

Research Article

Fine Needle Aspiration Cytology of apocrine Carcinoma of the Breast: Detection of Androgen Receptor, Gross Cystic Disease Fluid-15 and Intranuclear Vacuoles

Nobuzo Iwa¹, Chikao Yutani¹, Kunihiro Hiraoka², Takao Ichihara² and Shin-Ichi Nakatuka³

¹Department of Pathology, Amagasaki Central Hospital, Japan

²Department of Surgery, Amagasaki Central Hospital, Japan

³Department of Pathology, Kansai Rosai Hospital, Japan

***Corresponding author**

Nobuzolwa, Department of Pathology, Amagasaki Central Hospital, 1-12-1, Shioe, Amagasaki, Hyogo, Japan, Tel: 06-6499-3045; Fax: 06-6497-3196; Email: nobuiw@chuoukai.or.jp

Submitted: 05 August 2015

Accepted: 11 October 2015

Published: 13 October 2015

Copyright

© 2015 Iwa et al.

OPEN ACCESS**Keywords**

- Apocrine carcinoma
- Intranuclear vacuoles
- Breast
- Fine needle aspiration cytology

Abstract

To reach a morphological diagnosis of apocrine carcinoma (AC) of the breast, cytopathology and immunohistochemistry (IHC) was employed. Mammography showed an ill-defined mass in the central quadrant of the right breast. Fine needle aspiration (FNA) cytology showed that many fine granules were scattered throughout the necrotic background of the smear. AC cells were characterized by abundant cytoplasm with eosinophilic, dense to granular and foamy cytoplasm and eccentric nucleus. Bi nuclei and intranuclear vacuoles were noted in the tumor cells. The features of nuclei were as follows; anisocytosis, hyperchromasia, pleomorphism and oval to round shape with centrally located large nucleoli. The IHC showed that these tumor cells were diffusely positive for androgen receptor (AR) and gross cystic disease fluid protein-15 (GCDFP-15). Histopathology of the operatively resected breast and core needle biopsy (CNB) materials showed that most of tumor cells were consisted with abundant cytoplasm with eosinophilic granules, vesicular cytoplasm, and sheet-like proliferation and anisocytotic nuclei. The nucleus was round to oval shape with centrally located large nucleoli. The IHC showed diffusely positive for MIB-1, HER2, AR and GCDFP-15. However, estrogen receptor (ER) and progesterone receptor (PgR) showed no immune activity.

ABBREVIATIONS

AC: Apocrine Carcinoma; IHC: Immunochemistry; FNA: Fine Needle Aspiration; AR: Androgen Receptor; GCDFP: Gross Cystic Disease Fluid Protein -15; CNB: Core Needle Biopsy

INTRODUCTION

Apocrine carcinoma (AC) is a relatively rare neoplasm account for less than 1% all of breast carcinoma [1]. This neoplasm is characterized by the irregular and round-shaped nucleus containing of large nucleoli centrally located on the nucleus having an abundant eosinophilic granules or vesicles in the cytoplasm [2]. The prognosis and average age of this

tumor is not different with ordinary breast malignancies [1]. Recently; many investigators have been interested in hormonal expression of AR and GCDFP-15; because of the anti-androgenic therapies are useful for the treatment and management of the breast cancer patients [3]. Therefore; the detection of AR and GCDFP-15 is specially needed for this tumor to better treatment of the patients. While the histopathological presentation and the IHC studies on AC are well known; little has been written on the appearance of intranuclear vacuoles on the FNA cytology. AC is often confused with apocrine metaplasia and AC entities conventional pathological basis. Because of the apocrine proliferations are often seen various spectrum lesions such as atypical apocrine adenosis; [4] ductal adenomas; and papillomas.

Therefore; an accurate morphological diagnosis on FNA cytology or CNB material is crucial for adequate therapy planning. In this paper; we report here a case of AC to make a correct cytological and histopathological diagnosis utilizing IHC.

