

Sclerosis of gross cysts of the breast: a three-year study

C. Gomes, N. Amaral, C. Marques, R. Borralho, C. F. de Oliveira

Department of Gynaecology, University of Coimbra Hospital (Portugal)

Summary

Breast cysts can be separated into two types: Type I cyst with a lining epithelium which shows apocrine metaplasia, and Type II cyst with an epithelium which is markedly attenuated or absent. The risk of subsequent breast cancer among patients with Type I cysts can be up to 4. The standard treatment is fine needle aspiration, but 20% of the cysts recur. Pharmacological treatment has been tried, which reduces size and volume, but has side-effects and a high recurrence rate post-treatment occurs. The objectives of this prospective study were to sclerose the cyst, induce its regression and prevent or reduce recurrence rate, with the administration of a sclerosing solution (Sclerovein®) within the cyst post-aspiration. Fifty-seven patients were followed in the study, 37 with Type I cysts and 20 with Type II cysts. At the end of six months all patients with Type II cysts had no detectable cyst. On the other hand, two patients still had a residual Type I cyst. At the end of three years our recurrence rate appears to be less than 2%, with one patient with a possible recurrence. No significant side-effects were observed. The use of Sclerovein® is a simple and safe alternative in the treatment of recurring cysts.

Key words: Gross cysts; Cysts, Breast, Sclerosis; Fine needle aspiration.

Introduction

The term benign breast disorders encompasses a heterogeneous group of lesions that clinically and radiographically span the entire spectrum of breast abnormalities. The system for classifying these benign breast lesions employed by Dupont and Page [1-3] separate the various components into three groups, with different relative risks for the subsequent development of breast cancer: nonproliferative lesions, proliferative lesions without atypia, and atypical hyperplasias.

Nonproliferative lesions include cysts, papillary apocrine change, epithelial-related calcifications, mild hyperplasia of the usual type, and fibroadenomas. Cysts are fluid-filled round to ovoid structures that vary in size from microscopic to grossly evident, derived from the terminal duct lobular unit. The epithelium usually consists of two layers: an inner (luminal) epithelial layer and an outer myoepithelial layer. In some cysts, the epithelium is markedly attenuated or absent (Type II cysts); in others, the lining epithelium shows apocrine metaplasia, characterized by granular eosinophilic cytoplasm and apical cytoplasmic protrusions (Type I cysts) [4-6].

Multiple studies have been performed to determine the constitution of the cystic fluid, but for this study the determination of the concentrations of sodium (Na^+), potassium (K^+), and dihydroepiandrosterone sulphate (S-DHEA) were of interest. The relation Na^+/K^+ [7] allows the separation of Type I apocrine cysts ($\text{Na}^+/\text{K}^+ < 3$) and Type II simple cysts ($\text{Na}^+/\text{K}^+ > 3$) [6]. S-DHEA is considered to be a marker of the metabolic activity of the apocrine cells of the lining epithelium, where a greater concentration reflects greater metabolic activity [8-13].

The risk of subsequent breast cancer among patients with nonproliferative lesions is not increased when compared to patients with 'normal' breasts, except those with gross cystic disease alone (relative risk 1.5), a risk which increases if there is a family history of breast cancer, if there are multiple cysts, and if these are of Type I (relative risk up to 4.0) [14-19].

Treatment of these cysts includes needle aspiration, but routine cytological analysis of the fluid is not recommended because of the poor diagnostic yield. However, recurrence of the cyst post-aspiration occurs in 10 to 20% of the patients [20]. Other alternatives have been tried, from dietetic restrictions to the use of therapeutic drugs (bromocriptine, danazol, tamoxifen), which showed a marked decrease in number and volume of the cysts during treatment, complicated only by the side-effects of these drugs. However, after suspension of the treatment, the cysts reappeared [21-23]. Other studies suggest that the use of pneumocystography reduces the incidence of recurrence [24-26]. According to the American College, if a cyst is needle-aspirated two or three times and recurs, it should be surgically removed. But what should be done if there are multiple cysts? There is no therapeutic alternative for the group of patients that have multiple or recurrent cysts.

