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An evaluation of the preoperative diagnosis and management of cystosarcoma phyllodes

H C UMPLEBY MS FRCS
Lecturer in Surgery

I MOORE MRCPath
Consultant Pathologist

G T ROYLE MChir FRCS
Consultant Surgeon

P B GUYER MD FRCR
Consultant Radiologist

I TAYLOR MD FRCS
Professor of Surgery

University Surgical Unit and Departments of Histopathology and Radiology, Royal South Hants Hospital

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Summary

Cystosarcoma phyllodes is a rare tumour of the breast which is notoriously difficult to diagnose accurately preoperatively. In this review we report the clinical, imaging and histopathological features of 20 patients who have presented in our Centre over a 10-year period.

Introduction

In 1838 Muller reported a fleshy tumour of the breast which contained cystic spaces and the surface of which had a leaf-like configuration. He descriptively named the mass cystosarcoma phyllodes (CSP). It is a rare lesion accounting for less than 0.5% of all breast tumours *(1)* and 2.5% of fibroepithelial tumours *(2)*. Preoperative diagnosis, although difficult, is valuable in allowing correct primary surgical treatment. After surgery, accurate histopathology of excised specimens is essential to distinguish between fibroadenoma, benign CSP, and the 10% of tumours which might develop local recurrence or metastatic disease *(3–6)*.

We report the clinical, imaging and histopathological features of 20 women with CSP.

Patients and methods

All women with histologically confirmed CSP and who presented to the Southampton Hospitals between 1977 and 1987 were included in the study. Patient details were obtained from medical records. X-ray mammography was performed with a Senograph® mammogram unit, using Kodak MIN R film; sonomammography was performed on a Phillips B 7100 static B-scan ultrasound unit using a 7.5 MHz transducer. All X-ray and sonomammograms were reviewed by a single radiologist (PBG). Similarly, all histopathological and cytological material was examined by a single pathologist (IM).

Correspondence to: Professor I Taylor, University Surgical Unit, Centre Block, Southampton General Hospital, Southampton SO9 4XY

Results

CLINICAL

There were 20 women with histologically confirmed CSP. Their median age was 47 years (range 18–71 years). A unilateral breast mass was the presenting feature in all cases. In four patients with large tumours there was associated discomfort. The median duration of the mass prior to consultation was 2 months (range 0.5–128 months). In 16 cases the tumour was completely mobile but in four there was minor skin tethering but no ulceration. In five patients with large tumours prominent superficial veins were noted. The mass was considered solid in 17 patients but in three cases cystic areas were confirmed by needle aspiration. Maximum tumour diameter varied enormously with a median of 5.2 cm (range 1.0–13.5 cm), being greater than 10 cm in five patients and 2 cm or less in six cases.

The clinical impression was correct in only three patients, all of whom had tumours of 10 cm maximum diameter or greater. In six patients the diagnosis was fibroadenoma, in 10 carcinoma, and in the remaining case the mass was considered benign but of unknown nature.

Clinical lymphadenopathy, considered to indicate malignant involvement, was detected in two patients. In later cases subsequent axillary dissection showed no nodal involvement.

IMAGING

Imaging was available in 14 patients. Ten underwent X-ray mammography; one further tumour was too large to be X-rayed (Fig. 1), and three patients were too young to undergo X-ray mammography. Sonomammography was performed in 11 patients. With X-ray mammography, eight of the ten masses were well defined and tended to be lobulated; two were poorly defined in part. Coarse calcifications were present in three of the tumours (Fig. 2). Sonomammography revealed a homogeneous echo-containing mass in nine patients (Fig. 3*a*); one mass

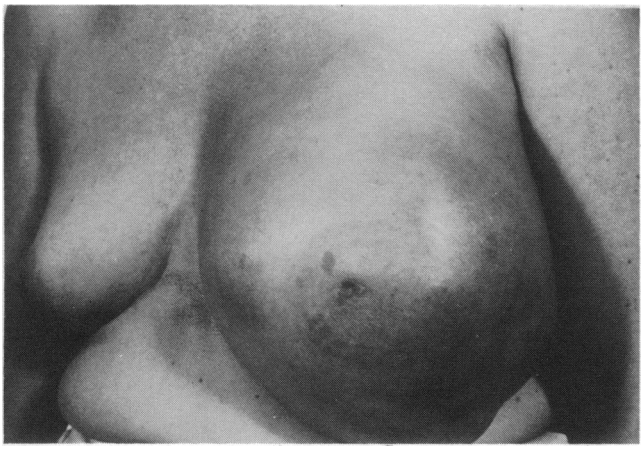


FIG. 1 Massive tumour of left breast which was too large for mammography.