MATERIALS AND METHODS

Tissues from CNB and excised surgical sample were fixed with 20% phosphate-buffered formalin. Totally; 4- μ sections were cut from the tissue blocks and stained with hematoxylin and eosin (H&E) stain; IHC; periodic-acid Schiff's reaction and Alcian blue stain. Aspirates and imprint smears were fixed in 95% ethanol and stained with a modified Papanicolaou stain. IHC was performed using the Envision-labeled polymer reagent(Dako; Glostrup; Denmark) and antibodies; AR (Dako); GCDFP-15(Dako); ER (Dako); PgR (Dako); HER-2 (Dako); MIB-1 (Dako); S-100 (Dako);P53 (Dako); MIB-1 (Dako); SMA (Dako) and Synaptophysin (Dako). Negative controls for the IHC were obtained by replacing the primary antibody with no immunized rabbit serum in the first steps of the indirect procedure. The sections were stained with [3]; 3'-diaminobenzidine and counterstained with hematoxylin. This study was approved by the local ethics committee and a patient gave written informed consent.

CASE REPORT

A 59-year old female was affected right mastitis at 39 years old and especially; she was no hormonal and medical histories in her life. The serum level of laboratory tests was within the reference ranges at clinical examinations. In 2016; she complained of a painless lump increasing in size in the central portion of the breast without the nipple discharge. And she was pointed out a right breast lump at the ultrasonographic examination in a private clinic. And she was introduced our hospital and physical examination revealed a tumor; measuring 3.4cm x 3.0cm in the central quadrant of the right breast. There were no palpable lymph nodes. Mammographic findings showed an ill-defined mass in the central quadrant of the right breast. And ultrasonographic findings showed a low echoic tumor mass

measuring 4.0cm x3.0 cm and the border was unclear. FNA cytology was highly suspicious of AC. And subsequently; CNB was performed to confirm the histopathological diagnosis and rendered to apocrine carcinoma. Operation was performed and FNA cytology and imprint materials were smeared onto several slides preventing air dry.

Cytology, Histopathology and IHC

Alcohol-fixed smears from the FNA cytology and imprint smears from operatively resected samples were stained with a modified Papanicolaou stain. The material was cellular and contained a mixture of many fine granular debris and tumor cells. The atypical cell components of the tumor cells were characterized as follows; individual cells; loosely cohesive clusters of enlarged cytoplasm and nuclei; irregular nuclear contours; thickness of nuclear membrane; anisocytosis; bi nuclei; hyperchromatic nuclei; centrally located large nucleoli; and eosinophilic or basophilic fine granules and vesicles in the cytoplasm. And intranuclear vacuoles were also noted (Figure 1A 1B 1C). But PAS stain was negative for the intranuclear vacuoles. The nuclear/cytoplasmic ratio was not increased. No malignant ductal elements were present in the FNA cytology material and imprint smears. The FNA cytology was interpreted as cells compatible with AC. The IHC showed that the cytoplasm was diffusely positive for AR; GCDFP-15 (Figure 2A 2B 2C). The excised breast tumor contained a soft grey tumor with spongy like appearance (Figure 3A). H&E stained sections showed that most of AC cells were occupied with irregular nuclei with sheet like proliferation having eosinophilic granules or vesicles in the cytoplasm (Figure 3B 3C). And also; intra nuclear vacuole bearing tumor cells were noted (Figure 3B) inlet. The sentinel lymph node was free from tumor cells. In the IHC; the AC cells showed diffusely and strongly positivity for AR (Figure 3D) and GCDFP-15 (Figure 3E).And also HER-2; P53; P53 and MIB-1 (tumor cells stained about 30%) showed positive. But ER; PgR; S-100 and Synaptophysin showed negative. The cytological features with present study and review of the literatures of AC were summarized in (Table 1).

