PATHOLOGY

The utility of microscopic findings and immunohistochemistry in the classification of necrotic testicular tumors: a study of 11 cases

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Necrotic testicular tumors are relatively frequent and can present a significant diagnostic challenge. Because of differing treatments for seminomas versus nonseminomas, accurate diagnosis is critical. Eleven totally (n = 9) or almost totally (n = 2) necrotic testicular tumors were retrieved from our consult files. The submitting pathologists favored benign processes in 4 cases, Leydig cell tumor in 1, and lymphoma in 1. The cases were evaluated for histologic features and, when material was available, by immunostaining with 7 antibodies: keratin (AE1/AE3), OCT4, placental alkaline phosphatase, alpha-fetoprotein (AFP), CD117, CD30, and S100. Only distinct reactivity in a cellular distribution in the necrotic zone was considered positive; nuclear reactivity alone was scored for OCT4 and membrane reactivity for CD117 and CD30. Mean patient age was 35 years (range 16-63). Mean tumor size was 19 mm (range 7-53). All patients presented with unilateral testicular masses (6 right, 5 left); 2 also had acute pain. The combination of histologic features, immunostains and, in 1 case, serum AFP permitted classification of 8 tumors (4 seminomas, 3 embryonal carcinomas, 1 yolk sac tumor). Three were not classifiable. The necrotic seminomas lacked associated coarse intratubular calcifications and were positive for OCT4 (4/4) and CD117 (3/3) but negative for keratin (0/4) and CD30 (0/4). The necrotic embryonal carcinomas had associated coarse intratubular calcifications and were positive for keratin (2/3), OCT4 (2/2), and CD30 (3/3). OCT4 stained 1 unclassifiable tumor, which lacked other specific markers. We did not find placental alkaline phosphatase, AFP, and S100 stains useful, although S100 did highlight tumor "ghost" cells in 1 case. Other features in most cases included intratubular germ cell neoplasia (6/11), tubular atrophy/hyalinization (10/11), tumor "ghost" cells (10/11), scar (9/11), and inflammation (10/11). Of the 5 patients with available follow-up, 3 were free of disease at 1, 5, and 8 years after orchiectomy (2 necrotic seminomas and 1 germ cell tumor, unclassified). One patient with yolk sac tumor (age 63 y) developed widespread metastases after 15 months and died of disease. The final case was initially misinterpreted as "testicular infarction, no malignancy" and 16 months later the patient developed a large retroperitoneal seminoma. Most totally necrotic testicular tumors can be placed into clinically important groups by assessment for coarse intratubular calcifications and staining reactions for keratin, OCT4, CD117, and CD30.

Editorial Comment

For a proper treatment, testicular tumors must be classified as seminomatous and non-seminomatous. In order to consider a tumor purely seminoma the neoplasia must be adequately processed. At least one section per centimeter of greatest diameter of the tumor is optimal. Each histological type has peculiar microscopic findings that allow a proper diagnosis. In some cases, the diagnosis is difficult. One example is the differential diagnosis in cases of solid embryonal carcinoma. Characteristically this tumor shows tubular arrangement. In cases it is solid it must be differentiated from seminoma. Some nuclear characteristics help in this distinction but immunohistochemistry is also very helpful (1).

In cases of necrotic tumors or totally necrotic the diagnosis is a challenge for the pathologist. The study by Miller et al. shows that immunohistochemistry and some other additional microscopic findings may be very helpful in the recognition of the type of tumor. As an example: necrotic seminomas lacked associated coarse intratubular calcifications and were positive for OCT4 and CD117 but negative for keratin and CD30, and necrotic embryonal carcinomas had associated coarse calcifications and were positive for keratin, OCT4,

and CD30. The study showed that in spite of necrosis, most tumors could be placed into clinically important groups for treatment.

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Focal prostatic atrophy: mimicry of prostatic cancer on TRUS and 3D-MRSI studies

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Prostatic atrophy which represents a form of adaptive response to injury most commonly to inflammation and/or chronic ischemia is a histological abnormality frequently found in prostate biopsies and autopsies. Although commonly found, this lesion is rarely reported in the prostatic biopsy reports. It is well known that histologically focal prostatic atrophy (FPA) is one of the most frequent mimics of prostatic adenocarcinoma. On conventional and color Doppler transrectal ultrasound and on magnetic resonance spectroscopic imaging studies (MRSI), FPA may also simulate prostate cancer. Thus, this entity should be considered together with prostatitis as an important cause of false-positive results in MRSI of the prostate. It has been shown that there is a positive and significant association between extent of FPA in biopsies and serum total or free PSA elevation. For this reason, pathologists should include the presence of FPA in the pathology report of a prostatic biopsy, particularly in those patients with absence of cancer. When extensive FPA is the only finding in patients with several negative prostatic biopsies, this lesion may be the source for PSA elevation.

Editorial Comment

Prostatic atrophy is one of the most frequent microscopic mimics of prostatic adenocarcinoma (1). In the study reviewed, the lesion is also an important mimicker of adenocarcinoma on conventional and color Doppler transrectal ultrasound and on magnetic resonance spectroscopic imaging studies MRSI). It occurs most frequently in the peripheral zone and gained importance with the increasing use of needle biopsies for the detection of prostatic carcinoma. The frequency of the lesion in autopsies is 85% and increases with age. Inflammation, radiation, antiandrogens and chronic ischemia due to local arteriosclerosis are all considered causes of the lesion although many examples of atrophy are still considered idiopathic in nature. The histological subtypes of prostatic atrophy do not represent distinct entities but a morphologic continuum of acinar atrophy and most of the times are seen concomitantly. The most common subtype that causes difficulty for pathologists is partial atrophy due to the pale cytoplasm lateral to the nuclei giving rise to pale staining glands that more closely mimic cancer.

Some reports suggest that focal atrophy may be causally linked to prostate cancer and to other pre-neoplastic lesions (2). However, other studies do not support this hypothesis (3). An intriguing finding is the association of extent of atrophy to serum PSA elevation (4). What would be a possible pathogenesis for the serum PSA elevation associated to focal prostatic atrophy? It is intriguing that cells of the secretory compartment of

atrophic acini may produce higher levels of PSA. It is speculated that injurious stimuli causing focal prostatic atrophy may interfere in the physiologic barrier that prevents the escape of any significant amounts of PSA to the general circulation.

Prostate-specific antigen is a single chain glycoprotein with proteolytic enzyme activity mainly directed against the major gel-forming protein of the ejaculate (semenogelin). PSA induces liquefaction of semen with release of progressively motile spermatozoa. There are several efficient physiologic barriers to prevent the escape of any significant amounts of PSA from the prostatic ductal system: basement membrane of the acini, basal cells lining the acini, prostatic stroma, basement membrane of capillary endothelial cells, and endothelial cells. These barriers normally prevent PSA from entering the general circulation at concentrations of more than 3 ng/mL.

Focal prostatic atrophy represents a form of adaptive response to injury most commonly to inflammation and/or local ischemia. Inflammation and/or ischemia are injurious stimuli resulting in diminished oxidative phosphorilation, membrane damage, influx of intracellular calcium, and accumulation of oxygen-derived free radicals (oxidative stress). Studies showing elevated levels of glutathione S-transferase P1, glutathione S-transferase A1, and Cox-2 in prostatic atrophic epithelial cells suggest a stress-induced response (5,6). We do not know which mechanisms are involved in the physiologic barrier that prevents the escape of any significant amounts of PSA to the general circulation, however, all these stress-induced responses may affect this barrier. Inflammation and particularly ischemia may have also a field effect affecting the physiologic barrier of normal acini close to atrophic acini.

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