INTRODUCTION

Cystic lesions are often found within mammary glands by ultrasound (US). This form of lesion is categorized into simple cysts, complicated cysts, and complex cysts based on US findings [1,2]. Of these, a complex cystic mass has a relatively high probability (23% to 31%) of malignancy, and thereby has important clinical implications due to the need for differentiation between benignity and malignancy [3-5]. BI-RADS® Ultrasound Lexicon Classification categories also support close examination and accurate diagnosis of this lesion [2]. In US findings, complex cystic masses are visualized as mixed lesions containing both a solid lesion and a cystic lesion. The pattern of the solid lesion and the intratumor occupancy of the solid component are variable.

In the histology, complex cystic masses consist either of an intracystic mass that contains a solid component in the cyst (duct) or a solid mass lesion that contains a fluid component in the mass. In some cases, it is difficult to determine lesion type based on US imaging; however, it is also important to observe the cystic composition. This can help determine the subtypes in addition to the histological types.

Summary: In ultrasound examinations, mixed mammary gland masses are divided into either intracystic masses that contain a solid component in the cyst or solid masses that contain a fluid component in the mass. The histological types and subtypes of three complex cystic masses that showed different internal compositions in ultrasound were determined using the ultrasound findings of three patients. Case 1: The mass showed a large cystic component (bleeding) inside and a broad-based solid lesion at the margin in the ultrasound finding. The histological type was encapsulated papillary carcinoma and the subtype was luminal A. Case 2: The mass was lobulated with a small cystic component at the margin. The histological type was solid papillary carcinoma and the subtype was luminal A. Case 3: The mass was lobulated with a circumscribed margin. Cystic components suspected of being hemorrhagic necrosis were observed at the margin and within the solid component. The histological type was squamous cell carcinoma and the subtype was triple negative. Case 2 was a solid mass in appearance, but a cystic component noted at the margin was possibly an intracystic mass. For Case 3, findings suggestive of necrosis were observed both at the margin and in the solid component and this suggested a mass with fluid degeneration. Complex cystic masses are usually examined with a focus on the solid component seen on ultrasound images; however, it is also important to observe the cystic composition. This can help determine the subtypes in addition to the histological types.

Key words  complex cystic mass, an intracystic mass, a solid mass with fluid components, subtype
ages. In this report, complex cystic masses detected in three patients were compared by US morphology to differentiate between (i) An intracystic mass and a solid mass with fluid components, and to determine (ii) histological type and (iii) subtype.

CASE REPORT

Case 1 (Fig. 1)

Subject was a 63-year-old female. She had noticed a mass in her right breast two years previously. The mass gradually increased in size and started to bleed. At the first US finding, the mass was more than 10 cm in size (Fig. 1a). After the drainage the mass was a circumscribed complex cystic mass (39 × 40 × 20 mm) with an irregular wall, and the center showed a fluid-fluid level (Fig. 1b). The mass corresponded to category 4b (moderate suspicion for malignancy) according to the BI-RADS® Ultrasound Lexicon Classification [2], and the tumor was suspected to be ductal carcinoma in situ (DCIS).

Macroscopically, the lesion appeared as a cystic-like mass with thick fibrous walls (Fig. 1c).

Histologically, the mass was sclerosed and encapsulated by fibrosis, and papillary and cribriform structures were seen within a network of fibrovascular cores (Fig. 1d). The histological diagnosis was an encapsulated papillary carcinoma (EPC). The tumor was estrogen receptor (ER) positive [Allred score 8], progesterone receptor (PgR) positive [Allred score 6] and human epidermal growth factor receptor 2 (HER2) negative. Its subtype was determined as luminal A.

Case 2 (Fig. 2)

A 74-year-old female noticed a mass in her left breast. On the mammography findings (MMG), there was an ill-defined high-density mass in the left breast. US findings showed a lobulated hypoechoic and non-circumscribed margin mass (28 × 16 mm) with anechoic area in the periphery (Fig. 2a). Also, the ducts besides the nipple were detected near the main mass (Fig. 2b). The mass corresponded to category 4b (moderate suspicion for malignancy) according to the BI-RADS® Ultrasound Lexicon Classification [2]. The tumor was suspected to be an intraductal papillary carcinoma.

