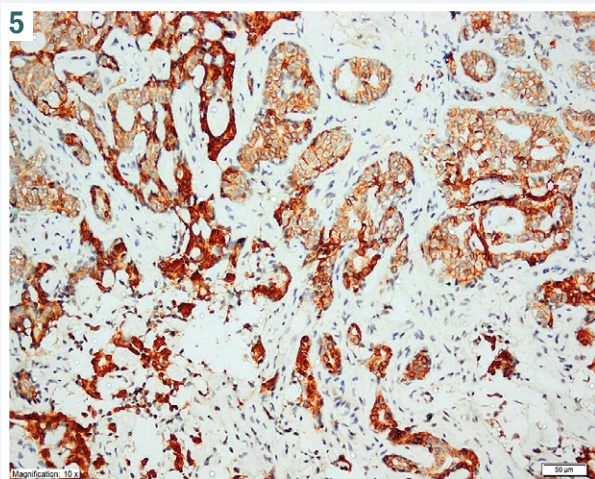
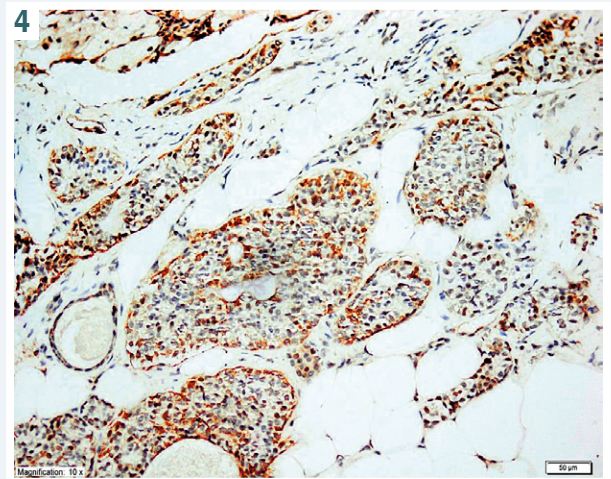
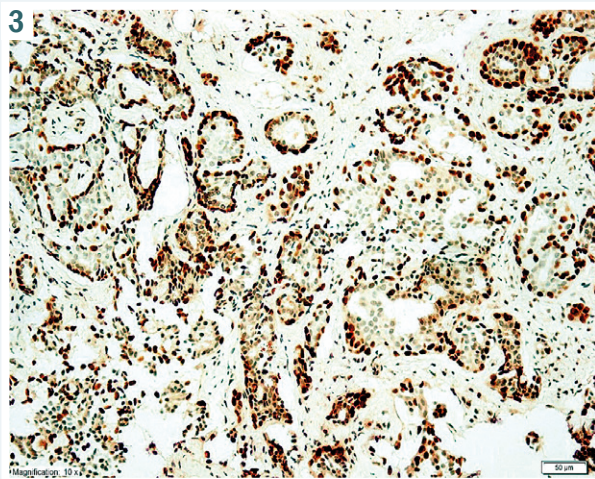
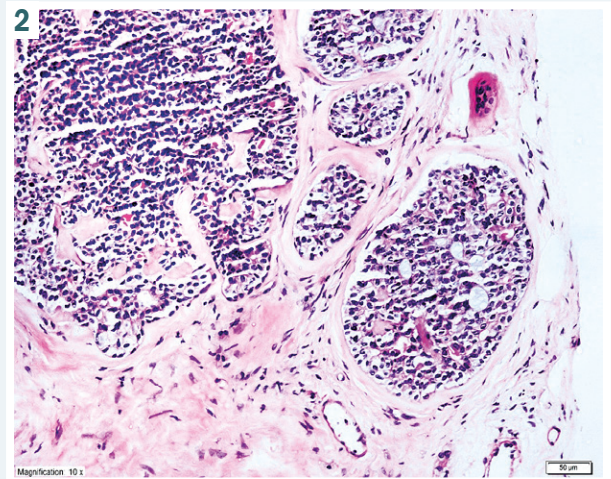
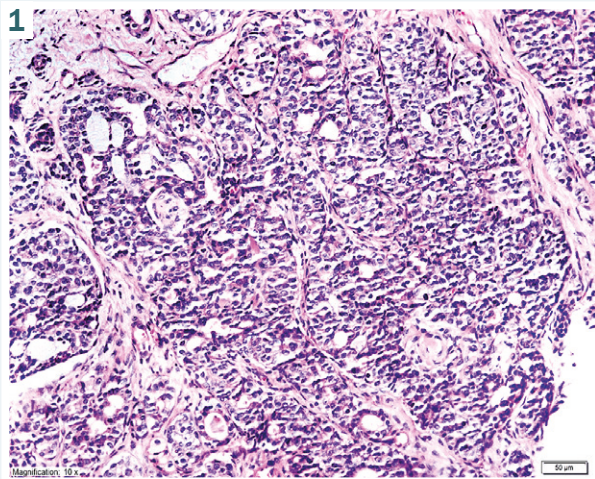
**Висновки.** У біоптатах грудної залози, крім подвійної популяції пухлинних клітин (епітеліальних і міоепітеліальних), важливо визначити різні патерни пухлини та звертати увагу на матеріал у просвітах трубчастих структур, що містять патерни AdCC і можуть призвести до помилкової діагностики IBC і DCIS. У сумнівних випадках під час імуногістохімічного дослідження корисним є використання хоча б одного міоепітеліального маркера та епітеліальних маркерів, як-от Cd117 і CK7.

