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Pseudo-neoplastic Lesions of Prostate and the Diagnostic Deception

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Abstract

Introduction: Many pseudo-neoplastic lesions of the prostate gland are recognized. Histologically these lesions mimic the adenocarcinoma of prostate. Pseudo-neoplastic lesions comprise of different glandular and non-glandular or solid patterns. Largely emphasized on the epithelial origin but some stromal and solid lesions are also important. In developing countries, the routine Hematoxylin and eosin (H&E) stain is most commonly used to stain the histological tissue sections. The other stains and molecular studies are not frequently used. The pseudoneoplastic lesions are so obscure and deceptive that sometimes it become very difficult to recognize. The diagnostic facilities both in government and private sector should have at least the facility of immunohistochemical staging to avoid misinterpretations.

Methodology: This retrospective study performed at Muhammad Medical College Mirpurkhas Sindh. 192 specimens of radical prostatectomy (RP) and transurethral resection of the prostate (TURP) received between January 2015 to December 2017 were retrieved for review. All retrieved blocks processed as per standard histopathological techniques. Fresh tissue sections taken and stained with H&E.

Results: All tissue sections reviewed to observe the glandular patterns, their architectural morphology, cytological changes and inflammatory process. The lesions were distinguished on epithelial origin and glandular patterns. Cases of benign prostatic hyperplasia were 169 (88 %), adenosis 06 (3.12 %), reactive hyperplasia 06 (3.12 %), Post atrophic hyperplasia 05 (2.6 %), benign stromal proliferation 02 (1 %) and prostate carcinoma 04 (2%).

Conclusion: Many pseudoneoplastic lesions of the prostate are the mimicker of adenocarcinoma. On H&E stains it sometimes become difficult to differentiate the lesions. The histomorphological diagnosis of these lesions should be facilitated at least by immunohistochemical stains at diagnostic tcenters.t

Keywords: Immunohistochemistry, Transurethral resection of prostate (TURP), Radical prostatectomy (RP). Hematoxylin and Eosin (H&E).

Introduction: Many retrograde lesions of prostate gland may mimic inversely with benign or malignant lesions[1]. These lesions are so deceptive that sometimes it become impossible to decide. The diagnostic perception arises when prostatic adenocarcinomas are morphologically present in two entities of low-grade adenocarcinomas Gleason score 2 and high grade adenocarcinomas[2]. Typical cytological atypia may not present in low grade adenocarcinoma. The tumors are usually identified on architectural morphology and basal epithelial layer[3]. In high grade tumors there is morphological abstraction and multidimensional mimicry to pseudoneoplastic lesions. The list of pseudoneoplastic benign lesions is given in table 1. Clear cell cribriform hyperplasia is not frequent form of benign prostatic pseudolesions[4]. It is nodular. Finger like out pouching or papillary projections are present. It involves transitional zone of prostate, usually identified in TURP specimenqs[5]. Histologically glands lie back to back with intraepithelial proliferation forming cribriform pattern. The cells are cuboidal or low columnar with clear cytoplasm, small uniform nuclei with inconspicuous nucleoli. Sometimes immunohistochemical stains are helpful to highlight basal cells at periphery of cribriform aggregates to differentiate it from high-grade prostatic intraepithelial neoplasia (HGPIN)[6]. Basal cell hyperplasia (BCH) is characterized by proliferation of basal cell layer[7]. It develops usually in the transitional zone of prostate. Basal hyperplasia includes basal cell adenoma and adenomatosis. The nuclei are hyperchromatic with prominent nucleoli. These are composed of basaloid cells present as nests separated by concentric layers of compressed stroma. Often is associated with chronic inflammation[8]. BCH do not raise problems of diagnosis but sometimes with cytologic atypia it may be confused with malignant lesion[9]. HGPIN raise important diagnostic problem. Although benign neoplastic lesion some time represent with atypical cells and necrosis. The mitoses are reported in 3% of HGPIN[10]. Acinar atrophy and post-atrophic hyperplasia (PAH) are commonly confused with adenocarcinoma. The acini are round, often dilated and distorted, lined by attenuated flattened epithelium. Benign atrophy may appear infiltrative wherever atrophic glands insinuate themselves as isolated units between benign glands[11]. Atypical adenomatous hyperplasia (AAH) or adenosis is also common mimicker of prostatic adenocarcinoma. It is localized usually in transitional zone of prostate and present in TURP specimens. In these lesions there is pseudo-infiltrative pattern. Some acini completely lacking basal cells[12]. Sclerosing adenosis is a pseudoneoplastic condition in which proliferating glands are compressed by myxoid spindle cell stroma. The lesions may simulate low grade adenocarcinoma. Reactive atypia is commonly associated with chronic non-specific inflammation. Proliferative small glands are lined by atypical epithelial c ells[13]. Granulomatous prostatitis is characterized by sheets of epithelioid, foamy macrophages and epithelial cells from ruptured prostate ducts and acini may resemble with adenocarcinoma[14]. Small glandular patterns of non-epithelial origin are the lesions which arise from seminal vesicle, ejaculatory duct and Cowper

