ADENOMYOEPITHELIOMA OF THE BREAST AS A DIAGNOSTIC PROBLEM

Zorica Mihajlovic [1, 2], Goran Azanjac [3], Zoran Protrka[1, 4], Drakce Radovanovic[1, 3], Vesna Stankovic [1, 2] and Slobodanka Mitrovic [1,2]
[1] Medical Faculty, University of Kragujevac, Serbia
[2] Center for Pathology, Clinical Center, Kragujevac, Serbia
[3] Surgery Clinic, Clinical Center, Kragujevac, Serbia
[4] Department of Gynecology and Obstretics, Clinical Center, Kragujevac, Serbia

ADENOMIOEPITELIOM DOJKE KAO DIJAGNOSTIČKI PROBLEM

Zorica Mihajlović [1, 2], Goran Azanjac [3], Zoran Protrka[1, 4], Drakče Radovanović[1, 3], Vesna Stanković [1, 2] and Slobodanka Mitrović [1,2]
[1] Medicinski fakultet, Univerzitet u Kragujevcu, Srbija
[2] Centar za patologiju, Klinički centar, Kragujevac, Srbija
[3] Hirurška klinika, Klinički centar, Kragujevac, Srbija
[4] Klinika za ginekologiju i akušerstvo, Klinički centar, Kragujevac, Srbija

Received / Primljen: 1. 6. 2009. Accepted / Prihvaćen: 21.10.2009.

ABSTRACT

Adenomyoepitheliomas are extremely rare breast tumours that were not described and classified until after the1990s. They are characterised by biphasic proliferation of ductal and myoepithelial cells organised in ribbon-like, solid, tubular or lobular arrangements. During years adenomyoepithelioma represent poorly understandable diagnostic entity which biological behaviour cannot be always predicted on the basis of the cytological characteristics and histological architecture. Diagnosis by clinical examination and imaging studies remains difficult, and frozen sections of selected areas can potentially be misdiagnosed as malignant.

In this study, we present a case of a breast adenomyoepithelioma in 68-year-old woman. The diagnosis was made with immunohistochemistry following a surgical excision.

Keywords: *breast tumours, adenomyoepithelioma, immunohistochemistry.*

SAŽETAK

Adenomioepiteliomi su retki tumori dojke, detaljno opisani i klasifikovani tek devedesettih godina prošlog veka. Karakteriše ih bifazna ćelijska proliferacija duktalnih i mioepitalnih ćelija organizovanih u trakaste, solidne, tubularne ili lobularne aranžmane. Godinama predstavljaju slabo razumljiv dijagnostički entitet, čije se biološko ponašanje ne može uvek predvideti na osnovu citoloških i histološko-arhitekturnih osobina. Postavljanje precizne dijagnoze, na osnovu kliničkog nalaza i radioloških-imidžing metoda, je veoma teško, a ex tempore analiza pojedinih tumorskih zona može biti pogrešno interpretirana kao maligna.

U ovom radu, prezentujemo slučaj adenomioepitelioma dojke kod žene stare 68 godina, koji je nakon hirurške ekscizije, dijagnostikovan određivanjem imunofenotipa ćelijske populacije ovog tumora.

Ključne reči: *tumori dojke, adenomioepiteliom, imunohistohemija.*

ABBREVATIONS

H&E - haematoxylin and eosin;
LMW CK - low-molecular weight cytokeratin;
HMW CK high-molecular weight cytokeratin;
α-SMA - smooth muscle actin;
GFAP - glial fibrillary acidic protein;
ER - estrogen receptor; PR - progesteron receptor.

SKRAĆENICE

H&E - hematoksilin i eozin
LMWCK - nisko-molekularni citokeratin
HMWCK - visoko-molekularni citokreatin
α- SMA - glatko-mišićni aktin
GFAP - glialni fibrilarni protein
ER - estrogen receptor PR- progesteron receptor

UDK ?????????? / Ser J Exp Clin Res 2009; 11 (2): 79- 83

Correspondence: Zorica Mihajlovic,Department of Pathology,
Medical Faculty, University of Kragujevac, Svetozara Markovica 69, Kragujevac 34000, Serbia
Home address: Sumaricka 6, 34000 Kragujevac, Serbia, Tel: +381 63 832 66 33; Fax: +381 34 330 435, E-mail: lmihajlovic@yahoo.com

INTRODUCTION

Adenomyoepitheliomas are extremely rare breast tumours. Hamperl (1970) was the first to describe this tumour1, and in 1991, Tavassoli classified it as a form of breast neoplasia2. Adenomyoepitheliomas are unique tumours formed of epithelial and myoepithelial cells, and other structures are sometimes present, as well. Classification is occasionally further complicated by papillary proliferation or microglandular adenosis within the foci of the tumour mass.