Objectives

The objective of this study was to induce sclerosis of the gross cysts of the breast with a detergent sclerosing solution (Sclerovein®) composed of polidocanol (10 mg) associated with ethanol (50 mg) in a 1% concentration. Our intention was to collapse the cystic formation, induce its regression, prevent its recurrence, and perform a three-year follow-up post-sclerosis.

Revised manuscript accepted for publication February 8, 2002

Methods

A prospective study was performed at the Gynaecology Department of the University of Coimbra Hospital, Portugal. Patients with recurrent gross cysts with ultrasound and mammograms that showed no suspicious images of malignant lesions were accepted. Under ultrasound control, the cyst was completely aspirated and, without removal of the needle, the sclerosing solution (Sclerovein® 1%) was administered in a volume that was half of the aspirated volume, up to a maximum of 3 cc. The colour and volume of the aspirated cysts were registered, the fluid sent for cytological analysis and dosage of Na⁺, K⁺, and S-DHEA. Ultrasound controls were performed at the first, third, and sixth months post-sclerosis. At the 12th and 36th month post-sclerosis ultrasound and mammography controls were performed. All patient complaints were registered, as well as all anomalies detected on breast evaluation by the examiner.

No control group comparison was performed since the patients all presented recurrent cysts.

Results

Sixty-two patients were admitted to this prospective study, with an average age of 44.6 ± 7.9 years; the youngest patient was 16 years of age and the oldest was 68. Of these, five were eliminated from the study (2 with multiple cysts which prevented follow-up of the sclero-

Age of the Patients

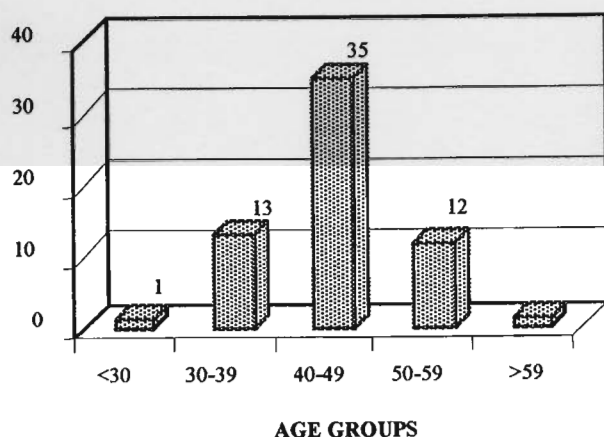


Figure 1. — Number of patients in each age group.

Cysts and the Breast

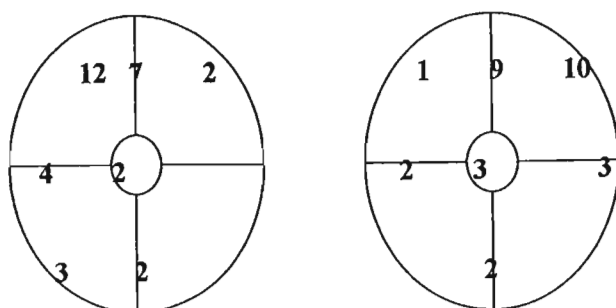


Figure 2. — Number of cysts in each breast quadrant.

TYPE I CYSTS: EVOLUTION POST-SCLEROSIS

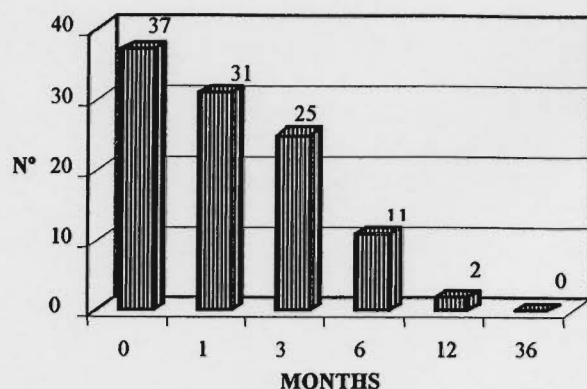


Figure 3. — Number of patients with Type I cysts after sclerosis in each month of observation.