Adenoid cystic carcinoma (AdCC), in which 3 subtypes are distinguished (classic adenoid cystic carcinoma, solid basaloid adenoid cystic carcinoma, adenoid cystic carcinoma with high grade transformation) is a very rare low-grade invasive carcinoma primarily in the breast [1]. It is generally observed as well-circumscribed lobular masses in the central region and subareolar area of the breast in the 6<sup>th</sup> and 7<sup>th</sup> decades [2].

Histopathologically, the structures in the cribriform pattern with myxoid or eosinophilic material within their lumens – which facilitates diagnosis – can also be found in tubular, solid, and trabecular patterns, Cd117

staining in epithelial cells by immunohistochemistry and detection of myoepithelial cells with markers such as p63 and calponin are helpful in diagnostics and differential diagnostics [1].

Breast AdCC treatment is sufficient with surgery alone and the prognosis is generally good [3]. The fact that similar patterns can be observed in invasive breast carcinomas (IBC) such as AdCC and carcinoma in situ (DCIS) in Tru-Cut biopsies creates difficulties in the differential diagnosis. Another point to be considered in the differential diagnosis is the limitation of the biopsy material to represent in the whole.



**Fig. 1.** IBC-like tubular structures and pink eosinophilic material in some part of the lumen. HE  $\times 200$ .

**Fig. 2.** DCIS-like pattern. HE  $\times 200$ .

**Fig. 3.** Myoepithelial cells interspersed in the basal layer and locally in epithelial cells. p63  $\times 200$ .

**Fig. 4.** Myoepithelial cells interspersed in the basal layer and locally in epithelial cells. Calponin  $\times 200$ .

**Fig. 5.** Diffuse staining of Cd117 epithelial cells. Cd117  $\times 200$ .

**Fig. 6.** Staining pattern of Ki-67. Ki-67  $\times 200$ .

In this article, the differential diagnosis of breast AdCCs with IBC and DCIS, and histopathological and immunohistochemical clues in a case of breast AdCC are discussed within the literature.

### Case presentation

A 70-year-old female patient was admitted to our outpatient clinic with the complaint of a palpable mass in the left breast subareolar region. A hard fixed mass was detected in this area on physical examination. Mammography showed a smooth contoured opacity 1 cm in diameter in the subareolar region of the left breast and ultrasonography showed a hypoechoic solid mass (BIRADS 4) at a distance of 5 cm from the left breast areola. A Tru-Cut biopsy was performed. The largest is  $0.6 \times 0.1 \times 0.1$  cm the smallest is  $0.2 \times 0.1 \times 0.1$  cm.

