

FIBROADENOMA OF THE BREAST IN A MAN ASSOCIATED WITH ADENOCARCINOMA OF THE RECTUM AND POLYPOSIS COLI

Z.H. Adibelli¹, M. Yildirim², E. Ozan¹, O. Oztekin¹, B. Kucukzeybek³

Fibroadenoma of the breast is an uncommon cause of breast lumps in men. Only a few cases have been reported in the literature, the majority of which were prescribed estrogen. We present herein the first case of a fibroadenoma of the breast in a 68-year-old man with adenocarcinoma of the rectum and polyposis coli. In this case, there was neither estrogen treatment nor any other medications which have been discussed in the literature as inducing fibroadenomas. Fibroadenomas in men without hormone treatment and with normal hormone levels are extremely rare and the developmental mechanism of the breast fibroadenoma in this man is under question.

Key-word: Breast, male.

Fibroadenomas of the breast are a common cause of benign breast lumps in premenopausal women. A clinical diagnosis of fibroadenoma is an unexpected presentation in male breasts due to the lack of fibroglandular tissue under the nipple in the normal male. Histologically, subareolar ducts are demonstrated in the normal male breast similar to those found in prepubertal girls (1). These ducts in a male may elongate and branch when stimulated by hormones or a variety of drugs (2). Most men who are referred for breast imaging have a palpable mass, breast enlargement, or tenderness. Benign conditions, such as gynecomastia, lipomas, epidermal inclusion cysts, and intraductal papillomas may mimic male breast cancer (3, 4). Fibroadenomas in males are rare, and only a few cases of fibroadenomas in males have been reported in the literature; most of the reported cases involved male-to-female transsexuals and iatrogenic male fibroadenomas due to estrogen therapy for medical conditions, such as prostatic carcinoma (5). Idiopathic male fibroadenomas are considered an extremely rare event (5-7). Our case had a fibroadenoma of the breast, adenocarcinoma of the rectum, and polyposis coli; however, we could not find any association between these events in the literature.

Case report

A man born in 1940 had diffuse bilateral breast enlargement without a palpable mass in 2002. On mammography and ultrasonography (US), diffuse gynecomastia was

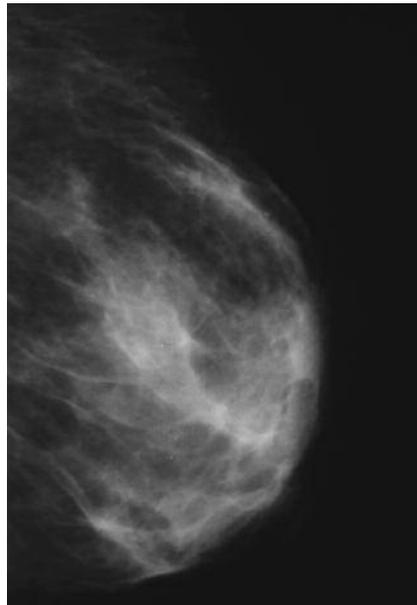


Fig. 1. — Mammographic appearance of the left breast of the patient in 2002. Left mediolateral oblique mammograms of the patient show very similar appearances to a heterogeneously dense female breast (diffuse gynecomastia).

demonstrated bilaterally (Fig. 1); however, no mass was found. The laboratory work-up was normal, a hormonal imbalance was not found, and he had not used any medications for a long time. He had never smoked nor chewed tobacco. He had worked as a building painter.

Three years later he presented with rectal bleeding and constipation. The laboratory work-up was normal. A rectal examination revealed a posterior rectal mass, nearly 6 cm distant from the anal

margin. At rectoscopy, a rectal tumor which was 4 cm in diameter and numerous polyps were visualized. At surgery, an abdominoperineal resection was performed. Histopathologically, adenocarcinoma of the rectum and polyposis coli (tubular adenoma) was demonstrated and no metastatic lymph nodes were found (Astler-Coller classification B2). The postoperative course was uneventful and the patient was discharged home on the 11th postoperative day. The patient received fluorouracil (5FU) and calcium leucovorin, administered as an infusion on day 1, and repeated every 3 weeks. The patient's brother died due to adenocarcinoma of the sigmoid and also had multiple polyps.

