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Case Report

Dimorphic variant of ductal carcinoma in situ of the breast

Nozomi Ueno, MD [a], Hajime Kuroda, MD [b,*], Yuji Kozuka, MD [c], Oi Harada, MD [d], Hiroyuki Kato, MD [a], Keiichi Kubota, MD [e], Yasuo Imai, MD [b]

[a] Department of Surgery I, Dokkyo Medical University, Japan
[b] Department of Diagnostic Pathology, Dokkyo Medical University, Japan
[c] Department of Pathology, Mie University, Japan
[d] Breast Center, Showa University Hospital, Japan
[e] Department of Surgery II, Dokkyo Medical University, Japan

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ABSTRACT

We report a case of dimorphic variant of ductal carcinoma in situ (dimorphic DCIS), composed of an epithelium intermixed with columnar cells and dimorphic cells. The findings of typical DCIS architecture support categorization as DCIS on a low-power view. Furthermore, there was no difference in the nuclear morphology of the two cell types on the high-power view. The two cell types comprising dimorphic DCIS were negative for p63, CK 5/6 and 14. On the contrary, both cell types were diffusely positive for nuclear ER and AR, as well as marked membrane-associated staining for E-cadherin and cytoplasmic staining for GCDFP-15. These immunohistochemical marker results are similar to conventional DCIS and there were no differences in expression patterns between the columnar epithelial cells and dimorphic cells. The morphological features of dimorphic cells may be confused with cells of other origins if the features of dimorphic DCIS are not recognized. Careful observation of morphological architecture and expression of immunohistochemical markers may support diagnosis.

1. Introduction

Ductal carcinoma in situ (DCIS) of the breast is usually composed of monomorphic epithelial cells that remain confined by basal myoepithelial cells [1–3]. However, there is evidence indicating that two types of epithelial cells are observed in DCIS. Lefkowitz et al. reported intraductal papillary carcinomas with cuboidal cells of abundant clear or faint cytoplasm, which were named dimorphic cells [4]. However, few articles on DCIS with dimorphic cells (dimorphic DCIS) have been published. The appearance of the dimorphic cells markedly contrasted with that of the conventional columnar cells in DCIS. There are many questions about the clinicopathological significance of this subtype, especially regarding differential diagnosis. Here we report a case of dimorphic DCIS of the breast.

2. Case report

A 42-year-old female presented at our department for medical examination with no constitutional symptoms. There was no complaint of pain or nipple discharge. There was no family history of breast cancer or history of any breast problems. Clinically and radiologically, there was a 1 cm lump in the right lower outer quadrant (Figs. 1, 2). An ultrasound-guided core biopsy was done that revealed ductal carcinoma in situ (DCIS). Immunohistochemical (IHC) studies showed the DCIS to be positive for estrogen receptor (ER) (100% strong) and progesterone receptor (PgR 80%, moderate), with a Ki-67 protein proliferation index of 5%. Breast-conserving surgery was performed, in association with a sentinel lymph node biopsy. Regarding the surgical specimen, macroscopically the tumor was 6 mm in diameter. Microscopically, on a low-power view, the dimorphic DCIS exhibited a cribriform pattern (Fig. 3). On the high-power view, the dimorphic cells have abundant clear or faintly eosinophilic cytoplasm similar to that seen in myoepithelial cells and the nuclei were identical to those in adjacent malignant columnar epithelial cells (Fig. 4).

Sections were immunostained for estrogen receptor (ER, clone SP1, VENTANA, prediluted, nuclear), progesterone receptor (PgR, clone 1E2, VENTANA, prediluted, nuclear), Ki-67 (Ki-67, MIB1, DAKO, 1:50, nuclear), p63 (p63, clone 6F11, Novocastra, 1:40, nuclear), E-cadherin (E-cadherin, clone 36, BD Transduction Lab., 1:2000, Membranous), cytokeratin 5/6 (CK5/6, clone D5/16 B4, DAKO, 1:25, cytoplasmic), cytokeratin 14 (CK14, clone LL002, Novocastra, 1:20, cytoplasmic), estrogen receptor (ER, clone 4A4, DAKO, 1:50, nuclear), androgen

* Corresponding author at: Department of Diagnostic Pathology, Dokkyo Medical University, 880 Kitakobayashi, Mibu, Tochigi 321-0293, Japan.
E-mail address: hajimek@dokkyomed.ac.jp (H. Kuroda).

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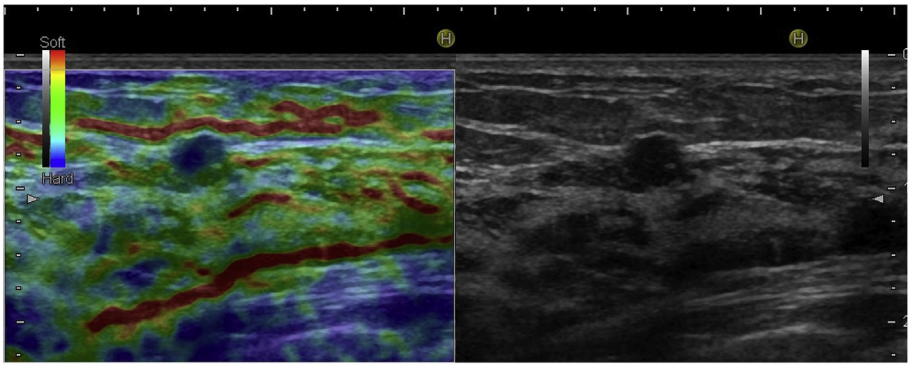

Fig. 1. Ultrasound examination showed an irregular hypoechoic mass in the lower outer quadrant of the right breast.

receptor (AR, clone 23A, Novocastra, 1:40, nuclear), gross cystic disease fluid protein 15 (GCDFP-15, clone AR441, DAKO, 1:50, cytoplasmic), synaptophysin (SYN, clone 27G12, Novocastra, 1:100, cytoplasmic), and chromogranin A (CgA, clone poly, Nichirei, prediluted, cytoplasmic). The two cell types comprising dimorphic DCIS were negative for p63, CK 5/6, CK 14, SYN and CgA. On the contrary, both cell types were diffusely positive for nuclear ER and AR. Weak membrane associated staining for E-cadherin and cytoplasmic staining for GCDFP-15 was observed in both cell types (Fig. 5A–D).