(Bulbourethral) glands. The branching small glandular structures may resemble adenomcarcioma[15]. Pseudoneoplastic lesions of mesonephric remnant s resemble adenocarcinoma[16]. In colonic gland remnants the diagnostic difficulty is when blue tinged mucin or prominent nuclei are evident. The basal layer may be absent[17]. Nephrogenic adenoma noticed in nephrogenic remnants within prostate glands. Lesions predominantly composed of small tubules. Cystically dilated tubules are lined by cuboidal to low columnar or hobnail shaped eosinophilic cells[18]. Solid and non-glandular patterns are comprising of xanthoma[19-22], signet ring like changes[20]. Paraganglia, Malakoplakia which may mimic the variants of adenocarcinoma of prostate[21]. Prostate xanthoma is rare pseudoneoplastic lesion in which there is a collection of lipid laden foamy macrophages can be confused with foamy gland variant of prostatic adenocarcinoma [(22)]. Paraganglia in peri-prostatic soft tissues may resemble adenocarcinoma in needle biopsies. Large lymphocytes and prostatic stromal cells rarely can exhibit a signet ring like morphology which may mimic the high-grade signet ring adenocarcinoma of prostate.

TABLE 1

List of pseudoneoplastic lesions of prostate gland

- Post atrophic hyperplasia.
- Adenosis.
- Sclerosing adenosis.
- Mesonephric hyperplasia.
- Nephrogenic adenoma.
- Cribriform hyperplasia.
- Malakoplakia.
- Xanthoma.
- Seminal vesicle, Cowper gland and paraganglia in prostate.
- Radiation hyperplasia.
- Squamous (and transitional cell) metaplasia.
- Basal cell hyperplasia.
- Postoperative spindle cell nodule.
- Benign stromal proliferation.
- Signet ring like change.
- Paraganglia.
- Granulomatous prostatitis.

Methodology: This retrospective study performed at the department of pathology Muhammad Medical College Mirpurkhas Sindh Pakistan. All 192 specimens of radical prostatectomy (RP) and transurethral prostate resection (TURP) received between January 2015 to December 2017 were retrieved for purpose of the review. All retrieved blocks processed as per standard histopathological techniques. Fresh tissue sections taken and stained with hematoxylin and eosin. The data collected from hospital record and previous histopathological reports.

Results: The age of patient ranges from 42–78 years with mean age 60 years. All the tissue sections examined to review and observe the glandular patterns with architecture, cytology, luminal contents and inflammatory processes. The arrangement of basal cell layer, preservation of lobules and acini. The cytological changes, nuclear atypia and nucleolar prominence. Cases of benign prostatic hyperplasia were 169 (88 %), adenosis 06 (3.12 %), reactive hyperplasia 06 (3.12 %), post atrophic hyperplasia 05 (2.6 %), benign stromal prolife ration 02 (1 %) and prostate carcinoma 04 (2 %).

Table 2: Total number of cases and their distribution according to lesion (n=192)

Lesion	No: of cases	Percentage
Benign prostatic hyperplasia.	169	88
Adenosis	06	3.12
Reactive hyperplasia	06	3.12
Post atrophic hyperplasia	05	2.6
Benign stromal proliferation	02	1.0
Prostate Carcinoma	04	2.0

Figure – 1 Atrophy of prostate. Disorderly arrangement of the glands.

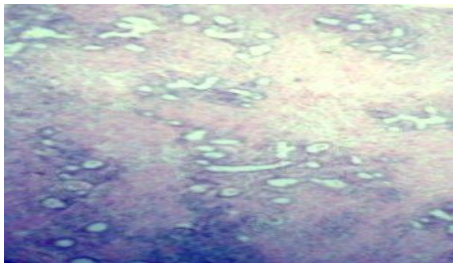


Figure – 2 Adenosis of prostate. Aggregates of glands present in fibromuscular stroma.

