



Sclerosing Adenosis

Paul E. Preece, M.D., F.R.C.S.(Edin.), F.R.C.S.(Engl.)

University Department of Surgery, Ninewells Hospital and Medical School, Dundee, Scotland, United Kingdom

The literature regarding sclerosing adenosis has been reviewed. The pathological and radiological aspects of this benign breast condition have been emphasized since they influence clinical practice.

Features of 43 patients diagnosed as having sclerosing adenosis have been reported. Cancer was suspected on mammography in 17, and 25 experienced breast pain. Thus, the lesion is important both as a mimic of malignancy and as a cause of mastalgia. The clinical and radiological features allow the condition to be suspected before biopsy, in which circumstance paraffin histology is greatly preferable to frozen section.

The benign disorder of the breast known as sclerosing adenosis is relatively uncommon. It has pathological, clinical, and radiological significance which will increase in importance as mammography is used more in investigating breast symptoms and screening for breast cancer.

Background

Sclerosing adenosis is a histopathological term referring to an entity of varying complexity which can be observed and recognized on microscopic examination of sections of human breast tissue. In 1923, a description of the condition was published in France [1], but not referred to as a form of adenosis since that term (which was probably coined by the Edinburgh pathologist, Harvey) was not widely publicized until 1933 [2]. Characteristically, the proliferating epithelial cells of the breast lobules are surrounded by a mass of fibers which the early observers regarded as myoepithelium [3]. A clear pathological description of sclerosing adenosis was published in 1968 [4]. Classically, the proliferating fibrous or myoepithelial tissue is disposed in whorls which distort the normal architecture of the lobules, the epithelium of which often shows hyperplasia [5, 6] (Fig. 1).

Pathological Implications of Sclerosing Adenosis

In 1938, the difficulty of distinguishing microscopically between carcinoma and sclerosing adenosis was demonstrated dramatically when, at a conference, 90% of pathologists who were shown the benign condition called it malignant [7]. The differ-

ential diagnosis has been shown to be particularly difficult to determine by frozen section [8]. Macroscopically, the hyper-vascularity and friability of sclerosing adenosis make it impossible to distinguish this from carcinoma. Microscopically, there are several features occasionally seen in sclerosing adenosis which can cause confusion with cancer. Thus, sclerosing adenosis may contain epithelial cells which appear to infiltrate—"pseudo infiltration" [9, 10]. These cells may surround neurones, giving the impression of perineural infiltration. In 1,000 consecutive cases of histopathologically diagnosed sclerosing adenosis, 20 showed neural or perineural invasion [11]. An independent series of 316 consecutive unselected benign mammary lesions revealed 4 examples of epithelial invasion of nerves or perineural spaces, and this occurred in 3.8% of cases of sclerosing adenosis [6].

In addition to neural and perineural invasion in sclerosing adenosis, 6 examples of infiltration of blood vessels with nonmalignant breast tubules have been described in a sequential series of 50 cases studied [12]. Eusebi and Azzopardi emphasize that there were no microscopic features, either in the overall tissue architecture or the individual cells, to suggest malignancy. Their benign nature is reinforced by the fact that, on follow-up of the affected patients, none developed carcinoma. The benign nature of sclerosing adenosis is not questioned in the papers cited above, many of which emphasize those features of it which could result in its being mistaken as malignant. The fact that the tissue planes invaded are the same as those infiltrated by malignant cells adds to the diagnostic difficulty. Electron microscopy has the ability to distinguish these lesions by virtue of the fact that infiltrating cells of ductal carcinoma do not have intact basement membranes [13]. This technique may be of practical value in differentiating these 2 lesions. Clearly, it can only be applied to fixed tissue, and is only likely to be available in specialized centers.

The Clinical Significance of Sclerosing Adenosis

Although sclerosing adenosis has been chiefly of concern to pathologists, clinical features have been described. Foote and Stewart [7] considered that it presented in 1 of 2 forms—palpable discrete tumors and minute foci found only incidentally by the pathologist. In their experience, the discrete form occurred most commonly in women between 20 and 30 years of

