

Palpable asymmetrical thickening of the breast: a clinical, radiological and pathological study

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Abstract. While management protocols for a discrete palpable breast lump are standardized in most centres, the approach to an area of palpable asymmetrical thickening in the breast has seldom been addressed. A diagnostic algorithm for palpable asymmetrical thickening of the breast was prospectively evaluated in 116 Oriental women, followed by a retrospective review of their mammograms and histology specimens. Most women (86%) were pre-menopausal and 82% complained of a lump. The thickening eventually resolved spontaneously in 93 (80%) women. None of these 93 women developed cancer at a median follow-up of 41 months. A total of 9 (7.8%) cancers were found in the series of 116 women, including two with a lobular component. The occurrence of cancer was more likely when the woman was older than 43 years or when the thickening was marked ($p < 0.04$). Mammographic review showed correlation of the palpable thickening with localized increase in breast tissue density and/or microcalcifications in 18% of cases. Histology review suggested fibrosis as an explanation for the clinical presentation. Although most cases of thickening tend to resolve with time, a significant number of cancers present in this way. A diagnostic approach with early and liberal imaging and biopsy for high risk women is required.

Although management protocols for a discrete palpable breast lump are standardized in most centres, the approach to an area of palpable asymmetrical thickening in the breast has seldom been addressed. Palpable asymmetrical thickening is defined as the presence of a palpable abnormality in the form of thickened breast tissue with an ill defined border that feels distinct from surrounding tissue. No such thickening should be palpable in the corresponding area of the contralateral breast. The present study is a prospective evaluation of a diagnostic algorithm designed for women presenting to a symptomatic breast clinic with asymmetrical thickening detected on physical examination [1]. At the end of the study, all available mammograms and histology specimens were reviewed to attempt to account for the clinical presentation.

Methods

The study involved women presenting to one breast surgeon (KLC) at a dedicated breast

referral clinic of a university teaching hospital. Women with palpable asymmetrical thickening of the breast were included, regardless of age. Women with a concomitant discrete lump in the same breast found on physical examination were excluded. Unless the thickening was marked or the woman was extremely anxious, no imaging was performed initially and a repeat clinical examination was carried out by the same surgeon at 6 weeks. The woman was discharged if the asymmetry had disappeared or if the thickening had become less obvious. Radiological examination was otherwise performed, using ultrasound for all cases as well as mammography for women above the age of 35 years. The radiological findings were reported in the usual manner: R1, normal; R2, benign; R3, indeterminate; R4, suspicious; and R5, malignant. If a mass lesion was seen on imaging, fine needle aspiration cytology (FNAC) was performed under image guidance and the mass was managed as a discrete lump according to a standard protocol. The mass was retained if it was less than 3 cm, it was radiologically and cytologically benign, and if the woman was not anxious to have it removed [2]. Core biopsy was performed if no mass lesion could be seen and the thickening was persistent. Core biopsy was chosen instead of FNAC because the thickened breast tissue is often fibrotic and

Received 23 August 2000 and in revised form 13 November 2000, accepted 24 January 2001.

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FNAC will often produce inadequate results. Open incisional biopsy was carried out if the thickening still caused concern or if the woman was anxious.

At the end of the study, a blind review of all available mammograms was carried out by one breast radiologist (LWCH) using the Breast Imaging Reporting and Data System (BIRADS) of the American College of Radiology [3]. Both breasts were compared to see whether there were consistent radiological features to account for the clinical findings. All histology specimens were reviewed by two dedicated breast pathologists (EYFL and USK) for the same purpose. This involved review of all core and incisional biopsies to see whether there were consistent features to account for the presentation as thickening. For women with cancer undergoing definitive surgery, mastectomy or wide local excision specimens were reviewed to look for features to account for the presentation as thickening rather than as a discrete lump. The Bloom and Richardson's classification with Elston's modification was employed in histological grading of all invasive cancer [4].

Follow-up was performed using the local histopathology registry to evaluate the outcome of those women who had been discharged. The median duration of follow-up was calculated from the time of presentation to the breast clinic.

The core and clinical part of the study was carried out in the form of a prospective evaluation of the diagnostic algorithm. Analysis was carried out with the aid of standardized biomedical computer programs (SPSSPC). Differences in data were compared to test for statistical significance using the χ^2 test, with Yates' correction when appropriate. Review of mammograms and histology specimens following the above evaluation was performed retrospectively.

