# Fine-Needle Aspiration Cytology of Apocrine Hidradenoma

Nina Petra Novak<sup>1</sup>, Gordana Kaić<sup>1</sup>, Čedna Tomasović-Lončarić<sup>1</sup>, Rado Žic<sup>1,2</sup>, Marija Škoro<sup>1</sup> and Karmen Trutin Ostović<sup>1,3</sup>

- <sup>1</sup> Dubrava University Hospital, Zagreb, Croatia
- <sup>2</sup> Zagreb University, School of Medicine, Zagreb, Croatia
- <sup>3</sup> University of Applied Health Studies, Zagreb, Croatia

# ABSTRACT

An apocrine hidradenoma is a benign adnexal neoplasm, usually covered by intact skin, but may show superficial ulceration and serous discharge. This feature is raising the possibility of malignancy as it was in our case of macroscopically suspicious tumour. We described cytomorphologic features of cutaneous nodule that might be a lead to the cytologic diagnosis of hidradenoma, but primary or secondary malignant tumour has been ruled out first.

Key words: skin tumours, hidradenoma, fine-needle aspiration, cytology, diagnosis

## Introduction

A cytologic study of skin nodules and distinction of metastatic lesions from primary cutaneous and subcutaneous neoplasms may be difficult. A hidradenoma is a benign adnexal neoplasm, closely related to poroma, that displays a limited degree of ductal differentiation. While historically considered eccrine, recent evidence suggests that the hidradenoma can be either apocrine or eccrine differentiation. The synonyms for this entity are: clear cell hidradenoma, nodular hidradenoma, poroid hidradenoma, acrospiroma and solid-cystic hidradenoma<sup>1,2</sup>. The hidradenomas have sporadic presentation and no sex predilection. Most of them develop in adults and those are usually solitary, asymptomatic, intradermal nodules, measure between 0.5 and 12 cm in diameter. They commonly develop on the scalp, the trunk and proximal extremities, presenting as skin-coloured to red-brown or blue nodules<sup>1,3</sup>. It's usually covered by intact skin, but may show superficial ulceration and serous discharge. This feature raises the possibility of malignancy<sup>3,4</sup>. The purpose of this article is to describe the clinical and cytomorphologic features of our case of an apocrine hidradenoma. We want to point out that these findings may be a potential pitfall even for experienced cytopathologists.

# **Case Report**

A 70-year-old, healthy man presented with a 2-year history of a subcutaneous nodular lesion on the right side of the chest under the breast. Since last six months the lesion has been growing faster. A physical examination revealed an red-coloured, egzulcerated tumour measured 2.5 cm in diameter. A serous-bloody discharge was noted on the tumor surface. A fine-needle aspiration cytology (FNAC) was performed, repeated several times at the different portions of the tumour. The yielded material was placed and smeared on the slides, air-dried and May--Grünwald Giemsa (MGG) stained. The cytology smears showed numerous large three-dimensional groups of monomorphic cells with small rounded nuclei and occasionally conspicous nucleoli. The cells had a scant basophilic cytoplasm and occasionally a moderate amount of clear cytoplasm. Some smaller and less cohesive cell clusters

displayed rounded rosette-like structures. In the background there were a few scattered naked nuclei, particles of amorphous extracellular basophilic material and blood. The immunocytochemical reactions were unsuccessful due to technical reasons. The cytologic diagnosis was: neoplasm of probably epithelial origin, metastatic tumour couldn't be excluded. A surgical excision was recommended.

Macroscopic patohistologic examination revealed extirpated skin measuring 8x3.5x3.5 cm with tumorous protuberance of 2.5 cm in diametar. Microscopically tumour has been well circumscribed from surrounding tissue and hasn't reached to the resection edges. It consisted predominantly solid areas of two cell types: eosinophilic and clear cells. The eosinophilic cells were occasionally forming tubular and cystic structures. An intervening, partly hyalinized stroma divided cell clusters into lobules of various sizes (Figure 1). The histologic diagnosis was apocrine hidradenoma. Three years after surgery, the patient was free of the disease.

The cytology smears were reviewed and described below. The cellular smears shows clusters of two cell types (Figure 2). The first type were cuboidal epithelial cells

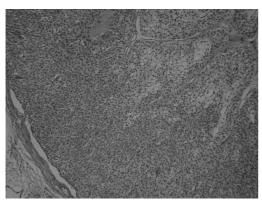


Fig. 1. Histologic section: Tumour tissue consists of solid areas and two cell types: eosinophilic cells and clear cells (Hematoxylin & Eosin, x100).

