

The significance of spontaneous resolution of breast calcification

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Abstract. Spontaneously resolving breast microcalcification is a rarely reported occurrence. A retrospective review was carried out on 33 cases of resolving benign and indeterminate microcalcification identified from 108 000 screening mammograms from the South West London Breast Screening Service. Four further cases are reported from The Jarvis Breast Screening Centre. No interval cancers were identified in women with microcalcification which initially showed benign appearances. However, 36.4% of the group with resolving indeterminate microcalcification subsequently developed cancers. It is recommended that this change should prompt full investigation and close follow-up or excision. While the majority of spontaneously resolving microcalcification is associated with benign processes, it is concluded that a significant proportion of disappearing indeterminate microcalcification is associated with malignancy.

Breast calcification is a common mammographic finding associated with both benign and malignant breast diseases. The aetiology of microcalcification is poorly understood, although radiological and histopathological correlation has been reported [1–3]. Microcalcification (MC) can be described according to mammographic characteristics including size, shape, density and distribution of individual particles or groups. MC can be differentiated on the basis of this morphology and grouped into categories indicative of malignancy risk [4].

Increasing numbers of calcifications or a change in appearance prompt full investigation and may reclassify the patient to a higher risk group [5, 6]. Similarly, the resolution of MC has been documented in association with various therapies [7–10], but spontaneous resolution has been reported in only two series [11, 12]. These two reports describe the finding as uncommon, although one obtained 17 cases prospectively over a 6-month period [12]. In addition, spontaneously resolving arterial calcification has only been reported once before [13]. There are no reports of an association with malignancy in any of these cases of spontaneous resolution of breast MC. We report 37 cases of spontaneously resolving MC, some of which subsequently developed histologically proven malignancy.

Method

Cases of spontaneously resolving MC were identified retrospectively from 108 000 screening

mammograms, in asymptomatic women, taken at the South West London Breast Screening Service (SWLBSS) between 1991 and 1997. All women had both craniocaudal and mediolateral views performed at all screening visits. Four additional cases are included from the Jarvis Breast Screening Centre, Guildford.

All MC identified were classified mammographically according to our experience into the categories of benign, indeterminate and malignant and could be located on both mammographic views. Table 1 indicates the criteria used. This classification then determined subsequent management of these patients, shown in Table 2.

Those women in the benign group, A, receive a normal screening result and undergo two view rescreening at 3-yearly intervals. Those in the indeterminate group, B, undergo full assessment. This involves taking a clinical history and examination and additional mammographic views, including magnification and compression views. Ultrasound is performed if the MC is associated with a soft tissue mass. MC still thought to be of an indeterminate nature is further evaluated by fine needle aspiration cytology (FNAC). Those women with benign cytology are recalled early at an interval of 12 months for reassessment. FNAC is repeated if the MC or soft tissues change in appearance or initial FNAC was thought to be unrepresentative. The women are returned to the routine screening programme if the MC is stable in appearance. Those with malignant or suspicious cytology are referred for excision biopsy. Women in group C, the malignant group, are referred to a specialist surgical unit for excision following full assessment which includes FNAC.

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Table 1. Mammographic characteristics used in the classification of microcalcification

	Benign	Indeterminate	Malignant
Distribution	Solitary, clustered or diffuse and bilateral	Clustered	Clustered
Cluster shape	Round	Round	Linear, triangular or rhomboid
Form	Ring, popcorn, parallel line or microcystic	Granular, round	Casting (linear, branching), pleomorphic
Size	Uniform	Uniform or variable	Variable
Density	Uniform	Uniform or variable	Variable within and between MC

The mammographic appearance of the microcalcification was classified in all cases by a radiologist (HRS) as to its distribution and location within the breast. The size of the focus of MC was measured directly from the relevant radiographs; a technique previously described [11, 12]. Assessment of mammographic change was recorded as a decrease in number or size of individual particles (diminishment) or an absence of a focus in the previously documented area (disappearance). All FNAC results were recorded, as were follow-up findings and histology where available.