Results

116 Oriental women (mean age 40 years, range 20–74 years) were included. The clinical presentations are summarized in Table 1. The median duration of symptoms prior to consultation was 1.5 months (range 0.5–120 months). 36 (31%) women had asymmetrical thickening that had resolved on repeat examination and were discharged without undergoing radiological examination. The mean age of these 36 women was 36 years (range 20–65 years) and they were predominantly pre-menopausal (94%). The remaining 80 women underwent imaging studies; all had ultrasound and 68 had also mammography examinations. The mean age of the 68 women who underwent mammography was 46 years (range 32–74 years). The radiological findings

Table 1. Clinical presentations of the women

Presentation	n (%)
Pre-menopausal	100 (86%)
Major presenting complaints	Lump 95 (82%) Mastalgia only 20 (17%)
Side of thickening	65% left breast
Site of thickening within the breast	63% upper outer quadrant
Degree of asymmetrical thickening ^a	Mild 57% Moderate 37% Marked 6%

^aArbitrarily graded by the examining surgeon according to the degree of difference compared with the breast tissue surrounding the thickening.

are summarized in Table 2. Mass lesions were seen on all ultrasound examinations and 10 on mammography in 17 women who had FNAC performed under ultrasound guidance. There were four malignant aspirates, while three aspirates showed features suspicious of malignancy, which were all subsequently proven to be cancer by either core biopsy ($n=2$) or open biopsy ($n=1$). The remaining 10 FNAs were benign and the women were managed similarly to those with a discrete lump [2]. All these 10 mass lesions were radiologically benign and less than 3 cm in size. For those cases without mass lesions, persistent asymmetrical thickening was found in 23 women who underwent core biopsy. Two cases of cancer were diagnosed, while 21 women had biopsy showing benign breast change. Two of them had long-standing thickening that felt suspicious of carcinoma and were subjected to open incisional biopsy, both of which showed benign findings.

93 (80%) women had complete resolution of the thickening after a median duration of 6 weeks (range 2–126 weeks). The resolution was spontaneous, as no medical treatment had been advised. The mean age of these 93 women was 40 years

Table 2. Radiological findings of women undergoing imaging studies

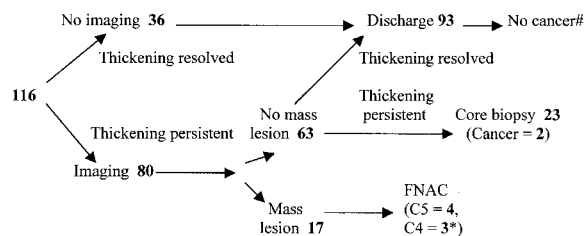
Findings	n
<i>Mammography</i>	
R1	58
R2	5
R3	0
R4	3
R5	2
Total	68
<i>Ultrasound</i>	
R1	63
R2	11
R3	1
R4	3
R5	2
Total	80

(range 20–74 years) and the majority of them were pre-menopausal (85%). A subsequent follow-up using the local histopathology registry was carried out at a median duration of 41 months (range 24–52 months). None of these 93 women who had been discharged due to resolution of their thickening were found to have developed breast cancer.

A total of 9 (7.8%) cancers were found in the whole series of 116 women (Figure 1). Statistical analysis was carried out to identify factors that could predict the presence of cancer. Cancer was more likely to be found when the woman was above the age of 43 years, when the degree of asymmetrical thickening was marked or when the mass lesion was radiologically indeterminate, suspicious or malignant (Table 3). No association was found with menopausal status, past history of breast diseases, family history of breast cancer, presentation and duration of symptoms, as well as the side and site of thickening.

At the end of the study, 55 sets of mammograms were reviewed, the others being unavailable since they had been performed privately. Most of them (55%) were categorized as having dense breast tissue, *i.e.* Category 3 or 4 according to BIRADS (Table 4) [3]. One mammogram showed a difference in generalized density between the two breasts (Category 1 vs 3), while a localized increase in breast tissue density corresponding to the palpable area of thickening was found in eight sets of mammograms. One of these eight mammograms also had localized microcalcifications in the area of thickening, while another mammogram had microcalcifications without an increase in density of breast tissue in the concerned area. Palpable asymmetrical thickening of the breast therefore had mammographic correlation in terms of increased density and/or microcalcifications in 10 out of 55 cases (18%). The microcalcifications on the two sets of mammograms were due to cancer, while malignancy was not found in the remaining eight cases.

