



Amyloidosis of the mammary gland (the breast)

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Abstract

Amyloidosis of the breast (AMB) is rare. Various internet search data bases were used to search for literature on amyloidosis of the breast. Amyloidosis refers to extra-cellular deposition of amorphous congophilic protein within tissues most commonly with structure types AL and AA. Patients’ ages have ranged between 43 and 86 years. Predisposing systemic diseases include systemic amyloidosis, rheumatoid arthritis, myeloma and walden strom’s macroglobulinemia. AMBs present with tender or non-tender palpable firm mass, generalized tenderness, peau d’orange or may be clinically asymptomatic, incidental breast screening radiological findings. Mammography may reveal clusters of micro-calcification whether the patient has a breast lump or not. Macroscopically AMB may appear as a gray-white, opalescent firm mass which is 5 cm or less. Microscopically AMB can appear as amorphous eosinophilic deposits in fat, stroma or vessels or have caused ductal atrophy, form rings around individual fat cells, or have associated multinucleated giant cell reaction or osseous metaplasia. The cytological findings include: amorphous acellular material with scattered plasma cells; lymphocytes; stromal cell; and epithelial cells. If limited to the breast AMB can be successfully treated with excisional biopsy. AMB has sometimes coexisted with carcinoma of the breast. We would conclude that the clinical course of AMB tends to be benign.

Key Words: Amyloidosis; breast; amorphous congophilic protein; micro-calcifications.

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Introduction

Amyloidosis in the breast was first reported by Fernandez and Hernandez in 1973. [1] Subsequently, a number of cases of amyloidosis of the breast had been published in the literature, and these had included women with bilateral breast involvement [2] [3] [4] [5] [6] [7]. The majority of the reported cases were in elderly women who had mammographically suspicious lesions. By definition, amyloidosis refers to extra-cellular deposition of amorphous congophilic protein within tissues. [8] According to Deoleker et al, [9] by 2002, 15 different protein structures of amyloid had been identified,

with AL and AA being the most common (see table 1).

Table 1: Shows a list of some of the types of amyloid with their precursor protein and associated syndrome [from Bull World Health Organ Nomenclature of amyloid and amyloidosis WHO-IUIS Nomenclature Sub-Committee 1993; 71(1): 105–112.PMCID: PMC2393434].

Name (or type) of amyloid	Type of Protein precursor	Associated Syndrome
AL	Variable fragments of immunoglobulin chain (unique to each patient)	Primary Systemic Asomemyloidosis
AA	Amino acid terminus-SAA + (the same in all patients)	Secondary Amyloidosis
ATTR	Transthyretin	Hereditary Systemic Amyloidosis
Aβ 2m	β2 microglobulins	Haemodialysis Related Systemic Amyloidosis
A cal	Calcitonin	Medullary Thyroid carcinoma
IAPP	Islet Associated Peptide	Type II Diabetes

Primary amyloidosis had been commonly reported in a number of other sites including: skin, tongue, the gastrointestinal tract, and the respiratory tract. Most of the cytology case reports had described the appreciation of amyloid material in fine needle aspiration preparations only in retrospect [4], [6], [9]. The ensuing document contains a review of the literature on amyloidosis of the breast as well as illustrations of various characteristics of the lesion in figures 1 to 6.

Methods

Literature Review: Various internet search data bases including PUB Med; Google, Google Scholar; Medline and Educus, were used to obtain case reports, case series, review papers and other documentations on amyloidosis of the breast to form a pivot for the literature review. The Key Words used were: Primary amyloidosis of the breast; Amyloidosis of the breast. In all 53 references were used to form a pivot for the literature review.

Definition: Amyloidosis is a mass which is composed of deposits of amyloid in fat, stroma or vessels [10]; thus amyloidosis of the breast is a mass of amyloid deposit within the fat, stroma or vessels within the breast.

Terminology: Amyloidosis is also called amyloidoma. [10]

Epidemiology: Amyloidosis of the breast is very rare it is usually found in women who are aged between 45 years and 79 years. [10] Sites 80% of amyloidosis of the breast occurs in the right breast and amyloidosis of the breast may be bilateral or unilateral; nevertheless, it is only on rare occasions that amyloidosis is confined to the breast. Amyloidosis may involve the breast alone or it may involve the breast as part of systemic amyloidosis [10].

Etiology: Amyloidosis of the breast is associated with a number of predisposing systemic diseases which include: systemic amyloidosis, rheumatoid arthritis, myeloma, Waldenstrom's macroglobulinemia. [10]

Clinical features: Amyloidosis of the breast may present as painless breast mass or it may occur late in systemic amyloidosis. [10] A thorough clinical examination is required to differentiate between primary and secondary amyloid tumours. [10]

Presentation: Amyloidosis of the breast may be presented as a palpable mass or it may be diagnosed as microcalcifications which may be detected incidentally or they may be diagnosed contemporaneously with a carcinoma of the breast. It may present as a mass: a focal or diffuse density with or without calcifications [11], [12] or as a diffuse infiltration of the mammary gland with skin thickening, mimicking an inflammatory carcinoma [13]. In cases where amyloid deposition presents as an irregular or spiculated mass, accompanied by irregular or

amorphous micro-calcifications, the radiological picture may be indistinguishable from invasive carcinoma [14].

Radiological findings: Radiological imaging of amyloidosis of the breast may manifest as micro-calcifications with or without presence of a breast lump.

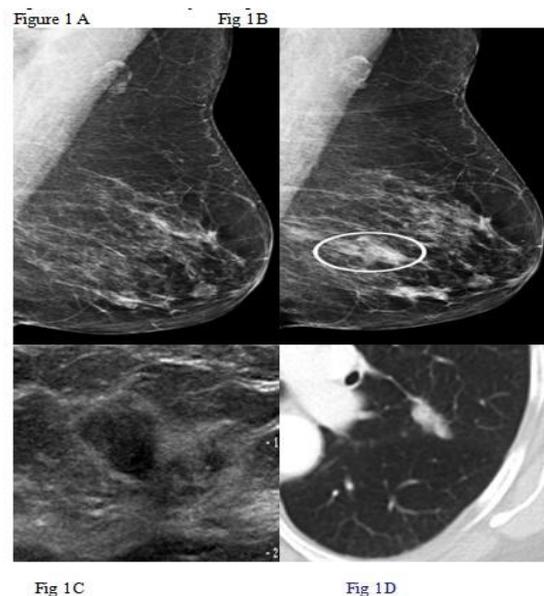
Mammography: Mammograms usually demonstrate an irregular, sometimes speculated mass, though various imaging appearances had been reported including clustered micro-calcifications and focal asymmetry [15] (see figures 1 a; and 1b). Mammography of the breast in amyloidosis of the breast may reveal clusters of elongated tubular homogenous well-defined opacities with coarse calcifications [16]

Ultrasound scan: Ultrasound scan may reveal an ill-defined hyper-echoic mass or an irregular hypo-echoic lesion with echogenic halo (see figure 1c). [15]

Computed tomography (CT) scan: Diverse imaging findings may be seen on computed tomography scan in amyloidosis [15], [17], (see figures 1d and 3).