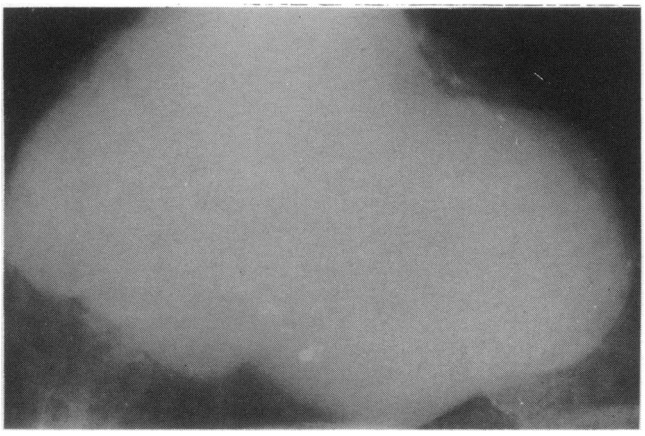
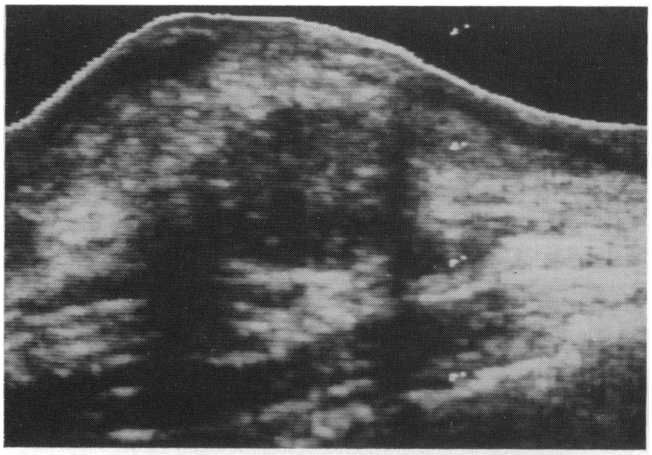
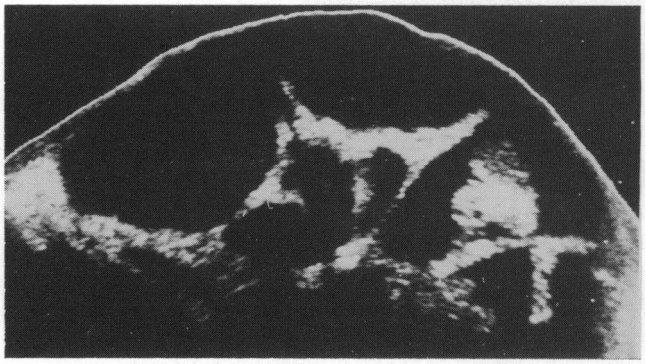


FIG. 2 X-ray mammography showing large lobulated mass occupying most of the breast tissue with coarse calcifications in the deeper portion of the tumour.



(*a*)



(*b*)

FIG. 3 *(a)* Ultrasound mammography showing a well-defined mass with fairly regular internal echoes—indistinguishable from a fibroadenoma. *(b)* Ultrasound mammography showing a massive tumour occupying the entire breast; there are large cystic spaces containing low-level echoes, into which project polypoid tumour masses.

was homogeneously echo poor, and one mass had a mixed internal echo pattern. Five tumours showed evidence of fluid spaces within the mass; in three of these there were small, round or cleft-like spaces (Fig. 3*b*) but in two the cystic spaces were massive, with polypoid processes projecting into the fluid spaces in one tumour (Fig. 4).

A diagnosis of cystosarcoma was suggested in seven of these tumours; four were diagnosed as fibroadenoma (one giant fibroadenoma) one was considered possibly malignant, and one was considered to be of indeterminate nature.

CYTOLOGY AND HISTOPATHOLOGY

Fine needle aspiration cytology was performed in 12 patients and in all cases demonstrated sheets of benign epithelial cells and fragments of myxoid stroma. Bipolar cells were seen in six aspirates, being present in abundance in five. Clusters of apocrine cells were also observed in four aspirates. The correct diagnosis of CSP was made in only one case.