TYPE II CYSTS: EVOLUTION POST-SCLEROSIS

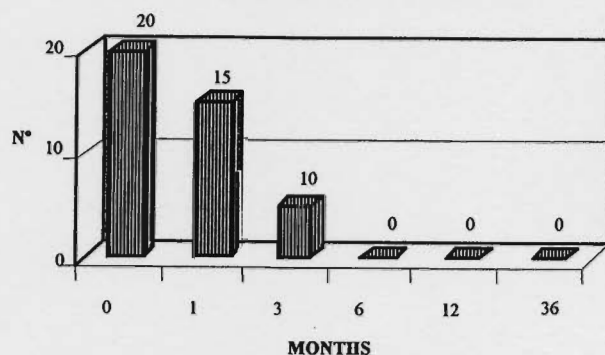


Figure 4. — Number of patients with Type II cysts in each month of observation.

sed cyst, 2 abandoned the study, and 1 had a large irregular cyst which prevented the full aspiration of the fluid). Figure 1 shows the age distribution, where 64.5% of the patients were 40 or older. Figure 2 shows the distribution of the gross cysts according to their localization in the breast. The preferential site of the cysts was the upper outer quadrant of both breasts. The average diameter of the cysts was 25.02 ± 10.33 mm, with a minimum of 6 mm and a maximum of 60 mm. The average volume aspirated was 6.0 ± 11.1 cc (0.6-30), and the volume of the detergent solution administered was 1.7 ± 0.9 cc (0.3-3).

Table 1 presents the colours of the cystic fluid. None of the samples showed a haemorrhagic colour, and after aspiration, no residual mass was detected. Table 2 shows the cytological analysis of the fluid, where the principal diagnosis was the presence of a 'cyst', followed by 'ductal ectasia' in 13 cases. Due to the necessity of biochemical analysis, in seven cases the fluid was insufficient for diagnosis.

Table 3 shows the concentrations of the ions and of S-DHEA of the 57 patients that concluded this investigation. Thirty-seven patients had Type I cysts and 20 patients had Type II cysts. In Type I cysts, there was a

Table 1. — *Colour of the cystic fluid.*

Colour	No.
Yellow	24
Greenish	21
Brown	17

Table 2. — *Cytological analysis of the cystic fluid.*

Cytology	No.
Cyst	42
Ductal ectasia	13
Insufficient	7

Table 3. — *Concentrations of sodium, potassium, and dehydroepiandrosterone sulphate.*

Cyst	Na ⁺	K ⁺	S-DHEA	No.
Type I	33.6 ± 19.8	115.5 ± 24.8	98.7 ± 72.9	37
Type II	133.6 ± 10.1	7.7 ± 7.3	10.5 ± 11.8	20

Table 4. — *Diameter in mm of the gross cysts at the different control periods.*

Diameter	TYPE I	TYPE II
Initial	26.4 ± 9.2 [10-50]	22.6 ± 11.6 [11-60]
1 st month	11.6 ± 6.8 [0-28]	7.4 ± 6.3 [0-26]
3 rd month	6.0 ± 5.2 [0-15]	1.2 ± 2.9 [0-12]
6 th month	1.9 ± 3.2 [0-10]	0 ± 0 [0-0]
12 th month	0.2 ± 1.1 [0-6]	0 ± 0 [0-0]
36 th month	0 ± 0 [0-0]	0 ± 0 [0-0]

Table 5. — *Patient complaints.*

Complaints	During introduction of Sclerovein®	Follow-up
Mastalgia	2	6
Burning sensation	5	7

significantly higher concentration of S-DHEA ($p = 0.002$), which revealed a much higher metabolic activity of these apocrine cysts.

Post-sclerosis evolution can be seen in Figure 3 (Type I) and Figure 4 (Type II). Due to the different metabolic activity, a greater resistance to the reduction in diameter of the cysts can be observed in Type I, where at the end of one year two patients still had cysts. On the other hand, Type II cysts disappeared at the end of six months.

Table 4 shows the diameter of cysts at the different control periods. Again, we note the behaviour of the two types of cysts. Type I has a gradual decrease in diameter, whereas Type II rapidly decreases in diameter. Table 5 shows the patient complaints.

Mastalgia and a local 'burning sensation' were the only two side-effects detected, and none of these were signifi-

cant. Only one patient used an anti-inflammatory drug (nimesulide, 1 pill), and two patients applied ice locally for a very short period of time.

