

CASE REPORT

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Lobular carcinoma of the male breast associated with the use of cimetidine

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Abstract A case of carcinoma in the breast of a male patient with a chronic gastric ulcer is described. The patient had received cimetidine for 17 years. Histological examination of an excisional biopsy showed lobular in situ and infiltrating carcinoma. In our review of the English literature, this is the 18th case of lobular carcinoma of the male breast to be reported; it is also the first report of lobular carcinoma associated with the use of cimetidine, and the second in a man with documentation of genotype.

Key words Lobular carcinoma · Male breast · Cimetidine

Introduction

A 62-year-old man presented with a left breast mass. Histological study of the specimen of a modified radical mastectomy showed lobular in situ and infiltrating carcinoma. The patient was a phenotypic and genotypic male. He had gynaecomastia and a past history of the use of cimetidine. This is the 18th case of infiltrating lobular carcinoma of the male breast [1, 10, 12, 15, 17–23, 25, 26] in the literature and the second in a genotypically proven male [17]. It is the first associated with the use of cimetidine.

Carcinoma of the male breast accounts for only 1% of breast malignancies [5, 10, 14, 18, 20]. In all large series, the predominant histological type is infiltrating ductal carcinoma. A review of the literature disclosed few previous reports of “small cell carcinoma” occurring in the male breast and only one example of lobular carcinoma in a patient with Klinefelter’s syndrome has been studied in our hospital [10].

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We report a case of infiltrating lobular carcinoma with an in situ component occurring in the breast of a phenotypic and genotypic male.

Case report

A 62-year-old white man presented with various medical complications, including a mass in the left breast which had appeared some months before. The patient was married and had two sons. Past history revealed gynaecomastia and there was a history of ingestion of cimetidine for 17 years (400 mg per 24 h) for a chronic gastric ulcer.

Physical examination revealed an ill-defined subareolar mass in the left breast measuring 1.8 cms in length. No nipple discharge was noted and there were no palpable lymph nodes in the axillary or supraclavicular regions. After a few days, a modified left radical mastectomy was performed.

Pathological findings

Macroscopically, the lesion was hard with irregular borders. On cut section, it showed a vague whitish-grey, multinodular pattern. We performed chromosomal and hormonal determinations.

Histological examination of paraffin sections stained with haematoxylin and eosin revealed inactive gynaecomastia (type II) [2] with proliferation of ducts without lobules (Fig. 1). The adjacent stroma was hyalinized without distinct differentiation of periductal stroma. Some groups of ductules were filled with cells that demonstrated a lack of regular cohesion or orientation. The nuclei were rounded or oval, usually with hyperchromatism. The cytoplasm was rather clear. The dense fibrous stroma was infiltrated with a uniform population of small neoplastic cells showing hyperchromatic nuclei, small nucleoli and a small amount of pale eosinophilic cytoplasm, some of which had signet-ring features (Fig. 2). Patterns included classic Indian files and solid areas. The most important finding was the presence of typical infiltrating lobular carcinoma with a minor in situ component, approximately 15% of the infiltrating lobular carcinoma (Fig. 2); residual ducts and fibrous gynaecomastia. Thirty-four lymph nodes were found in the left axilla; all of them were tumour free.

Results of oestrogen and progesterone receptor studies, using the dextran-coated charcoal biochemical method, were positive: 350 fmol/mg and 10 fmol/mg, respectively. Using the immunocytochemical assay, there was nuclear staining in most of the tumour cells for oestrogen receptors (prediluted; Biogenex; 86% total nuclear area). Progesterone receptors (1:50; Novocastra) were negative.

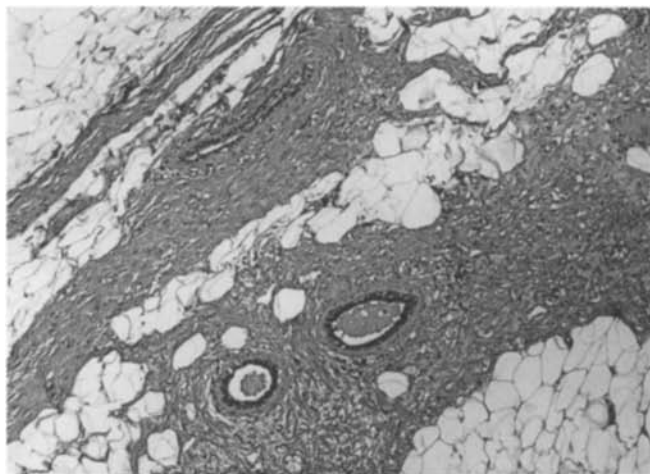


Fig. 1 Inactive gynaecomastia. Note the fibrotic stroma without periductal differentiation. Haematoxylin and eosin (H&E) $\times 150$