Results

37 women were identified with spontaneously resolving MC. 15 women were classified as clearly benign MC (Group A). 22 women, including the four from the Jarvis Centre, were classified as indeterminate MC (Group B). Each group is discussed separately due to the differing management strategies employed.

Group A, clearly benign

15 women were identified in this group (Table 3). All changes were first seen at 36 months, following a repeat screening mammogram. No interval cancer has been identified in this group with a follow-up ranging from 37 to 66 months (average 51.5 months). None had a significant breast history. The woman with vascular-type calcification had no significant medical history. Figures 1–3 show examples of resolving, typically benign MC.

Group B, indeterminate

22 women had indeterminate MC and most were fully assessed (Table 3). 14 women showed

Table 2. Management protocols for breast microcalcification

Benign	36 month screening with 2 views
Indeterminate	Full assessment
Malignant	Full assessment and excision biopsy

diminishment ($n=7$) or disappearance ($n=7$) of the MC with no other mammographic change and all have remained well (12 had benign FNAC, 2 had no FNAC).

Eight women (36.4%) from this group developed cancers (Figures 4 and 5). A diagnosis of lobular carcinoma *in situ* (LCIS) was included in the malignant group, in accordance with the directive from the NHS Breast Screening Programme Pathology Reporting Draft [14]. The mammographic features and change in MC of these women with proven cancers is shown in Table 4.

Discussion

The aetiology of breast MC is poorly understood. They may be produced either by secretion from the glandular epithelium or by mineralization of necrotic debris, depending on the local conditions of tissue and the matrix into which the calcium is deposited [1–3]. MC may thus be associated with both benign and malignant processes, possibly reflecting increased cellular activity. It is the morphology of MC that helps radiologically to differentiate them into the risk groups, which determine management. Temporal changes in MC are recognized and an increase in number may reclassify the patient to a higher risk group.

Resolving MC may be a feature of treatment for breast carcinoma. Decreasing amounts of both fine and coarse calcification have been described

Table 3. Results of mammographic analysis and follow-up of disappearing microcalcification

	Benign	Indeterminate
Number of women	15	22
Mean age, years (range)	56.6 (52–63)	55.6 (50–65)
Location: Rt or Lt	10 Lt, 4 Rt, 1 bilateral	13 Lt, 9 Rt
Type: solitary (SOL) or clustered (CL)	4 SOL, 10 CL, 1 vascular	All CL
Follow-up interval months (range)	51.5 (37–66)	21.4 (5–69)
Focus disappeared	7	12
Focus diminished	8	10
Number of cancers (%)	0 (0)	8 (34.6)