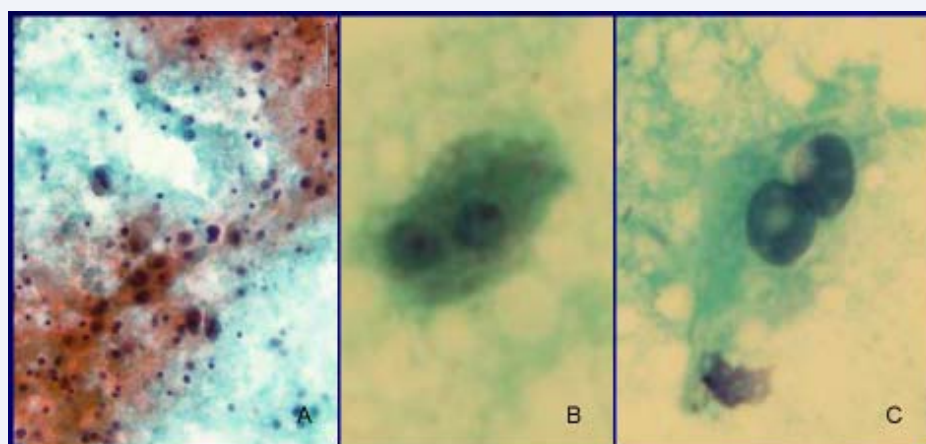


Figure 1 A: Fine needle aspiration cytology showed many tumor cells in a background of the tumor diathesis. (Papanicolaou stain; x200). B: Fine needle aspiration cytology showed many fine granules in the abundant cytoplasm. (Papanicolaou stain; x400) C: Fine needle aspiration cytology showed intracytoplasmic nuclear invagination in the tumor cells. (Papanicolaou stain; x400)

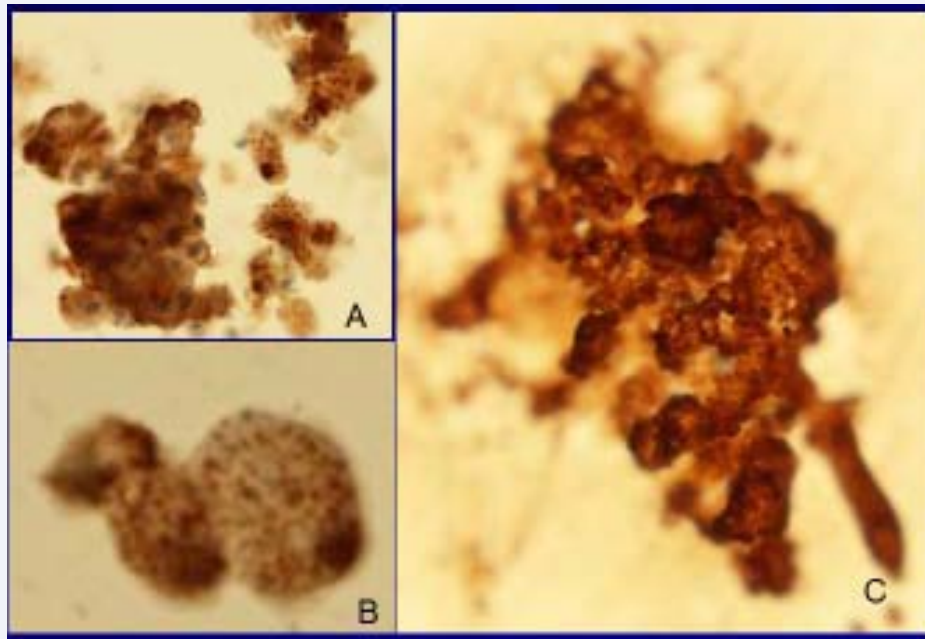


Figure 2 A: Immunocytochemistry of the imprint smear; the tumor cells showed strongly positive for androgen receptor throughout the nucleus and cytoplasm (hematoxylin counterstain; x20). B: Immunocytochemistry of the imprint smear; cytoplasmic granules showed positive for androgen receptor. (hematoxylin counterstain; x40). C: Immunocytochemistry of the imprint smear; the tumor cells showed strongly positive for gross cystic disease fluid protein-15. (hematoxylin counterstain; x400)