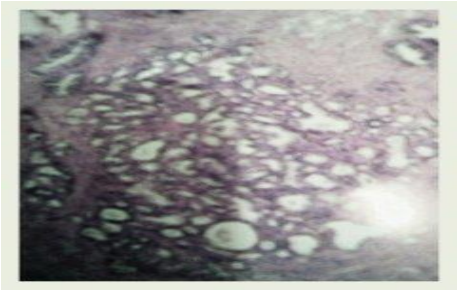
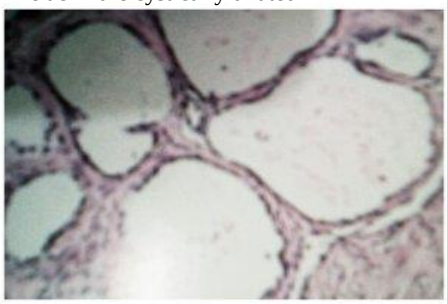


Figure – 3 Post-atrophic hyperplasia. The acini are cystically dilated



Discussion: Prostate is the discrete organ of body in which lesions are so obscure that sometimes it is very difficult to diagnose on conventional histological methods, even if the lesion is well differentiated carcinoma, deceptive in their morphological and cytological order and arrangement[23]. Sometimes it become difficult to sort them out on conventional

methods. In developing countries with few exceptions, the tumor markers and even the immunohistochemical stains are not used in diagnostic centers. The basic stains hematoxylin and eosin is usually used to stain the tissue sections. The misinterpretation of benign and malignant lesion is pitfall in pseudoneoplastic lesions of prostate gland[24]. Small glandular patterns are most frequently confusing with carcinoma as compare to other pseudoneoplastic lesion s of the prostate gland. Adenosis as reported in 1983 is still deceptive pseudo lesion due to its resemblance to adenocarcinoma[25]. Reactive atypia is also one of the most frequent pseudoneoplastic lesion seen in prostate specimens. Acute and chronic prostatitis foci can present glands with cribriform architecture and nuclear atypia. These aspects of reactive hyperplasia may be interpreted as HGPIN or as cribriform carcinoma. In prostate gland the epithelial abnormalities, glandular architectural patterns, inflammatory lesions, stromal proliferation and normal finding that may cause confusion are the basic elements to alter the structure[26]. In 1983 Chen and Sciff reported the sclerosing adenosis that resembled an adenomatoid tumor[25-26]. Subsequently Philip B. Clement encountered the similar case noted as resemblance to sclerosing adenosis of the breast[26]. Gikas and associates misdiagnosed one case of mesonephric remnant hyperplasia as adenocarcinoma of the prostate. The small acini of this process are generally similar in size and shape to those of prostatic carcinoma[27]. In 1984 Proppe and colleagues described pseudoneoplastic mesenchymal lesion. The original submitting of all cases was leiomyosarcomas[28]. The large glandular patterns are present in central zone of the prostate around ejaculatory duct adjacent to seminal vesicles. It contains glands of large size and more complex architecture than the transitional and peripheral glands with papillae, arches, epithelial bridges and cribriform structures. The cribriform glands from central zone may be confused with cribriform HGPIN, as HGPIN is reported in central area of prostate with the incidence of 13% [5,29]in cystoprostatectomy specimens. In current study, it was not difficult to diagnose the 169 cases of benign prostate hyperplasia and 04 cases of well differentiated carcinoma, although 19 cases of pseudoneoplastic tumors were deceptive in their morphological patterns. In 06 cases of adenosis the basal epithelial layer of glands was not discernable. In 06 cases of reactive hyperplasia due to chronic non-specific inflammation, there was proliferation of small glands which lined by single layer of reactive atypical cells. In 05 cases of post atrophic hyperplasia, the glands were cystically dilated and lined by single layer of flattened cells. In 02 cases of stromal proliferation, most glands were small in size and compressed. The scanty epithelium was obvious and due to pseudo-sarcomatous appearance the morphology was undecidable. It is sometimes very difficult to differentiate between benign and malignant features by routine H & E stain. For diagnostic awareness of the salient histological features, relevant immunohistochemical features of these prostatic pseudo neoplasms is critical to avoid rendering false positive diagnosis of malignancy[30].

Conclusion:

Pseudoneoplastic lesions of the prostate gland are mimickers of adenocarcinoma of prostate. On H & E stain sometimes, it is difficult to differentiate these lesions. The histomorphological diagnosis of these lesions should be facilitated by molecular and immunohistochemical stains to avoid the misdiagnosis.

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