In the light microscopy examination of 3 tissue samples with a size of 3 measurements, IBC-like tubular structures (Fig. 1), some of which were formed by tiny uniform cells with narrow cytoplasm, and some with eosinophilic material, and solid nest structures suggesting DCIS in focal areas were observed (Fig. 2).

In addition, cribriform structures with mixed material in their lumens were observed in several areas. Immunohistochemical examination showed continuity of myoepithelial cells with p63 (Fig. 3) and calponin (Fig. 4). Diffuse staining was observed in epithelial cells with Cd117 (Fig. 5), while CK7 focal staining was observed. No staining was observed with progesterone, estrogen, and Cerbb2. The staining rate of Ki-67 was determined as 2 percent (Fig. 6). A diagnosis of AdCC was made with these findings.

Written consent from patient was taken.

### Discussion

Breast AdCC differs significantly from breast IBC and DCIS in terms of treatment and prognosis [4]. Therefore, diagnosis and differential diagnosis with Tru-Cut biopsy is important. There are difficulties in differential diagnosis with Tru-Cut biopsy. At this point, histological and immunohistochemical clues can be guiding. In our experience, histologically solid and tubular patterns in large areas are indeed a problem in Tru-Cut biopsy materials and may cause the misdiagnosis of IBC or DCIS. At first sight, tissue samples with a large solid and tubular pattern should be carefully examined for further trabecular or cribriform patterns. In addition, a double cell population consisting of basaloid cells located in the basal of epithelial cells with large cytoplasm indicates AdCC [1]. Eosinophilic and/or myxoid material in tubular structures or lumens of cribriform structures is an important clue for AdCC for differential diagnosis from IBC and DCIS. In addition, in histochemical staining, the eosinophilic material is stained pink with alcian blue and PAS, and the myxoid material in blue [1].

As another histopathological finding, perineural invasion is a valuable finding in breast AdCCs [1]. In case of perineural invasion, the diagnosis of AdCC should be considered. Immunohistochemically, myoepithelial cell markers such as p63 and calponin provide important helpful

findings [1]. While IBC myoepithelial cells are not observed with markers such as p63 and calponin, continuity can be observed around the ducts in DCIS, but as in our case, myoepithelial cells are observed as embedded in epithelial cells in AdCCs. Cd117 is highly sensitive for AdCC in epithelial cells [1]. For this reason, it is a point to be considered that it should be added to the routine as a marker, especially in breast Tru-Cut biopsies with tubular or solid patterns. In addition, CK7 stains epithelial cells while myoepithelial cells do not [5]. This finding is valuable for understanding the dual cell population. In AdCCs staining with estrogen-progesterone and cerbB2 is not expected [6].

It should be kept in mind that similar staining characteristics can be observed in some DCIS and triple-negative IBC, although it is a finding in favor of AdCC. The very low numbers of mitoses and staining pattern of Ki-67 may also indicate AdCC [1].

It is a helpful finding in the differential diagnosis of high-grade DCIS and IBC, but this is not the same for low-grade DCIS and well-differentiated IBC. MYB and SOX 10 are markers whose sensitivity and specificity have been reported for recently studied AdCCs but require further studies [5, 7].

### Conclusions

In conclusion, it is important to search for different patterns in addition to double cell population and pay attention to the material in the lumens in breast Tru-Cut biopsies that contain AdCC patterns that may cause the diagnosis of IBC and DCIS in error. However, in cases that cannot be resolved, using at least one myoepithelial marker and epithelial markers such as Cd117 and CK7 will be helpful in the immunohistochemical staining routine.

**Conflicts of interest:** authors have no conflict of interest to declare.  
**Конфлікт інтересів:** відсутній.

Надійшла до редакції / Received: 01.12.2021  
Після доопрацювання / Revised: 31.03.2022  
Прийнято до друку / Accepted: 15.04.2022

### Information about authors:

Ilyas Sayar, MD, Associate Professor of the Department of Pathology, Erzincan Binali Yildirim University, Turkey.