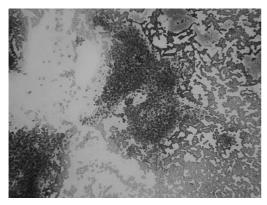


Fig. 2. Cytologic smear: The cohesive clusters of cuboidal, occasionally squamoid cells and the second type of cells with more abundant, occasionally clear cytoplasms. In the background there is basophilic extracellular material (top right) (MGG, x100).

which formed large, cohesive, three-dimensional papillary-like, dense packing clusters. These cells had rounded to ovoid nuclei, small nucleoli and a scant to moderate, slight granular, basophilic cytoplasm. Occasionally they were reminiscent to squamoid cells and their nuclei show overlapping, mild hyperchromasia and anisonucleosis (Figure 3). The rounded rosette-like formations were rare but discernible (Figure 4). The second type of cells had round, eccentric nuclei, fine granular chromatin and small nucleoli. The cytoplasms of these cells were more abundant, slight eosinophilic or gray to watery-clear coloured (Figure 5). They formed middle sized, flatter clusters. In the background there was an amorphous basophilic extracellular material, some histiocytes, fibrocytes, pigmentophages, naked nuclei and blood. The periodic acid-Schiff-diastase (PAS-D) reaction is demonstrated in both cell types, but the strongest in the cells with an abundant clear cytoplasm (Figure 6).

#### Discussion

Neoplasms of cutaneous appendages are relatively uncommon lesions, and because they are encountered so infrequently in clinical cytology practice sometimes pose difficulty in diagnosis. The hidradenoma is usually covered by intact skin, but may show superficial ulceration

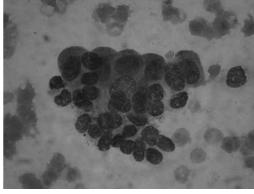


Fig. 3. The cuboidal cells show mild hyperchromasia, anisonucleosis, overlapping nuclei and conspicious small nucleoli (MGG, x1000).

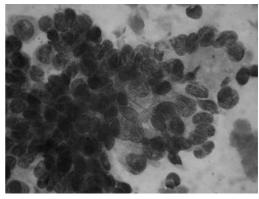


Fig. 4. The cell cluster with rosette-like formations (MGG, x1000).

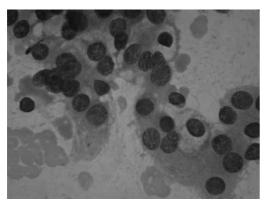


Fig. 5. The apocrine cells with eosinophilic cytoplasm and clear cells (MGG, x1000).

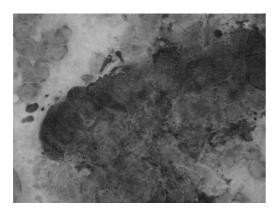


Fig. 6. The cytochemical PAS-D reaction demonstrated the strongest positivity in the clear cells (x1000).

and serous discharge as it was in our case of macroscopically suspicious tumour. Microscopically, it is composed of several types of cells. When predominate clear or pale cells with distinct cell borders, the name clear cell hidradenoma is appropriate<sup>1</sup>. Hybrid lesions include compact poroid cells with prominent ductal differentiation have been referred to as poroid hidradenomas<sup>1</sup>. The clear cells contain glycogen and periodic acid-Schiff-positive, diastase-resistant material, but no lipid<sup>5</sup>. The squamoid cells are polygonal with a central vesicular nuclei and an eosinophilic cytoplasm, often arranged in whorls<sup>1</sup>. They may even be cornified with formation of horn pearls<sup>6</sup>. Mucinous cells are the least common component. These are large cells with fine basophilic granular cytoplasm, cuboidal or columnar in shape. The cells line the tubules and may show evidence of apocrine differentiation. Transition between different types of cells is frequent. When we reviewed cytology smears we noted two types of the cells, corresponding to the description above. Cellular smears revealed large cohesive three-dimensional papillary-like clusters of dense packing cuboidal epithelial cells and middle sized, flatter clusters of cells with abundant, partially clear cytoplasm. As the quantity of different cells type vary markedly in different tumours, one must be aware of the resemblance to metastatic renal cell carcinoma, squamous cell carcinoma or signet-ring adenocarcinoma<sup>4,5</sup>. In the case of apocrine hidradenoma with pseudopapillary cell clusters, metastases of papillary carcinoma must be excluded<sup>7</sup>. The nuclear grooving recently described as a common finding in these tumours, also confirmed by electron microscopy<sup>6</sup> hasn't been noticed in our case.

The nuclei of neoplastic cells may be hyperchromatric and exhibit coarsely clumped chromatin, but presence of marked pleomorphism and frequent or atypical mitoses is not observed<sup>3</sup>. In our case we have seen mild hyperchromasia, anizonucleosis and overlapping nuclei with small distinct nucleoli. Some authors describe mild pleomorphism, multinucleation and occasional mitotic figures in rare case of recurrent poroid hidradenoma<sup>8</sup>. Close follow-up is necessary because histology is not always a reliable indicator of biologic behaviour<sup>9</sup>.