These tumours are most commonly restricted in growth and benign in character. However, sometimes their biological behaviour is unpredictable as assessed by macroscopic, histological and immunohistochemical features.

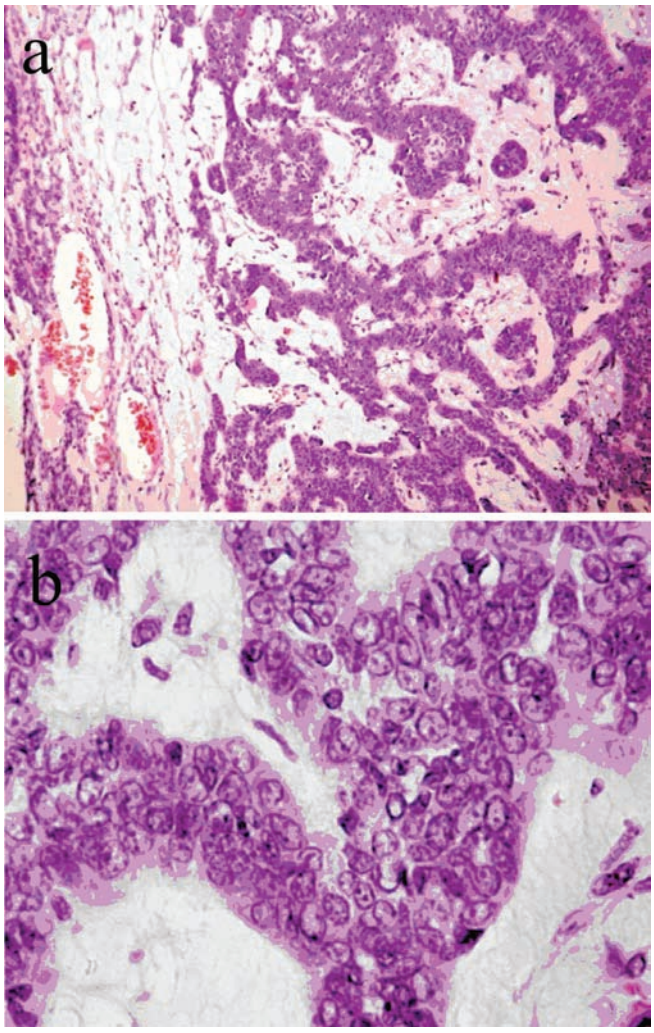


Figure 1: Histological features of adenomyoepithelioma (H&E staining). a) The well-restricted tumour is composed of proliferated ductal epithelial cells, myoepithelial cells and myxoid stroma (original magnification, x100). b) The tumour cells demonstrate a slight polymorphic morphology, with pale eosinophilic cytoplasm and vesicular nuclei with prominent nucleoli (original magnification, x400).

CASE REPORT

A 68-year-old woman was admitted by her family doctor because of a change in the upper outer quadrant of the left breast that was first noticed a few months ago. Planar X-ray mammography was suspicious for neoplasia, but ultrasound results were nonspecific. Clinical examination revealed the presence of a subcutaneous, localised, solid, mobile mass of approximately 4 cm diameter, nontender to palpation. Axillary lymphadenopathy was absent. A multidisciplinary oncology team recommended surgical treatment. A biopsy of the mass was performed, and an intraoperative ex tempore histological analysis was done.

Macroscopically, the specimen was a round, solid, well-circumscribed, irregular mass 35×25×20 mm in diameter. Tissue sections revealed a white-yellow interior. The findings of the microscopic ex tempore analysis were nonspecific, as the frozen section showed microscopic structures with both benign and malignant features, varying by tissue area.