Magnetic Resonance Imaging (MRI) Scan: MRI scan of the breast of patients with amyloidosis of the breast may reveal tubular lesions which demonstrate low T1 signal and high T2 and Short Tau Inversion Recovery signal with no significant enhancement; however, there may be some faint peripheral delayed enhancement. [16]

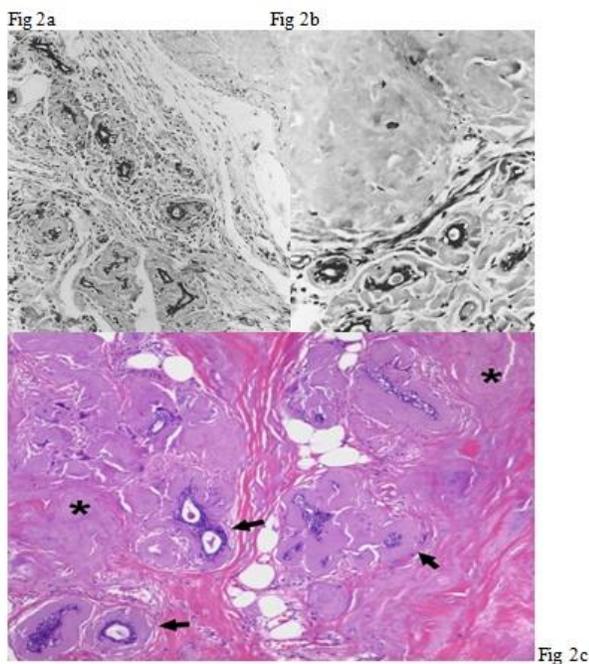
Figures 1a, 1b, 1c and 1d: Amyloidosis in a 66-year old woman with a history of right breast cancer who presented for screening mammography (a) (b) Left MLO mammography obtained in 2007 (a) and 2009 (b) demonstrate the development of a new irregular mass at middle depth in the lower portion of the breast (circled in b). The smaller area of opacity located more inferiorly was found to represent stable glandular breast tissue (c). Ultrasound image shows an irregular hypo-echoic lesion with an echogenic halo. Positive Congo red staining of the biopsy specimens was diagnostic for amyloid deposition. (d) Axial chest CT scan (lung window) shows a juxtafissural lobulated pulmonary nodule in the left upper lobe, a finding that was confirmed at biopsy to represent additional amyloid deposition



Macroscopic features: Macroscopic examination of amyloidosis of the breast may reveal a 5 cm or less mass which is firm, gray-white, and opalescent (see figure 6 for an example). [10]

Microscopic features: Microscopic examination of amyloidosis of the breast may reveal amorphous eosinophilic deposits in fat, stroma or vessels. Amyloidosis may at times be seen at microscopy to have caused ductal atrophy, form rings around individual fat cells, or have associated multinucleated giant cell reaction or osseous metaplasia (see figures 2 to 5 which show examples of the histological features of amyloidosis of the breast). [9] [10]

Figure 2a: Amyloid occurs in lobule (lower left) and as a separate stromal nodule (upper right AFIP). Figure 2b: Thick wavy bands of amyloid around lobular glands and a nodular deposit that is virtually acellular; Figure 2c: Diffuse deposit of dense amorphous material (*) surrounding ductal structures (arrows) reproduced from Pernick N, Nassar H. Breast nonmalignant Benign tumors Amyloid tumor Pathology Outlines.com. URL: www.pathologyoutlines.com/topic/breastamyloidtumor.html with permission from PathologyOutlines.com. Copyright permission was granted by PathologyOutlines.com



Cytology Findings: The cytological findings in amyloidosis of the breast include:

Amorphous acellular material with scattered plasma cells, lymphocytes, stromal cells and epithelial cells [10]

- Rarely, multinucleated giant cells may be seen
- Metachromatic by modified Wright's stain [18]

- A typical description of the cytological features of amyloidosis of some breasts reported by some authors [18] was: The amyloid appeared as dark-blue to purple clumps of acellular material on Diff-Quik stain, accompanied with chronic inflammatory cell infiltrates and multi-nucleated giant cells, simulating granulomatous inflammation. Papanicolaou stain demonstrated cyanophilic to orangophilic acellular material (Based upon these findings amyloid was suspected in the reported cases and this was confirmed by positive Congo red staining of the breast specimen). [18]

Figure 3: Amyloidomas in a 52-year-old woman with palpable breast nodules Axial CT scan images show nodules of soft tissue attenuation in the left breast (arrow), some of which are calcified. Biopsy results were diagnostic of amyloidomas Reproduced from Geogiades C, Heyman E, Barish M A, Fishman E. Amyloidosis: Review and CT manifestations. *Radiographics* 2004 Mar; 24: 405 – 416. Copyright permission was granted by Radiographics and the Radiological Society of North America

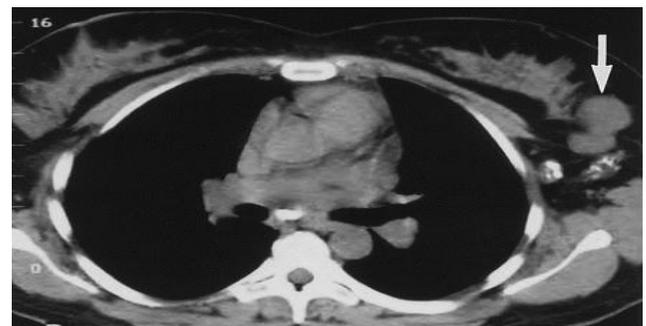


Figure 4: Amyloidosis (bilateral breast masses); figure reproduced with permission of the editor in chief of the journal on behalf of the American College of Pathology and the journal. Figure 4.1; 1.7-cm ill-defined mass containing coarse calcifications. Figure 4.2; Haematoxylin and eosin stain. Figure 4.3; Congo red stain of the specimen. Figure 4.4; Polarized light examination of Congo red stain

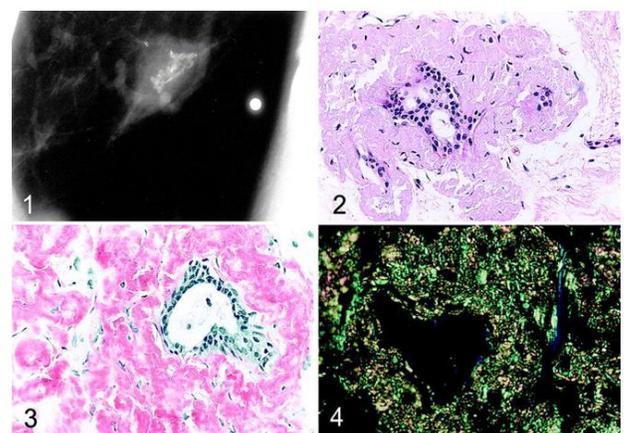


Figure 5a

Fig 5b

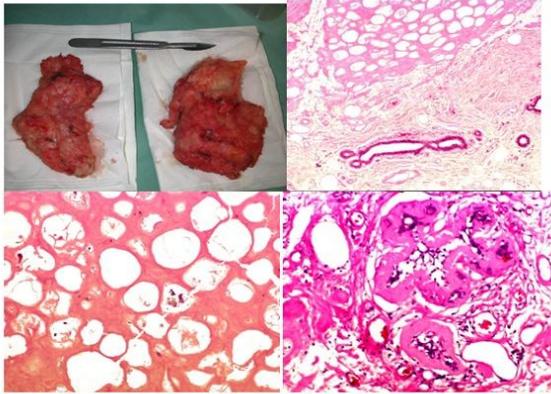


Fig 5c

Fig 5d

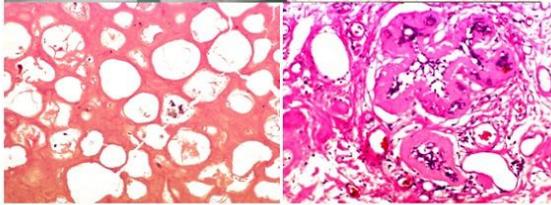


Figure 5a: Macroscopic appearances of bilateral breast amyloidosis showing two grayish-yellow masses which measured 12 cm and 13cm in diameter

Figure 5b: Microscopic examination of the breast mass showed a dense fibrous stroma surrounding adipocytes no replacement nucleated with a thick eosinophilic cell membrane.

