

NIPPLE ADENOMA – A CASE REPORT

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Summary

The paper presents a case of a rare benign lesion of the breast - nipple adenoma. Nipple adenoma is a benign tumor without connective tissue cores composed of small tubules lined by epithelial and myoepithelial cells with or without proliferation of the epithelial component around collecting ducts. In 1955, Jones considered it as a separate clinical pathologic entity. The tumor most often develops in women between 40-50 years of age in the form of erythema, crust or ulceration, and it is therefore often mistaken for Paget's disease. We report a case of a patient referred to our cytology laboratory for clinical suspicion of malignancy, with an erythematous, exulcerated nipple and occasional hemorrhagic discharge. The mammographic finding was normal and sonography indicated a smaller hypoechogenous zone immediately below the nipple. Scraping material for cytologic analysis was stained by the standard MGG staining raising the suspicion of a malignant tumor.

The nipple containing a tumor of a firm consistency underwent PHD analysis. Bipsies of standard H&E-stained sections showed the tumor partly covered with multilayered squamous epithelium, with ducts revealing scattered epithelial proliferation and the diagnosis of nipple adenoma was made.

Due to its rare occurrence, clinical presentation and cytologic pattern of increased cellularity, dissociation of epithelial cells with occasional signs of atypia, the tumor is often misinterpreted and cytologically classified as carcinoma. For nipple lesions presented as exulcerated changes, and any changes in the nipple's appearance in general, except for Paget's disease, the possibility of a benign tumor, such as adenoma of the nipple, should always be taken into consideration.

The treatment of choice consists of the removal of the entire nipple since foci of carcinoma can sometimes, although rarely, be found in a nipple adenoma, too.

KEY WORDS: *nipple adenoma, cytology diagnostics*

ADENOM BRADAVICE DOJKE – PRIKAZ SLUČAJA

Sažetak

U radu je prikazan slučaj rjeđega benignog tumora dojke – adenoma bradavice. Adenom bradavice je benigni tumor bez vezivne čahure građen od malih tubula obloženih epitelnim i mioepitelnim stanicama sa ili bez proliferacije epitelne komponente oko sabirnih kanalića. Kao zasebni kliničko patološki entitet 1955. ga izdvaja Jones. Tumor se najčešće pojavljuje u žena između 40-50 godine uz simptome često krvavog iscjetka te promjene bradavice u obliku eritema, kruste ili ulceracije zbog čega se klinički često zamijeni s Pagetovom bolesti.

Izveštavamo o pacijentici koja je u citološki laboratorij upućena pod kliničkom sumnjom da se radi o malignoj bolesti, s eritematoznom, egzulceriranom bradavicom uz povremeni krvavi iscjedak. Mamografski nalaz je bio uredan, a UZV nalaz je pokazivao manju hipoechogenu zonu neposredno ispod bradavice. Materijal za citološku analizu dobije se metodom struganja, oboji standardno MGG-om te se citološki postavi sumnja na zloćudni tumor.

Na PHD analizu se zaprimila bradavica s tumorom čvršće konzistencije. Biopsije standardnog H&E bojenja pokazivale su tumor koji je dijelom bio pokriven višeslojnim pločastim epitelom uz kanaliće u kojima se mjestimice vidjela i proliferacija epitela te se postavila dijagnoza adenoma bradavice.

Zbog rijetke pojave ovog tumora, njegove kliničke prezentacije te citološke slike jake celularnosti, disocijacije stanica uz mjestimice izražene znakove atipije, nije neobično da se tumor citološki klasificira kao karcinom. Za lezije bradavice

koje se prezentiraju kao egzulcerirane promjene, te općenito promijenjeni izgled bradavice, osim Pagetove bolesti treba svakako razmišljati i o benignim tumorima kao što je adenom bradavice.

Terapija izbora je uklanjanje bradavice u cijelosti zato jer se, iako rijetko, mogu naći i žarišta karcinoma.

KLJUČNE RIJEČI: *adenom bradavice, citološka dijagnostika*

INTRODUCTION

Adenomas, benign breast tumors are sharply delineated tumors consisting of tubular formations lined by epithelial and myoepithelial cells, while their stromal elements can be variable. There are many different types of adenomas, including tubular adenoma, lactating adenoma, apocrine adenoma, ductal adenoma, pleomorphic adenoma, syringomatous adenoma and adenoma of collecting ducts (1, 2).

