

Urological Survey

compression or penetration. In other words, the injury that causes the most shearing forces to the urethra should cause an injury.

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PATHOLOGY

The role of P501S and PSA in the diagnosis of metastatic adenocarcinoma of the prostate

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Background: Adenocarcinoma of the prostate can present as metastatic carcinoma with no known primary. Prostatic origin can be confirmed in most of these cases by immunohistochemistry for prostate-specific antigen (PSA) and prostate-specific acid phosphatase. In a small subset of high-grade prostate carcinomas, both markers are negative and therefore are not helpful for confirming prostatic origin. Recently, novel marker proteins that are preferentially expressed in prostate tissue were identified. One such marker is P501S or prostein, a 553-amino acid protein that is localized to the Golgi complex. It is expressed in both benign and neoplastic prostate tissues, but not in any other normal or malignant tissue examined to date. Owing to its apparent specificity, prostein may be a good marker to demonstrate prostatic origin in metastatic prostate cancer.

Design: Five-micron sections of a tissue microarray were subjected to immunohistochemistry with a monoclonal mouse anti-P501S (clone 10E3, Dako, Carpinteria, CA) antibody and a monoclonal mouse anti-PSA (clone ER-PR8, Dako, Carpinteria, CA) antibody. The tissue microarray contains 78 cases of metastatic prostatic adenocarcinoma, 20 cases of primary prostatic adenocarcinoma, and 20 cases of benign prostate tissue from the peripheral zone as well as samples of benign brain, pancreas, kidney, thyroid, testis, skeletal muscle, and fibroconnective tissue.

Results: Similar staining (intensity and extent) was identified for both markers in the majority of metastatic tumors (11 distant sites, 42 pelvic lymph nodes), in all 20 primary tumors and in all benign prostate and nonprostate tissues. The P501S stain had perinuclear cytoplasmic (Golgi) distribution even in poorly differentiated tumors and metastases. Two distant metastases were negative for PSA but retained focal weak positivity for P501S. Two other distant metastases were weakly PSA positive, but strongly P501S positive. Metastases in the pelvic lymph nodes were positive for both markers in 53 cases and 1 lymph node metastasis was strongly PSA positive but P501S negative. In summary, 67 of the 69 cases (97%) of metastatic prostate carcinomas were PSA positive, whereas 68 of the 69 cases showed at least focal weak reactivity for P501S (99%). None of the tumors were negative for both markers.

Conclusions: Immunohistochemistry for P501S is a sensitive and highly specific marker for identifying prostate tissue. The large majority of metastatic prostatic adenocarcinomas are P501S positive (99%). A small subset of metastatic prostatic adenocarcinoma shows significant differences in staining intensity and extent for PSA and P501S and, therefore, combined use of these markers may result in increased sensitivity for detecting prostatic origin.

Editorial Comment

In 2001 (1), Xu et al. identified P501S or prostein, a novel prostate-specific protein expressed in normal and malignant prostate tissues. Characterization of the prostein gene showed that prostein cDNA encodes a 553-amino acid protein. The protein is predicted to be a type IIIa plasma membrane protein with a cleavable signal peptide and 11 transmembrane-spanning regions. Prostein gene is located on chromosome 1 at the WI-9641 locus between q32 and q42. Prostein mRNA is shown to be uniquely expressed in normal and cancerous prostate tissues using Northern blot, cDNA microarray, and real-time PCR analysis. Furthermore, prostein mRNA expression does not appear to be prostate tumor grade related and is restricted exclusively to prostate cell lines. Immunohistochemical staining using a mouse monoclonal antibody generated against prostein demonstrates that this protein is specifically detected in prostate tissues both at the plasma membrane and in the cytoplasm.

P501S or prostein should not be confounded with P504S (alpha-methylacyl coenzyme A racemase or AMACR). In 2000, Xu et al. (2) using cDNA library subtraction in conjunction with high throughput microarray screening, identified 3 genes: P503S, P504S and P510S that showed differential expression in malignant and benign prostate glands. It was demonstrated AMACR (P504S) immunoreactivity in prostatic adenocarcinoma but not in benign prostatic glands, while P503S immunoreactivity was present in both malignant and benign glands. Furthermore, it was found AMACR overexpression in colorectal, ovarian, breast, bladder, lung, and renal cell carcinomas, as well as lymphomas and melanomas (3). This findings makes AMACR unsuitable for the diagnosis of metastatic adenocarcinoma of the prostate.

In the study surveyed, P501S or prostein showed that is a good marker in metastatic adenocarcinoma of the prostate. The authors found that 67 of the 69 cases (97%) of metastatic prostate carcinomas were PSA positive, whereas 68 of the 69 cases showed at least focal weak reactivity for P501S (99%). None of the tumors were negative for both markers. They conclude that Immunohistochemistry for P501S or prostein is a sensitive and highly specific marker for identifying prostate tissue. The large majority of metastatic prostatic adenocarcinomas are P501S positive (99%).