Figure 5c: Microscopic examination also revealed cystic appearances with diameters ranging from 1 mm to 15 mm compounds coated fibrous wall, sometimes partially but in most cases completely, a similar membrane; sometimes microcalcifications intracyst found in the stroma.

Figure 5d: Microscopic picture of the breast mass an eosinophilic homogenous deposit, distributed in the fat surrounding the cysts, in the stroma, and perlobular periductal areas and around vessels. Reproduced from with Copy right permission from PathologyOutlines.com on their behalf and on behalf of the authors

Figures 5a; 5b; 5c; 5d

Fig 6a

Fig 6b

Fig 6c

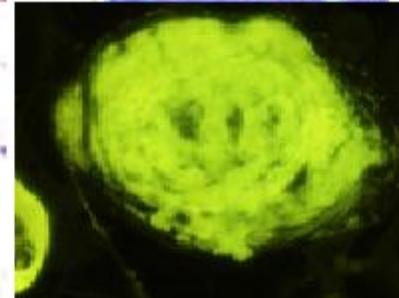
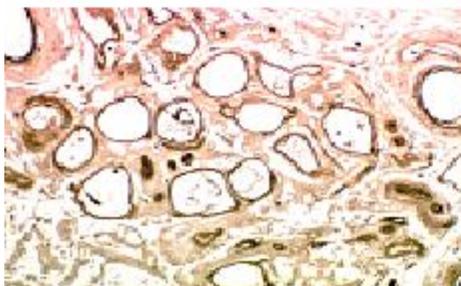
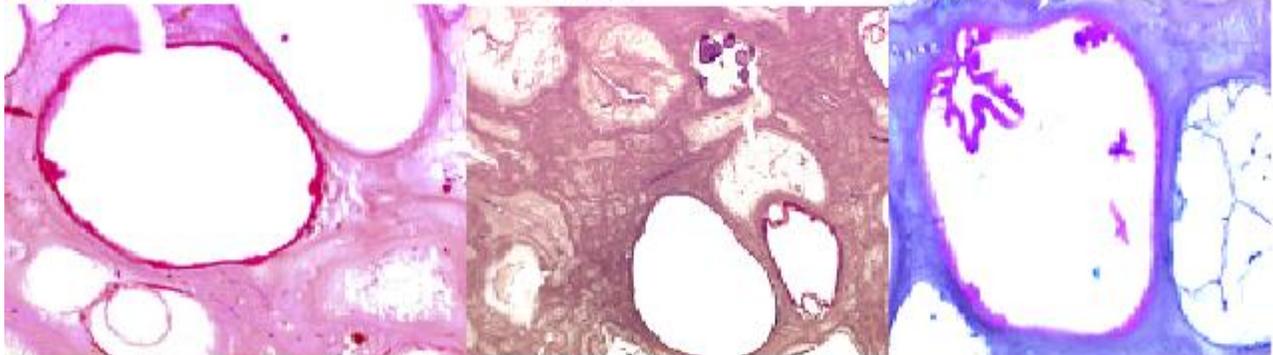


Fig 6d

Figure 6e

Fig 6f

Figures 6a; 6b; 6c; 6d

Figure 6a: Immunofluorescence histochemical findings: Eosinophilic membrane was stained with PAS with enzyme digestion this showed autofluorescence in the in the yellow-green fluorescence microscope. The pattern showed ceroid nature of this material Amyloid was demonstrated by Congo red. **Figure 6b:** Immunofluorescence histochemical findings: Eosinophilic membrane was stained with PAS without enzyme digestion – this showed autofluorescence in the in the yellow-green fluorescence microscope. The pattern showed ceroid nature of this material Amyloid was demonstrated by Congo red. **Figure 6c:** Immunofluorescence histochemical finding: Eosinophilic membrane was stained with Alcian Blue and PAS; this showed autofluorescence in the in the yellow-green fluorescence microscope. The pattern showed ceroid nature of this material Amyloid was demonstrated by Congo red. **Figure 6d:** Immunohistochemical finding: This exhibited positive scoring with collagen IV, demonstrating its membrane nature. **Figure 6e:** Immunohistochemical finding: This exhibited positive scoring with laminin, demonstrating its membrane nature. **Figure 6f:** Amyloid was stained with Thioflavin; **Figure 6g:** Amyloid was stained with Thioflavin; Reproduced from with Copyright permission from PathologyOutlines.com on their behalf and on behalf of the authors

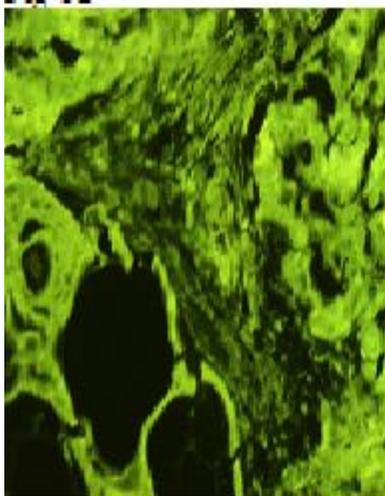


Fig 6g

Staining characteristics

The ensuing stains are positive for amyloidosis

- Congo red (red-orange with apple green birefringence under polarized light) (see figure 4) [5d], [6f]
- Metachromatic with crystal violet [10]

Electron microscopic features: The ensuing microscopic features have been reported in amyloidosis of the breast:

Straight, non-branching, haphazard amyloid fibrils, 5-10 nm, mixed with collagen fibers [6]

Differential Diagnosis: The differential diagnoses of amyloidosis of the breast include:

- Plasmacytoma which contain immature plasma cells but no amyloid [10]
- Stromal fibrosis may have hyaline material, but it has different histologic features from amyloid and it is also Congo-Red negative [10]

Treatment: If amyloidosis of the breast is limited to the breast then excisional biopsy is a successful treatment. [10]

Narrations from reported cases

Silverman et al. [6] reported two examples of localized primary amyloid tumour of the breast which included one patient who had metachronous bilateral lesions. They stated that:

- This rare lesion occurs predominantly in elderly females and can be mammographically and clinically confused with carcinoma.
- Fine-needle aspiration biopsy could be a useful procedure to make a preliminary diagnosis.
- Congo red staining with prior potassium permanganate incubation confirmed the AL type of amyloid in their two cases; this might be the predominant type in the localized form involving the breast.
- Immunofluorescence studies demonstrated IgA, with kappa and lambda light-chain deposition within the amyloid foci in one case, and intra-cytoplasmic IgG with both light chains within plasma cells and amyloid deposits of the second case.
- Ultra-structural examination of one of the cases showed characteristic findings of straight, non-branching fibrils of 4-9 nm, diagnostic of amyloid.
- From their findings and a review of the literature, they concluded that amyloid tumours of the breast can occur in three separate settings: secondary amyloidosis, systemic or multiple myeloma associated amyloidosis, and as a localized primary type having a benign course.