The samples were fixed in 4% formaldehyde solution and embeded in paraffin. Five- μm-thick tissue sections were stained with hematoxylin and eosin (H&E).

On further microscopic exam, the tumour was well-encapsulated, but in several foci the tumour appeared to invade the surrounding tissue in tiny bands. The tumour consisted of myxoid stroma and cells of slightly polymorphic morphology with a myoepithelial-like shape that formed anastomosis-like bands, ranging in width from one to more than 10 cells (figure 1a). The cytoplasm was pale, nuclei were large and vesicular and nucleoli were prominent (figure 1b). Inside the bands and occasionally outside of them, foci of pseudo-luminal glandular structures suggesting ductal differentiation of the tumour were noted. Within those foci, the cells had lightly eosinophilic cytoplasm and hyperchromic nuclei. There were 5 mitotic figures per 10 areas of large microscopic magnification. Because of suspicion for double histological differentiation, additional immunohistochemical analyses were performed.

On immunohistochemical analysis, tumour cells demonstrated a diffuse, moderate-to-strong positivity for vimentine, low-molecular weight and high-molecular weight cytokeratin (LMW and HMW CK, respectively) (figures 2a, c, and d). They also displayed sporadic positivity for S-100 protein, smooth muscle actin (α-SMA), and glial fibrillary acid protein (GFAP) (figures 3a, b, and c). About 8% of the nuclei of tumour cells stained positive for Ki-67 (figure 3d). Staining for desmin, HER-2, estrogen (ER) and progesterone (PR) receptors was negative.

Based on this microscopic analysis and immunophenotype, a diagnosis of benign adenomyoepithelioma was established. The patient was discharged and advised to follow up regularly. The patient remained well throughout two years of follow-up after the surgery, with no apparent recurrence.