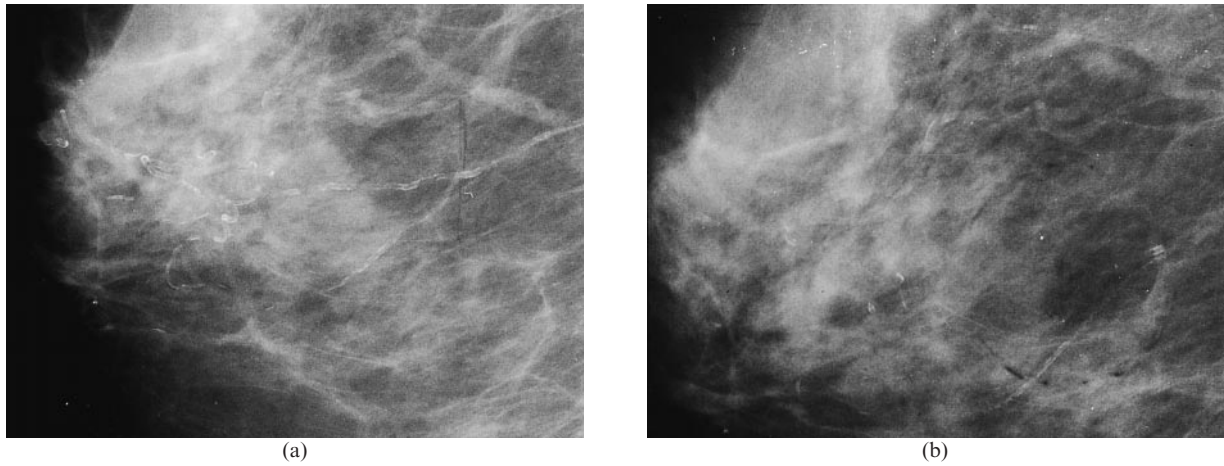


Figure 1. (a) Detail from right mediolateral (ML) mammogram showing extensive vascular calcification. (b) Detail from the same area at 36-month rescreening showing a marked reduction in vascular calcification.

in association with surgery, chemotherapy, radiotherapy and hormonal treatments [7–10]. The mechanism of resolution is unknown and possible causes include increased clearance of mineralized debris by macrophages or an alteration in the rate of secretion by cells. It is unlikely that extrusion of the original MC via a ductal system is possible, since in none of the cases was MC seen to migrate toward the nipple.

Vascular calcification is associated with increasing age, diabetes, hypertension and chronic renal

failure, possibly a result of deranged calcium metabolism and secondary hyperparathyroidism [15, 16]. This is supported by reports of resolution of vascular calcification in patients with chronic renal failure treated by renal transplantation [17]. Treatment with hormonal steroids is thought to delay breast arterial calcification or possibly to be a factor in observed resolution of breast arterial calcification [13]. The woman in our series with disappearing arterial MC was known to be on hormone replacement therapy.