Deoleker et al. [9] reported an 86-year old white woman who presented with a palpable left breast lump. Her breast lump was suspicious of malignancy, both clinically and mammographically, with malignant looking micro-calcification. Fine needle aspiration cytology was performed, which was negative for malignancy, and was reported to show a non-specific inflammatory reaction

only. In view of the clinical and mammographic suspicion, excision biopsy of this lesion was performed. On macroscopic examination, the breast tissue weighed 7.5 gm. ‘Serial slicing’ of the excised mass, showed a 1.6 cm size firm nodule close to the excision margins. All the tissue had been processed. Subsequent histological examination revealed a mass which was composed of hyaline eosinophilic material surrounded by giant cells. There were foci of osseous metaplasia. At the periphery, numerous plasma cells containing Russel bodies and lymphocytes were present. The Congo red stain was positive in this hyaline material and showed apple green birefringence on polarising microscopy. Apart from the localized mass, amyloid was seen around occasional breast ducts and blood vessels. Nevertheless, there was no amyloid within the walls of the blood vessels. There was no evidence of malignancy in the specimen submitted. In order to evaluate the nature of this amyloid further, the sections were pretreated with potassium permanganate and then a Congo red stain was carried out. [19] The material resisted potassium permanganate treatment and retained its orange- brown colour, thus, it confirmed the AL type of amyloid. Considering the nature of amyloid the patient was investigated further. Her chest, spine, and skull radiographs were normal. The serum electrophoresis was also unremarkable. Urinary Bence-Jones proteins were negative. The haematology profile was normal. The cytology preparations were reviewed and showed amorphous homogenous material surrounded by giant cells and lymphocytes.

Gluck et al. [11] reported a 76 -year-old woman with a 15-year history of indolent multiple myeloma who presented for annual screening mammography. Her myeloma had been diagnosed 15 years earlier by bone marrow biopsy and serum protein immune-electrophoresis but she was not treated in view of the fact that she had remained asymptomatic. Annual screening mammography revealed grouped, generally smooth branching rod-like calcifications in the upper outer quadrant of her right breast. These calcifications were new since the previous examination a year earlier. No correlative palpable abnormality was present on physical examination. Because of the short-interval appearance of calcium and the branched morphology, biopsy was recommended to exclude breast malignancy. The patient underwent needle localization and surgical excision. Histological examination of the specimen revealed diffuse dense hyalinized material associated with fibrosis, chronic inflammation (including foreign body-like reaction), and micro-calcifications. This was present in and around ducts, vessels, and stroma. The material exhibited apple-green birefringence with Congo red stain under polarized light, characteristic of amyloid deposition. No malignancy was identified at pathological examination.

Gluck et al. [11] stated that:

- Amyloid deposition in the visceral organs may be seen in patients with primary amyloidosis (no preexisting or coexisting disease), multiple myeloma, chronic infectious disease, and chronic inflammatory disease (such as rheumatoid arthritis).
- Amyloid tumour of the breast is rare and may present as a similar clinical appearance to carcinoma of the breast, with a palpable breast mass and mammogram showing a mass or focal or diffuse density with or without calcifications [1] [2] [6] [7] [20] [21]
- Even though there are sporadic case reports in the literature, amyloid deposition in the breast had been previously reported only once in the radiology literature to their knowledge [14]
- Though it had been incidentally observed as breast nodules or infiltration at autopsy with negative mammograms [21], they were at the time of their report unaware of amyloid presenting as a non-palpable mammographic abnormality consisting of only indeterminate calcifications on annual screening mammography.
- The mammographic appearance of non-palpable amyloid had not been described and was not commonly thought of in the differential diagnosis of non-palpable breast disease or, more specifically, indeterminate calcifications.
- In their case, the absence of ill-defined density or a nodule on mammogram might be related to the overall relative increased breast density; nevertheless, a discrete lesion was not present on gross pathologic examination either.
- Amyloid fibrils have an affinity for calcium and deposition around mammary ducts and in blood vessels [6] [7] [22].
- In their case, perhaps the branched morphology of the calcium was related to deposition in or around vasculature or mammary ducts. When limited to the breast, primary amyloid tumor is benign. Nevertheless, secondary amyloidosis might have an ominous significance and poor prognosis [23].

Munson-Bernadi and DePersia [24] reported a 58-year-old African American woman who presented for a routine mammogram. She did not report any palpable abnormality, nipple discharge, or breast tenderness. She had a stereotactic biopsy of the left breast in 1999 for indeterminate micro-calcifications. The pathological examination revealed severe atypical ductal hyperplasia and papillomatosis with the surrounding breast tissue heavily involved with amyloid and amyloid micro-calcifications. She subsequently underwent excisional biopsy which revealed two foci of ductal carcinoma in situ (DCIS), solid and cribriform type of low nuclear grade, fibrocystic change, and florid ductal hyperplasia with micro-calcifications as well as micro-calcifications consistent with amyloid. One surgical margin was positive for DCIS for which repeat excisional biopsy was required.

On re-excision, four specimens were obtained that showed no residual tumour.

Two years subsequently, routine cranio-caudal and medio-lateral oblique (MLO) views of both breasts were performed. The MLO view of the left breast revealed new, rounded, loosely clustered micro-calcifications in the upper outer quadrant of the left breast that did not possess the anticipated morphologic characteristics of amyloid calcifications. At the same time, the right breast MLO view showed interval development of a cluster of round micro-calcifications in the upper central region which were thought to be indeterminate in morphology and again not clearly indicative of amyloid calcification. Stereotactic core biopsies of both the left and right breasts were performed. The result of the pathological examination was reported to have shown benign breast tissue with scattered associated micro-calcifications that had characteristic yellow-green birefringence under polarized light. No malignancy was evident.

Although not clearly an interval change, in 2003 4 years after the initial presentation, at the time of a screening mammography, biopsy for the right breast retro-areolar micro-calcifications was advised because of the segmental distribution, varying size, and fine branching appearance. The surgeon elected to perform a needle localization biopsy, which yielded atypical ductal hyperplasia and foci of fat necrosis with foveated micro-calcifications associated with amyloid deposition. No malignancy was found.

Munson-Bernadi and DePersia [24] stated that:

- The patient did not have a personal or family history of primary or secondary amyloidosis.
- Unfortunately, immunohistochemical staining was not performed to further characterize the amyloid protein as either of the amyloid associated or the amyloid light chain subtype. Nevertheless, several breast biopsies of both the left and right breasts since 1999 (from the time of her first presentation) had yielded amyloidosis.
- Several cases of primary amyloidosis of the breasts had been reported in the surgical and pathology literature, usually of the amyloid light chain type, with few cases in the radiology literature.
- Amyloidosis had presented as pruritus of the nipple mimicking inflammatory carcinoma, [25] as a palpable mass [2], and in association with scirrhous and tubular carcinoma. Even though there had been articles documenting cutaneous amyloidosis in patients on long-term hemodialysis, their patient was not undergoing such treatment [26]
- The mammographic appearance of amyloidosis involvement can vary, ranging from a solitary mass to segmental and branching suspicious micro-calcifications.
- In their case, scattered calcifications in each breast were thought to be consistent with amyloid as they were smooth, elongated, curvilinear, and radiolucent centered. The micro-calcifications in the right retro-

areolar region appeared to be of different morphology and in a ductal distribution. Biopsy was therefore advised for these indeterminate calcifications.