Nipple adenoma is a benign tumor without connective tissue cores composed of small tubules lined by epithelial and myoepithelial cells with or without proliferation of the epithelial component around collecting ducts. Some of the ducts communicate with the surface of the nipple replacing the superficial squamous epithelium and resulting in clinical occurrence of erosions (3). The tumor can also communicate with lumens of lactiferous ducts and squamous metaplasia of superficial or cystically dilated ducts may occur. Foci of noninvasive ductal carcinoma are rarely found within an adenoma. The tumor was first mentioned by Miller and Lewis in 1923, then by Stowers in 1935, and Jones singled it out as a separate clinical pathologic entity in 1955 (4, 5). Adenoma of the nipple is a rare tumor that occurs in both sexes, most often between 40-50 years of age, but some authors report cases of its occurrence among early adolescent females and males (6, 7).

The commonest symptom is discharge from the nipple which is often bloody, but there may be pain and burning sensation in the nipple region, too. In the majority of cases, the mamillary region is enlarged and a tumor nodule may be palpated. The nipple surface may be ulcerated, red or covered by crust. For the above symptoms, the tumor may be clinically mistaken for Paget's disease or papilloma (8). Mammographic and sonographic findings may also suggest a malignant diagnosis (9).

Histologically, papillomas are divided into four groups: 1. Sclerosing papillomatous form characterized by papillary hyperplasia of the ductal epithelium and also stromal proliferation with an intact squamous epithelium on the surface; 2. Papillomatous form characterized by florid papillary hyperplasia of the ductal epithelium that may be partly or completely replaced by squamous epithelium on the surface; 3. Adenous form consisting of condensed glandular structures demonstrating both epithelial proliferation and hyperplasia of myoepithelial cells; 4. Mixed proliferative form in the majority of cases characterized by squamous metaplasia on the surface, accompanied by hyperplastic ductal epithelium and cystic dilatation of the ducts (6).

Glandular cells are uniformly immunoreactive for cytokeratin, and focally immunoreactive for carcinoembryonic antigen (CEA), the basement membrane showing reactivity for collagen type IV, and myoepithelial cells for myosin, actin and calponin (1). Flow cytometric analyses show the lesions are diploid and do not show immunoreactivity for c-erbB2 (10).

CASE REPORT

A patient was referred to the Cytology Laboratory of the University Hospital for Tumors, Zagreb, Croatia, for changes in the nipple manifested by itching, scaling of the skin and occasional bloody secretion that the patient first noticed three months ago. At examination, the nipple was exulcerated with redness of the surrounding skin. The mammographic finding was normal and sonography indicated a smaller hypoechoic zone immediately below the nipple. Material for cytologic analysis was obtained by scraping and then smeared on a glass slide and MGG stained. Cytologic analysis indicated that the lesion was most probably a malignant epithelial tumor. Due to the cytologic diagnosis, the patient underwent a complete excision

of the nipple. The nipple containing a tumor, 4x3.4 cm in size, firmer in consistency was received for PHD analysis. Within one hour of the excision, the surgical material was fixed in 10% buffered formalin and processed using the standard pathohistologic method of paraffin-embedding and H&E staining. On thus obtained preparations, the pathohistologic diagnosis of nipple adenoma was made using a light microscope.

RESULTS

Smears obtained using the scraping method showed increased cellularity with numerous clusters of glandular epithelial cells partly displaying moderate to severe anisonucleosis, hyperchromasia, with occasionally observable nucleoli and mildly to moderately extended basophilic cytoplasm. Dissociation of cells showing signs of atypia was occasionally present, too (Figure 1). Smears contained numerous anuclear squama and individual cells of the squamous epithelium with some neutrophil granulocytes (Figure 2). Such cytologic pattern raised suspicion of a malignant epithelial tumor. Histologically, the tumor was partly covered with a thicker, regular, keratinized multilayered squamous epithelium which was partially exulcerated. Beneath the tumor, compressed larger collecting ducts were observable showing a pattern of sclerosing adenosis (Figures 3,4). Some ducts were cystically dilated containing some horny substance, while some