Significant fibrosis was seen in all except one



C5 = Malignant
 C4 = Suspicious of malignancy
 * All proven to be cancer (See text)
 # After 41 months (median) (See text)

Figure 1. Outcome of women with palpable asymmetrical thickening of the breast.

Table 3. Prediction of the presence of cancer

	Cancer	
	No	Yes
<i>Age (years)^a</i>		
≤43	73	3
>43	34	6
<i>Degree of asymmetrical thickening^a</i>		
Mild/moderate	102	7
Marked	5	2
<i>Radiological findings</i>		
<i>Mammographic^b</i>		
R1–2	59	4
R3–5	0	5
<i>Ultrasound^b</i>		
R1–2	71	3
R3–5	0	6

^a*p*<0.04; ^b*p*<0.001.

core biopsy specimen in this series. A moderate to marked degree of sclerosis was seen in the background of the tumour in all nine cases of cancer. The presence of tumour was not obvious on gross examination of the operative specimen owing to marked sclerosis in four of these nine cases.

The histological features of the nine cases of cancer, with radiological correlation, are summarized in Table 5.

Discussion

This study is a prospective evaluation of a diagnostic algorithm designed for a condition that has seldom been directly addressed in the literature, namely palpable asymmetrical thickening of the breast. An attempt has also been made to draw a correlation of the condition with established mammographic and histological features of the breast.

Most palpable asymmetrical thickening is due to benign breast change, which tends to resolve spontaneously with time, as seen in 80% of cases in this series. Most women presenting with such condition do not require radiological assessment at the initial consultation, provided that repeat clinical examination is carried out at 6 weeks to ensure spontaneous resolution. None of these women in the present study developed breast

Table 4. Breast tissue density according to the Breast Imaging Reporting and Data System (BIRADS)

BIRADS category	<i>n</i>
1	8
2	17
3	18
4	12
Total	55

Table 5. Histological features and radiological correlation of cancer cases

Age (years)	Size (cm)	Grade	Type (all invasive carcinoma)	Sclerotic background	Gross suspicion of tumour	Other features	Findings on mammogram	Findings on ultrasound
44	1.8	III	Ductal, NST	Marked	No	Marked fibrocystic change	Mass (R5)	Mass (R5)
67	1.0	II	Ductal, NST	Moderate	Yes	Radial scar-like area	Mass (R5)	Mass (R5)
51	3.0	II	Mixed ductal and lobular	Moderate	No	Extensive DCIS and LCIS	Mass (R3)	Mass (R3)
38	2.2	III	Ductal, NST	Moderate	No		Microcalcifications (R1)	Normal (R1)
42	7.0	III	Mixed ductal and lobular (predominantly lobular)	Moderate	No	Multicentric tumour	Normal (R1)	Normal (R1)
47	2.5	II	Ductal, NST	Marked	Yes		Normal (R1)	Mass (R4)
39	3.0	I	Ductal, NST	Moderate	Yes		Mass (R4)	Mass (R4)
49	1.7	I	Ductal, NST	Moderate	Yes		Normal (R1)	Normal (R1)
45	3.5	II	Ductal, NST	Moderate	Yes	Extensive DCIS	Microcalcifications (R4)	Mass (R4)

NST, no special type; DCIS, ductal carcinoma *in situ*; LCIS, lobular carcinoma *in situ*.

cancer after a follow-up of more than 3 years. A 6-week observation period was chosen so that normal cyclical breast change every 4 weeks would not lead to misinterpretation of the clinical findings. In fact, most women with cyclical mastopathy complained of specific or generalized breast lumpiness [5], although only a small proportion of women in this series presented with mastalgia.

On the other hand, breast cancer sometimes presents in the same way, amounting to nearly 8% in this series. Palpable asymmetrical thickening may be the only presentation of an underlying breast cancer without any radiological abnormality, as seen in two of the nine women with breast cancer in this study. The diagnosis was made only after core biopsy of the area of thickening that had remained persistent. Statistical analysis showed that the chance of breast cancer would tend to increase when the woman was slightly older, *i.e.* from mid forties onward, or when the degree of the thickening was marked.