In 2008, he presented with a left breast mass. On mammography, the patient had bilateral diffuse gynecomastia, and there was a round, well-circumscribed, and homogenous lesion in the upper outer quadrant of the breast (Fig. 2). The lesion was 2 cm in diameter. On US, the lesion was solid, hypoechoic, homogenous, and well-circumscribed (Fig. 3). The lesion corresponded to BI-RADS 3 on mammography; however, because of the solid character and history of malignancy, it was considered suspicious for a malignancy. The histological diagnosis was made by surgical biopsy and the lesion was proven to be a fibroadenoma. Hematoxylin-eosin-stained slides of the biopsy were available for review. Macroscopically, the mass was measured as 2 x 1.5 x 1.3 cm. Microscopically, the mass was typically a fibroadenoma with a knobby and circumscribed contour (Fig. 4). The mass showed nearly equal portions of epithelial and stromal components. Also, the epithelial component of the specimen showed diffuse gynecomastia.

Besides using 5FU and calcium leucovorin in 2005, the other med-

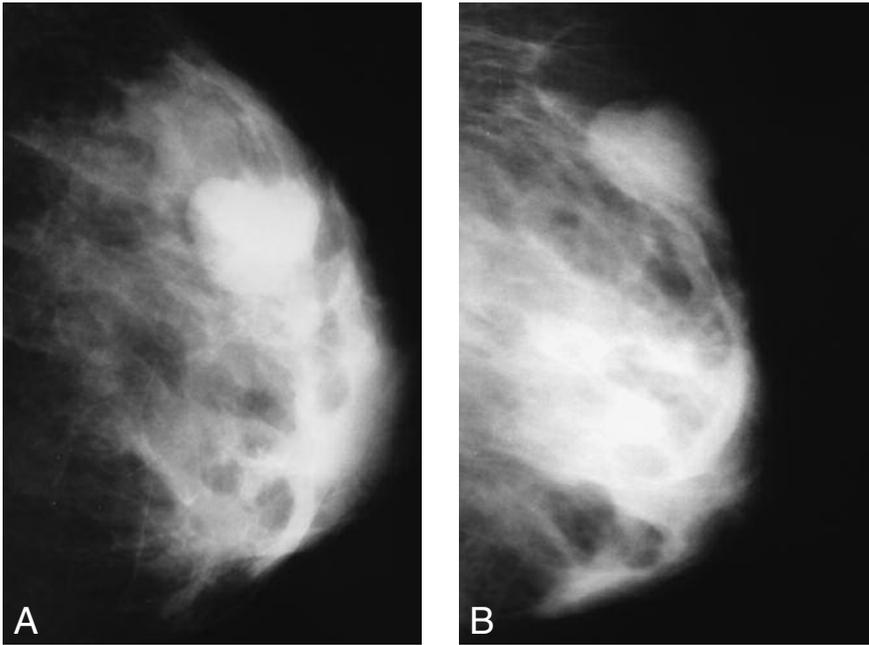


Fig. 2. — Mammographic appearances of the left breast of the patient in 2008. A. Craniocaudal and B mediolateral oblique mammograms show a bilobulated and homogenous mass in the upper lateral quadrant besides gynecomastia.

ications of the patient were warfarin sodium and acetylsalicylic acid after a deep venous thrombosis since 2007, furosemide since 2006, and citalopram since 2008. His hormone levels were normal for his age group.

Discussion

Fibroadenomas in the male breast are rare, and only a few cases have

been reported. Holleb et al. (8) concluded that there was no true fibroadenomas of the male breast. It has been concluded by some authors that most of the reported lesions are poorly documented and nodular foci of gynecomastia have been reported as fibroadenomas (9). However, it is now apparent that fibroadenomas in the male breast are true events because there have been some reports in which

fibroadenomas were well-documented (5-10).