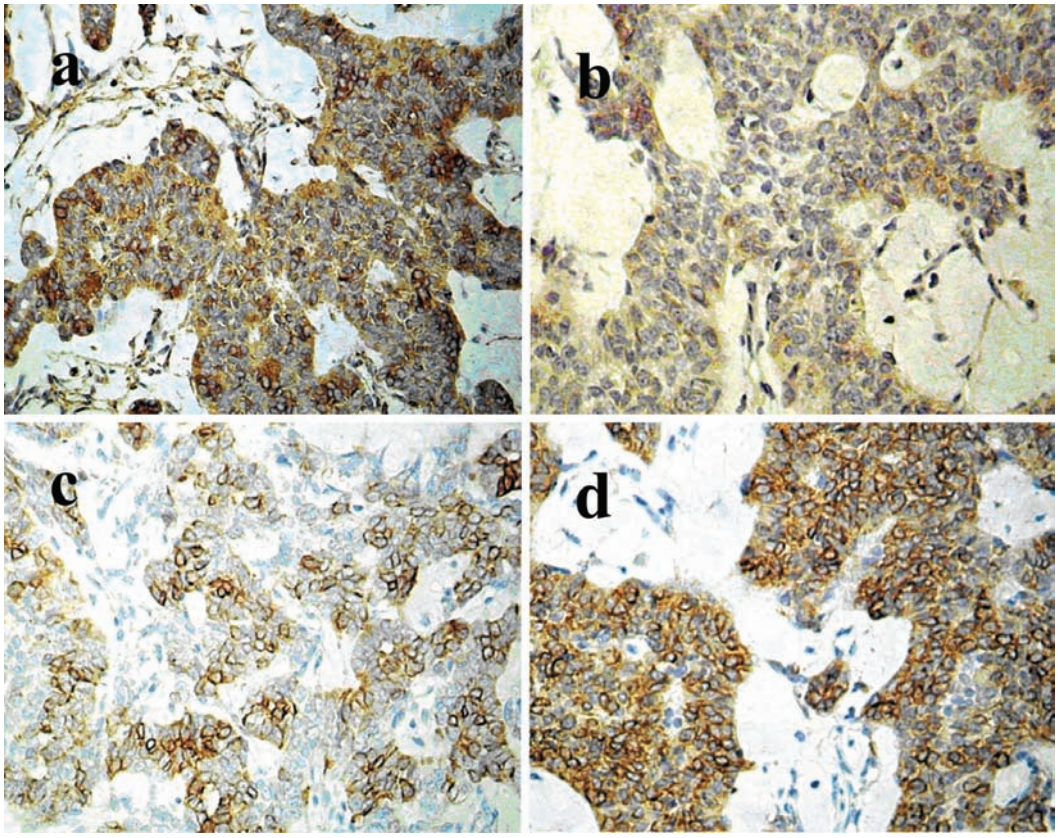


Figure 2: Immunohistochemical staining (original magnification, x200).
a) The tumour cells demonstrate moderate to strong expression of vimentin, and
b) discret and weak expression of desmin.
c) Approximately 50% of tumour cells are strongly positive for CK HMW.
d) Diffuse, strong staining for CK LMW.

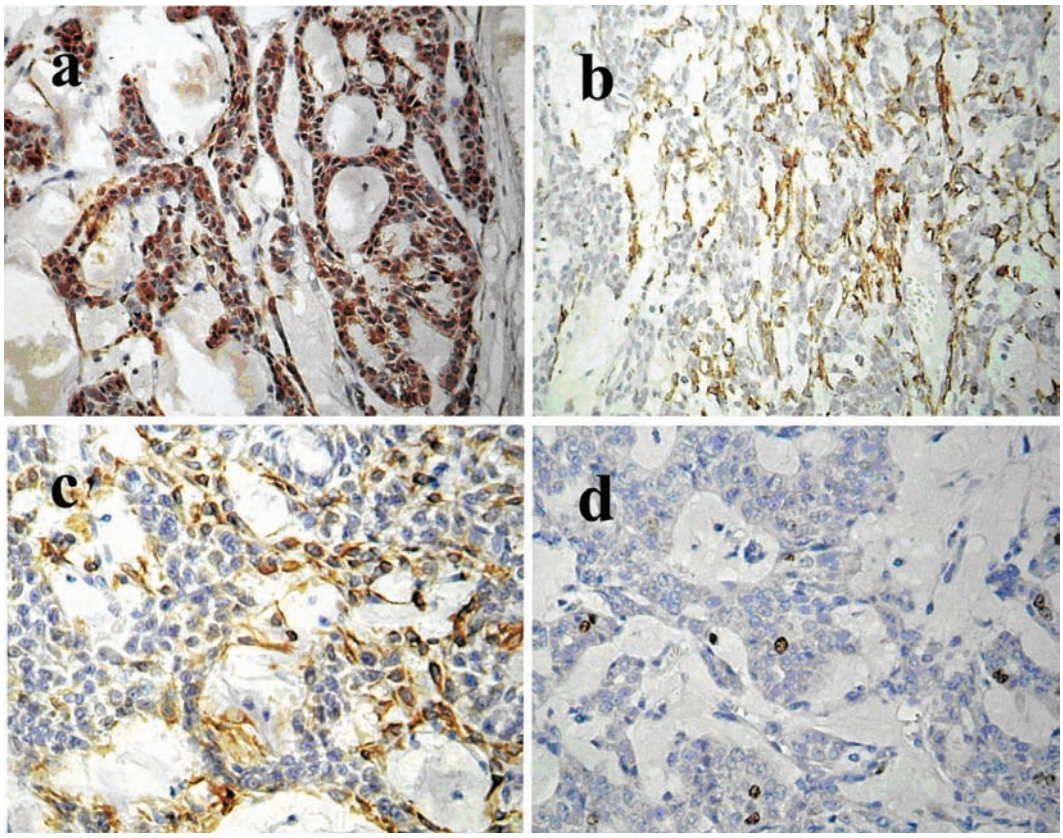


Figure 3: Immunohistochemical staining (original magnification, x200).
a) The tumour cells demonstrate moderate to strong expression of S-100 protein.
b) Myoepithelial cells positive for α-SMA and
c) GFAP.
d) The nuclei of the tumour cells show focal positivity for Ki67 (Ki67 index = 8%).