- Gluck et al. [11] described grouped, generally smooth branching rod-like calcifications, whereas O'Connor et al. [21] documented amyloid as a nodule.
- Despite the incidental finding of concomitant one and two foci of DCIS, all of the indeterminate micro-calcifications biopsied in their patient had proven to be benign and secondary to amyloidosis.
- Isolated primary amyloidosis of the breast must be considered in the differential diagnosis of micro-calcifications with or without an associated palpable or non-palpable mass. Localized primary amyloidosis of the breast occurs more frequently in elderly women but is not limited to unilateral disease. [6]
- Their case served as a reminder to clinicians and mammographers that isolated primary amyloidosis may be mistaken for or co-existing with carcinoma.
- When limited to the breast, amyloidosis had proven to be a benign diagnosis, unlike secondary amyloidosis, which may have a less favorable prognosis.

Kersemans et al. [27] reported a 63-year-old asymptomatic postmenopausal woman who presented to the radiology department for a two-yearly screening mammography. She had mammogram which revealed in the upper outer quadrant of the right breast a focal density containing micro-calcifications. Her physical examination was within normal limits. She was referred for additional imaging. She had a Magnification mammogram which showed an irregularly shaped, linear and branching micro-calcifications of variable density which occurred in an ill-defined density. She had ultrasound scan which showed an ill-defined small hypo-reflective -structure which contained internal reflections. The micro-calcifications were considered suspicious for malignancy (BI-RADS category 4) and stereotactic vacuum biopsies were performed. Microscopic examination of H&E-stained slides showed a lymphocytic inflammatory infiltrate with peri-ductal and intra-lobular localisation. Furthermore, deposits of amorphous, eosinophilic material were seen, localized around mammary ductules and acini, in the wall of blood vessels and diffuse within the connective and fatty tissue of the breast, the latter resulting in a mass effect. Numerous large calcifications were found within this area of diffuse deposition. Focally, a foreign body giant cell reaction was encountered. The amorphous material, stained red with the Congo red stain, and green after polarisation. Stains for amyloid AA and kappa and lambda were negative. These histological findings were consistent with a diagnosis of amyloid deposition in the breast. The medical history of the patient revealed primary Sjögren syndrome (PSS), which was diagnosed 9 years earlier, and was characterized by positive ANF and anti-Ro/SSA antibodies. At the time of diagnosis of amyloid deposition in the breast, mild leucopenia (3700), elevated total protein, elevated IgG (28,5g/l), and IgA (7.14 g/l)

were found. Immuno-fixation showed only polyclonal light chains, no monoclonality. Because renal function was normal, without proteinuria, no additional therapy was given.

Kersemans et al. [27] stated that:

- Amyloidosis can be subdivided into systemic and localised forms as well as into different types, including primary, secondary, hereditary familial, endocrine and senile amyloidosis.
- Amyloidosis is a heterogeneous group of diseases characterized by deposition of amyloid fibrils in the extracellular spaces of tissues and organs.
- Amyloid fibrils are composed of low molecular weight sub-units of a variety of proteins, many of which circulate as constituents of plasma.
- Immunoglobulin components are often the major source of the amyloid fibril protein.
- Amyloidosis may present as a mass: a focal or diffuse density with or without calcifications [11], as micro-calcifications without mass or density [12] or as a diffuse infiltration of the mammary gland with skin thickening, mimicking an inflammatory carcinoma [13].
- In cases where amyloid deposition presents as an irregular or spiculated mass, accompanied by irregular or amorphous micro-calcifications, the radiological picture may be indistinguishable from invasive carcinoma [14].
- In their case it presented as a focal density containing micro-calcifications.
- Histological suspicion of amyloidosis can be confirmed by histochemical and immunohistochemical stains [12].
- Amyloid fibrils are anionic and chelate calcium, leading to deposition of amorphous calcified matrix material mainly around mammary ducts, acini and in the wall of blood vessels [1], [1].
- May be the branching and linear calcifications are related to the deposition of amyloid around mammary ducts and in blood vessels.
- The history of their patient revealed primary Sjögren syndrome (PSS).
- Sjögren syndrome is an autoimmune disease of exocrine glands, especially the salivary and lacrimal glands. On histology, a dense lymphocytic infiltrate forming lymphoepithelial lesions was seen. These histological features might be an indication of B-cell hyperactivity that may uncommonly result in the development of extra-nodal marginal zone B cell lymphoma.
- The coexistence of primary amyloidosis and PSS is rare. Only eight cases had been reported in the English literature at the time of publication of their paper [28], their localisation limited to dermis, lung or tongue.
- To the best of their knowledge, the association of primary Sjögren syndrome and amyloid deposition in the breast had not been previously reported

Lynch and Moriati [29] detailed the cytologic features of primary localized amyloid tumour of the breast which presented as bilateral breast masses in a 72-year-old woman. Clinically and radiographically, the masses simulated metastatic or multifocal carcinoma. Fine-needle aspiration revealed irregular globules of acellular amorphous material and numerous multinucleated giant cells resembling granulomatous inflammation. Histological examination confirmed amyloid tumours with a foreign-body giant cell reaction in response to amyloid and foci of osseous metaplasia. She underwent subsequent clinical work-up which included a serum electrophoresis and immunofixation which showed a small IgG k monoclonal protein. Her urine immunofixation was negative for Bence Jones protein. Her bone marrow examination revealed no evidence of a plasma cell dyscrasia. Up to the time of publication of the paper the patient had not developed clinical or laboratory evidence of systemic amyloidosis or multiple myeloma.

Lynch and Moriati [29] stated that:

- Amyloidosis involving the breast, and specifically localized primary amyloid tumors of breasts are infrequently reported entities.
- To their knowledge, osseous metaplasia within isolated primary amyloid tumors of the breast has not been reported.
- They presented the unusual case to illustrate the intratumoral calcification patterns mimicking carcinoma and to characterize the cytological features.
- Emphasis should be placed on the inclusion of amyloidosis in the differential diagnosis of breast masses.

Rossett et al. [30] reported a woman who had mammograms which showed an area of clustered microcalcifications, with irregular and pleomorphic morphology, mimicking the onset of a cancer. The core biopsy specimens resulting in breast amyloidosis were in disagreement with the radiological Breast Imaging Reporting and Data System (BI-RADS) risk, category 4. Furthermore, specimens from abdominal sub-cutaneous fat and bone marrow biopsies showed no evidence of deposition of amyloid material, allowing exclusion of a systemic disease. Because of the reported frequent association between breast amyloidosis and malignant lesions, a surgical excision of the micro-calcifications was performed. The final histology confirmed the benign nature of the lesion consisting in a solitary amyloid tumour of the breast. They stated that the case stressed the importance of multidisciplinary collaboration between Radiologists, Surgeons and Pathologists to achieve a correct diagnosis and treatment of this rare breast disease. Rocken et al. [30] reported on three cases of amyloidosis of the breast, two of which had coincided with carcinoma of the breast cancer. Patient no. 1, a 60-year-old woman, presented with two mass lesions which measured 2 cm in diameter, one in each breast. Histological examination

revealed a tubulo-lobular carcinoma in the left breast accompanied by vascular, interstitial, and periductal amyloid deposits; the lesion in the right breast consisted of amyloid deposits only. Patient no. 2, an 86-year-old woman, presented with an ulcerated breast tumour which measured 5 cm in diameter on the left side. A poorly differentiated invasive ductal carcinoma was found in the mastectomy specimen, and it coincided with interstitial and vascular amyloid deposits. In both patients, the tumour cells had invaded the amyloid deposits. Patient no. 3, a 73-year-old woman, presented with a mass which measured 5 cm x 3 cm x 3 cm in her left breast. Fibrocystic changes, as well as interstitial and periductal amyloid deposits, were found histological examination of the specimen. In each case electron microscopy showed rigid, non-branching fibrils of indefinite length and measuring 10nm to 12 nm in diameter; and these were consistent with amyloid fibrils. Clinical data, immunohistochemistry, and/or amino acid sequencing of the fibril proteins extracted from formalin-fixed and paraffin-embedded tissue specimens provided evidence that the amyloid deposits were of immunoglobulin light chain origin in all three cases. Rocken et al. [30] then reviewed the literature and found that that kappa-light chain had been described more frequently than lambda-light chain in the breast and that there are no specific clinical or radiological symptoms of amyloidosis affecting the breast; a diagnosis can be achieved only by histology. White et al. [32] in 2004 reported a case of primary amyloid deposit confirmed by immunohistochemistry, which occurred in a patient with early breast cancer.