In five patients a preoperative biopsy using the Trucut® needle was performed to establish a diagnosis. In only one case did this provide the correct diagnosis. Diagnosis in the remaining cases included fibroadenoma, chronic inflammation, papillary cystadenocarcinoma and normal tissue.

The histopathological review of all 20 cases showed 14 benign phyllodes tumours and six tumours which fulfilled the criteria for malignancy described by Azzopardi *(7)*; namely, an infiltrating tumour margin, stromal overgrowth, cellular atypia of stromal cells and three or more mitoses per 10 high power fields.

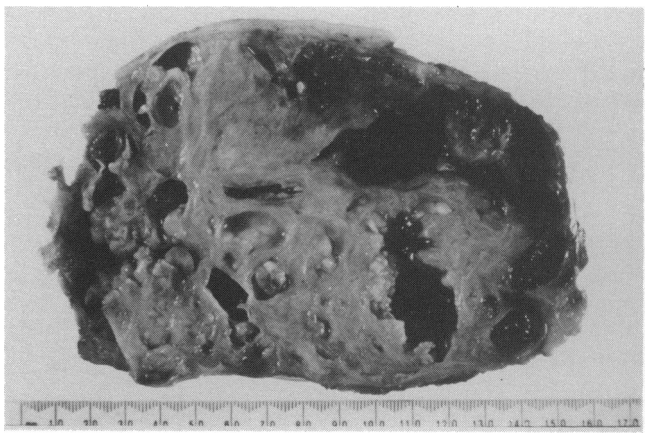


FIG. 4 Macroscopic appearances of tumour in Fig. 3*(b)* showing large spaces into which project polypoid tumour masses.

There was a mild increase in stromal cellularity in 12 cases of benign CSP and only in two cases was a moderate degree of cellularity observed. This finding contrasted with the appearances of the malignant tumours in which marked stromal hypercellularity was seen in two and moderate cellularity in four cases.

The highest mitotic rate noted in the stromal cells of benign tumours was two mitoses per 10 high-power fields, whereas in the group of malignant tumours the mean mitotic count was nine mitoses per 10 high-power fields (with a range from 6 to 12 mitoses per 10 high-power fields).

Stromal degenerative changes including myxoid change and hyalinization were more prominent in benign than in malignant tumours. However, highly specialised stroma such as osseous metaplasia was only observed in one case of malignant CSP.

TREATMENT

Wide excision alone was performed in 14 patients and mastectomy in six. In three patients with enormous tumours (maximum diameter >20 cm) wide excision was not feasible; on histology one of these patients was found to have a malignant tumour. In two patients with moderate sized lesions (5.5 cm×10 cm maximum diameter) an initial excision biopsy discovered an incompletely excised malignant CSP and therefore mastectomy was deemed advisable. In the final patient a large tumour (15 cm diameter) was considered to be a malignant carcinoma but no histological proof was obtained. After an unsuccessful course of chemotherapy the patient underwent mastectomy, the histology of which showed a benign CSP.

Discussion

Cystosarcoma phyllodes is a fibroepithelial tumour unique to the breast. It is of uncertain origin. A long history of a lump and the finding of possible remnants of fibroadenoma imply development of CSP from fibroadenoma in some cases *(8)*, in other cases the tumour appears to arise spontaneously. Although aptly named by Muller *(9)* on morphological appearance this title is generally considered unsatisfactory. Cysts are not always present and the majority of these tumours have an entirely benign clinical course following complete excision, in spite of some histological features of malignancy. Likewise the commonly used alternative term giant fibroadenoma is unsatisfactory as CSP is distinguished from fibroadenoma by an increased stromal cellularity, pleomorphism, and mitotic activity. The average age of women with CSP is some 10 to 20 years older than the average women with fibroadenomas *(10)*, although there is a wide age range for both breast tumours. Unlike fibroadenomas, CSP tend to recur following simple enucleation.

There is no classical history for CSP. A lump may have been noted for several weeks or several years; occasionally, recent rapid growth may be reported. Characteristically CSP is mobile and painless. However, symptoms can lead to confusion with a carcinoma in older patients, as frequently occurred in this series. At the other extreme, small tumours may well be considered a fibroadenoma.