Conclusion and Discussion

The majority of the patients were in the age group 40-49 years which coincides with other studies [4, 27]. The preferential locations of the cysts were in the upper-outer quadrants of the breasts but, unlike the references made in the literature consulted, we did not observe the left breast as the preferential location. The cystic fluid was submitted to cytological analysis and, as is suggested in the literature, no anomalies were detected [28-30].

The evolution of the sclerosed cysts is different when we compare Type I cysts with Type II. In patients with Type I, there is a progressive reduction in size and number of patients with cysts. At the sixth month of observation, 11 of the 37 patients still had a remaining cyst, although the average diameter was 1.9 mm. At the 12th month only two patients had a cyst with a 0.2 mm diameter. On the other hand, patients with Type II cysts had no remaining cysts at the sixth month observation. In both cases there were no recurrent cysts observed at the 36th month observation. However, in the Type I patient group, at the 36th month evaluation, three patients had a cyst in the same quadrant of the sclerosed cyst. In two cases we cannot assume that it is a recurrence of the original cyst since the present location of the cyst is not equal to the original description (as measured by sonogram as the distance from the areola and the union of the respective quadrants). But in the third case, the location is compatible with the original cyst, which, being a recurrence, provides us with a recurrence rate of less than 2%.

Sclerovein® is a product largely used in the sclerosis of veins where it is safely employed. In this study the use of Sclerovein® proved to be safe and showed no major side-effects. The only side-effects observed were mastalgia and a burning sensation, none of which required any type of medication to relieve the pain.

For the one patient that had the irregular Type I cyst, the detergent product was administered (3 cc) and the cyst was surgically removed six months later. The pathologist's report showed no atypical cells present in the cyst's inner epithelium, even though a reduction in the size of the cyst was registered. Another patient with multiple cysts was submitted to a subcutaneous mastectomy and the pathologist's report showed no cellular damage in the area of the sclerosed cyst.

The absence of a cyst and of a residual lesion allows for a clear imageable, vision of the breast, so that an infra-clinical suspicious image may be detected earlier.

In our study breast cancer was detected in one patient with a Type I cyst in the breast contralateral to the sclerosed cyst.

In conclusion we can affirm that the sclerosis of recurrent cysts with Sclerovein® is a safe procedure in that it has no significant side-effects and prevents recurrence of all cysts post-sclerosis.