The margins and sentinel lymph node were negative for carcinoma. The patient received adjuvant radiation therapy. The patient had no sign of local recurrence or distant metastasis 36 months after the operation.

3. Discussion

Lefkowitz et al. reported 20 cases of intraductal papillary carcinomas (IPCs) of cuboidal cells with abundant clear or faintly eosinophilic cytoplasm [1–4]. These cells were located mainly near the basement membrane singly, in small clusters, or in broad sheets. The appearance of the polygonal cells contrasted with that of the adjacent malignant columnar epithelial cells, and was similar to the appearance of the myoepithelium. The report suggested that the presence of these tumor cells could create a problem in the differential diagnosis of an IPC due to possible misinterpretation as myoepithelial cells. Despite the difference in cytoplasmic features, the nuclei resemble those in adjacent malignant columnar epithelial cells. Because of the variable appearance of these cells, they were designated as dimorphic cells. Furthermore, there was no difference in nuclear morphology between the two cell types in dimorphic DCIS in our case on a high-power view. Lefkowitz et al. also reported the resemblance between dimorphic cells of intraductal papillary carcinoma and myoepithelial cells, and described the nuclei as identical to those in the adjacent malignant epithelial cells [4].

This morphology raises the issue of whether dimorphic DCIS should be diagnosed as a type of DCIS. The primary differential diagnosis of dimorphic DCIS is with usual ductal hyperplasia, which is characterized by a heterogeneous population of ductal cells implying a dimorphic DCIS. The duct lumen spaces that are found in ductal hyperplasia have distinctive features [1–3]. The lumen spaces in a ductal hyperplasia usually have varied shapes, rather than being rounded, which tends to be found in dimorphic DCIS. In dimorphic DCIS, the observation of typical DCIS architecture, such as a cribriform pattern, supports the categorization of DCIS on a low-power view. Further, the cytoplasmic borders in ductal hyperplasia are often indistinct and the nuclei are overlapping and distributed in a “streaming” fashion. In contrast, the tumor cells usually show uniform round to oval nuclei, with prominent nucleoli in dimorphic DCIS on a high-power view, which is also helpful. Thus, dimorphic DCIS may be an accurate diagnosis on the basis of architectural pattern and careful observation of cytological features.

It must be emphasized that dimorphic cells should be carefully evaluated for morphological evidence on hematoxylin-eosin-stained slides to avoid a misleading diagnosis. However, immunohistochemical markers that can aid in accurate diagnosis of dimorphic DCIS have been identified. The immunohistochemical marker p63 proved to be the most sensitive marker for the detection of myoepithelial cells of the breast, and may also be helpful for evaluation of dimorphic cells, which resemble myoepithelium [5,6]. In our case, despite the differences in cytoplasmic features between the eosinophilic and clear stained cytoplasm cells (columnar epithelial cells and dimorphic cells), there was no reactivity for p63 in both cell types. Furthermore,

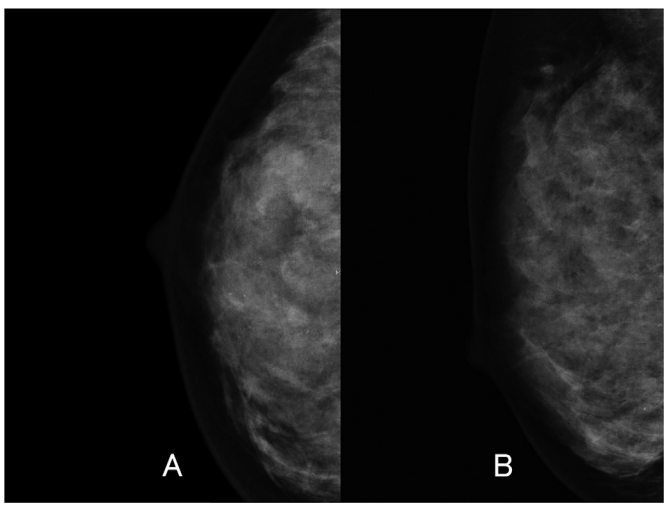

Fig. 2. Craniocaudal (A) and mediolateral oblique (B) mammogram views of the right breast showing no obvious tumor lesion.

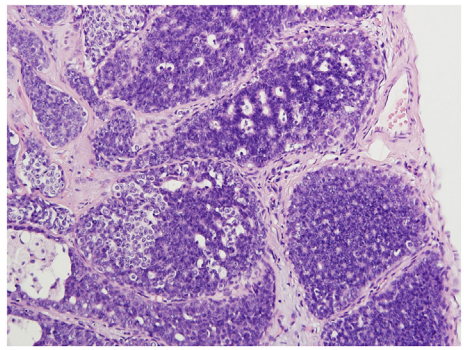

Fig. 3. Dimorphic DCIS on low-power view. The finding of typical DCIS architecture, such as a cribriform pattern, supports categorization as DCIS.