With X-ray mammography, the tumours were generally well-defined and lobulated, appearing benign *(11)*. Although calcification is stated to be rare *(12)*, coarse calcification was present in three of the 14 tumours. Sonomammographic appearances have previously been reported in only 11 patients *(13)*; characteristically, they have good border definition with a homogeneous internal echo pattern. Fluid spaces within these masses, mentioned by Paulus *(12)*, and recorded in one of eight cases described by Cole-Beuglet *et al. (13)*, were present in no fewer than five of 11 patients we have investigated, an example of the macroscopic appearances being shown in Fig. 4. This combination of imaging features led to a suggestion of cystosarcoma phyllodes in seven of the 14 patients undergoing imaging, whereas the clinical diagnosis was made in three, and a cytological diagnosis in two patients. Thus imaging has been the most useful of the preoperative diagnostic procedures, and is dependent to a considerable extent on the sonomammographic findings.

Mitotic activity in the stromal cells (more than three mitoses per 10 high-power fields) is considered the most important criterion in assessing the malignant potential of CSP. Other features such as an infiltrating margin, stromal overgrowth and stromal cellular atypia aid the differential diagnosis between benign and malignant tumours. This distinction can be very difficult, as many tumours may show borderline appearances and the histological appearances may not reflect the clinical behaviour of the tumour. Approximately 20% of all CSP are histologically malignant, although reports vary widely between 1% and 40% *(14–19)*, probably due to difficulties in histological interpretation and case selection. A longer history of a mass, recent increase in size, larger tumour size *(19)*, and older patients *(20)* have all been reported to be associated with malignant CSP, but this has not been our experience.

Histological malignancy does not necessarily imply a malignant clinical course. Although most benign and malignant CSP may be cured by adequate primary excision, others exhibit considerable variation in clinical behaviour. Apparently benign CSP has been reported to metastasise and this may represent subsequent malignant transformation *(21)*. Earlier reports have documented local recurrence in up to 30% of all patients with CSP, usually within 2 years of excision; however, this may represent inadequate local excision, since lower recurrence rates have been noted for malignant CSP treated by mastectomy than for benign CSP treated by local excision. Local recurrence can develop over 10 years after excision and may be fatal by direct extension into the pleural cavity.

The preoperative diagnosis of CSP is difficult, small tumours being likely to be considered fibroadenomas, and large tumours carcinomas, as happened in our series. The diagnosis was made clinically in only three of our 20 patients, and cytologically in two patients. Cytology would normally be expected to be positive in carcinomas of the size described here, so that a benign cytology result, together with the imaging findings, should lead to consideration of CSP as the diagnosis.

Treatment of CSP by enucleation (a technique suitable for fibroadenomas) carries a high risk of local recurrence *(20–22)*. Conversely, treatment by mastectomy is only necessary for massive tumours, to ensure total removal or for cosmetic reasons, as in six of our patients. The use of frozen section at operation does not obviate these problems, because the differentiation between CSP and carcinoma can be difficult. Although the follow-up period in our series is short (6–72 months), our results support the suggestion of Briggs *et al. (18)* that wide excision, performed in the remaining 14 of our

patients, is the treatment of choice *(14,23)*. There have been no instances of local or distant recurrence in our patients. Radiotherapy, chemotherapy and hormone therapy have not proved useful. Risk of local and distant spread with histologically malignant tumours demands close long-term follow-up.

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Book review

Eighteenth century medics (subscriptions, licences, apprenticeships) by P J and R V Wallis. 2nd ed. 690 pages, illustrated. Newcastle-upon-Tyne: Project for Historical Bibliography, 1988.

The first edition of this work was published in 1985 in the form of photocopied sheets, but this new, revised edition, appears in conventional book form with the text printed from computer print-out which is legible, if rather small. The work consists of a single alphabetical list of references to eighteenth-century medical practitioners, using the term in its broadest sense to include barbers, chemists, druggists and apothecaries, as well as physicians and surgeons. The coverage is mainly the British Isles but there are some entries for Europe and North America. There are over eighty thousand entries in the list taken from such diverse sources as university registers, livery company members' lists and apprenticeship records, dictionaries of national biography, society records, sale catalogues and book subscription lists. The serious omissions from these sources are the examination and membership records of the Surgeons Company but this is through no fault of the compilers and it is to be hoped that they will be included in time for the next edition.

The compilation of a work of this magnitude is possible only with the use of a computer to generate the many cross-references required. Most entries are condensed into a single line and rely heavily on abbreviations. Consequently at first sight the listings appear rather daunting, especially as the work is in no sense interpretive and one individual may have several adjacent entries, one for each source in which they are cited.

For any serious worker in the field of eighteenth-century medical history this work will prove invaluable as a starting point for biographical research.

I LYLE
College Librarian