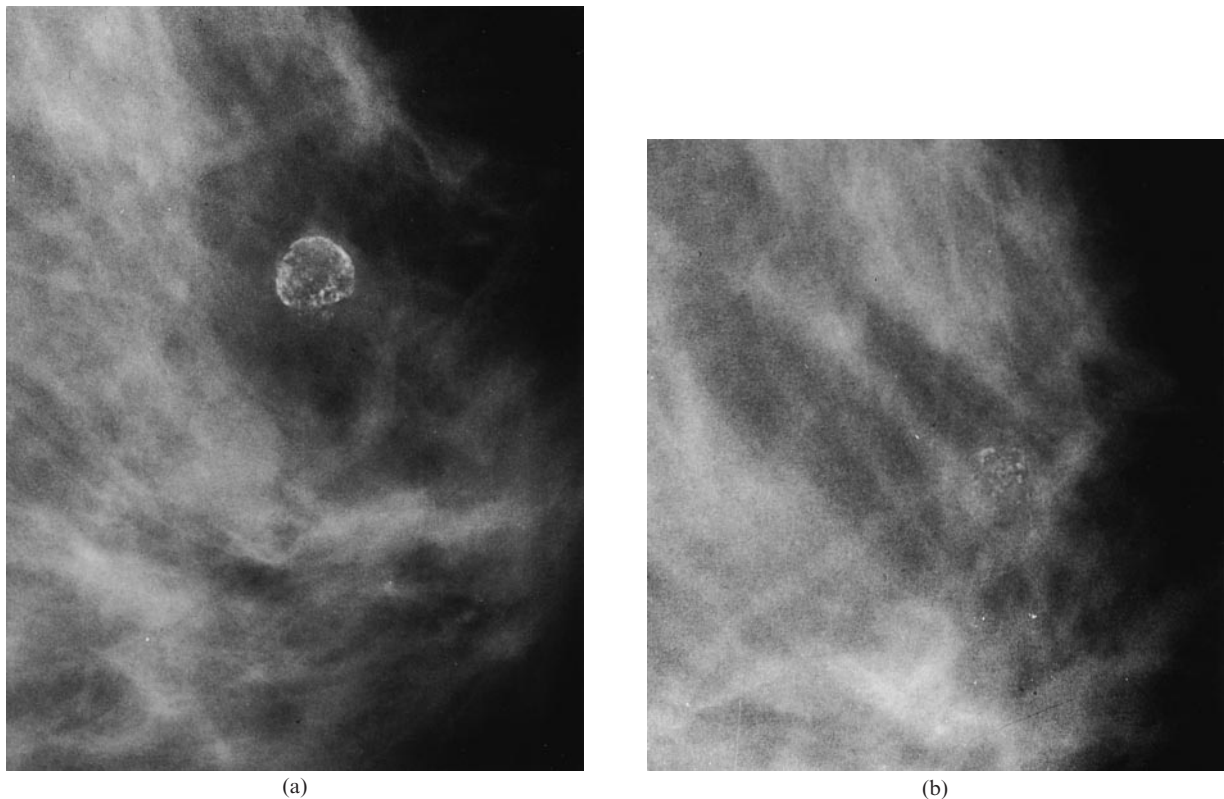


Figure 2. (a) Detail from a left ML mammogram showing a focus of benign calcification. (b) Detail from the same area of the left breast at rescreening showing diminishment of the previously identified focus. However, this woman had developed a new group of more suspicious MC adjacent to the above focus, which yielded C3 on FNAC. She had an excision biopsy, which showed BBD.

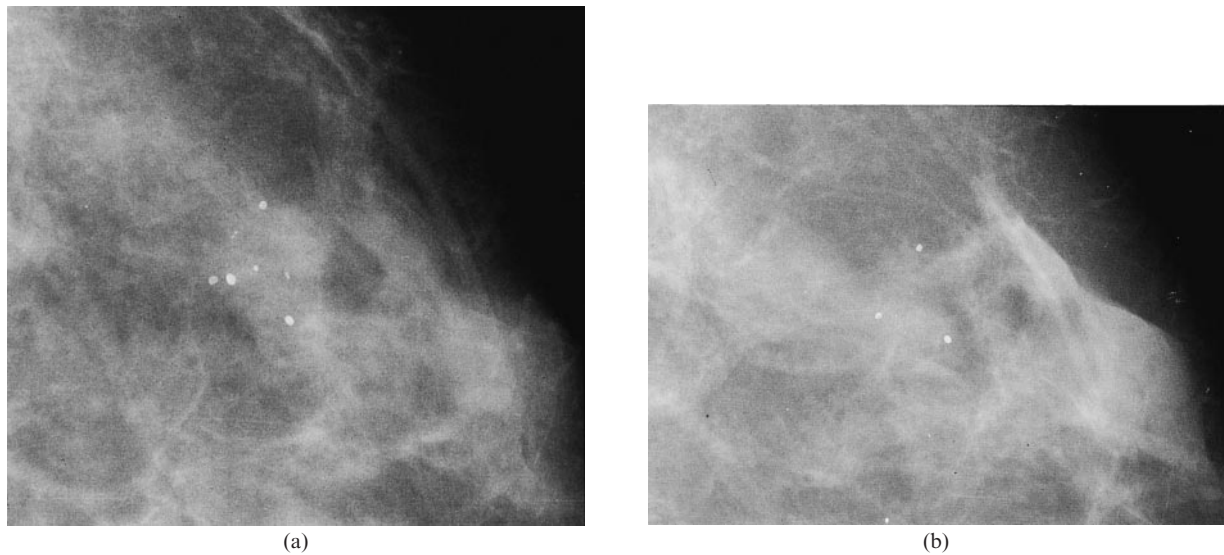


Figure 3. (a) Detail from a left craniocaudal (CC) mammogram showing a benign group of MC. (b) 3 years later, at rescreening, a diminishment in the same MC focus was noted.

This study shows that spontaneously resolving breast MC is uncommon, being seen in 0.03% of screening mammograms, in keeping with the findings of Parker et al [12]. While they commented that resolving MC were rarely of an indeterminate nature suggestive of malignancy, 22 out of 37 women had indeterminate calcifications in our experience. These results correlate better with those of Fewins and co-workers who identified MC “suggestive of malignancy” in six of their fifteen foci [11]. They did not state whether any of these cases subsequently went on to develop malignancy and to our knowledge this has not been reported before.