Bisceglia et al. [33] in 1995 reported a lady who was admitted due to a breast lump which mammographically was thought to be suspicious for malignancy by virtue of a cluster of variously sized microcalcifications. At histology the excised lesion was diagnosed as an amyloid deposit on special stains and disclosed of the AL type with Congo red stain on sections previously treated with KMnO₄, according to standard methods.

Toohy et al. [34] reported a case of amyloidosis of the breast in which asymptomatic mammographic findings were suspicious for locally recurrent disease in a patient with previously treated breast cancer.

Chiang et al. [35] reported a 72-year-old female, with no significant past medical.

History, who presented for stereotactic vacuum assisted needle core biopsy of an already known suspicious 2.3 cm cluster of micro-calcifications within the 11 o'clock region of the left breast. There were no other suspicious mammographic abnormalities noted in the left breast. Stereotactic biopsy demonstrated peri-ductal and peri-vascular amyloid deposits, with the calcifications being related to amyloid deposition. There was no evidence of malignancy or atypia. Nevertheless, in view of the highly suspicious mammographic appearance, the pathology was felt to be discordant and the patient with given a BIRADs 4 with recommendation for surgical excisional biopsy. WC

instead underwent a repeat stereotactic vacuum assisted needle core biopsy of the same cluster of micro-calcifications, which demonstrated DCIS and foci of atypical ductal hyperplasia; it should be noted that the repeat needle core biopsy was negative for amyloid. With the new diagnosis of DCIS, the patient underwent a staging bilateral breast Magnetic Resonance Imaging. Additional the known focus of DCIS within the 11 o'clock region of the left breast, a 0.9 cm avidly enhancing spiculated mass was also found within the posterior 3 o'clock region of the left breast. There were no abnormalities visualized within the right breast. Nevertheless, the magnetic resonance imaging also showed a 2.1 cm × 1.2 cm nodule within the lingula of the left lung. In view of the fact that the left breast 0.9 cm spiculated mass was not visualized on mammography, the patient then underwent a magnetic resonance imaging (MRI) guided biopsy of this second lesion. Pathological examination of the specimen revealed a coexistent invasive pleomorphic lobular carcinoma. She underwent total left mastectomy, as breast conservation therapy was not plausible because of the multi-centricity of her carcinoma. Pathological examination of the specimen revealed invasive pleomorphic lobular carcinoma and lobular carcinoma in situ at 2-3 o'clock position. DCIS, intermediate nuclear grade, and solid and cribriform subtypes were demonstrated at the previous biopsy site around the 11 o'clock position. The sentinel lymph node was negative for metastatic carcinoma. Following the total left mastectomy, the patient also underwent a wedge resection of the lingula nodule. Histopathological examination, of the nodule, demonstrated extra-nodal Castleman's disease of the plasma cell variant. The pathologist noted that there was no evidence of amyloid within this lingula nodule.

Some authors [13] [31] stated that breast amyloidosis typically presents in women from 43 to 86 years of age, with only recent case reports describing their coexistence with breast cancers. Rocken et al. [31] stated that patients with breast amyloidosis may be clinically asymptomatic or they may present with palpable firm lesions, generalized tenderness, or peau d'orange skin findings.

Chiang et al. [35] stated that their patient presented with a non-tender, palpable lump at around the 11 o'clock position of the left breast. She had no other clinical symptoms or radiographic findings to indicate multi-organ involvement of systemic amyloidosis. Even though amyloidosis presented mammographically in their patient as a suspicious cluster of pleomorphic micro-calcifications, it is difficult to determine whether this was solely due to amyloid because it was intermixed with DCIS.

Chiang et al. [35] also stated that:

- Previous case reports had described amyloidosis as distinct lesions or as lesions inter-mixed with breast cancers.
- Reported co-existing breast carcinomas had included tubular carcinoma, invasive ductal carcinoma with

extensive intra-ductal components, and invasive lobular carcinoma [36].

- Their case was unique in that the patient presented with both focal amyloidosis inter-mixed with DCIS in addition to a separate focus of invasive pleomorphic lobular carcinoma within the same breast; the patient's localized breast amyloidosis was secondary to an underlying extra-nodal Castleman's disease within the lingula.
- Amyloidosis can be classified as either primary or secondary, with most cases of breast amyloidosis being classified as the later [36].
- Secondary amyloidosis is characterized by the deposition of the acute phase protein, serum amyloid A (SAA) [37].
- While primary amyloidosis is considered an idiopathic process, secondary amyloidosis is caused by an underlying chronic inflammatory disease such as inflammatory bowel disease, rheumatoid arthritis, or tuberculosis [36] [37].
- In their patient, extra-nodal Castleman's disease within the lingula was the underlying inflammatory process. Castleman's disease is an atypical lymphoproliferative disorder noted for giant lymph node hyperplasia [38]. Its association with amyloidosis is believed to have occurred secondary to the production of IL-6 by its hyperplastic lymph nodes. IL-6 results in the production of acute phase proteins in the liver, including SAA [38].
- Complete surgical excision is considered curative for localized unicentric Castleman's disease [38].

Tutar et al. [39] reported a 58-years-old woman with amyloid tumour of the breast which developed secondary to long-standing rheumatoid arthritis. She presented with a palpable in her right breast which had led to an erroneous clinical diagnosis of carcinoma of the breast. Tutar et al. [39] stated that amyloid involvement of the breast has no has no specific diagnostic features on mammography and on occasions this causes diagnostic challenges.

Turner et al. [40] both sclerosing lymphocytic lobulitis (SLL) and amyloidosis of the breast are rare. They reported the case of a 59-year old woman who presented with suspicious micro-calcifications on routine mammography. She underwent wire-guided excision biopsy which showed features typical of sclerosing lymphocytic lobulitis (SLL) but also localized amyloid deposits within the specimen. Turner et al. [40] stated that:

- Amyloidosis and sclerosing lymphocytic lobulitis (SLL) may have similar immunological causes.
- The patient represented the first documented association of these two disorders.