Fibroadenomas have both estrogen and progesterone receptors (11). It has been discussed that proliferative changes in the male breast, like gynecomastia, lobular differentiation, and fibroepithelial lesions are caused by hormonal imbalances and some medications. In the literature, fibroadenomas in the male breast appear to be always associated with gynecomastia. Like Shin and et al. (6), we could not find any reports of fibroadenoma in male patients who did not have concurrent gynecomastia. However, the presence of lobular differentiation with or without associated gynecomastia is less common (6). Lobular differentiation and fibroadenomas were found in two reported cases of male-to-female transsexuals who were undergoing demasculinization and feminization by hormonal therapy using ethinyl-oestradiol and cyproterone acetate and surgical treatment (5). Davis et al. (11) reported a case of a 19-year-old female with complete androgen insensitivity syndrome (CAIS) and a fibroadenoma of the breast. Four cases of male fibroadenomas have been reported in which gynecomastia with lobular differentiation was present in each case (12). One of the four patients had been treated with estrogens, whereas another patient had been treated with methyl dopa and chlor diazepoxide. As Asscheman et al. (13) reported, there are genetic differences in estrogen sensitivity to



Fig. 3. — Ultrasound of the mass demonstrates a solid, homogenous, and lobulated mass with a well-defined contour.

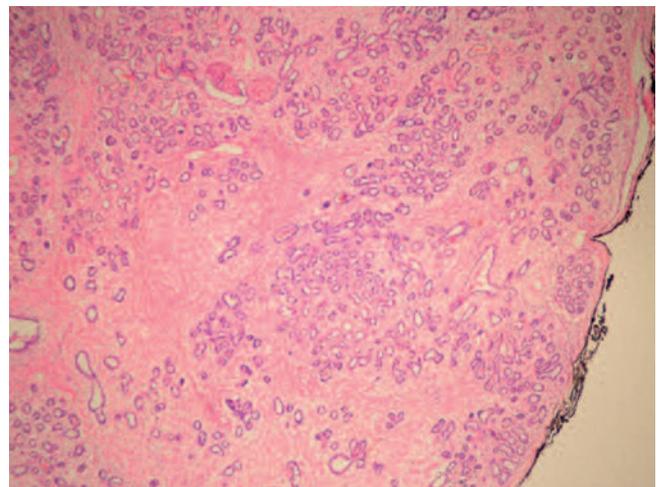


Fig. 4. — Photomicrograph of the surgical biopsy specimen reveals that connective tissue invaginates into the glandular spaces (x 40 H&E stains).

dopaminergic regulation of prolactin secretion, and in the latter case, methyldopa was thought to play a role. For the other two patients, the possible causes of fibroadenoma formation remain elusive. In our case, the presence of lobular differentiation was carefully sought; however, not found.

In idiopathic prepubertal or senile gynecomastia, the increase in the plasma estrogen-to-androgen ratio usually will not induce acinar and lobular formation in the male breast. However, in transsexuals, in whom progestagenic antiandrogens, such as cyproterone acetate, are combined with feminizing estrogen therapy, acini and lobular formation will occur (6, 14). The use of a luteinizing hormone-releasing hormone agonist to decrease testosterone levels for the treatment of advanced prostate cancer has contributed to the development of gynecomastia and fibroadenoma (6). Gynecomastia has also been associated with digitalis and spironolactone, which interfere with the production of testosterone and its conversion to the potent metabolite, 5- α -dihydrotestosterone (2, 5). Cimetidine is also a big precursor of gynecomastia (15). Nielsen (16) reported a case of bilateral fibroadenomatoid hyperplasia in a 69-year-old man whose breasts had become diffusely enlarged with multiple fibroadenomatoid nodules when spironolactone was added to his prior therapy with digoxin and furosemide during the last 4 years before presentation.

In the literature, we did not find any reports about the relationship between 5FU, calcium leucovorin, and fibroadenomas of the breast. However, a combination of different therapies can lead to some side effects. Since 2002, gynecomastia was known to be present. Perhaps citalopram (since 2008) gave the boost to develop the fibroadenoma. The patient had worked as a painter,

so he had some chemical contacts which may have assisted the development of fibroadenoma. Also, there were no reports about the association of adenocarcinoma of the rectum and polyposis coli with fibroadenomas of the breast in a man. Our patient's brother also had polyposis coli (tubular adenoma) and died because of colorectal adenocarcinoma. The prevalence of fibroadenomas of the breast among patients who have polyposis coli is unknown. The co-occurrence may have arisen by chance, or maybe in the future, new research will show an association.