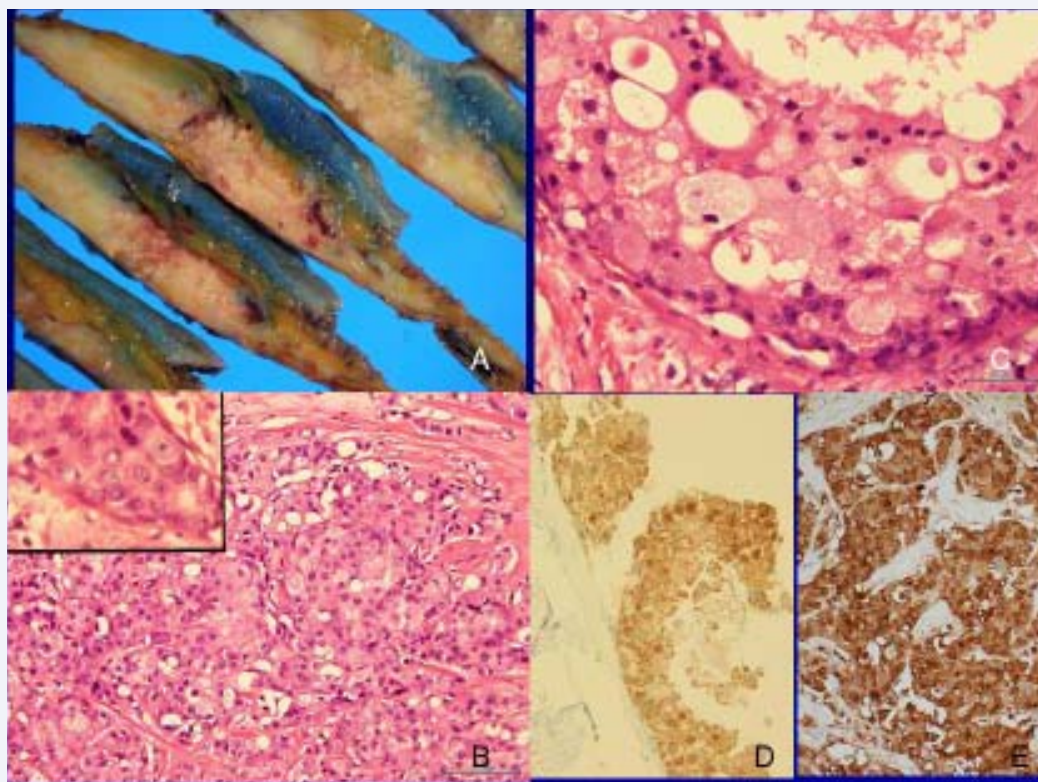


Figure 3 A: Gross appearance of the breast; the tumor cut surface in a surgical specimen showed gray and spongy like appearance. B: Histopathological appearance of the resected breast tumor revealing abundant cytoplasm with eosinophilic granules and vesicles in a sheet-like proliferation. And the inset showed intracytoplasmic nuclear invagination. (H&E; x200; inset; x200). C: Histopathological section showed abundant cytoplasm with eosinophilic granules. (H&E; x400). D: Immunohistochemistry of the tumor showed positive for androgen receptor. (hematoxylin counterstain; x200). E: Immunohistochemistry of the tumor showed positive for gross cystic disease fluid protein-15. (hematoxylin counterstain; x200)

Table 1: Cytological findings of present study and review of literature in apocrine carcinoma [10,11].