References

- [1] Dupont W. D., Page D. L.: "Risk factors for breast cancer in women with proliferative breast disease". *N. Engl. J. Med.*, 1985, 312, 146.
- [2] Page D. L., Dupont W. D., Rogers L. W. *et al.*: "Atypical hyperplastic lesions of the female breast: a long-term follow-up study". *Cancer*, 1985, 55, 2698.
- [3] Consensus Meeting: "Is 'fibrocystic disease' of the breast pre-cancerous?". *Arch. Pathol. Lab. Med.*, 1986, 110, 171.
- [4] Haagensen C. D., Bodian C., Haagensen D. E.: "Breast Carcinoma: Risk and Detection". *Philadelphia WB Saunders*, 1981, 55.
- [5] Azzopardi J. B.: "Problems in Breast Pathology". *Philadelphia WB Saunders*, 1979, 92.
- [6] Dixon J. M., Miller W. R., Scott W. N., Forrest A. P.: "The morphological basis of human breast cyst populations". *Br. Med. J.*, 1984, 288, 275.
- [7] Dixon J. M., Miller W. R., Scott W. N.: "Subpopulations of human breast cyst fluid as defined by sodium, potassium and dehydroepiandrosterone content". *Arch. Surg.*, 1982, 357, 195.
- [8] Dogliotti L., Orlandi F., Torto M. *et al.*: "Cations and dehydroepiandrosterone sulphate in cyst fluid of pre- and menopausal patients with gross cystic disease of the breast. Evidence for the existence of subpopulations of cysts". *Eur. J. Cancer Clin. Oncol.*, 1986, 22, 1301.
- [9] Miller W. R., Dixon J. M., Scott W. N., Forrest P. M.: "Classification of human breast cysts according to electrolyte and androgen conjugate composition". *Clin. Oncol.*, 1983, 9, 227.
- [10] Secreto G., Recchione C., Bellerini P. *et al.*: "Accumulation of active androgens in breast cyst fluids". *Eur. J. Cancer*, 1991, 27 (1), 44.
- [11] Lai L. C., Ghilchic M. W., Shaikh N. A. *et al.*: "Relationship between epidermal growth factor and dehydroepiandrosterone and its sulphate in breast cyst fluid". *Br. J. Cancer*, 1988, 60 (3), 320.
- [12] Zanardi S., Valenti G., Torrisi R. *et al.*: "Identification of breast cyst subpopulations: biochemical and morphological features". *Cancer Detect. Prev.*, 1991, 15 (4), 273.
- [13] Nahoul K., Kottler M. L.: "Relationships between androgen and estrogen sulfates in breast cyst fluid". *Clin. Chem. Acta*, 1992, 31, 209 (3), 179.
- [14] Leis H. P.: "Gross breast cysts: significance of apocrine type, identification by cyst fluid analysis, and management". *Breast Dis.*, 1989, 1, 277.
- [15] Roberts M. M., Jones V., Elton R. A. *et al.*: "Risk of breast cancer in women with a history of benign disease of the breast". *Br. Med. J.*, 1984, 288, 275.
- [16] Black M. T., Barklay B., Cutler B. *et al.*: "Association of atypical characteristics of benign breast lesions in the subsequent risk of breast cancer". *Cancer*, 1972, 29, 338.
- [17] Cancer Committee of the College of American Pathologists: Consensus Meeting: is "fibrocystic disease" of the breast precancerous?. *Arch. Pathol. Lab. Med.*, 1986, 110, 171.
- [18] Ciatto S., Biggeri A., Rosselli T. M. *et al.*: "Risk of breast cancer subsequent to proven gross cystic disease". *Eur. J. Cancer*, 1990, 26, 5, 555.
- [19] Devitt J. E., To T., Miller A. B.: "Risk of breast cancer in women with breast cysts". *Can. Med. Assoc. J.*, 1992, 1, 147, 45-9.
- [20] Dixon J. M., Scott W. N., Miller W. R.: "Natural history of cystic disease: the importance of cyst type". *Br. J. Surg.*, 1985, 72, 1990.
- [21] Mauvais-Jarvis P., Kuttann F.: "Benign breast disease". *Curr. Ther. Endocrinol. Metab.*, 1994, 5, 364-70.
- [22] Hockenberger S. J.: "Fibrocystic breast disease: every woman is at risk". *Plast. Surg. Nurs.*, 1993, 13(1), 37.
- [23] Hurst J. L., Mega J. F., Hogg J. P.: "Tamoxifen-induced regression of breast cysts". *Clin. Imaging.*, 1998, 22(2), 95.
- [24] Dyreborg U., Blichert-Toft M., Boegh L., Kiaer H.: "Needle puncture followed by pneumocystography of palpable breast cysts: a controlled clinical trial". *Acta Radiol.*, 1985, 26, 277.
- [25] Ikede D. M., Helvie M. A., Adler D. D. *et al.*: "The role of fine needle aspiration and pneumocystography in the treatment of impalpable breast cysts". *AJR*, 1992, 158, 1239.
- [26] Tabar L., Pentek Z., Dean P. B.: "The diagnostic and therapeutic value of breast cyst puncture and pneumocystography". *Radiology*, 1981, 41, 659.
- [27] Haagensen C. D. Gross cystic disease. In Haagensen C. D. (ed): "Diseases of the Breast". 3rd ed. Philadelphia: W.B. Saunders, 1986, 250.
- [28] Ciatto S., Cariaggi P., Bularesi P.: "The value of routine cytologic examination of breast cyst fluids". *Acta Cytol.*, 1987, 31, 301.
- [29] Smith D. N., Kaelin C. M., Korbin C. D. *et al.*: "Impalpable breast cysts: utility of cytologic examination of fluid obtained with radiologically guided aspiration". *Radiology*, 1997, 204(1), 149.
- [30] Czernobilsky B.: "Intracystic carcinoma of the female breast". *Surg. Gynecol. Obstet.*, 1967, 127, 93.

Address reprint requests to:
 C. GOMES, M.D.
 Hospitais da Universidade de Coimbra
 Servico de Ginecologia
 Praceta Prof. Mota Pinto
 Coimbra 3000-075 (Portugal)