Neuroendocrine differentiated breast carcinoma: imaging features correlated with clinical and histopathological findings

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Abstract The aim of this study was to describe the imaging features of neuroendocrine differentiated breast carcinoma (NEDBC) and to correlate the radiological findings with the clinical and histopathological findings. A retrospective review of the mammograms of 1845 histopathologically proven breast cancer cases revealed five NEDBC. The clinical, imaging, and histopathological findings were analyzed. On mammography, a high-density mass was seen in all patients. The shape of the mass was round in 4 and irregular in 1 patient. The margins were spiculated in 2, indistinct in 1, microlobulated in 1, and partially obscured in 1 patient. On sonography, 4 patients had homogeneously hypoechoic masses with normal sound transmission. In 1 patient the mass was heterogeneously hypoechoic with mild posterior acoustic enhancement. The margins were microlobulated in 2, irregular in 2, and well-circumscribed in 1 patient. Neuroendocrine differentiated breast carcinoma should be included in the differential diagnosis of mammographically dense, round masses with predominantly spiculated or lobulated margins. Sonographically, they mostly present as irregular or microlobulated, homogeneously hypoechoic masses with normal sound transmission.

Keywords Breast · Neuroendocrine differentiated breast carcinoma · Mammography · Sonography

Introduction

Some breast tumors are classified as primary neuroendocrine carcinomas because of argyrophilia and positivity for neuroendocrine markers (chromogranins A and B and neuron-specific enolase), regardless of their cellular rest and cord structures [1]. Although neuroendocrine tumors can originate from various parts of the body and can cause a diverse group of well-defined clinical entities, primary neuroendocrine tumor of the breast is very unusual [2]. Currently, several reports on neuroendocrine differentiated carcinomas of the breast have been reported in the pathology literature [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13]; however, imaging features have been described in only two cases [1, 4]. Wade et al. [4] described the first neuroendocrine carcinoma of the breast in 1983 as a case report. Since then, there has been only one other case with imaging features reported [1]. The aim of this study was to describe the imaging (mammographic, sonographic, and MR imaging) features of this very rare tumor, and to correlate the radiological findings with the clinical and histopathological findings.

Materials and methods

A retrospective review of the mammograms of 1845 histopathologically proven breast cancer cases diagnosed in our mammography unit during the past 15 years revealed five histopathologically proven neuroendocrine differentiated breast carcinomas. The history, physical examination, and radiological (mammographic and sonographic) findings were analyzed in all patients. Patients were all women and their age ranged between 43 and 70 years (mean age 58 years).

Mammography with two routine positions (craniocaudal and mediolateral oblique) was performed in all of the patients by Se-
nographe Senix 600T (General Electric CGR S.A., Issy Les Moulineaux, France) or Mammomat 3000 (Siemens, Sweden, TA). All mammograms were retrospectively reviewed by two radiologists who are specialists in breast imaging. The evaluation was done as consensus readings. Mammograms were evaluated blinded to the information from physical examination or sonographic records but aware of the histopathological diagnosis. Each mammographic lesion was characterized according to size, mass characteristics (shape, margins, density, size, and location), presence and type of microcalcifications, associated architectural distortion, and skin changes using the criteria given by American College of Radiology’s Breast Imaging Reporting and Data System (BI-RADS) [14]. Parenchymal patterns were categorized as fatty, scattered fibroglandular tissue, heterogeneously dense, and extremely dense using BI-RADS criteria [14].

Sonography was performed in all of the patients by using a 7.5-MHz transducer (SAL 70, Toshiba, Tokyo, Japan; or Sonoline Adara, Siemens, Erlangen, Germany) or a broadband 5- to 11-MHz transducer (HDL 1000, Advanced Technology Laboratories, Bothell, Wash.). The sonographic prints and records (original reports) of each patient were reviewed after the mammograms, in the same evaluation session. Sonograms were assessed for lesion shape, margin, echo texture, echogenicity, and posterior acoustic phenomena, and lesions were classified according to the criteria established by Stavros et al. [15].

Magnetic resonance imaging was performed in 1 patient with a 1.5-T MR imaging system (Magnetom Vision, Siemens, Erlangen, Germany), using a dedicated double breast coil. Dynamic contrast-enhanced MR mammography was obtained using three-dimen-
tional fast low-angle shot (FLASH) gradient-echo sequences in an axial orientation. One sequence pre- and five sequences post-contrast medium injection at 58-s intervals were carried out. The imaging parameters were TR=12 ms, TE=5 ms, field of view=300 cm, and slice thickness 3 mm. Gadopentetate dimeglumine (Gd-DTPA; Magnevist, Schering, Berlin, Germany) was administered as bolus injection using an injector at a dose of 0.2 mmol per kilogram body weight after the first sequence, followed by a saline flush of 20 ml. Additional subtraction images were obtained, and time–intensity curve was drawn from a region of interest within the mass.

Preoperative fine-needle aspiration biopsy was performed in 4 patients. All lesions were surgically excised. In 1 patient the nonpalpable mass was preoperatively localized by mammographically guided needle-wire localization system.

Microscopic slides were reviewed by two pathologists who are breast pathology specialists. Each case was reviewed by two pathologists as consensus evaluation. In all of the cases, the tissues were fixed in formalin and routinely processed. Histological and immunohistochemical studies were performed on paraffin sections. All cases had more than 50% cells positive for at least two neuroendocrine markers (chromogranin A, neuron-specific enolase, synaptophysin). Immunohistochemical studies were carried out with avidin–biotin method using the following antibodies: neuron-specific enolase (NSE, prediluted; Dako, Carpinteria, Calif.); synaptophysin (Dako, Glostrup, Denmark, 1:50); chromogranin (prediluted; Dako, Carpinteria, Calif.). Mammographic and sonographic findings were then correlated with histopathology. Pathological size, predominant pathological findings, and lymph node status were obtained from surgical pathological reports.

Results

Our patients were all women and their age varied between 43 and 70 years (mean age 58 years). One of the patients had three risk factors (breast cancer in her mother, no childbirth, contralateral breast cancer), and the other patients did not have any risk factors. One of the patients presented for screening, and the other 4 patients