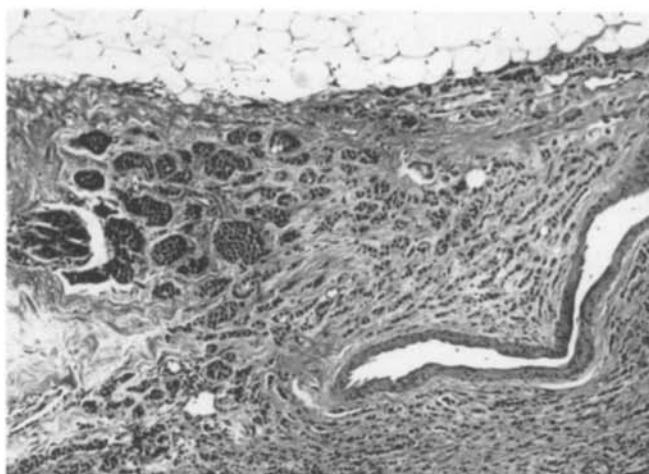


Fig. 2 Invasive carcinoma cells in contiguity with in situ lobular carcinoma. Note the linear growth pattern of invasive lobular. (H&E $\times 150$)

Table 1 Clinical and pathological data in 18 cases of lobular carcinoma of the male breast (*W* white, *B* black; – node-negative, + node-positive, *A* alive)

Authors	Number of patient's	Age (years)	Race	Size (cm) ^a	Axillary node status	Follow-up (months)	Karyotype
Norris and Taylor [18]	1	?	?	?	?	?	?
Haagensen [11]	1	?	?	?	?	?	?
Giffler and Kay [9]	2	67/74	B/B	1, 5/3	-/?	12/12	?
Yogore and Sahgal [25]	1	56	B	2, 5	–	?	?
Schwartz [21]	1	66	?	?	?	?	?
Wolff and Reinis [24]	3	55/75/?	W/B/?	1, 5/4/?	-/+/?	200/48/?	?
Vercoutere and O'Connell [22]	1	?	?	?	?	?	?
Sanchez et al. [19]	1	61	W	3	+	36 (A)	47XXY
Aghaudino [1]	2	75/60	B/B	?/?	+/+	12/24	?
Nance and Reddick [17]	1	80	W	2, 5	?	5 (A)	?
Simon et al. [20]	1	?	?	?	?	?	?
Michaels et al. [16]	1	59	W	3	–	21 (A)	46XY
Joshi et al. [14]	1	31	?	?	?	?	?
San Miguel (this case)	1	62	W	1, 5	–	6 (A)	46XY

^a Maximum dimension

Measurements of the proliferation fraction with MIB 1 (prediluted; Dianova) were positive in only 10% of the neoplastic nuclei. The proliferation index, the hormone receptors and the imprints of fresh tumours, stained by the Feulgen method, with the staining pit from cell analysis system (CAS, Lombart, Ill., USA) were analysed with a CAS 200 image analyser and software (CAS). Tumour cells were diploid with a single peak diploid position. They did not stain for p53 protein (1:100; Biomed), C erb B2 oncogen (prediluted; Biogenex) and carcinoembryonic antigen (prediluted; Biogenex).

Discussion

Male breast cancer is uncommon and represents only approximately 1% of all breast cancers [5, 10, 14, 18, 20] and 1.6% of malignant cancer in men. The mean age at which breast cancer is detected in men is 60 years, which is 5 years more than the mean age in women [14]. The mean age of the cases reported in the English language literature of lobular carcinoma in the male breast is 66

years. Lobular breast cancer is less often bilateral in men than in women although a case of bilateral breast cancer in a male patient with Klinefelter's syndrome has been reported [10]. As the male breast is small, the breast tumour is frequently subareolar, with nipple retraction and ulceration of the skin surrounding the nipple [11]. The case report describes a 62-year-old male who had a subareolar mass in the left breast. The overlying skin was normal.

The histopathological patterns of breast carcinoma are almost identical in men and women [6, 13]. One important exception is lobular carcinoma or small cell carcinoma. Several reports have confirmed that this is presumably due to a lack of lobules in normal male mammary tissue. Mammary cancer is usually divided into ductal and lobular types, according to their origin. However, since Wellings and Jensen's description in 1975, ductal and lobular carcinomas are considered to arise from the terminal ducts lobular unit, especially in the lobular for-

mation [24]. We think that the lack of lobules in the male breast is sufficient to explain the rarity of breast cancer in males and not only that lobular carcinoma is an uncommon occurrence in itself. It has been suggested that changes in steroid levels can stimulate the formation of acini and lobules in the male breast cancer [4–7, 14]. In the reported cases of male lobular breast cancer, one patient was receiving therapy for prostatic carcinoma, and one patient had Klinefelter's syndrome [20, 22]. In the case we describe in this report the patient had a chronic gastric ulcer and had been taking cimetidine for 17 years. Various abnormalities have been described in patients treated chronically with cimetidine: hyperprolactinaemia, gynaecomastia, galactorrhoea and breast cancer; but this is the first report of lobular carcinoma in a man. The incidence of oestrogen and progesterone receptors seem to be greater in men than in women with breast carcinoma. In a recent study of male breast cancer, 85% were oestrogen receptor positive and 64% were progesterone receptor positive [8]. In our case, oestrogen receptors were positive and progesterone were negative.

The cases reported in the English language literature of lobular carcinoma of the male breast are summarized in Table 1. This is the 18th case in the English literature of lobular carcinoma [1, 10, 12, 15, 17–23, 25, 26] and the second case of lobular carcinoma of the breast in a phenotypic and genotypic proven man [17]. Unfortunately, most of the reports do not give explicit complementary chromosomal studies. Gynaecomastia is known to occur in men treated with cimetidine; this report shows that lobular carcinoma may also develop.

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