Metastatic Prostatic Adenocarcinoma Within a Primary Solid Papillary Carcinoma of the Male Breast

Application of Immunohistochemistry to a Unique Collision Tumor

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We report the case of a 78-year-old man who developed a breast mass 12 months after hormonal therapy for palliation of prostatic adenocarcinoma. On histologic and immunohistochemical examination, the breast tumor revealed a unique collision tumor composed of metastatic prostatic adenocarcinoma and solid papillary breast carcinoma.

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The differential diagnosis of a breast mass developing in a male patient who has prostatic carcinoma includes gynecomastia secondary to estrogen therapy, metastatic prostatic carcinoma in the breast, or a primary carcinoma of the breast.1 The sporadic occurrence of concurrent separate primary prostatic and mammary carcinomas has been reported.2

The distinction between primary carcinoma of male breast and metastatic prostatic adenocarcinoma in the breast can be difficult, because the morphology of the 2 tumors is similar in some instances. Immunohistochemical markers are usually useful in this situation.

We describe a patient with metastatic prostatic adenocarcinoma in a primary intraductal solid papillary carcinoma of the male breast, a form of collision tumor. Immunohistochemistry was extremely helpful for distinguishing the 2 structurally similar neoplasms. To the best of our knowledge, this is the first reported example of such an occurrence.

REPORT OF A CASE

A 78-year-old white man had undergone transurethral resection of the prostate in September 1999 for prostatic adenocarcinoma. Laboratory studies revealed a serum prostate-specific antigen (PSA) level of 109 ng/mL, elevated alkaline phosphatase value of 577 U/L, and a normal serum chemistry panel. A computed tomographic scan demonstrated multiple areas of uptake consistent with metastatic disease. He received leuprolide acetate and flutamide, but no estrogen therapy. Initially, the patient's PSA level returned to normal, but it subsequently increased, indicating resistance to hormonal therapy.

In August 2000, the patient presented with a firm left breast mass. Physical examination revealed a hard, partly cystic, nontender mass in the superior half of the breast distorting the nipple-areola complex. The patient's serum alkaline phosphatase level was 504 U/L; carcinoembryonic antigen, 2.9 μg/L; PSA, 57.0 ng/mL; and CA 27.29, 74 U/mL. Computed tomographic scans of the chest, abdomen, and pelvis showed a new 2-cm lesion in the left lobe of the liver that was not present in the baseline computed tomography studies. There was also evidence of bony metastases, which had progressed compared with a prior study, as well as adenopathy in the retroperitoneum and left iliac region.

Fine-needle aspiration of the solid breast mass revealed atypical cells. A left modified radical mastectomy was performed.

PATHOLOGIC FINDINGS

Gross Description

The mastectomy specimen contained a 5-cm, well-demarcated, partly cystic mass filled with thick brown fluid immediately beneath the skin of the nipple and areola. A 3.0 × 2.0 × 1.5-cm, tan-red, solid mass was present in the posterior wall of the cyst. The remainder of the specimen consisted of fatty breast tissue. Level I and level II axillary lymph nodes were grossly unremarkable.

Microscopic Examination

Prostate.—The transurethral resection specimen revealed a moderately to poorly differentiated prostatic adenocarcinoma with a combined Gleason score of 8/10 and a predominant pattern 3. The tumor exhibited a spectrum of histologic patterns, including microacinar growth with irregular outlines, solid sheets, and diffuse single-cell infiltration. The tumor cells contained abundant clear cytoplasm and large nuclei with prominent nucleoli.

Breast.—The cystic portion of the mass had a thickened fibrous wall with aggregates of foamy histiocytes, multinucleated giant cells, cholesterol clefts, and numerous hemosiderin-laden macrophages. Necrotic material and cellular debris were present in the interior of the cyst.

Sections of the solid mass revealed remnants of a cystic and solid papillary carcinoma with low to intermediate nuclear grade and cribriform architecture beneath the fibrous capsule. The remainder of the solid mass was composed of carcinoma with solid nests and microacinar ar-
A. Photomicrograph showing both components of the collision tumor. The darker cells with hyperchromatic nuclei and cribriform architecture on both sides of the fibrous band (center) represent the solid papillary breast carcinoma. The cells with abundant clear cytoplasm forming microacini and solid sheets adjacent to the darker cells represent metastatic prostatic carcinoma (hematoxylin-eosin). B. Immunohistochemical stain for estrogen receptor exhibits strong nuclear reactivity in the breast carcinoma and no reactivity in the prostatic carcinoma. C. Immunohistochemical stain for prostate-specific antigen exhibits cytoplasmic reactivity in the prostatic carcinoma and no reactivity in the breast carcinoma. D. Immunohistochemical stain for cytokeratin 7 shows focal cytoplasmic reactivity in the breast carcinoma and no reactivity in the prostatic carcinoma.

