Venue: ANUKIS
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1130-1245 hr

Symposium 1D: Diagnostic challenges in urogenital pathology

S1D-1. Mimickers of high grade prostatic intraepithelial neoplasia (HGPIN)

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Central zone histology
Glands within the central zone up at the base of the prostate are complex and large with numerous papillary infoldings, and often are lined by tall pseudostratified epithelium with eosinophilic cytoplasm. Central zone glands are frequently overdiagnosed as HGPIN because their nuclei are piled up and they may be arranged in Roman bridge and cribriform glandular patterns. Central zone glands are distinguished from HGPIN by their lack of cytological atypia.

Clear cell cribriform hyperplasia
Clear cell cribriform hyperplasia consists of crowded cribriform glands with clear cytoplasm sometimes growing as a nodule and in other instances more diffusely. The key distinguishing feature of clear cell cribriform hyperplasia from HGPIN is the lack of nuclear atypia. Furthermore, within a nodule of clear cell cribriform hyperplasia, at least some of the cribriform glands show a strikingly evident basal cell layer, which is unique for this entity.

Basal cell hyperplasia
Otherwise typical basal cell hyperplasia may show prominent nucleoli along with mitotic activity. Because of the prominent nucleoli, these lesions may be mistaken for HGPIN. The nuclei in basal cell hyperplasia tend to be round and at times form small solid basaloid nests. In contrast, the nuclei in HGPIN tend to be more pseudostratified and columnar and do not occlude the glandular lumina. Within areas of basal cell hyperplasia, atypical basal cells can be seen undermining overlying benign appearing secretory cells. HGPIN has full thickness cytological atypia with the nuclei oriented perpendicular to the basement membrane. Basal cell hyperplasia reveals high molecular weight cytokeratin or p63 positivity in multilayered nuclei. In HGPIN, high molecular weight cytokeratin or p63 labels only flattened cytologically benign basal cells beneath the negatively stained atypical cells of PIN. Whereas cribriform HGPIN glands represent a single glandular unit with punched out lumina, many of the glands within a focus of cribriform basal cell hyperplasia appeared as fused individual basal cell hyperplasia glands (pseudocribriform).

Acinar (usual) adenocarcinoma
Almost always when there are atypical cribriform glands, they are accompanied by small atypical infiltrating glands where the diagnosis of infiltrating tumor can be made. Only when cytologically atypical cribriform glands are so large, back-to-back, or outside of the prostate that they are inconsistent with cribriform PIN should infiltrating cribriform carcinoma be diagnosed on H&E stained sections in the absence of small atypical infiltrating glands. The other more common scenario where it is difficult to distinguish acinar adenocarcinoma from HGPIN is when there are a few atypical glands immediately adjacent to HGPIN. The differential diagnosis is whether these small glands represent tangential sectioning or outpouching off of the HGPIN glands or a small focus of carcinoma adjacent to the HGPIN. We refer to these foci at PINATYP. A diagnosis of carcinoma can be rendered only if the small atypical glands are too numerous or too far away from the HGPIN glands to represent outpouching or tangential sectioning from the PIN glands. Racemase does not differentiate between HGPIN and cancer, as both typically express this antigen.

Ductal adenocarcinoma

Ductal adenocarcinomas are often centrally located in the periurethral region and sampled on TURP. PIN is uncommonly found within the periurethral region and infrequently seen on TURP. Ductal adenocarcinomas often contain true papillary fronds with well-established fibrovascular cores, whereas HGPIN more frequently reveals micropapillary fronds with tall columns of epithelium without fibrovascular stalks. Ductal adenocarcinomas frequently contain comedonecrosis, which may be extensive. HGPIN usually lacks comedonecrosis, and when present is focal. Finally, ductal adenocarcinomas may consist of very large and/or back-to-back glands, whereas glands involved by PIN are of the size and distribution of benign glands. The use of basal cell markers in this differential diagnosis may be problematical, as both HGPIN and ductal adenocarcinoma may display a patchy basal cell layer. However, absence of a basal cell layer in numerous glands rules out PIN.

S1D-2. Testicular tumours

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The current classification of testicular tumours is based on a revised scheme originally put forward by Dixon and Moore. Although the histological features of the prototype tumours are well described, the pathological diagnosis of testicular tumors can still be problematic. As with other neoplasms, accurate diagnosis rests firmly with the appreciation of gross morphology, thorough sampling of the lesion(s), meticulous study of the histological features and the judicious use of immunohistochemistry.

Knowledge of the existence of histological mimics within each of the broad diagnostic categories of testicular tumours minimizes diagnostic errors. For example, in the diagnosis of seminoma, nuances in the morphology and architectural variation may pose difficulties differentiating seminoma from embryonal carcinoma, Sertoli cell or yolk sac tumour. Similarly, calcification in Leydig cell tumours may erroneously suggest a diagnosis of large cell Sertoli cell tumour; and infarction in large adenomatoid tumours may imitate malignancy.

Among some of the new developments in the field, the existence of an anaplastic variant of testicular seminoma , long considered controversial, has been re-visited in a recent paper , where the researchers showed that anaplastic seminoma cells tended to be *c-kit* negative, and compared with classic seminoma, showed a larger proportion of cells staining for MIB-1 activity. Similarly, recent studies have also looked at features for predicting malignant behavior in Sertoli cell tumours.

The practicing pathologist must therefore remain alive to these new developments, so that accurate diagnosis can be rendered which can then be translated into optimum patient care.