Calcifications in the mammogram. The good the bad and the ugly. With pathologic correlation.

Poster No.: C-2034
Congress: ECR 2015
Type: Educational Exhibit
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Keywords: Cancer, Calcifications / Calculi, Biopsy, Digital radiography, Breast
DOI: 10.1594/ecr2015/C-2034

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Learning objectives

- Review basic anatomy of the breast.
  
  Show different types of calcifications that can be found on mammograms.

  Comprehend the nature of the lesions that produce such calcifications correlating mammogram features with the histology images.

Background

Calcifications are a frequent finding on mammograms, the form or morphology of calcifications is the most important factor in deciding whether calcifications are typically benign or not. The morphology and distribution of the calcifications are related to the histology of the lesions that produce them. Different pathological entities may give rise to different calcifications.

Benign calcifications "the good" do not require further study because are related to benign entities such a fibroquistic changes, fibroadenomas or fat necrosis. Malignant calcifications "the bad" are most likely malignant (ductal carcinoma in situ and invasive duct carcinoma), so they do not offer a diagnostic challenge. "The ugly" ones pose a diagnostic challenge, because benign and malignant entities may give rise them.

Findings and procedure details

The good (BI-RADS 2):

- Pop corn (fig. 1)
- Round(fig. 2)
- Milk of calcium
- Rod like (Fig. 3)
Fibroadenomas are benign masses that include collagen and fibroblast, typically seen as ovoid nodules that calcify when then involute. The early involution of fibroadenomas may present intermediate concern calcifications and may require biopsy to confirm, but once involutes, they present typical "pop corn" calcifications.

Most breast calcifications form either within the terminal ducts (intraductal) or within the acini (lobular), both of which compose the terminal duct lobular unit (TDLU), the basic functional unit of the breast. The ducts and lobules are lined by breast epithelium. When secretions calcify in the acini (lobular calcifications), this results in uniform, homogeneous and sharply outlined calcifications, that are often punctate or round, these calcifications isolated are typically benign, although when grouped might be suspicious, a cluster of round calcifications has been defined as a group of 5 or more round calcifications within 1cm$^3$ of tissue.

When the acini became large and dilated, another typical calcification appears, the milk of calcium, which has an amorphous look on a craneo-caudal projection, but on a lateral view they look concave. When a dilated duct contains calcified secretions, they take the form of the duct, taking the rod like appearance.

Radiolucid center calcifications are also typically benign, they include the fat necrosis, or colicuative necrosis, a lesion that calcifies peripherally over time and develops after trauma, surgery or radiation. Most skin calcifications are easy to identify as benign, because of their position, shape and radiolucid center, but some of them may be mistaken for mammary calcification, so additional views may be necessary.

Suture and distrophic calcifications are quite common, we need to be aware of the patient history. Suture material tends to calcify over time in a linear way (Fig. 5). Dystrophic calcifications are coarse and present with architectural distortion on patients with history of surgery and radiation therapy or some trauma cases.
Filariasis is an infestation of the breast by a round worm Wuchereria bancrofti. Host response is variable, and can cause from a silent disease, to a inflammatory response mimicking inflammatory carcinoma. Over time, the parasite body calcifies and shows on mammograms as a serpinginous calcification.

Vascular walls tend to calcify and are quite easy to detect, double wall, tubular and in vascular distribution, do not biopsy these calcifications.

The ugly (BI-RADS 4B):

Amorphous (Fig. 8)
Coarse heterogeneous (Fig. 9, 10)
Pleomorphic (fig. 11, 12)

Intermediate suspicion calcifications may have benign or malignant origin, so in order to properly assess these lesions we have to biopsy them. Amorphous calcifications (Fig. 8) have a non clearly shape, diffuse borders, they indicate frequently fibrocystic changes, but maybe associated with high risk lesions such a atypical duct hyperplasia, atypical lobular dysplasia, lobular dysplasia and in a 20% are associated with DCIS or invasive ductal carcinoma, since the calcification occur in the duct.

Coarse heterogenous are irregular, conspicuous calcifications that are generally between 0.5 mm and 1 mm and tend to coalesce but are smaller than dystrophic calcifications, initial degeneration of fibroadenomas and other benign lesions such as lobulillar sclerosis (Fig.9) may present them, but in situ and infiltrating ductal carcinomas, (Fig. 10) may also have these type of calcifications (DCIS is considered when they have a clustered, linear or segmental distribution).