| Present study | Review of literatures | |
|---------------|---|---|
| Smears | Highly cellular with granular debris | Moderate to high cells, necrotic debris |
| Cells | Isolated or loosely cohesive cluster | Loosely cohesive cluster |
| Cytoplasm | Elongated and Granular cytoplasm | Dense to granular cytoplasm |
| Nucleus | Irregular nuclear borders, thickness of nuclear membrane, anisocytosis, binuclei, intercytoplasmic vacuoles | Pleomorphism, binuclei, irregular nuclear borders |
| Nucleoli | Centrally located large nucleoli | Macro nucleoli |

DISCUSSION

AC of the breast is a relatively rare entity whose endocrinal behavior is increasing interest by its hormonal expression such as ER; PgR; AR and GCDFP-15 as clinical treatment and management of the patient. AC of the breast is characterized by a >90% of AC tumor cells and almost these tumor cells are negative for ER and PgR and positive for HER-2; [5] therefore; this neoplasm is characterized by the expression of AR and GCDFR-15 [6]. Sasahara et al [7] reported that AR expressed in 100% (54/54) and fork head-box A1 protein 93% (50/54) in AC. Present case; the cytoplasm of the AC cells from smears and paraffin sections showed diffusely positive for AR and GCDFP-15.

Therefore; the detection of AR and GCDFP-15 is a specific marker for AC to make correct diagnosis in cytology as well as histopathology. And also; MIB-1 labeling index was 30%; and P53 was positive for tumor cells.

On cytological findings; there are two types of tumor cells; type A is abundant granular; intensely eosinophilic; cytoplasm and type B is fine empty vacuoles resulting in a foamy appearance which are variously intermingled. Nuclei are similar to those in type A cells [1]. Although our case is belonging to type B; until now; the feature of intranuclear vacuoles is not described from others. Neoplastic entities in the differential diagnosis of AC include atypical apocrine metaplasia which characterized by abundant pink; sometimes granular cytoplasm and bland or monotonous with centrally located in the nucleus. Nucleus is small and regular sheets [8]. Cytological; there is seldom any difficulty in recognition the presence of malignancy because; it is well known that the cytological features of AC cell show as follows; nuclear overlapping; nuclear pleomorphic and hyperchromatic nuclei; loosely cohesive clusters; large and polygonal cells; with large nucleoli and abundant; basophilic and granular cytoplasm [9-11]. Although these cytological features of AC were similar to our experienced case; AC cells allow the differential diagnosis with other tumors having cytoplasmic granules. And cutaneous apocrine carcinoma is mimic in the breast carcinoma [12]. Occasionally; only the cytological features of AC are difficult to correct diagnosis. Because, there are similar tumors having cytoplasmic granules or vesicles in the cytoplasm such as glycogen-rich carcinoma; [13] lipid-rich carcinoma; [14] oncocytic carcinoma [15] and sclerosingadenosis [16] however, the breast lesions with these malignancies are rarely encountered in breast FNA cytology materials. Moreover; these tumors do not over express AR and GCDFP-15.

In this study; AC cells showed diffusely positive for AR and GCDFP-15. However; ER; PgR and Synaptophysin showed

no immune activity. Therefore; we suggest that. The IHC is helpful for the differential diagnosis for this tumor .Although; metastatic malignant melanomas of the breast are rare; AC allows differentiation with AC cells. The cytological features of malignant melanoma are as follow; predominant single cells with eccentric nuclei; predominant nucleoli; intranuclear cytoplasmic inclusions and dense cytoplasmic vacuoles with melanin pigment [17]. However; malignant melanoma could not be identify the hormone receptors. The meanings of internuclear vacuoles in AC cells need further investigations. In our knowledge; it is the first cytological description for the detection of the intra nuclear vacuoles in the tumor cells from FNA cytology as well as tissue sections. We hope that this cytological and the IHC findings and intra nuclear vacuoles could be of further utility in elucidating its cytological features; although IHC and histopathological confirmation are required for diagnosis.