Fig. 1. Case 1 [Encapsulated papillary carcinoma (EPC)]
a. (US) First visit: more than 10 cm (depth 4.5 cm).
b. (US) After the drainage: A circumscribed complex cystic mass (39 × 40 × 20 mm) with an irregular wall, and the center showed a fluid-fluid level.
c. The mass showed a cystic-like mass with thick fibrous walls.
d. The mass was encapsulated by fibrosis and sclerosed, and papillary and cribriform structures were seen by network of fibrovascular cores.
Macroscopically, the mass showed a solid mass with cystic space in the periphery (Fig. 2c).

Histologically, papillary structure is represented by a network of fibrovascular cores among the solid cellular proliferations. Invasion was not clearly observed (Fig. 2d). The histological diagnosis was a solid papillary carcinoma (SPC) in situ. The tumor showed ER positive [Allred score 8], PgR positive [Allred score 7] and HER 2 negative. Its subtype was luminal A.

Case 3 (Fig. 3)
A 58-year-old female noticed a painful mass in her right breast. MMG findings revealed a high-density microlobulated mass in the right breast (Fig. 3a). US findings were a lobulated hypoechoic and circumscribed margin mass (40 × 20 × 26 mm) with posterior acoustic enhancement. Cloudy fluid areas were seen in the mass and at the periphery (Fig. 3b). The mass corresponded to category 4c (high suspicion malignancy) according to the BI-RADS® Ultrasound Lexicon Classification [2]. The tumor was suspected to be a squamous cell carcinoma (SCC), mixed type mucinous carcinoma or invasive carcinoma- solid type [no special type (NST)].

Macroscopically, there were necrotic spaces within the solid mass (Fig. 3c).

Histologically, eosinophilic adenocarcinoma cells with squamous differentiation showed a solid proliferation (Fig. 3d). The histological diagnosis was metaplastic carcinoma, SCC. The tumor was triple-negative (TN) for ER, PgR and HER2.

Comparison of the three cases (Table 1)
In US findings, case 1 (EPC) presented a large, cloudy cyst (bleeding) inside the mass. Case 2 (SPC) had a clear cystic component at the margin. Both cases were intracystic masses of luminal A subtype. Case 3 (SCC) was a solid mass type that included cloudy cysts (necrotic bleeding) at the margin and within the solid component of the mass. The subtype was TN.

DISCUSSION
(i) Differentiation between an intracystic mass and a solid mass with fluid components on US
Histological type is predicted from US findings depending on the type of mass, i.e. an intracystic mass or a solid mass with fluid components. Case 1 (EPC), a large possibly bleeding cystic mass, was classified as an...
Fig. 3. Case 3 [Squamous cell carcinoma (SCC)]
a. (MMG) The mass was a high density microlobulated mass in the right breast.
b. (US) The lobulated hypoechoic and circumscribed margin mass (40 × 20 × 26 mm) with posterior acoustic enhancement, and bleeding areas were shown in the mass (△) and in the periphery (→).
c. The mass showed necrosis spaces.
d. The mass showed eosinophilic adenocarcinoma cancer cells with squamous differentiation showed a solid proliferation.

|        | Case 1 EPC | Case 2 SPC | Case 3 SCC |
|--------|------------|------------|------------|
| US findings | Intracystic(ductal)mass (Solid parts in a cyst) | Solid mass (Liquid parts in a solid mass) |
| Position of the cystic area | Inside and margin | anechoic area in the periphery | margin and inside |
| Property in the cyst | bleeding | clear | bleeding |
| US type schema | ER + / PgR + / HER2 – Luminal(A) | ER - / PgR - / HER2 – Triple negative |
| Subtype | solid : cystic area: anechoic(clear) bleeding | |

TABLE 1: Comparison of three cases
intracystic mass that was suspected of being intracystic cancer based on the absence of infiltration to the surrounding tissues. Case 2 (SPC) was largely occupied by a solid component with a small cystic component. The cyst itself was clear and extended along the margin. There was also a finding suggestive of intraductal involvement. Therefore, case 2 was classified as an intracystic mass that was suspected of being an intracystic papillary carcinoma. The cyst observed in case 3 (SCC) was not as clear as that observed in case 2; it contained opacified cystic components suggestive of necrosis both at the margin and within the solid component. This finding was considered likely to be necrotic degeneration of the solid mass, rather than dilated ducts or an intracystic mass. Case 3 was thus classified as a solid mass with fluid components. US can provide an accurate picture of complex cystic masses, such as the location and properties of solid and cystic components [1,6]. Using this diagnostic modality, it is important to focus not only on the solid components but also on the cystic conformation.