Conclusion

Fibroadenomas in men without hormone treatment and with normal hormone levels are extremely rare. This is the first report of a man who had a fibroadenoma of the breast, gynecomastia, adenocarcinoma of the rectum, and polyposis coli. In light of the literature, the causative agent of the fibroadenoma in this unique case is unknown and the developmental mechanism of the breast fibroadenoma in this man is under question.

References

1. Kopans D.: Breast imaging, 3rd Edition. Pa: Lippincott Williams and Wilkins, 2007, pp 671-672.
2. Asscheman H., Gooren L.J.G.: Hormone treatment in transsexuals. *J Psychol Human Sexual*, 1992, 5: 39-54.
3. Appelbaum A.H., Evans G.F., Levy K.R., Amirkhan R.H., Schumpert T.D.: Mammographic appearances of male breast disease. *Radiographic*, 1999, 19: 559-568.
4. Chen L., Chantra P.K., Larsen L.H., Barton P., Rohitopakarn M., Zhu E.Q., Bassett L.W.: Imaging characteristics of malignant lesions of male breast. *Radiographics*, 2006, 26: 993-1006.
5. Kanhai R.C., Hage J.J., Bloemena E., van Diest P.J., Karim R.B.: Mammary

fibroadenoma in a male-to-female transsexual. *Histopathology*, 1999, 35: 183-185.

6. Shin S.J., Rosen P.P.: Bilateral presentation of fibroadenoma with digital fibroma-like inclusions in the male breast. *Arch Pathol LAB Med*, 2007, 131: 1126-1129.
7. Adibelli Z.H., Oztekin O., Postaci H., Uslu A.: The diagnostic accuracy of mammography and ultrasound in the evaluation of male breast disease: a new algorithm. *Breast Care*, 2009, 4: (DOI:10.1159/000226284).
8. Holleb A.I., Freeman H.P., Farrow H.J.: Cancer of male breast, part II. *N Y State J Med*, 1968, 68: 656-663.
9. Rosen P.P.: Benign proliferative lesions of the male breast. In: Rosen P.P., ed. *Rosen's Breast Pathology*. 2nd ed. Philadelphia, Pa: Lippincott Williams and Wilkins, 2001, 703-712.
10. Lemmo G., Garcea N., Corsello S., Tarquini E., Palladino T., Ardito G., Garcea R.: Breast fibroadenoma in a male-to-female transsexual patients after hormonal treatment. *Eur J Surg, Suppl*, 2003, 588: 69-71.
11. Davis S.E., Wallace A.M.: A 19 year old with complete androgen insensitivity syndrome and juvenile fibroadenoma of the breast. *Breast J*, 2001, 7: 430-433.
12. Ansah-Boateng Y., Tavassoli F.A.: Fibroadenoma and cystosarcoma phyllodes of the male breast. *Mod Pathol*, 1992, 5: 114-116.
13. Asscheman H., Gooren L.J.G., Assies J., Smits J.P.H., de Slegte R.: Prolactin levels and pituitary enlargement in hormone-treated male-to-female transsexuals. *Clin Endocrinol*, 1988, 28: 538-588.
14. Kankai R.C., Hage J.J., van Diest P.J., Bloemena E., Mulder J.W.: Short-term and long-term histologic effects of castration and estrogen treatment on breast tissue of 14 male-to-female transsexuals in comparison with chemically castrated males. *Am J Surg Pathol*, 2000, 24: 74-80.
15. Rodriguez L.A., Jick H.: Risk of gynecomastia associated with cimetidine, omeprazole, and other antiulcer drugs. *BMJ*, 1994, 19: 503-506.
16. Nielsen B.B.: Fibroadenomatoid hyperplasia of the male breast. *Am J Surg Pathol*, 1990, 14: 774-777.