

CASE REPORT: CYSTIC GYNECOMASTIA IN A MALE TREATED WITH CLOMIPHENE CITRATE

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Clomiphene citrate has been found to be quite effective in the treatment of subfertile men with idiopathic oligospermia¹⁻³ and more recently in the treatment of men with varicoceles.⁴ In general, the drug is well tolerated by men with minimal (if any) side effects such as slight weight gain and occasional transient visual disturbances. The patient reported below represents the first case of cystic mastalgia in a male related to clomiphene citrate therapy.

CASE REPORT

The patient was a 32-year-old male evaluated for primary infertility. His baseline sperm count 3 years prior to his initial visit was 11 million/ml, 55% motility grade 2+. Over a 1½-year period his sperm counts waxed and waned but became persistently low at about 5 million/ml. He was then treated with clomiphene citrate, 25 mg for 25 days with 5 days' rest. The patient had had several complete physical examinations prior to starting the drug, and no abnormalities were found other than the possibility of mild prostatitis.

The patient showed considerable improvement on clomiphene. His sperm count improved to 20 million/ml with good motility after 2 months, and his counts after 5 months were over 60 million/ml with good motility. After 5 months on the drug he noticed some tenderness in the left breast, and

small nodules were noted. This tenderness increased significantly after 3 more months of therapy and then involved the right breast.

Since no pregnancy had been achieved, a laparoscopy on his wife was performed and endometriosis was found. The patient's clomiphene treatment was stopped while his wife was placed on Danocrine therapy. Four months later the breast nodules were still present, although the tenderness had diminished.

A mammogram was performed and revealed an increase in density in the subareolar areas bilaterally, but more marked on the right. These cystic gynecomastia changes are evident in Figure 1. The chest x-ray was negative.

The following blood studies were performed while the patient had been taking clomiphene citrate after the cystic gynecomastia was noted: luteinizing hormone, 16.3 mIU/ml (normal range 6 to 30 mIU/ml); follicle-stimulating hormone, 5.1 mIU/ml (normal range 5 to 25 mIU/ml); cortisol, 9.9 µg/100 ml (normal range 5 to 25 µg/100 ml); total estrogen, 0.5 ng/100 ml (normal up to 0.25 ng/100 ml); T₄, 10.3 ng/100 ml (normal range 4.5 to 13 ng/100 ml); T₃ uptake, 34.5% (normal 25% to 35%); β-subunit of human chorionic gonadotropin, 0; testosterone, 624 ng/100 ml (normal range 300 to 960 ng/100 ml). After 4 months off clomiphene the same serum tests were performed. The serum estrogen level dropped to 0.3 ng/100 ml, just slightly above normal for a male. The remaining studies remained normal as they had been previously.

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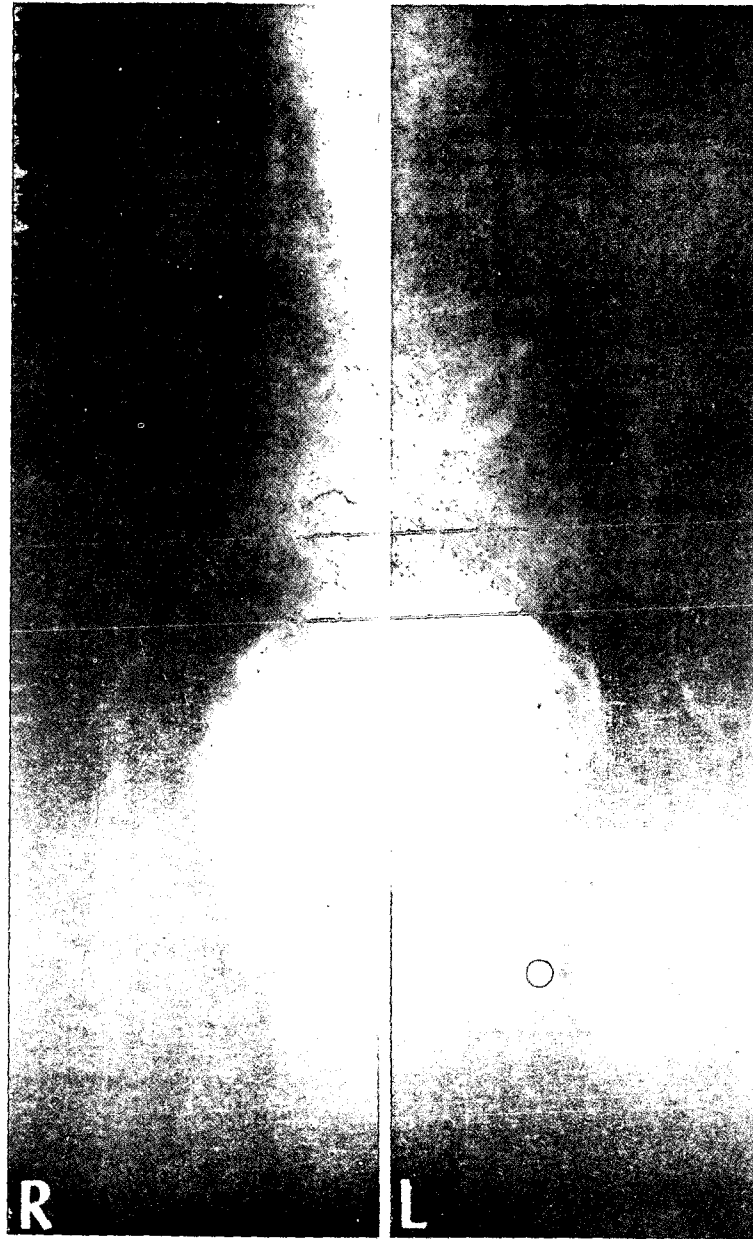


FIG. 1. Cystic gynecomastia in a male treated with clomiphene citrate. Bilateral mammography shows evidence of homogeneous density in the subareolar areas bilaterally. The appearance is that of bilateral cystic gynecomastia. The opaque marker in the inferior portion of the left breast marks the area that was clinically palpable on the left.

The patient's sperm count dropped to 4 million/ml off clomiphene. He elected to resume taking the drug, so a bilateral mastectomy was performed. Histologic study showed a generally fibrous background containing proliferating ductal elements. Some ducts were simple but most were moderately tortuous. The lining was moderately to markedly hyperplastic, forming papillary

infoldings. Some sections showed a periductal round cell infiltrate and periductal edema.

DISCUSSION

Gynecomastia presenting suddenly in a male this age is unusual. Its development while he was taking clomiphene citrate raises suspicion that the

drug itself was responsible. However, a coincidental tumor secreting human chorionic gonadotropin, prolactin, or estrogen would first need to be excluded. Most of the laboratory data would exclude the first two conditions; however, the elevated serum estrogen level suggests the presence of an estrogen-secreting lesion or the clomiphene itself to be responsible for the increase in estrogen. This latter hypothesis seems most reasonable in view of the absence of any testicular lesions by examination, the normal serum cortisol levels, and a reduction in the estrogen level to close to normal when the patient had been off the drug for

4 months along with some reduction of the size of the breast nodules.

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