A selective combination approach is probably the appropriate way to arrive at the diagnosis for a woman presenting with palpable asymmetrical thickening. The 8% incidence of breast cancer found in this series is not a small proportion and subjecting all women presenting with palpable asymmetrical thickening to re-examination could cause delay in the diagnosis of a cancer by at least 6 weeks. All women with cancer in this series were older than 35 years and statistical analysis showed that women older than 43 years were at higher risk of cancer. The authors therefore suggest changing the present algorithm to perform imaging for all women older than 35 years at

the first visit (Figure 2). The results in this series showed that the mammogram was normal while a mass was found on ultrasound examination in one woman with cancer (Table 5). Ultrasound examination of the area of thickening should therefore be carried out in addition to mammography or at least when mammography does not show any abnormality, especially in women with thickening judged by the clinician to be marked. Liberal use of core biopsy should be considered when a marked degree of asymmetrical thickening is encountered, even if imaging is unremarkable. For women with normal imaging and less than marked thickening at initial examination, re-examination at 6 weeks, prior to core biopsy, is acceptable.

Although over half of the mammograms reviewed in this series showed a generalized dense pattern of breast tissue, actual correlation

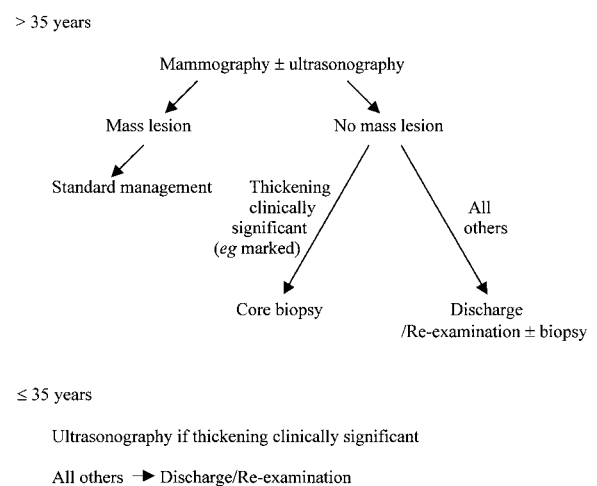


Figure 2. Suggested clinical management algorithm.

with the palpable area of thickening, as evidenced by localized radiological features such as increase in breast tissue density, was uncommon. In a case control review of 250 mammograms in each arm, Scutt et al [6] suggested that breast asymmetry as found in mammography was likely to be a predictor of breast cancer. The present series reviewing 55 mammograms may be too small to substantiate this observation. Interestingly, localized microcalcifications seemed to correlate with the clinical finding of thickening in two women with cancer in this series. The phenomenon might well be due to associated ductal carcinoma *in situ* (DCIS). Although in the present era most cases of DCIS are screen-detected, Sneige et al [7] found that up to 16% of symptomatic DCIS presented with thickening.

On the other hand, fibrosis was a consistent feature on histological examination of the palpable area of thickening. This supports the use of core biopsy or even open incisional biopsy in suspicious cases. Blindly-performed FNAC is often inadequate. Carrying out FNAC, especially under image guidance, is acceptable if a mass lesion is seen. In a number of cancer cases in this series, sclerosis was so marked that the tumour was masked on gross examination. This could probably account for the distinct clinical presentation as an area of thickening rather than a discrete lump. Radial scar-like features were found on the histology of one mastectomy specimen. Radial scar and complex sclerosing lesion are well known sclerosing lesions of the breast [8]. Despite the small number, the presence of two cases of invasive lobular carcinoma (mixed with invasive ductal carcinoma) might also be consistent with the well recognized, ill defined and infiltrating presentation, *i.e.* as palpable asymmetrical thickening, sometimes without mammographic abnormalities [9].

Most thickening in this series was found in the upper outer quadrant of the breast where there is the greatest bulk of breast tissue and where cancer is also most commonly found. However, the

preponderance of the area of thickening in the left breast, whether it is related to the non-dominant hand, remains unexplained.

Acknowledgment

The authors are grateful to Ms Joan Mow for carrying out the follow-up using the histopathology registry.

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