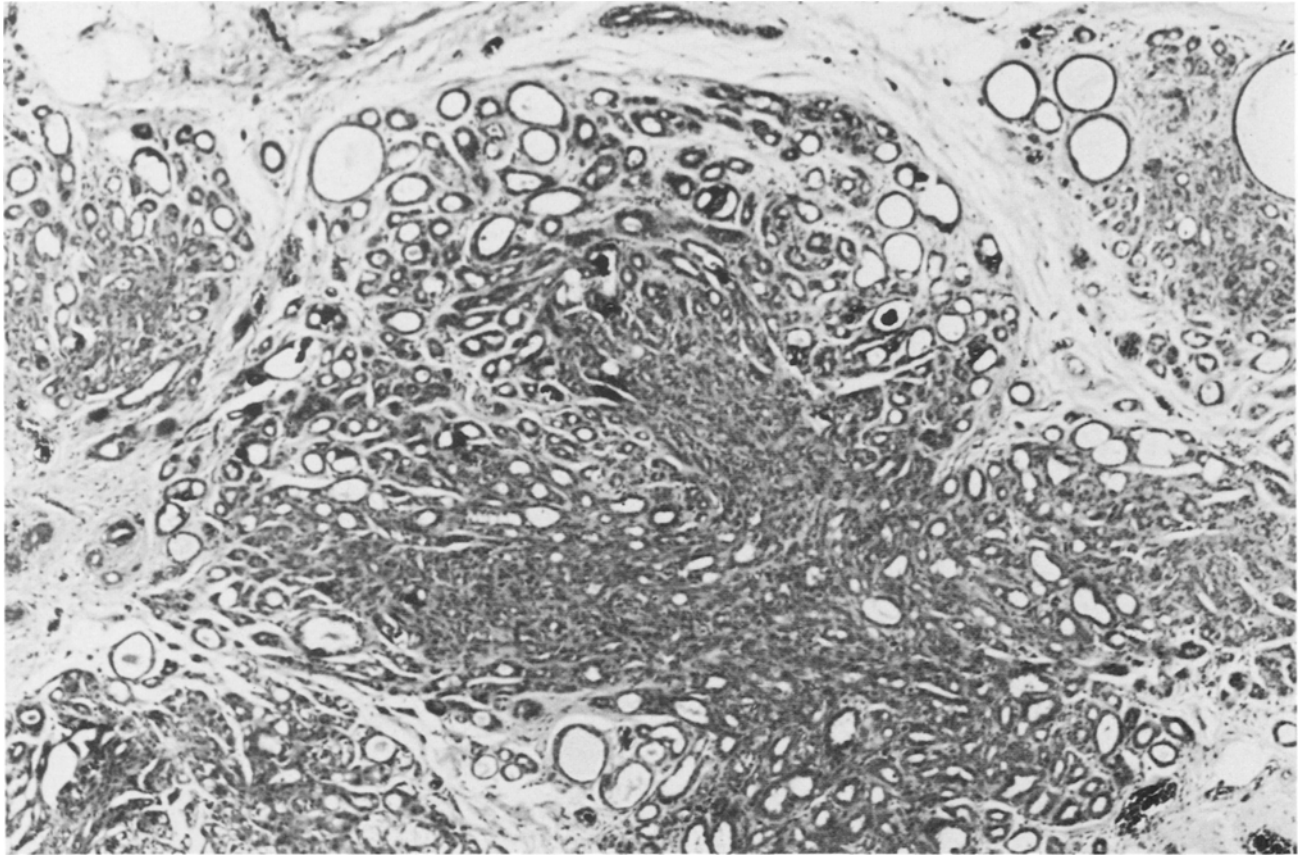


Fig. 1. Photomicrograph of sclerosing adenosis showing whorls of sclerosis distorting the normal architecture (H. & E. $\times 4$ objective magnification $\times 65$).

age, in whom the palpable lump was freely mobile with no accompanying skin changes. The incidental foci were 20–30 times more common than the discrete ones. Urban and Adair [8] found the disorder in women between 20 and 50 years of age, their cohort having a mean age of 31 years. Pain and tenderness was experienced by 45% of their patients with sclerosing adenosis. Heller and Fleming [14] found this to make up 2% of all lesions seen at their breast clinic. The average age of their affected patients was 34 years. Sandison, in a study of surgically removed breast tissue, looking especially for sclerosing adenosis [15], confirmed that it is much more frequently found incidentally than as a discrete palpable entity. In a prospective study of 232 patients presenting with breast pain, sclerosing adenosis was present at the location of this in 5% [16]. Sclerosing adenosis was the most frequent single benign lesion masquerading as subclinical breast cancer in a series of 24 cases published in 1977 [17]. There were 9 cases of sclerosing adenosis, 9 of invasive carcinoma, and 2 of in situ carcinoma, all in symptomatic patients. These 2 series [16, 17], led us to review all of our patients diagnosed as having sclerosing adenosis.