DISCUSSION

Breast adenomyoepitheliomas are extremely rare, so data about these tumours are limited to individual case-reports.3-13 They appear to occur in a wide age range, from 26 to 82 years of age. In the majority of the patients, the mass's initial presentation was as a solid, clearly circumscribed, painless lesion, localised in a peripheral quadrant of the breast. The usual tumour size is from 0.6-17 cm, with the largest mass described in a 30-year-old woman.13 They more frequently appear as solitary rather than multifocal masses.8 Reported colors include light brown, grey, white or yellow. X-ray mammography and ultrasound imaging often suggest malignancy.4,7

The specific histological presentation depends on the presence of glandular-epithelial and myoepithelial proliferation, the degree of spindle-cell differentiation and the extent of fibrosis. Thus, adenomyoepitheliomas appear closely related to ductal adenomas14 and pleomorphic adenomas.15 However, these tumours are more commonly found in subareolar regions rather than in the lateral breast quadrants, and they probably originate from large lactiferous ducts.6,15

The most common microscopic appearance of adenomyoepithelioma is tubular with glandular structure proliferation, though myoepithelial differentiation can be found in peripheral islands of solid tumour or in the basal cells of tubular structures. Rarely, myoepithelial proliferation appears as wide bands and trabeculae that are both separated by fibrovascular stromal cells. Epithelial and myoepithelial cells are incorporated into abundant mixed stroma12 that sometimes contain areas of calcification, cystic degeneration, and cartilaginous and bony metaplasia. In our case, myoepithelial cells formed anastomosing bands of one to many cells thick, with additional foci of ductal differentiation. Abundant mixed stroma was found in the area of this epithelial "building block."

Cytological atypia and mitotic activity were rare or absent in the lesions where myoepithelial cells were seen to have a polygonal configuration or a clear papillary form. These cells were often found in the lesions that appeared to be growing in spindle-shaped formations. They were noted to contain increases in mitosis, nuclear polymorphism, and hyperchromasia, and rare multinuclear cells were seen in them. However, cytological atypia is not a valid criterion for diagnosing adenomyoepithelioma, because some tumours without that feature progressed aggressively.2,7 Therefore, in the absence of an obviously malignant pattern of cytomorphology, invasive development remains the only reliable criterion for establishing a diagnosis of malignancy.

The immunohistochemical analysis of cell phenotype, and thus the establishment of a diagnosis, is greatly aided when the pathologist is familiar with the great morphological diversity of adenomyoepitheliomas. Normal myoepithelial cells strongly express LMW CK, α-SMA, myosin, S-100, CD-10 and maspin.8 Because S-100 protein is expressed in both glandular and myoepithelial cells, it cannot be used as diagnostically specific tumour marker for adenomyoepithelioma.11 Epithelial cells regularly stain positive for cytokeratin and carcinoembryonic antigens.5,6 Both cell types are variably positive in response to vimentine and immunonegative staining for epithelial membrane antigen, p53 and HER-2.8 Also, the response to staining for ER and PR receptors is variable; if they are immunohistochemically present, they are restricted to the nuclei of epithelial cells.7,9 In our case, most tumour cells were positive for vimentine, LMW and HMW CK, and a smaller number were positive for S-100 protein, GFAP and α-SMA. Ki-67 was visualised on 8% of tumour cells. In the available literature data about mitotic indices, data about the association between number of mitotic figures and tendancy towards malignancy are scarce. One paper reported a series in which 7 per 10 areas of large microscopic magnification were considered a diagnostic sign suggesting malignancy.16

Adenomyoepitheliomas are most commonly benign, well-circumscribed, and encapsulated tumours that are most frequently treated with surgical excision.7 However, although they are enclosed within a pseudo-capsule of connective tissue, masses often infiltrate their surrounding structures.10 Due to this invasive tendency, the natural course of these lesions is ultimately unpredictable. Local recurrence usually occurs two years after initial excision.2 In some cases, multiple recurrences were reported, likely resulting from incomplete tumour excision.3,7 Mastectomy, radiotherapy and axillary dissection for benign adenomyoepithelioma should be avoided, except in the case of frequently recurrent lesions or tumours with malignant characteristics.16-19

The reports concerning malignant adenomyoepithelioma are rare. Neoplasm can be detected incidentally as a separated mass or after an excision of the adenomyoepithelioma.2 Histological characteristics include increased mitotic activity, necrosis, cellular polymorphism, and, frequently, invasion of tissue surrounding the tumour. Malignant alteration could be limited to the epithelial or myoepithelial zones, or rarely to both of them. The location of malignant zones might alternate within the same tumour , e.g., the the foci of benign characteristics and obviously malignant lesions could be bounded by the zones with benign features.16,17 Some tumours described as malignant adenomyoepitheliomas recurred locally, while other masses metastasised, resulting in fatal outcomes.16-19

CONCLUSION

Breast adenomyoepithelioma is usually a well-circumscribed tumour; as such, complete surgical excision of the mass remains the preferred therapeutic strategy. The definitive diagnosis is established with vigilant microscopic analysis and immunohistochemical staining. This approach avoids an incorrect pathological diagnosis that could lead to an unnecessary procedure such as a major surgery.