**Immunohistochemical Findings in Prostatic and Breast Carcinomas**

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* CK indicates cytokeratin; PSA, prostate-specific antigen; PsAP, prostatic acid phosphatase; AR, androgen receptor; ER, estrogen receptor; PR, progesterone receptor; GCDFP-15, gross cystic disease fluid protein 15; –, negative; and +, positive.

architecture formed by larger tumor cells with clear cytoplasm, large nuclei, and prominent nucleoli, similar to the prostatic carcinoma. The prostatic carcinoma component showed frequent atypical mitoses, focal necrosis, and dystrophic calcification. Intimate mingling of the papillary mammary carcinoma and metastatic prostatic carcinoma was present in some regions (Figure, A).

**Liver.**—A needle core biopsy of the liver lesion revealed metastatic prostatic adenocarcinoma.

**Immunohistochemistry**

A panel of antibodies was utilized to study the prostate and breast tumors. The results are presented in the Table and shown in the Figure. In summary, the primary prostatic carcinoma, as well as the metastatic prostatic carcinoma in the breast, displayed strong and diffuse staining for PSA (BioGenex, San Ramon, Calif) and androgen receptor (BioGenex), focal staining for prostatic acid phosphatase (PsAP; BioGenex), and negative staining with cytokeratin (CK) 7 (Dako, Carpinteria, Calif), CK 20 (Dako), estrogen receptor (ER; Dako), and gross cystic disease fluid protein 15 (GCDFP-15; Signet, Dedham, Mass). The breast carcinoma component showed strong immunoreactivity with GCDFP-15, ER, progesterone receptor (Novocastra, Newcastle upon Tyne, United Kingdom), and CK 7, and complete absence of staining with PSA, PsAP, and CK 20. The distribution of immunostaining correlated completely with the histologic distinction between the
prostatic and mammary carcinoma components in the collision tumor.

**COMMENT**

Malignant neoplasms originating from 2 or more distinct topographic organs form a collision tumor. Four instances of collision tumor of the male urogenital tract in which prostatic carcinoma was one of the components have been described.\(^3\)\(^-\)\(^4\) These include 2 examples of combined metastasis of bladder and prostatic carcinoma in pelvic lymph nodes,\(^4\) prostatic adenocarcinoma and rectal leiomyosarcoma,\(^5\) and prostatic adenocarcinoma and liposarcoma of the seminal vesicle.\(^6\) We report a rare and, to our knowledge, yet-undescribed type of collision tumor composed of prostatic adenocarcinoma in male breast carcinoma.

Prostate-specific antigen and PsAP expression are very useful in identifying the origin of metastatic tumors because they are positive in all but the most undifferentiated prostatic carcinomas.\(^7\) Prostatic adenocarcinoma cells also express low-molecular-weight keratins and are positive for androgen receptor. Mammary carcinomas are relatively specific in reactivity for GCDFP-15, they usually express estrogen and progesterone receptors, and they are typically negative for androgen receptor, PSA, and PsAP. Prostate-specific antigen expression in human breast carcinoma has been reported, but reactivity is uncommon, weak, and tends to be focal.\(^8\)\(^-\)\(^10\) This issue did not arise in our case, because the primary breast carcinoma was negative with PSA and PsAP, whereas both primary and metastatic prostatic carcinomas were strongly reactive for these markers. The biphasic growth pattern of the tumor in the breast raised the suspicion of coexistent primary and metastatic carcinoma, leading us to perform additional immunostains. In the current case, the primary breast carcinoma component was strongly reactive with GCDFP-15, ER, progesterone receptor, and CK 7. On the other hand, the metastatic prostatic carcinoma showed absence of staining with ER, progesterone receptor, GCDFP-15, and CK 7.

It is important to differentiate between metastatic prostatic carcinoma in the breast and primary breast carcinoma because of the marked difference in prognosis. The prognosis of a primary male breast carcinoma is determined by the stage at diagnosis and is likely to be more favorable than the prognosis for metastatic prostatic carcinoma. Therefore, we suggest that breast carcinomas in patients with prostatic adenocarcinoma should be carefully evaluated using immunostains to clearly distinguish primary from metastatic tumor when the distinction is not clearly evident on the basis of routine hematoxylin-eosin-stained sections and clinical data. The antibodies that are helpful in distinguishing metastatic prostatic adenocarcinoma from primary breast carcinoma include CK 7, ER, GCDFP-15, PSA, and PsAP. However, the selection of immunostains in a particular case will depend on the immunoreactivity of the primary prostatic carcinoma.

**References**