Intraductal calcifications represent calcified cellular debris or secretions within the distal aspect of the TDLU and typically vary in size, density, and shape. Fine-Pleomorphic calcifications are less than 0.5mm. and extremely variable in size, density and form (i.e. pleomorphic from the Greek pleion 'more' and morphe 'form'). They are associated with malignancies like ductal carcinoma in situ but also with benign entities like fibrocystic changes, adenosis (Fig. 11).

The bad (BI-RADS 4C):
Fine linear and branching (fig.13) microcalcifications occur when the tumor grows within and along the duct, expanding the duct and assuming its shape, secretions calcify forming casts, so the branching follows the ductal anatomy. The uneven calcification of the cellular debris explains the fragmentation and irregular contours of the calcifications. (when these calcifications appear in a segmental distribution are highly suggestive of malignancy- BI-RADS 5).

Images for this section:

Fig. 1: MLO view of a breast, showing the typical "pop corn" calcification that correspond to involuted fibroadenomas.
Fig. 2: Zoomed MLO view of an isolated round calcification.
Fig. 3: Zoomed MLO view that shows rod-like calcifications, a benign finding, these correspond to calcified casts on ectatic ducts. A round calcification is also seen.

Fig. 4: Left: MLO view of the breast with peripheral ovoid calcifications with radiolucid center that corespond to skin calcifications. Right: MLO view that shows the typical appearance of "eggshell" calcification that occur after fat necrosis.
**Fig. 5:** 4 years evolution to show how suture material calcifies progressively and in a linear fashion on mammography.
**Fig. 6:** MLO view of a post surgical breast that show architectural distortion and a coarse distrophic calcification.

**Fig. 7:** Serpiginous calcifications of a dead Wuchereria bancrofti, the patient is a spanish woman who had travelled to India.

**Fig. 8:** Left: amorphous calcifications. Middle: HE Hyperplastic duct lined by multiple layers of benign cells. Right: HE of the same biopsy specimen, a calcification is seen inside a dilated duct.
**Fig. 9:** Left: coarse heterogeneous calcifications on in a CC view. Right: HE. Biopsy of the lesion showed a lobular sclerosis with collagenous proliferation, the calcifications on the left image corresponded to these thick calcifications surrounded by collagen and fibroblasts.

**Fig. 10:** Left: coarse heterogeneous grouped calcifications; we also see 2 pop corn calcifications that correspond to fibroadenomas. Middle: HE Intraductal microcalcification in a benign duct. Right: HE Malignant cells forming nests and gland-like structures diagnosed as ductal carcinoma. A stromal microcalcification is seen.
Fig. 11: Left: Radiography of 3 biopsy cylinders, in which pleomorphic microcalcifications are seen. Right: HE Benign proliferation of ducts lined by a double layer of cells.

Fig. 12: Left: Radiography of a surgical specimen with a better view of pleomorphic microcalcifications. Middle: HE Intraductal proliferation of evenly distributed round and oval proliferating cells in a duct showing a normal columnar layer of luminal cells. Right: HE An area of fibrocystic changes with presence of microcalcifications in the lumens of cysts. Presence of atypical ductal hyperplasia was diagnosed close to this area.
Fig. 13: Left: MLO view of a breast that shows extensive, diffuse, pleomorphic and linear branched microcalcifications that strongly suggest malignancy. Middle: Hematoxilin-Eosin (HE) that shows neoplastic cells arranged in nests, strings and single-cell, with pleomorphic shapes and hyperchromatic nuclei with conspicuous nucleoli that infiltrate the stroma. Right: HE Calcification surrounded by collagen fibers and fibroblasts.
Conclusion

Proper knowledge of the histopathology and the processes of formation of the different types of calcifications in the breast can help the radiologist to better classify them for optimal Management according to the BI-RADS.

Morphology and distribution of the calcifications on the mammogram gives us clues on the histology of the lesions that causes them, that way we are able to classify them and determine which will require histological study because of high or intermediate suspicion for malignancy and which are certainly benign.

Personal information

References

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