In the present series, 36.4% of those with resolving indeterminate MC developed malignancy. All

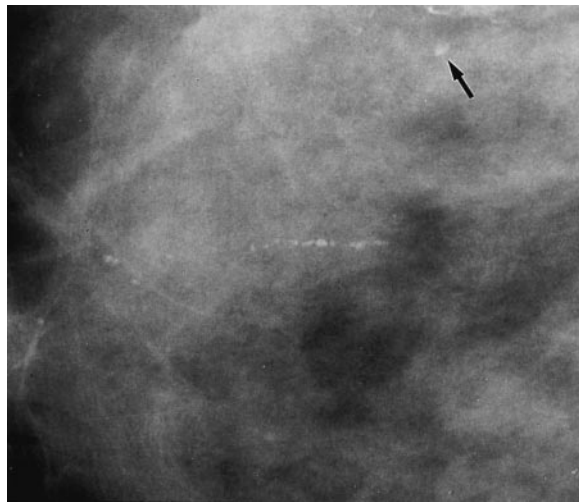
those found to have cancers had additional parenchymal change with new masses or distortion or newly appearing adjacent MC. In contrast, those with resolving MC but otherwise stable parenchymal appearances have all remained well.

The women in Group B were retrospectively compared with a cohort of women ($n=27$), who also had initially indeterminate MC and benign cytology following full assessment (unpublished data). All were recalled early at 12 months. All the women in the second group had stable indeterminate MC at reassessment and were discharged. None of this group with stable indeterminate MC has been found to develop cancers and all remain well at follow-up. It is therefore suggested that the spontaneous diminution of indeterminate breast

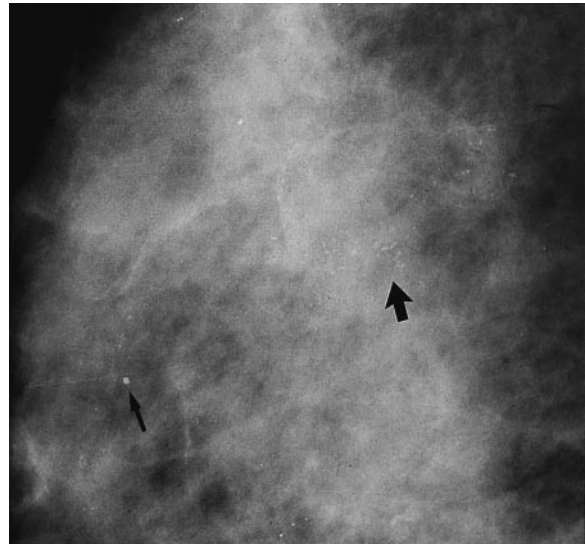
Table 4. Mammographic and histological features of women with proven carcinomas

Patient number	Mammographic change in original MC	Additional features	Cytology result preceding biopsy	Histology
1	Disappeared	New soft tissue mass	C4	Radial scar with focus of LCIS
2	Disappeared	New soft tissue mass and MC	C2	14 mm high grade IDC and separate focus of DCIS
3	Disappeared	New adjacent MC	C5	50 mm high grade IDC, 1/15 nodes positive
4	Diminished	New soft tissue mass	C5	23 mm low and intermediate grade IDC, 3/17 nodes positive
5	Diminished	New distortion and contralateral new MC	C5 and contralateral C5	Multifocal bilateral low grade IDC, no nodes involved
6	Diminished	New soft tissue mass	C5	17 mm moderate grade IDC, 0/21 nodes
7	Disappeared	New soft tissue mass	C5	12 mm focus of IDC, no nodes involved
8	Disappeared	New soft tissue mass	C5	Extensive high grade lobular carcinoma and 12 mm focus of moderate grade IDC, 6/19 nodes positive

LCIS, lobular carcinoma *in situ*; IDC, invasive ductal carcinoma; DCIS, ductal carcinoma *in situ*.