REFERENCES

1. World Health Organization Classification of the Tumors. Tumours of the breast. IARC Press: Lyon. 2002; 53-54.
2. Hoda S, Brogi E, Koerner FC, Rosen PP. Rosen's Breast and Pathology; 4rd Ed; Wolters Kluwer; Philadelphia. 2015; 645-666.
3. Laforga JB, Gasent JM, Sánchez I. Encapsulated apocrine papillary carcinoma of the breast: case report with clinicopathologic and immunohistochemical study. *Diagn Cytopathol.* 2011; 39: 288-293.
4. Fuehrer N, Hartmann L, Degnim A, Allers T, Vierkant R, Frost M, et al. Atypical apocrine adenosis of the breast: long-term follow-up in 37 patients. *Arch Pathol Lab Med.* 2012; 136: 179-182.
5. Khandeparkar SG, Deshmukh SD, Bhayekar PD. A rare case of apocrine carcinoma of the breast: Cytopathological and immunohistopathological study. *J Cytol.* 2014; 31: 96-98.
6. Lehmann-Che J, Hamy AS, Porcher R, Barrिताult M, Bouhidel F, Habuellel H. Molecular apocrine breast cancer are aggressive estrogen receptor negative tumors overexpressing either HER2 or GCDPF15. *Breast Cancer Res.* 2013; 15: 37.
7. Sasahara M, Matsui A, Ichimura Y, Hirakata Y, Murata Y, Marui E. Over expression of androgen receptor and forkhead-box A protein in apocrine breast carcinoma. *Anticancer Res.* 2014; 34: 1261-1267.
8. Gerhard R, Costa JL, Schmitt F. Benign and malignant apocrine lesions of the breast. *Expert Rev Anticancer Ther.* 2012; 12: 215-221.
9. Jayaram G, Yacob RB, Yip CH. Apocrine carcinoma of the breast diagnosed on fine needle aspiration cytology. *Acta Cytol.* 2007; 51: 664-667.
10. Nagarekha K. Fine needle aspiration cytology of apocrine mammary carcinoma: Report of five cases. *Oncocytology* 2012; 2:6-9.
11. Ng WK. Fine needle aspiration cytology of apocrine carcinoma of the

- breast. Review of cases in a three-year period. *Acta Cytol* 2002; 46: 507-512.
12. Toledo PT, Lombart CB, Traves ZP, Requena CC, Sanmartin JO, Angles SM, et al. Case report: differential diagnosis between primary cutaneous apocrine adenocarcinoma versus extrammary or metastatic breast a. *Am J Dermatopathol* 2014; 36:175-178.
13. Das AK, Verma K, Aron M. Fine-needle aspiration cytology of glycogen-rich carcinoma of breast: report of a case and review of literature. *Diagn Cytopathol*. 2005; 33: 263-267.
14. Machalekova K, Kajo K, Bencat M. Unusual occurrence of rare lipid-rich carcinoma and conventional invasive ductal carcinoma in the one breast: case report. *Case Rep Pathol*. 2012; 387045.
15. Damiani S, Eusebi V, Losi L, D'Adda T, Rosai J. Oncocytic carcinoma (malignant oncocytoma) of the breast. *Am J Surg Pathol*. 1998; 22: 221-230.
16. Cho EY, Oh YL. Fine needle aspiration cytology of sclerosing adenosis of the breast. *Acta Cytol*. 2001; 45: 353-359.
17. Cangiarella J, Symmans WF, Cohen JM, Goldenberg A, Shapiro RL, Waisman J. Malignant melanoma metastatic to the breast: a report of seven cases diagnosed by fine-needle aspiration cytology. *Cancer*. 1998; 84: 160-162.

Cite this article

Iwa N, Yutani C, Hiraoka K, Ichihara T, Nakatuka SI (2015) Fine Needle Aspiration Cytology of apocrine Carcinoma of the Breast: Detection of Androgen Receptor, Gross Cystic Disease Fluid-15 and Intranuclear Vacuoles. *Ann Clin Cytol Pathol* 1(3): 1011.