ORCID ID: [0000-0002-7204-4112](https://orcid.org/0000-0002-7204-4112)

Ufuk Memiş, MD, Assistant Professor of the Department of General Surgery, Erzincan Binali Yildirim University, Turkey.

ORCID ID: [0000-0003-3393-3301](https://orcid.org/0000-0003-3393-3301)

Sami Bilici, MD, Assistant Professor of the Department of General Surgery, Erzincan Binali Yildirim University, Turkey.

ORCID ID: [0000-0003-1076-1447](https://orcid.org/0000-0003-1076-1447)

Nurten Arslan Isik, MD, Assistant Professor, Health Faculty, Erzincan Binali Yildirim University, Turkey.

ORCID ID: [0000-0002-5192-6263](https://orcid.org/0000-0002-5192-6263)

### Відомості про авторів:

Ільяс Саяр, доцент каф. патології, Університет Ерзінджана Біналі Йілдірима, Туреччина.

Уфук Меміш, асистент, каф. загальної хірургії, Університет Ерзінджана Біналі Йілдірима, Туреччина.

Самі Білічі, асистент, каф. загальної хірургії, Університет Ерзінджана Біналі Йілдірима, Туреччина.

Нуртен Арслан Ісік, асистент, факультет здоров'я, Університет Ерзінджана Біналі Йілдірима, Туреччина.

## References

- [1] WHO Classification of Tumours Editorial Board. (2019, December 3). *Breast Tumours: WHO Classification of Tumours (Medicine)* (5th ed.). World Health Organization.
- [2] Ghabach, B., Anderson, W. F., Curtis, R. E., Huycke, M. M., Lavigne, J. A., & Dores, G. M. (2010). Adenoid cystic carcinoma of the breast in the United States (1977 to 2006): a population-based cohort study. *Breast cancer research : BCR*, 12(4), R54. <https://doi.org/10.1186/bcr2613>
- [3] Miyai, K., Schwartz, M. R., Divatia, M. K., Anton, R. C., Park, Y. W., Ayala, A. G., & Ro, J. Y. (2014). Adenoid cystic carcinoma of breast: Recent advances. *World journal of clinical cases*, 2(12), 732-741. <https://doi.org/10.12998/wjcc.v2.i12.732>
- [4] Treitl, D., Radkani, P., Rizer, M., El Hussein, S., Paramo, J. C., & Mesko, T. W. (2018). Adenoid cystic carcinoma of the breast, 20 years of experience in a single center with review of literature. *Breast cancer*, 25(1), 28-33. <https://doi.org/10.1007/s12282-017-0780-1>
- [5] Yang, C., Zhang, L., & Sanati, S. (2019). SOX10 Is a Sensitive Marker for Breast and Salivary Gland Adenoid Cystic Carcinoma: Immunohistochemical Characterization of Adenoid Cystic Carcinomas. *Breast cancer : basic and clinical research*, 13, 1178223419842185. <https://doi.org/10.1177/1178223419842185>
- [6] Defaud-Hénon, F., Tunon-de-Lara, C., Fournier, M., Marty, M., Velasco, V., de Mascarel, I., & MacGrogan, G. (2010). Le carcinome adénoïde kystique du sein: étude clinique, histologique, immunohistochimique et revue de la littérature [Adenoid cystic carcinoma of the breast: clinical, histological and immunohistochemical characterization]. *Annales de pathologie*, 30(1), 7-16. <https://doi.org/10.1016/j.annpat.2010.01.003>
- [7] Poling, J. S., Yonescu, R., Subhawong, A. P., Sharma, R., Argani, P., Ning, Y., & Cimino-Mathews, A. (2017). MYB Labeling by Immunohistochemistry Is More Sensitive and Specific for Breast Adenoid Cystic Carcinoma than MYB Labeling by FISH. *The American journal of surgical pathology*, 41(7), 973-979. <https://doi.org/10.1097/PAS.0000000000000878>