INTRODUCTION

Amyloidosis refers to the extracellular deposition in tissues of fibrils composed of low molecular weight subunits of a variety of proteins, many of which circulate as constituents of plasma. Amyloid deposits can occur in any body site such as skin, tongue, gastrointestinal tract, urogenital tract and the respiratory tract. However, the breast is an unusual site for amyloidosis involvement (1). Here, we describe a case of breast involvement of amyloidosis in patient with underlying multiple myeloma, detected on a baseline screening mammogram and subsequent ultrasonography focusing on imaging finding.

CASE REPORT

A 56-year-old menopausal woman with a history of multiple myeloma visited our breast center for a screening mammogram. She had a prior history of multiple myeloma which was diagnosed 6 years previously. Even though the multiple myeloma had been treated with chemotherapy and autologous peripheral blood stem cell transplantation, she was diagnosed 3 years later with plasma cell neoplasm for pleural mass by aspiration biopsy, and she was treated with radiation therapy for this lesion. She had no prior history of breast disease or familial history of breast cancer, and had received hormone replacement therapy for 5 years at the gynecology department due to postmenopausal symptoms.

The screening mammogram revealed a focal asymmetry in the outer central portion of the right breast, in the middle third of the breast (Fig. 1A, B), and there was no combined suspicious microcalcification or architectural distortion in her breast. The focal asymmetry was interpreted as Breast Imaging Reporting
and Data System (BI-RADS) category 0. Since this was an incomplete assessment, ultrasonography was recommended for further evaluation.

Ultrasonography revealed the lesion to be an approximately 1.1 cm sized, oval shaped, isoechoic mass with a microlobulated margin in the 9 o'clock direction of the right breast, 5 cm away from the nipple (Fig. 1C). Based on ultrasonography findings, the lesion was considered a BI-RADS category 4a, i.e., low suspicion for malignancy, and biopsy was recommended for confirmation.

Ultrasound-guided core biopsy using a 14-gauge needle was performed four times. Ductal and lobular atrophy due to diffuse amyloid deposits in the stroma was revealed by the pathologic examination of the cores (Fig. 1D). Congo-red staining produced red-orange coloring, and polarized light microscopy showed apple-green birefringence, both results confirming amyloidosis (Fig. 1E, F). Subsequently a large, irregular, enhancing mass was found by chest computed tomography (CT) (Fig. 2). The patient underwent a follow-up surgery for the pleural mass and the lesion was diagnosed as a plasma cell myeloma forming amyloid tumor by surgical wedge resection. The patient was treated with adjuvant chemotherapy for uncontrolled multiple myeloma. Follow-up breast ultrasonography and chest CT 1 year after receiving chemotherapy revealed a slight increase in the size of the breast mass and a newly developed pleural lesion, suggesting the progression of the multiple myeloma.

Fig. 1. Amyloidosis of the breast in a 56-year-old woman with multiple myeloma.
A, B. Mammograms with craniocaudal (A) and mediolateral oblique (B) views show focal asymmetry (arrows) at the outer central portion of the right breast without microcalcification or masses.
C. Ultrasonogram shows oval shaped, isoechoic mass with microlobulated margin and parallel orientation, which is located at the 9 o'clock position of the right breast and 5 cm away from the nipple (the largest diameter: 1.1 cm).
D–F. Microscopic examination of 14-gauge core biopsy specimens of breast amyloidosis (D) shows amyloid deposition (arrow) in the periductal stroma of the breast. (H&E, × 200). Congo red stain (× 100) (E) reveals diffuse orange red coloring (arrow) consistent with a strong positive identification of amyloid. Polarizing microscopy (× 100) (F) reveals the characteristic apple-green birefringence (arrow) of amyloid.
DISCUSSION

Amyloidosis can be divided into two major groups according to the type of accumulated amyloid: 1) amyloid light-chain amyloidosis (AL; primary) associated with plasma cell dyscrasia such as multiple myeloma, in which a monoclonal immunoglobulin (Ig) is detectable in the serum; and 2) amyloid A (secondary) amyloidosis associated with amyloid complicated by chronic infections or inflammatory diseases such as rheumatoid arthritis, spondyloarthropathy, inflammatory bowel disease or periodic fever syndromes (2).

Breast amyloidosis lacks specific clinical or radiographic features, and has rarely been reported (2). It can be part of systemic disease or may be isolated to the breast (2, 3), but it mostly occurs as a focal involvement of systemic disease (3). Systemic amyloidosis is associated with clonal B-cell or plasma cell proliferation such as in multiple myeloma. The incidence of systemic amyloidosis is approximately one-tenth that of multiple myeloma (4). Systemic amyloidosis associated with hematologic malignancy is reported to involve the breast in over half of the cases, and breast involvement is usually found as a late presentation and typically associated with AL amyloidosis (2). Amyloid fibril protein produced from free Ig light chains secreted by a monoclonal population of plasma cells (5, 6) might be the cause of AL amyloidosis in this condition (5). In our case, monoclonal light chain was positive in the serum immune histochemical stain analysis.

Breast amyloidosis typically occurs in women from 43 to 86 years of age. The majority of breast amyloidosis patients have no clinical symptoms, and only a few patients have a painless palpable mass or localized skin thickening, edema, or erythema (3, 5). In our case, the patient complained of no symptoms or signs, and the lesion was detected by radiologic screening examination.

The common mammographic finding of breast amyloidosis is described as a variety of multiple solid masses, with or without calcifications (7). In our case, only focal asymmetry without a demonstrable mass or microcalcification was identified as an amyloidosis lesion by mammography. Although there are several reports related to mammographic descriptions of amyloidosis, detailed reports on ultrasonographic findings are rare. Our case presented an oval shaped, isoechoic, microlobulated mass on ultrasonography. Pathologic examination showed amyloid deposits around ducts, vessels, and within lobules, leading to atrophy, obliteration of glandular components, and calcification or a foreign body–like reaction (8). We think that these pathologic features of periductal infiltration, lobular atrophy and inflammatory reaction may cause the low suspicious ultrasonographic features of breast amyloidosis.

The confirmative diagnosis for breast amyloidosis should be made histologically, as it has been reported that radiologic findings can mimic malignancy and several coexisting breast cancers such as tubular carcinoma, invasive ductal carcinoma, and invasive lobular carcinoma (9). The distinctive amorphous pink or red color obtained with Congo red stain, and the apple-green birefringence seen by polarizing microscopy are the pathognomonic findings for diagnosis of amyloid deposits.

The prognosis for patients with systemic involvement of amyloidosis is poor (2, 8), and the prognosis for those with associated hematologic disorders is dependent on the underlying hematologic disease (2). In patients with localized amyloidosis without hematologic disease, treatment is unnecessary (2). However, patients with systemic amyloidosis associated with hematologic disease require chemotherapy, with or without radiation therapy. Resorption of amyloid deposits after treatment of the associated disease has been reported, but it is rare (8). Patients with myeloma-associated amyloidosis have a poorer prognosis than those with other types of systemic amyloidosis (8). The prognosis for...
patients with localized amyloidosis is much better (2, 8).

In conclusion, we report a case of breast involvement by systemic amyloidosis in a 56-year-old woman with underlying multiple myeloma. Despite its rarity, if radiologists recognize radiographic breast abnormality in multiple myeloma patients, the possibility of breast amyloidosis should be considered as a differential diagnosis, and systemic evaluation should also be considered to rule out possible disease progression.

REFERENCES