The Criteria for Diagnosis of Sclerosing Adenosis

The diagnosis was made by histology or mammography (or both). The pathological criteria we used to define sclerosing

adenosis were those described above, outlined by McDivitt and associates [4] and summarized by Davies [6] as nodular epithelial lesions in which fibrosis or myoepithelial proliferation was associated with a stellate or whorled distortion of the normal type of lobular pattern (Fig. 1). We regarded 1 of 4 mammographic signs to indicate the presence of sclerosing adenosis in the breast [18]. The first was distortion of breast architecture of a type very similar to that caused by a small cancer (Fig. 2). The second sign consisted of fine, smooth calcifications scattered widely throughout the breast tissue, usually bilaterally (Fig. 3). The third was the presence of a few microcalcifications, up to 10 in number, arranged in a small localized group (Fig. 4). These may occur alone or in association with the widely scattered type of calcification. They are radiologically indistinguishable from malignant microcalcification [19] (such that biopsy is mandatory). The fourth change was a combination of architectural distortion and microcalcification, which was rare in our experience.

Patients with Sclerosing Adenosis

The diagnosis of sclerosing adenosis was made by histology or mammography or both in 43 patients. These are subdivided into 2 groups: A and B. In group A, the diagnosis was made first by histology. Group B patients were diagnosed primarily by mammography.

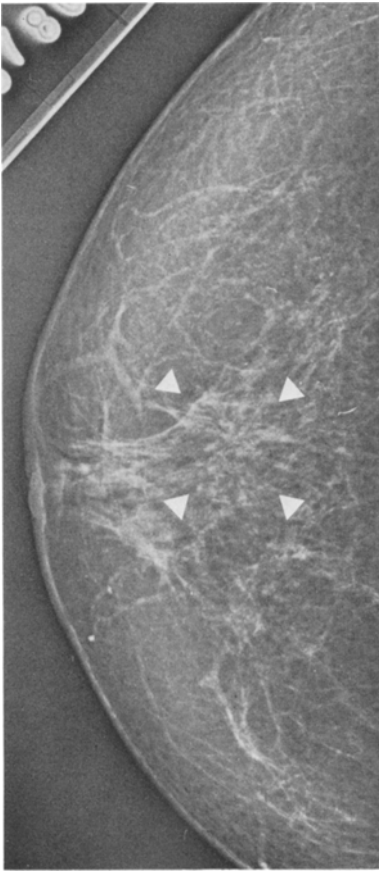


Fig. 2. A mammogram showing distortion of breast architecture caused by sclerosing adenosis but similar to that caused by a small cancer.



Fig. 3. A mammogram showing fine, smooth calcifications scattered widely throughout the breast tissue in a case of sclerosing adenosis.

Group A was comprised of 28 patients who had breast biopsies. In 8, this was for mammographic features suggestive or diagnostic of cancer but without any palpable mass. Accurate localization of the site of mammographic abnormality was achieved by radiological control. Physical as well as radiological signs suspicious of cancer were present in 9. The other 11 had discrete palpable masses which were biopsied on clinical grounds alone, there being no significant radiological signs.

Group B consisted of 15 patients who had a diagnosis of sclerosing adenosis on mammography. For clinical reasons, 7 of these had tissue diagnoses. These supported the radiological diagnosis in 3, were equivocal in 3, and showed no evidence of sclerosing adenosis in one. Table 1 shows the age and the incidence of pain in these subjects.

Of 28 patients with unequivocal histopathological diagnosis of sclerosing adenosis, 16 (57%) experienced mastalgia. In this series, 6 (67%) of 9 patients diagnosed preoperatively as having sclerosing adenosis on mammogram had this confirmed at biopsy. Adjusting for possible radiological overdiagnosis, there are 23 of 38 cases of sclerosing adenosis, 60% of the overall series, who had significant mastalgia.

Clinical features were documented for half of the patients who had breast pain, since these were studied prospectively. Their ages ranged from 24 to 64 years, with a mean of 36 years. Nine were premenopausal. Their ages at menarche ranged from



Fig. 4. Small localized group of microcalcifications magnified by 5.

11 to 17 years. Three had been on oral contraceptives. Two were nulliparous. Of the 9 parous patients, only 3 had breast fed for more than 4 months. The pain had been present for 2 years or more in 8 and for less than 6 months in the other 3. In 5 patients, the pain had a definite relationship to the menstrual cycle, being worse premenstrually. Pain was left-sided in 10 and

Table 1. Age and incidence of breast pain in patients with sclerosing adenosis.

