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Treatment of Bicalutamide-Induced Gynecomastia With Breast-Reduction Surgery in Prostate Cancer

Nine years after radical prostatectomy and salvage radiation therapy, a 64-year-old man with prostate cancer presented with a rising prostate-specific antigen in the absence of metastatic disease. The patient opted for high-dose bicalutamide (Casodex, 150 mg daily; AstraZeneca, Wilmington, DE) monotherapy, as trials have suggested that bicalutamide offers improvements in quality of life in terms of sexual function compared with androgen deprivation therapy. The patient refused recommended prophylactic radiotherapy to his breasts before treatment. Two years after starting bicalutamide, he developed severe gynecomastia, and was referred to a plastic surgeon. On physical examination, his breasts were characterized by glandular proliferation, excess fatty tissue, enlarged areolae, and ptosis. Gynecomastia was classified as stage 3 according to the Rohrich scale (Fig 1A).[1] Twenty-seven months after initiating bicalutamide, he underwent bilateral periareolar mastopexies with peripheral liposuction under general anesthesia. Approximately 300 mL of fatty tissue was aspirated. The pathologic report showed no malignant change. The patient tolerated surgery well and was pleased with the results (Fig 1B).

It is well known that gynecomastia is a vexing complication of hormonal therapy in men with prostate cancer both because of associated psychologic stress, as well as breast pain. Its etiology is thought to be an altered ratio of estrogen to androgen levels.[2,3] The use of high-dose bicalutamide monotherapy has certain quality of life benefits in terms of improved energy level, libido, and hot flashes, and better maintenance of bone mineral density when compared with medical or surgical castration, although this approach may lead to a small difference in survival in metastatic patients.[4,5,6] Estrogens and antiandrogen monotherapy are particularly prone to inducing gynecomastia. Approximately 70% of patients develop gynecomastia and breast pain after initiation of bicalutamide.[4] Issues of body image and sexual identity have been noted as important concerns for men with prostate cancer. Men may suffer psychologic effects from a perception of feminization.[7] Breast radiation has been reported to be effective with minimal adverse effects in the management of gynecomastia; although, it is mostly used prophylactically. It may be effective in alleviating breast pain, but is generally ineffective in reducing breast size. Although gynecomastia is partially reversible after discontinuation of the androgen deprivation therapy, long-term gynecomastia can be irreversible due to fibrosis and hyalinization of the stroma.[3,8] It is noteworthy that some patients are reluctant to receive radiation therapy to their breasts, and that some men develop gynecomastia despite prophylactic radiation. Surgery is effective for long-standing gynecomastia, as in this case.[8] Risks of surgery include infection, bleeding, numbness, asymmetry, contour irregularities, the possible need for revision surgery, and high cost that is usually greater than several thousand dollars and is not often reimbursed by insurance. More cases of gynecomastia will be reported as an adverse effect as increasing numbers of prostate cancer patients are treated with antiandrogens and estrogens. This disturbing adverse effect can

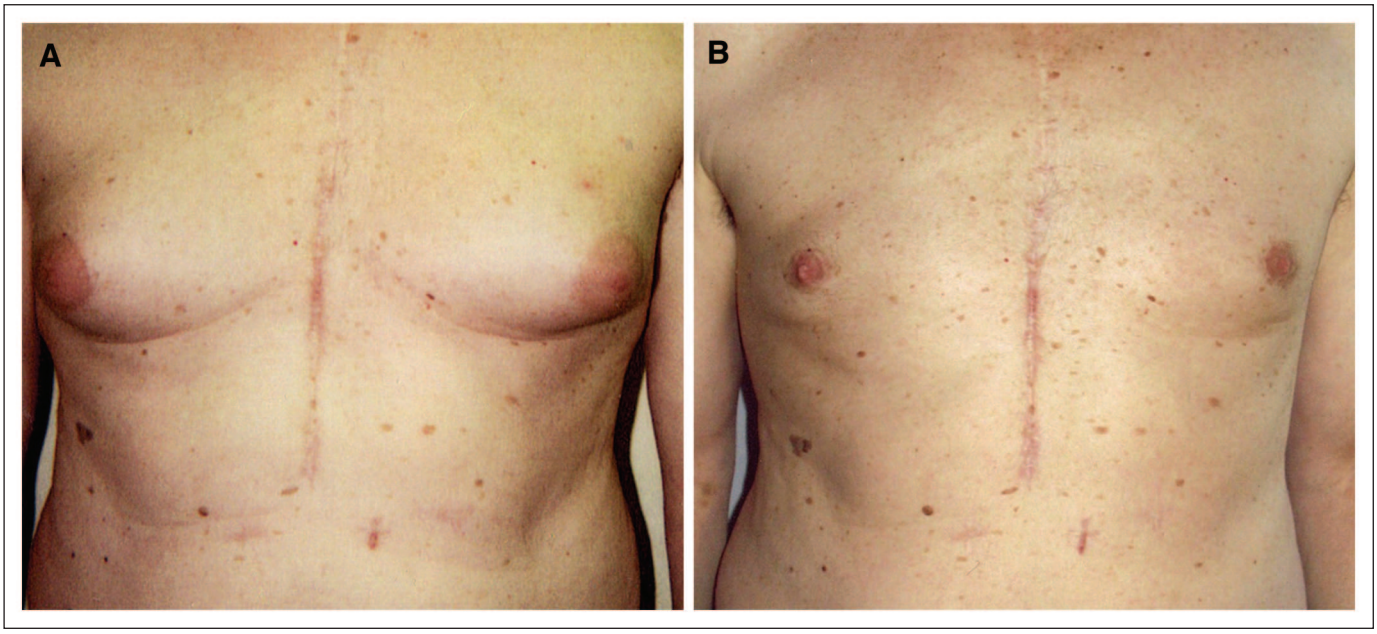

Fig 1.

sometimes be serious enough to influence a patient's treatment decision in the management of prostate cancer. For physicians, it is important to be aware of patients concerns regarding their body image and to consider available therapeutic options.