Fleury et al. [41] reported a 77-year-old African American woman, who was admitted with a pulmonary embolism secondary to bilateral deep venous thromboses, and on physical examination was incidentally found to have bilateral breast masses. The mass in the right breast was found at the 4 o'clock position and it was larger than

that in the left breast. On palpation, the mass was adjudged to be firm and irregular in shape, so a carcinoma was suspected. She had an extensive past medical history which included end-stage renal failure requiring tri-weekly hemodialysis secondary to Wegener granulomatosis, a right upper pole renal mass which was radiologically suggestive of renal cell carcinoma, monoclonal gammopathy of unknown significance, iron deficiency anemia, pseudomonas sepsis, post-menopausal bleeding, bullous pemphigoid, and recent-onset chronic diarrhoea and pancytopenia. She had mammography of both breasts which revealed a 1.7-cm, ill-defined mass containing coarse calcifications in the lower inner quadrant of the right breast (Figure 4.1) and an un-calcified 1.5-cm lesion in the upper inner quadrant of the left breast. She underwent an ultrasound-guided biopsy of the right breast mass (see figures 4.2, 4.3 and 4.4 which show haematoxylin and eosin stain, Congo red stain and Congo red stain visualized under polarized light respectively Fleury et al. [41] stated that:

- There is a wide range of possible etiologies for bilateral breast masses. Fibrocystic changes and fibroadenomas comprise the majority of cases. Invasive breast carcinoma presents as bilateral tumours less than 1% of the time.[42]
- Other rare causes include stromal proliferations, such as pseudo-angiomatous stromal hyperplasia and diabetic mastopathy, along with metastases to the breast from extra-mammary malignancy. [43]
- The literature contains descriptions of several cases of bilateral breast masses due to amyloidosis.
- Amyloid deposits are typically closely related to the connective tissue framework of the involved organs and they are often found to be interposed between parenchymal cells and their blood supply. This configuration promotes parenchymal cell death via ischemia and pressure atrophy.
- In the breast, amyloid accumulates surrounding ducts, terminal duct lobular units, vessels, and fat; in the former 2 locations, the differential diagnosis is the far more common periductal stromal elastosis.
- Amyloidosis can be divided into systemic and localized forms.
- Systemic amyloidosis is a relatively uncommon condition and is rare in people younger than 40 years, with less than 1% of the population affected.
- Systemic amyloidosis can be further subdivided into 2 main types: primary amyloidosis (AL) and secondary (inflammation associated) amyloidosis (AA).
- Plasma cell dyscrasias, including multiple myeloma, have long been recognized as being responsible for the AL variety.
- AL amyloid accounts for 75% of all cases of amyloidosis, and this sub-type has a predilection for tissues such as the heart, gastrointestinal tract, peripheral nerves, skin, and tongue. Here, the fibrils are composed of monoclonal k or l immunoglobulin

light chains. AA amyloid is formed from serum amyloid protein (SAA), an acute-phase protein produced by the liver in response to inflammation. Before the advent of antibiotics, the most common causes of systemic AA amyloidosis were chronic infectious diseases, such as tuberculosis and bronchiectasis.

- Currently these conditions are usually adequately controlled with antibiotics, so chronic inflammatory diseases such as rheumatoid arthritis are now the most common causes of AA-type amyloid. Up to 3% of rheumatoid arthritis patients develop amyloid deposits.
- Less common types of systemic amyloidosis include that associated with long-term haemodialysis, which affects the joints of 70% of these patients. This subtype of systemic amyloid is derived from a component of the major histocompatibility complex class I molecule, b2-microglobulin, that fails to be filtered by the membrane used in haemodialysis and therefore accumulates.
- On the contrary, localized amyloidosis refers to amyloid deposits that are limited to a single organ, such as the lung, larynx, or heart. Localized amyloidosis may also be associated with specific endocrine neoplasms, such as medullary carcinoma of the thyroid, islet cell tumour of the pancreas, and pheochromocytoma; in these circumstances, the amyloid is derived from specific polypeptide hormones.
- Amyloidosis of the breast is a rare entity. Fernandez and Hernandez [new 1 old 40] recorded the first case in 1973. Deolekar et al [9] recently reviewed the literature and found 13 well described cases of localized AL amyloid tumour of the breast, that is, amyloid protein deposits in the breast tissue without any evidence of systemic disease. Of these cases, 2 were bilateral. Their own review of the literature revealed several additional cases of systemic amyloidosis as the cause of bilateral breast masses. One described diffuse amyloidosis involving the lungs and breast, which was associated with a k-chain restricted gammopathy. [44] Another case reported bilateral amyloidosis secondary to rheumatoid arthritis. [45]
- Localized mammary amyloidosis typically presents in postmenopausal patients and has a benign clinical course, although it simulates carcinoma clinically and mammographically. [7] [45].The difficulty of this distinction was compounded in 2002, when 3 additional cases of amyloidosis of the breast were reported, 2 of which were found to have breast carcinoma in conjunction with the protein deposits. [31] Overall, AL-type amyloid is more common in the breast than AA-type, and in unilateral cases the right breast is affected 3 times more frequently than the left. k- Light-chain restriction has been described in

mammary amyloidosis more frequently than I-light-chain restriction.[31]

- Their patient's mammary amyloidosis had a number of potential etiologies. Her renal failure and history of hemodialysis make her a candidate for systemic b2-microglobulin-associated amyloidosis, although her relatively short time on dialysis and absence of joint involvement make this unlikely. Another consideration is the suspected renal cell carcinoma, which has been associated with systemic amyloidosis of the AA variety. The third and most probable consideration is systemic amyloidosis secondary to monoclonal immunoglobulin production.
- In their patient, serum protein electrophoresis and urine protein electrophoresis demonstrated monoclonal immunoglobulin G I restriction, but her M-component was quantitatively insufficient to meet diagnostic criteria for multiple myeloma. Immunohistochemistry performed on the biopsy specimens did not demonstrate light-chain restriction, although this is commonly the case due to technical limitations in formalin-fixed tissue. Assuming that the patient's amyloidosis is related to her plasma cell dyscrasia, their patient could no longer be considered to have asymptomatic monoclonal gammopathy of unknown significance, and she was then considered to have systemic amyloidosis. While at the time of discovery of her breast masses the patient had not met the criteria for multiple myeloma, it was possible that her monoclonal gammopathy/plasma cell dyscrasia would progress to multiple myeloma in the future.
- In their patient, the diagnosis of amyloidosis in the right breast raises further questions. Her left-sided breast mass was clinically presumed to be amyloidosis due to its similar radiographic appearance to the right breast. As for her renal mass, thought to be a renal cell carcinoma, one wonders if this could be an amyloid deposit mimicking renal cell carcinoma, as has been reported previously.[46] Could the recent-onset chronic diarrhoea in the patient be due to amyloid deposits in her colon? It was also possible that her pancytopenia could be the result of amyloid deposition or plasma cell infiltration in the bone marrow.
- In summary, they had reported a rare case of amyloidosis of the breast in the setting of a patient monitored for monoclonal gammopathy of unknown significance. Amyloid should, however, be a differential diagnosis in postmenopausal women presenting with unexplained bilateral breast lesions. Localized primary amyloid tumour of the breast is benign; however, secondary (systemic) amyloidosis involving breast tissue does carry a poorer prognosis. [6] Therefore, it is important to try to seek out and exclude

Shim et al [47] reported a 72-year-old woman who was referred for further evaluations of calcifications which were detected on a screening mammography

taken at another hospital. She had a 5-year history of diabetes mellitus. She did not have any breast symptoms: such as pains, palpable masses, or nipple discharges. Her mammography demonstrated multiple, irregular calcifications in the sub-areolar area of the left breast; they were regionally distributed, generally smooth-branched, linear, and rod-like, and varied in sizes and shapes. The calcifications were classified as Category "4A": low suspicious findings at final assessment according to the Breast Imaging Reporting and Data System [48]: In view of this, a biopsy was recommended, and she underwent surgical excisional biopsy with mammo-guided needle localization. Her specimen mammography revealed several irregular-shaped calcifications. There were no discrete mass evidences on the gross pathology. Histopathology examination of the specimen revealed dystrophic calcifications in ectatic mammary ducts, amorphous in her physical or laboratory results. There was no interval change in calcifications of the left breast on follow-up mammography for five years. During the follow-up period of five years, no clinical or laboratory evidence of systemic amyloidosis was found.