Group	No.	Mean age (yr)	Age range (yr)	Mastalgia
A	28	37	24-71	16
B	15	44	30-53	11
Total	43	40	24-71	27

right-sided in 3, two women experiencing it bilaterally. Radiation of the pain to the lateral chest wall, neck, and back occurred in 4.

Seven women described their symptom as a pain, 3 as an ache, and 1 as a tenderness to the touch. Half of the women used an adjective describing a "sharp" quality—for example, pricking or stabbing. In 7 patients, the pain was intermittent, but for the other 4 it was continuous, lasting months at a time in 2 patients. Sleep loss occurred frequently in 2 patients and occasionally in 4. Without exception, contact, pressure, and activities resulting in breast movement exacerbated symptoms. There were no consistent methods of obtaining relief. On examination, half of the group had pendulous, obese breasts. Four had diffuse nodularity, whereas the breast tissue of the other 7 was smooth to palpation.

Discussion

The radiological difficulty of distinguishing between this benign lesion and cancer is emphasized by the present study. Thirty-eight percent of cases were either suspected of or diagnosed definitely as being malignant, usually because of the pattern of calcification. The calcification accompanying sclerosing adenosis is characteristically of the fine type, very much as it is seen in cancer. In a specific study of these calcifications, Millis and associates [19] could not differentiate between those of cancer and sclerosing adenosis. This raises the possibility that similar processes occur in both lesions. When, on x-ray, these calcifications are few in number and localized to a small area, the appearances are indistinguishable from malignant microcalcifications [18]. When, as is so often the case, no lump is palpable, the radiologist, recognizing that it is equally possible to make a false-positive diagnosis as a false-negative one, almost always advises that the pathologist be the referee.

The significance of sclerosing adenosis to the histopathologist and radiologist is well established. Currently, the clinician rarely anticipates this diagnosis [20]. The recognition that some 60% of cases of sclerosing adenosis are painful will make it possible to think of this diagnosis preoperatively, and the fact that 35% of suspected subclinical cancers prove to have this condition [17] make it important for the clinician to do so. The patients and laboratory can be prepared for urgent (48-72 hours) paraffin histology and the chance of misdiagnosis is minimized [21].

This study has shown that mastalgia was a symptom in 60% of patients in whom sclerosing adenosis was identified in the symptomatic breast. Among his series of consecutive unselected cases of benign breast lesions, Davies found sclerosing adenosis to be the one most frequently found to contain neural invasion by mammary epithelial cells [6], a feature observed

independently by Ackerman [9], and Taylor and Norris [11] as well as by Eusebi and Azzopardi [12]. Is the direct invasion ("pseudoinfiltration") [4] of nerve tissue the cause of pain in patients with sclerosing adenosis?

Conclusions

The benign lesion, sclerosing adenosis, mimics carcinoma on microscopy [22], and is often indistinguishable from cancer on mammograms [23, 24]. Pain is a symptom in 60% of cases of sclerosing adenosis that are diagnosed in practice. This may enable the lesion to be suspected preoperatively when paraffin rather than frozen section histology is more certain and, therefore, more satisfactory, as advocated 40 years ago [8].

Résumé

L'adénose scléreuse a fait l'objet d'une analyse de la littérature. Les aspects histologiques et radiologiques de cette affection bénigne du sein, si importants pour la pratique clinique, sont décrits.

Les dossiers de 43 patientes ayant une adénose scléreuse du sein sont exposés. Un cancer a été suspecté sur l'aspect mammographique chez 17 patientes; 25 patientes se plaignaient de mastalgies, soulignant la fréquence avec laquelle cette lésion peut simuler une maladie maligne ou donner lieu à une symptomatologie douloureuse. Les données cliniques et radiologiques permettent de soupçonner le diagnostic avant de pratiquer la biopsie. La lecture des coupes fixées par la paraffine est préférable à l'examen extemporané.

Resumen

Se revisó la literatura sobre adenosis esclerosante. Los aspectos patológicos y radiológicos de esta entidad mamaria benigna son resaltados, en la medida que influyen sobre la práctica clínica.

Se informan las características de 43 pacientes con el diagnóstico de adenosis esclerosante. Se sospechó la presencia de cáncer en la mamografía en 17 casos, y 25 experimentaron dolor mamario. Esto indica que la lesión es importante tanto como una mímica de neoplasia maligna, así como causa de mastalgia. Las características clínicas y radiológicas permiten sospechar la presencia de esta lesión con anterioridad a la biopsia, para la cual definitivamente se prefiere la histología por cortes de parafina sobre los cortes por congelación.

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