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Renal medullary carcinoma: report of seven cases from Brazil

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We report seven cases of renal medullary carcinoma collected from several institutions in Brazil. In spite of a relatively high incidence of sickle cell trait in Brazil, this is a rare tumor. All patients were males between the ages of 8 and 69 years (mean 22 years). From the collected information, the most frequent presenting symptoms were gross hematuria and flank or abdominal pain. The duration of symptoms ranged from 1 week to 5 months. Most of the tumors were poorly circumscribed arising centrally in the renal medulla. Size ranged from 4 to 12 cm (mean 7 cm) and hemorrhage and necrosis were common findings. All seven cases described showed sickled red blood cells in the tissue and six patients were confirmed to have sickle cell trait. All cases disclosed the characteristic reticular pattern consisting of tumor cell aggregates forming spaces of varied size, reminiscent of yolk sac testicular tumors of reticular type. Other findings included microcystic, tubular, trabecular, solid and adenoid-cystic patterns, rhabdoid-like cells and stromal desmoplasia. A peculiar feature was suppurative necrosis typically resembling microabscesses within epithelial aggregates. The medullary carcinoma of the 69-year-old patient was associated with a conventional clear cell carcinoma. To our knowledge, this association has not been previously reported and the patient is the oldest in the literature. The survival after diagnosis or admission ranged from 4 days to 9 months. The 8-year-old African-Brazilian patient with a circumscribed mass is alive and free of recurrence 8 years after diagnosis. This case raises the question whether a periodic search for renal medullary carcinoma in young patients who have known abnormalities of the hemoglobin gene and hematuria could result in an early diagnosis and a better survival.

Editorial Comment

Renal medullary carcinoma is a rare, rapidly growing tumor that affects young individuals with sickle cell trait. This tumor was described in 1995 by Davis et al. (1), which considered it the seventh sickle cell nephropathy. The six sickle cell nephropathies previously described by Berman (2), in 1974, are gross hematuria, papillary necrosis, nephrotic syndrome, renal infarction, inability to concentrate the urine and pyelonephritis. All of them are to a certain extent related to the obstruction of blood vessels and tissue hypoxia resulting from red blood cell sickling. The renal medulla is particularly susceptible to damage in sickle cell disease due to its unique environment characterized by anoxia, hyperosmolarity and low pH that tend to promote hemoglobin S polymerization and red blood cell sickling. Over a period of 22 years, the Armed Forces Institute of Pathology had collected only 34 cases (1) and over the next 5 years, only 15 more had been described (3).

The incidence of sickle cell trait in Brazil is 6.7% in African-Brazilians, 5.4% in Mulattos (persons with mixed White and African-Brazilian ancestry) and 0.21% in Whites (4). Considering the large population at risk, the tumor is, in fact, very rare suggesting that additional factors are likely necessary. This is the first report from Brazil as a result of the collaboration of several pathologists that searched for cases of renal medullary carcinoma in their institution's files.

Renal medullary carcinoma is typically seen in young patients with the sickle cell trait and exceptionally with sickle cell disease. All seven cases described in the study showed sickled red blood cells in the tissue and six patients were confirmed to have sickle cell trait. Renal medullary carcinoma shows a male predominance (2:1) and the mean age at presentation is approximately 22 years, with ages ranging from 5 to 40 years.

The most frequent presenting symptoms are gross hematuria and flank or abdominal pain. A palpable abdominal mass is often observed. Some patients may present with symptoms of metastatic disease. Spontaneous gross hematuria, the first sickle cell nephropathy, is usually unilateral and occurs at the same age range that renal medullary carcinoma. It is worth noting, however, that most of these spontaneous benign bleedings occur from the left kidney and most of the renal medullary carcinomas arise on the right kidney. The origin and pathogenesis of renal medullary carcinoma are not completely understood.

The prognosis of renal medullary carcinoma is very poor due to the highly aggressive behavior of this neoplasm and to its resistance to conventional chemotherapy. Metastases are both lymphatic and hematogenous with liver and lungs most often involved. The mean duration of life after surgery is about 15 weeks (5) and the

longest documented survival for renal medullary carcinoma was 15 months (6). Exceptionally, the 8-year-old African-Brazilian patient with a circumscribed mass described in the study is alive and free of recurrence 8 years after diagnosis. Chemotherapy has been known to prolong survival by few months but generally, neither chemotherapy nor radiotherapy has altered the course of the disease (7).

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INVESTIGATIVE UROLOGY

Structural organization of fibrous connective tissue in the periacinar region of the transitional zone from normal human prostates as revealed by scanning electron microscopy

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Objective: To analyse, using scanning electron microscopy (SEM), the organization of stromal fibrous components in the transitional zone (TZ) from normal human prostates; because of its association with disease, greater emphasis was placed upon the periacinar region of the stroma.

Materials and Methods: TZ specimens were obtained from normal prostates during autopsy of six men, aged 18-30 years, who had died from accidents. Tissue was fixed for SEM in a modified Karnovsky solution for 48 h at 4 degrees C, and to visualize the three-dimensional organization of the stroma, samples were treated to remove cells.

Results: In acellular preparations, narrow fibrous septa formed a dense and supportive scaffold for ducts and acini, and a smooth and homogeneous fibrous sheet, herein identified as pars fibroreticularis, lined the acinar