(a)

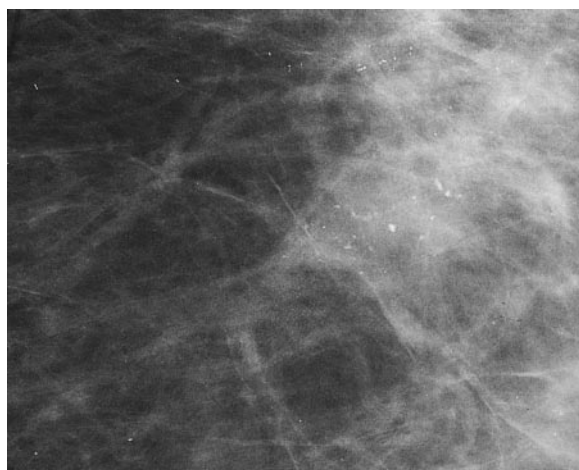


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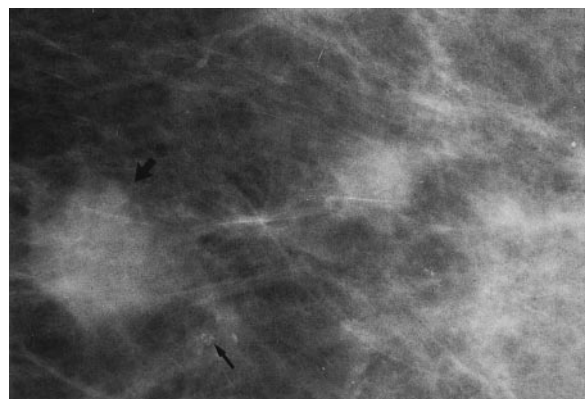


(c)

Figure 4. (a) (Patient 3, Table 4). Detail from right ML mammogram showing a new retroareolar linear focus of MC. Previous screening mammograms were normal. A benign focus of MC is marked (arrow). FNAC of the area was benign. (b) (Patient 3, Table 4). Detail from right ML mammogram at 6 months early recall showing a new area of more suspicious MC in an adjacent site (large arrow). The retroareolar linear focus had disappeared at the time of attempted needle localisation, prior to this mammogram. The benign MC (small arrow) and faint vascular calcification was unchanged. (c) (Patient 3, Table 4). Detail of new MC from the ML mammogram (Figure 4b) at 6-month early recall. This was a 50 mm focus of high grade invasive ductal carcinoma extending to the retroareolar region at mastectomy with axillary node metastasis.



(a)



(b)

Figure 5. (a) (Patient 2, Table 4). Detail from the initial assessment magnified CC view showing a focus of indeterminate MC, which yielded benign cytology. (b) (Patient 2, Table 4). At the second early recall, magnified CC view showed resolution of the original focus of MC, but a new soft tissue mass (large arrow) and new MC (small arrow), posterior to the original area. Excision biopsy showed a 14 mm focus of high grade invasive ductal carcinoma and separate focus of DCIS, 8 mm from the main mass, without nodal spread.

MC carries an increased risk of malignancy compared with that in women with stable indeterminate MC and benign cytology followed-up over a similar time interval.

Full initial assessment, including FNAC, in most of the women in series Group B, suggested that these MC were probably benign, despite the indeterminate mammographic appearance. The policy of continuing to follow-up women with indeterminate calcifications at 12-monthly intervals before returning them to routine rescreening, if the MC is stable, enabled us to identify changes which then prompted surgical excision. This study was performed before the use of core biopsy was advocated in the assessment and management of indeterminate MC. This latter technique may have obviated the need for early recall by allowing earlier histological identification of malignancy.

Women with mammographically benign disappearing MC were followed-up over an average of 51.5 months, and none of these women developed cancers. Conversely, eight (36.4%) of the 22 women with indeterminate MC, which resolved over the follow-up period of between 5 and 69 months, developed cancers in either the same or an adjacent area of the same breast. This finding suggests that any change in MC, whether it is an increase or a diminution, may indicate a malignant process.

It is concluded that the majority of spontaneously resolving MC is associated with benign processes and when initial appearances are clearly benign, no further action is needed. It is recommended that resolution of indeterminate MC should prompt full investigation and close follow-up or excision since over a third of disappearing indeterminate MC progress to cancers.

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