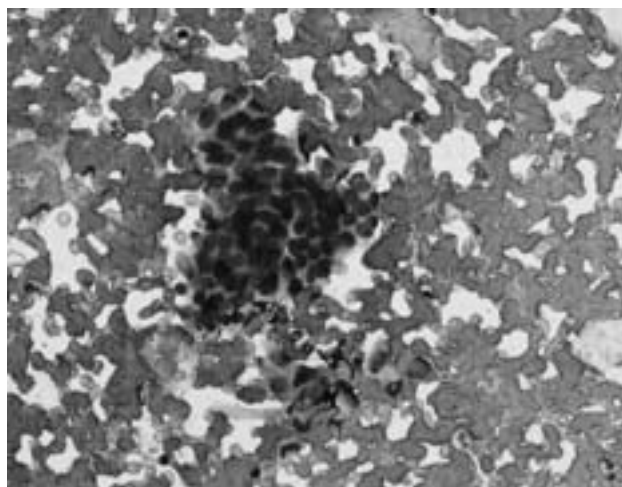


Figure 1. Nipple adenoma (MGG x 400)

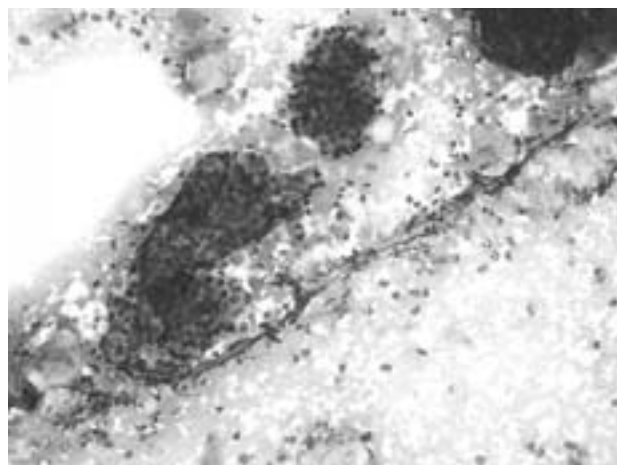


Figure 2. Nipple adenoma (MGG x 200)

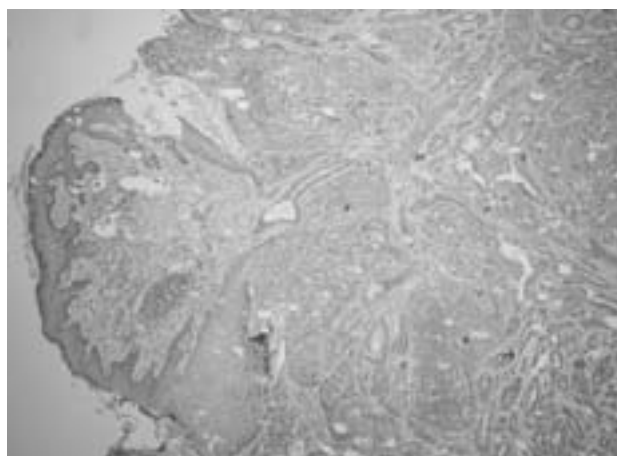


Figure 3. Nipple adenoma lined by multilayered squamous epithelium; ductal regions lined by epithelium (H&E x 40)

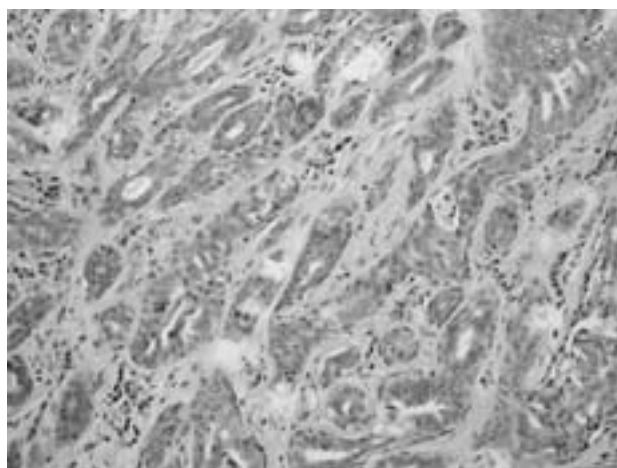


Figure 4. Nipple adenoma, areas of epithelial proliferation and sclerosing adenosis (H&E x 100)