REFERENCES

1. Hamperl H. The myothelia (myoepithelial cells) state, regressive changes, hypoplasia tumors. Curr Top Pathol 1970; 53: 194-8.
2. Tavassoli FA. Myoepithelial lesions of the breast. Myoepitheliosis, adenomyoepithelioma, and myoepithelial carcinoma. Am J Surg Pathol 1991; 15:554-568.
3. Young RH, Clement PB. Adenomyoepithelioma of the breast. A report of three cases and review of the literature. Am J Clin Pathol 1988;89:308-314.
4. Gusterson BA, Sloane JP, Middwood C, et al. Ductal adenoma of the breast-a lesion exhibiting a myoepithelial/epithelial phenotype. Histopathology 1987;11:103-110.
5. De Dominicis E, Perrone G, Verzi A, et al. Pleomorphic adenoma of the breast. Breast J 2005;11:513–4.
6. Sato K, Ueda Y, Shimasaki M, et al. Pleomorphic adenoma(benign mixed tumor) of the breast: a case report and review of literature. Pathol Res Pract 2005;201:333–9.
7. Rosen PP.Adenomyoepithelioma of the breast.Hum Pathol 1987; 18:1232 -37.
8. Pia-Foschini M, Reis-Filho JS, Eusebi V, Lakhani SR. Salivary gland-like tumours of the breast: surgical and molecular pathology. J Clin Pathol 2002;56:497–506.
9. Vielh P, Theiry JP, Validire P, et al. Adenomyoepithelioma of the breast: fine-needle sampling with histologic, immunohistologic and electron microscopic analysis. Diagn Cytol 1993;9:188-193.
10. Molland JG, Morgan GJ, Walker DM, Lin BP. Pleomorphic adenoma of the parotid and breast in a male patient. Pathology 2005; 37:263–5.
11. Gillett CE, Bobrow LG, Millis RR. S100 protein in human mammary tissue-immunoreactivity in breast carcinoma including Paget's disease of the nipple, and value as a marker of myoepithelial cells. J Pathol 1990;160:19-24.
12. Reid-Nicholson M, Bleiweiss I, Pace B, Azueta V, Jaffer S. Pleomorphic adenoma of the breast. A case report and distinction from mucinous carcinoma. Arch Pathol Lab Med 2003;127:474–7.
13. Williams RW, Leach WB. Mixed tumor of female breast of unusual duration and size. South. Med. J. 1975; 68: 97-100.
14. Guarino M, Reale D, Squillaci S, et al. Ductal adenoma of the breast. An immunohistochemical study of five cases. Pathol Res Pract 1993;189:515-20.
15. Biku J, Griffiths C, Ebbs SR. Pleomorphic Adenoma of the Breast Should Be Excised with a Cuff of Normal Tissue. The Breast Journal, 2007;13: 418–420.
16. Rasbridge SA, Millis RR. Adenomyoepithelioma of the breast with malignant features. Virchows Arch 1998;432:123-130.
17. Loose JH, Patchefsky AS, Hollander IJ, Lavin LS, Cooper HS, Katz SM. Adenomyoepithelioma of the breast. Am I Surg Pathol 1992;16: 868-876.
18. Hungermann D, Buerger H, Oehlschlegel C, Herbst H and Werner Boecker W. Adenomyoepithelial tumours and myoepithelial carcinomas of the breast – a spectrum of monophasic and biphasic tumours dominated by immature myoepithelial cells BMC Cancer 2005, 5:92.
19. Nadelman CM, Leslie KO, Fishbein MC."Benign", Metastasizing Adeno-myoepithelioma of the Breast. Arch Pathol Lab Med. 2006;130:1349–53.