Shim et al. [47] stated that:

- Amyloidosis is the deposition of amyloid at connective tissues framework of organs. It is divided into the systemic eosinophilic material deposition; the infiltration of periductal lymphocytes and multinucleated giant cells were revealed upon hematoxylin-eosin staining (Fig. 1D). The calcifications were stained with Congo-red and exhibited apple-green birefringence under polarizing microscopy (Fig. 1E) which were consistent with amyloidosis. No malignancies were pathologically identified. Immunohistochemistry confirmed the AL type amyloidosis.
- Their patient refused further investigations, and there was no clinical evidence suggesting generalized amyloidosis

Shim et al. [47] also made the ensuing statements:

- Primary breast amyloidosis presenting as micro-calcifications and localized form, according to the extensions of the disease can be classified as a primary or secondary form according to the aetiology.
- Amyloidosis can also be classified as the AA or AL type based upon the chemical compositions.
- In clinical practice, the most commonly diagnosed form of amyloidosis is primary idiopathic amyloidosis, the AL type [7] [49].
- Amyloidosis of the breast typically appears as diffuse breast involvements in the systemic form of amyloidosis with the primary AL type rather than AA type [49].
- Isolated breast involvement is a less common manifestation that occurs as a localized form of disease [7] [49].

- The clinical course of amyloidosis of the breast tends to be benign, and typically, patients complain for hard, non-painful, and palpable masses in the affected breasts [50].
- At times, a patient may manifest with abnormalities on the mammograms without any clinical symptoms. Previous studies had reported that common mammographic findings of breast amyloidosis have revealed a variety of solid shapes or multiple masses or nodules, whether including or excluding calcifications [31] [13].
- Primary amyloidosis of the breast which consists of only micro-calcifications excluding the associated mass is very rare. Only five cases that were presented solely as micro-calcifications had been reported at the time of publication of their paper [11] [12] [50] [51] [52] One case was breast involvements of systemic amyloidosis within a patient with a 15-year history of multiple myeloma. [11] The remaining four reports were in localized forms. In the previous reports, the shapes of the micro-calcifications had varied according to clustered [50] [52], pleomorphic [50] [52], fine linear and branching [12] [51], and smooth branching rod-like [11] [12] shapes. All the previous mammographic findings were assessed either as intermediate or suspicious of malignancy, and pathological confirmations were recommended [11] [12] [50] [51] [52]. In their reported case, there were irregularly linear distributed, multiple, smooth, rod-like calcifications as evident by mammography, similar to the two previously reported cases [11] [12]. Among these two prior reports, one was of localized form, and the other being breast involvements of systemic amyloidosis [11] [12]. This implied that mammographic findings between systemic amyloidosis and localized amyloidosis are not different which is probably due to the same pathophysiology.
- In breast amyloidosis, the amyloid is histologically evident as depositions at periductal, interstitial, or perivascular spaces with multiple multinucleated giant cells and calcifications. Amyloid fibrils have an affinity for calcium and deposition around mammary ducts and are found in blood vessels [7], thus, this pathophysiology is strongly correlated with the mammography-evident branching or linear distribution of micro-calcifications deposited in or around the vasculature or mammary ducts.
- Few cases of breast amyloidosis had been associated with breast cancers such as ductal carcinoma *in situ*, invasive carcinoma, invasive lobular carcinoma, or tubular carcinoma [13] [31] [49]. And, some cases had been associated with diffuse skin thickening which mimics inflammatory breast cancer [13]. In their reported case, no malignancy was identified on pathological examination. Although no distinctive findings have been reported for breast amyloidosis, the previously reported cases presenting suspicious

masses with or without micro-calcifications that mimic malignancy and pathologic diagnosis were needed.

Fernandez et al [53] reported a 64-year-old woman who presented with painless swelling of both breasts with continued growth for three years. There was no history of previous breast disease of any kind and the masses were relatively well defined. There was no abnormal secretion from the nipple. She had five years earlier undergone hysterectomy for endometrial cancer and radiotherapy. Her comorbidities included asthma, obesity, and hypertension. Her physical examination showed that the masses had occupied the upper quadrant of both breasts with 12 cm diameter, adherent deeply to the skin with skin retraction. She had mammography which revealed calcifications and confirmed the dimensions of the masses. Her serum and urine electrophoresis were negative. She underwent excision of the masses. Macroscopic appearance of the excised pieces of breast masses revealed that both masses were firm and grayish-yellow 12 and 13 cm. Histological examination of the specimens showed a dense fibrous stroma surrounding adipocytes, no replacement nucleated with a thick cell membrane, eosinophilic membrane. More often appeared cystic with diameters which ranged from 1 mm to 15 mm Compounds coated fibrous walls sometimes partially but in most cases completely, a similar membrane. Sometimes, micro-calcifications, as well as intra-cyst found in the stroma. A deposit was homogenous eosinophilic amorphous and distributed in the fat surrounding the cysts, in the stroma and perilobulillar periductal areas and around vessels, decreasing light immuno-fluorescence. With regard to immunofluorescence and histological the eosinophilic membrane was stained with PAS (with and without enzyme digestion), Alcian Blue and PAS showed auto-fluorescence in the yellow ceroid nature of the material. Amyloid was demonstrated by Congo red. With regard to immunohistochemical finding, the membrane scored positively with collagen IV and laminin demonstrating its membranous nature. Amyloid was stained with Thioflavin (figures 5a to 5d and 6a to 6g illustrate various characteristics of the lesion described above). She had not developed any clinical or analytical evidence of systemic amyloidosis, multiple myeloma, or local recurrence.

O'brien et al. [16] reported a 64-year-old lady with a remote history of Non-Hodgkin's lymphoma who presented with a palpable lump in her left breast. She had mammography which revealed that both breasts contained clusters of elongated tubular homogenous well-defined opacities with coarse calcifications which was indeterminate on ultrasound scanning. She had magnetic resonance imaging that the tubular lesions demonstrated low T1 signal and high T2 and Short Tau Inversion Recovery signal, with no significant enhancement; nevertheless, there was some faint peripheral delayed enhancement. Histological examination with positive

Congo red histological staining of the excised breast lump was consistent with the presence of amyloid.

In summary, breast amyloidosis is a rare entity that is usually evident as clinical or radiological palpable masses. Breast amyloidosis which only presented micro-calcifications without mass is still rare, and only a few cases have been reported [11] [12] [13] [50] [51] [52].

Conclusions

Amyloidosis of the breast is a rare phenomenon which can present incidentally through breast screening, or as a palpable breast lump. On mammography lesions can sometimes be seen as micro-calcifications in the breast. If confined to the breast, amyloidosis acts as a benign entity but if not confined to the breast it may be associated with poor outcome for patients. Few cases have been reported but in some of these cases amyloidosis of the breast was found to coexist with carcinoma of the breast. Treatment tends to be by excisional biopsy if the lesion is confined to the breast.

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