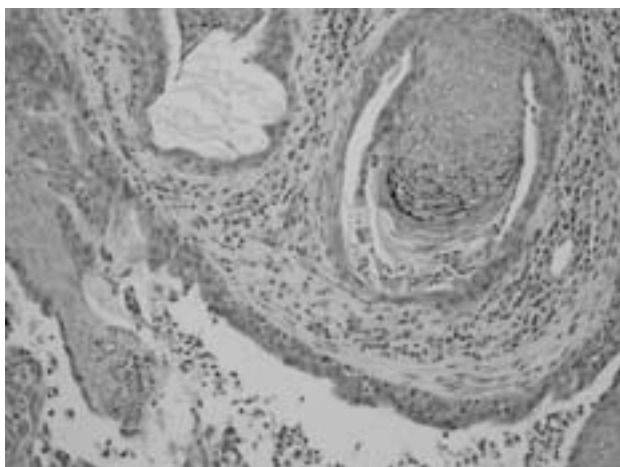


Figure 5. Nipple adenoma, area of squamous metaplasia (H&E x 200)

ducts also displayed squamous metaplasia (Figure 5). In the stroma, there were also occasional inflammatory cells, and focally, there was an epithelial proliferation. The diagnosis of a nipple adenoma was made (mixed proliferative form).

DISCUSSION

Adenoma of the nipple is a rare lesion of the breast which is often mistaken clinically for Paget's disease. This usually happens for changes in the nipple that also occur in Paget's disease including erythema, crusts, ulcerations and bleeding. The tumor most often develops in middle-aged women, but there were also cases reported in younger females and men (6, 7). For the rare occurrence of this benign tumor, its clinical presentation and cytologic pattern, it is not unusual that the tumor is often cytologically classified as carcinoma. Considering that the aspirate shows extreme cellularity, the dissociation of epithelial cells, papillary pattern, furthermore mild atypia with variation in size and shape and hyperchromatic nuclei with prominent nucleoli, could misleadingly create a suspicion of malignancy (11, 12).

The cytologic pattern of Paget's disease, especially if the cellular material is collected using the scraping method, displays a more severe inflammatory underlying infiltrate with clusters and individual malignant cells demonstrating

moderate pleomorphism and occasional vacuolated cytoplasm in bloody smears (13) which differentially may lead to a diagnosis of nipple adenoma. Positivity of Paget's cells for CAM 5.2 may be of great assistance to differential diagnostics.

Histologically, differential diagnosis of Paget's disease includes, besides nipple adenoma, inflammatory changes of the skin, Toker cells, malignant melanoma, basalioma and squamous cell carcinoma (14).

In addition, nipple adenoma coexists with breast carcinoma in 16.5% of patients (6). It is often difficult to diagnose morphologically for hyperplastic zones within an adenoma. Such zones demonstrate an atypical pattern which may also include foci of comedo-type necrosis as well as cribriform and micropapillary growth pattern, mitoses and cytologic atypias.

Incision biopsy as well as fine-needle aspiration biopsy (FNA) and scraping as a method of collecting material, cannot exclude the presence of focal carcinoma cells within the lesions. For that reason, the definitive therapy includes a complete excision of the nipple, while mastectomy is not indicated without signs suggestive of malignancy. Local recurrences may occur if a subtotal excision is performed (6). The majority of authors believe that the occurrence of breast carcinomas with nipple adenoma is usually a coincidence and that nipple adenoma cannot be considered a precancerous lesion (15-17).

CONCLUSION

Adenoma of the nipple is a rare benign tumor most often developed by middle-aged women, although it may occur among both early adolescent females and males. For nipple lesions presented as exulcerated changes, and any changes in the nipple's appearance in general, except for the commonest tumor of the breast (Paget's disease), it is very important to take into consideration the possibility of a benign tumor, such as adenoma of the nipple.

It therefore requires careful sample collection, and if anyhow possible, additional immunohistochemical staining that may help distinguish a benign from malignant lesion of the

nipple. Immunocyto/histochemical reaction for actin from ductal cells demonstrates myoepithelial cells which are one of the significant factors confirming the tumor benignity.

Differential diagnostics reliable for distinguishing between benign and malignant lesions will help avoid unnecessary surgical ablation for benign breast lesions.

The treatment of choice consists of the removal of the entire nipple since foci of carcinoma can sometimes, although rarely, be found in a nipple adenoma, too.

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