(ii) Determination of histological type

Determination of the histological type was discussed in terms of an intracystic mass and a solid mass with fluid components. Representative malignancies of an intracystic mass include intracystic papillary carcinoma, EPC, and SPC [7]. EPC is a kind of papillary carcinoma, which is listed in the fourth edition of the WHO classification as a new independent disease entity [7]. US imaging of EPC generally shows a hypoechoic mass or a complex cystic mass [8]. Some of the lesions can grow rapidly, dilating and compressing nearby tissues, and as in this case, EPC can protrude on the breast surface [9]. Case 1 was also a large self-destructive cystic mass. SPC basically refers to intraductal carcinoma, which was proposed by Maluf and Koerner and shows solid, papillary development. SPC is often characterized by the expression of neuroendocrine phenotype [10]. SPC is listed in the WHO classification in 2012 as a new independent disease entity [11]. SPC can be a complex cystic type presenting in US imaging as a lobulated intraductal or intracystic mass, or otherwise, as a uniform solid mass. SPC is often enhanced in posterior echo [12]. Case 2 was a mass occupied by a solid component. EPC and SPC, relatively new disease entities, should be considered in histological determination of lesions suspected of being an intracystic mass.

Representative malignancies of a solid mass with fluid components include SCC, phyllodes tumor, mucinous carcinoma, and invasive carcinoma- solid type (IC-NST) [13]. All these lesions show expansive growth in an ovalized or lobulated form. These masses are hypoechoic (hyper to isoechoic mass in mucinous carcinoma), and are often enhanced in posterior echo [13]. Similar findings were observed in case 3. These findings described above should be considered when evaluating a solid mass with fluid components.

(iii) Determination of subtype

In these cases, case 1 (EPC) and case 2 (SPC), both classified as intracystic masses, generally manifest as papillary lesions with nuclear atypia of lower grades. Most EPC and SPC have been associated with luminal subtypes [14, 15]. Weigelt et al. also reported the association between histological special types and subtypes [16]. Among the histological types, neuroendocrine type is associated with luminal types, in which category SPC is also included. Determination of subtypes would be possible if EPC and SPC could be differentiated by US.

Reports on the characteristics in US findings and subtypes of solid mass suggest that morphology, posterior echo property, and margins have important relationships with subtypes and histological grades [17, 18]. Circumscribed margins and posterior acoustic enhancement are often observed in patients with TN breast cancer [17, 18]. TN cancer is also characterized by expansive growth and round, oval or lobulated shapes [17, 19]. Case 3 also presented SCC findings that were suspected of indicating TN based on the form and properties. TN cancer has higher grades of biological malignancy and a generally poor prognosis due to the intrinsic subtype [19-21]. As TN cancer shows characteristic US findings such as round/lobulated masses and enhanced posterior echo, US is especially helpful in the differentiation of subtypes, specifically in TN cancer.

We classified complex cystic masses into (i) An intracystic mass or a solid mass with fluid components by US findings including the locations and properties of cystic components; (ii) papillary lesions such as EPC or SPC have been recognized recently as new disease entities and should be taken into account as possibly malignant intracystic masses, and SCC and/or IC-NST may be useful for differentiation from a solid mass with fluid components; (iii) An intracystic mass may be likely to have luminal subtypes, while a solid mass with fluid components that is differentiated from SCC or IC-NST was likely to be TN cancer. Reading US findings is critical when deciding whether to perform additional examinations and determining a treatment strategy. As regards treatment strategy, it would be very helpful to clinicians if US findings could be used to differentiate histological types and subtypes. Further studies are needed in a case series.
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