The hidradenoma often has cystic spaces that may contain eosinophilic, homogenous material as a result of degeneration of the tumour cells<sup>6</sup>. That material should not be mistaken for tumorous diathesis which with another features of malignancy like aggresive local growth, pleomorphism, numerous mitotic figures, angiolymphatic and perineural invasion lead to diagnosis of hidradenocarcinoma<sup>5,6,9,10</sup>. Most of malignant forms of nodular hidradenoma are malignant from their inception, but some develop from benign hidradenoma<sup>6</sup>. The hidradenocarcinomas are rare and tend to be moderate size, but a growth rate of both malignant and benign tumours is slow. Cytologic features indicative for malignancy may not be obvious. Futher, in differential diagnosis we should consider other primary appendageal benign and malignant tumours same as other malignant skin tumours like a basal cell carcinoma, Merkel cell carcinoma or malig $nant\ melanoma^{2,8,11}$ .

The PAS stain with diastase digestion were done additionally on a residual smears. We demonstrated a positivity in the cytoplasm of the clear cells as other authors claimed<sup>8,11</sup>. Hidradenomas could react with different monoclonal antibodies such as: citokeratin, specially CK LMW, EMA, CEA, S-100 protein, vimentin<sup>3,5</sup>.

Complete excision is usually curative, but hidradenoma may occasionally recure after local excision<sup>1,3</sup>. The first case of nodular hidradenoma diagnosed by fine-needle aspiration cytology was reported in 1996<sup>12</sup>. Knowledge of the cytologic features of primary skin adnexal neoplasms helps distinguish them from the cutaneous metastases which were more commonly referred for FNAC evaluation. Detailed clinical history, physical findings, and ancillary studies are essential add for correct diagnosis. Even more skill is required to recognize specific entities in a broad group of appendageal tumours. Considering that hidradenoma is an uncommon tumour and an experience in FNAC of such lesions is insufficient, we hope we made a useful contribution with this report.

# Conclusion

Despite the fact that we missed the correct diagnosis, FNAC determined the need for surgical excision and histologic evaluation. We belive that cytologic findings of three-dimensional papillary-like clusters with mild atypia, two types of cells and specific background in smears of cutaneous nodule might be a lead to the diagnosis of hidradenoma, but primary or secondary malignant tumour has been ruled out first.

#### REFERENCES

1. LEBOIT PE, Appendageal skin tumours. In: LEBOIT PE, BURG G, WEEDON D, SARASIN A (Eds) WHO Classification of Tumours, Pathology and Genetics: Skin Tumours, (IARC, Lyon, 2006). — 2. LAYFIELD LJ, MOONEY E, Acta Cytol, 42 (1998) 1064. — 3. RAGSDALE BD, MURPHY GF, Tumors of the skin. In: SILVERBERG SG, DELELLIS RA, FRABLE WJ (Eds). Principles and practice of surgical pathology and cytopathology (Churchill Livingstone, New York, 1997). — 4. MANNION E, MCLAREN K, AL-NAFUSSI AI, Cytopathology, 6 (1995) 100. — 5. VOLMAR KE, CUMMINGS TJ, WANG WH, CREAGER AJ, TYLER DS, XIE HB, Arch Pathol Lab Med, 129 (2005) 113. — 6. KHURSHID A, YAQOOB

N, DEVAN HA, PERVEZ S, J Cutan Pathol, 34 (2007) 871. — 7. PÉREZ-GUILLERMO M, SOLANO JG, Diagn Cytopathol, 30 (2004) 275. — 8. HOSHIDA Y, HANAI J, MATSUSHITA N, YONEKAWA M, KOBAYASHI Y, KAWAKAMI H, UCHINO N, AOZASA K, Acta Cytol, 42 (1999) 471. — 9. HOLDEN B, COLOME-GRIMMER M, SAVAGE C, STIERMAN K, POU AM, Ear Nose Throat J, 81 (2002) 352. — 10. POHAR-MARINŠEK Ž, LAMOVEC J, Acta Dermatoven APA, 12 (2003) 94. — 11. CHO S, KIM JS, SHIN JH, KIM JH, KIM HJ, WHANG KK, HAHM JH, Int J Dermatol, 40 (2001) 62. — 12. GOTTSCHALK-SABAG S, GLICK T, Diagn Cytopathol, 15 (1996) 395.

## N. P. Novak

Department of Clinical Cytology and Cytometry, Dubrava University Hospital, Av. G. Šuška 6, 10040 Zagreb, Croatia e-mail: dr.nina.novak@gmail.com

# CITOLOŠKA PUNKCIJA APOKRINOG HIDRADENOMA

## SAŽETAK

Apokrini hidradenom je benigna novotvorina kožnih adneksa, najčešće prekrivena nepromijenjenom kožom. Ponekad na koži može biti izražen površinski vrijed sa seroznim iscjetkom, obilježje koje budi sumnju u zloćudnost promjene, što je bio slučaj i u našeg bolesnika. Opisali smo citomorfološke značajke punktiranog kožnog čvora koje mogu pomoći u citološkoj dijagnozi hidradenoma, uz preduvjet da su isključene moguće primarne i sekundarne zloćudne novotvorine.