Mari Nakabayashi, Richard A. Bartlett, and William K. Oh
Lank Center for Genitourinary Oncology, Department of Medical Oncology, Dana-Farber Cancer Institute, and the Department of Surgery, Children's Hospital, Harvard Medical School, Boston, MA

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Acute Coronary Syndrome Secondary to Fluorouracil Infusion

The patient, a 41-year-old man, presented with a neck mass on his right side, and was diagnosed with stage IV (T3N3M0) squamous cell carcinoma of the right tonsillar fossa. The patient underwent radical neck dissection, as well as radiation therapy for his squamous cell carcinoma, and did well for 1.5 years. Subsequently, the patient was found to have recurrence when a lung mass as well as a bony metastasis was found in his left shoulder. The patient was entered onto a clinical trial and was randomly assigned to the standard treatment arm with cisplatin and infusional fluorouracil (FU). The patient was admitted to begin his chemotherapy and was given cisplatin as well as a 5-day continuous infusion of FU. The patient was treated with 1,000 mg/m^2 per day, which was calculated to be 2,210 mg in 500 mL normal saline. He developed severe substernal chest pain on the morning of the third day, which was partially relieved by nitroglycerin. The patient had mild ST elevation in leads II, III, AVF, and V4-V6 (Fig 1).

He also had an elevated troponin, with a peak of 18.6. A diagnosis of acute ST elevation myocardial infarction was made. The patient's echocardiogram at that time showed that there was global hypokinesis with an ejection fraction of 25%. He was taken emergently for cardiac catherization, which revealed that he had normal coronaries without any evidence of plaque, stenosis, or vasospasm (Figs 2 and 3). The patient transiently required pressor support with dobutamine, but was able to be sent home safely. Repeat echocardiogram performed 3 weeks after the myocardial infarction showed that his ejection fraction had improved to 50% with only mild global hypokinesis. Finally, another repeat echocardiogram performed 2 months after the myocardial infarction showed that his ejection fraction had recovered to 65% and that the global hypokinesis had entirely resolved.

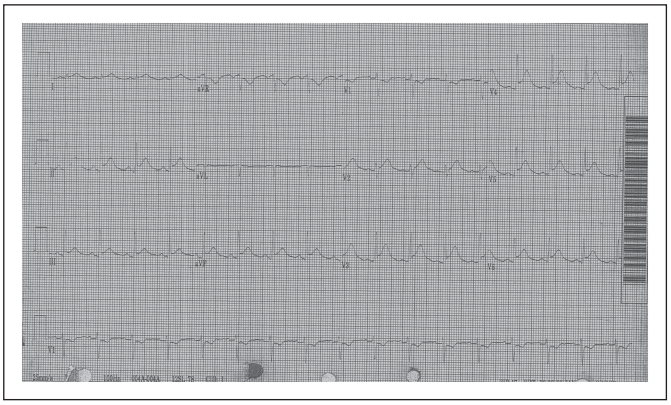

Fig 1.

There have been case reports in the literature documenting the incidence of cardiotoxicity due to fluorouracil infusions. In one prospective study of 367 patients, de Forni et al[1] found that the incidence of high-dose FU continuous infusion related cardiotoxicity was 7.6%. There were ECG changes in 65% of patients with cardiac events. However, only two of their 28 patients with cardiac events had elevated cardiac enzymes, and nine of 16 patients who were examined were noted to have partial or global hypokinesia. However, in a large retrospective study of 1,083 patients, the incidence of FU cardiotoxicity was reported to be 1.6% with bolus dosing.[2] Meydan and Kundak[3] found that the incidence of cardiac events was 3.9% in a

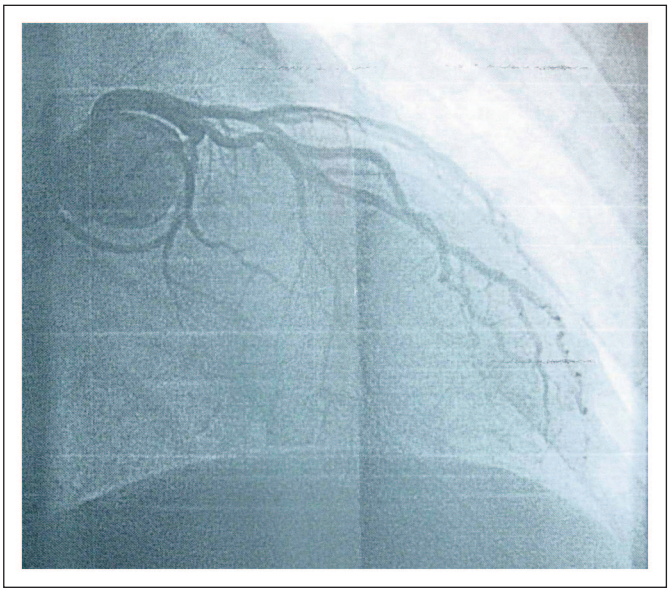

Fig 2.