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Review article

Clinical implications of the forgotten Skene's glands: A review of current literature

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ABSTRACT

Introduction: The clinical and pathological aspects of the Skene's glands have not been addressed in the current scientific literature.
Aim: To review the current literature to focus on the clinical and pathological aspects of the Skene's glands. The historical perspective including embryology, anatomy, histology, and current role of prostatic specific antigen (PSA) as a tumor marker of lesions which develop from the Skene's glands, 'female prostate.'
Material and methods: Medline searches were performed to review the current literature regarding Skene's glands pathology, clinical manifestations, diagnosis, role of PSA, and its treatment options.
Discussion: Anatomical pathology including inflammatory, cystic, solid, benign, and malignant tumors of Skene's glands is emphasized. The unique role of PSA in these lesions is reviewed. Cognizance of periurethral, perimeatal and urethral masses is essential for anatomical pathologists, radiologists, urologists and gynecologists who encounter complex female urethral masses in their clinical practice. Imaging techniques of Skene's glands to diagnose urethral, perimeatal and periurethral masses in female are reviewed.
Conclusions: The literature of the interesting scientific concepts related to the Skene's glands are reviewed. The role of PSA in these lesions is expanded for diagnoses and treatment options of pathology of the Skene's glands. Methods of imaging are necessary for radiologist, pathologists, and clinicians alike, for the proper treatment of Skene's gland lesions.

1. Introduction

In 1880, Alexander Skene discovered prostatic glandular tissue proximally located next to two large ducts adjacent to the female urethra, thus proving the existence of the female prostate.[1] Before Skene's discovery, several researchers speculated the idea of the existence of a female prostate. A researcher named Galen first discussed the idea of the female prostate, but he believed the prostatic tissue was located closer

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to the fallopian tubes than the urethra. In 1672, de Graaf described ducts in close proximity to the female urethral meatus, and believed that these structures drained the female prostate.[2] In 1853, Virchow described stone-like masses inside the ducts surrounding the urethral meatus. He concluded these urethral glands and ducts were homologous to the male prostate. In 1889, Tourneaux similarly described glands adjacent to the urethral meatus, stating that these glands were structurally similar to the prostatic glands of a five- to six-month-old male fetus.[3] Pallin, in 1901, found that the Skene's glands are not homologous to the whole male prostate, but to the cranial and ventral portions. In 1922, Johnson examined female fetuses at different developmental stages comparing female embryology with that of a male. He noted that the Skene's glands first appear in 60-mm female embryo, and that the glands were distributed along the anterior, posterior, and lateral walls of the urethra. He also stated that compared to their male counterpart, Skene's glands are 'fewer in number, less closely packed together, have fewer branches, thicker epithelial walls, smaller lumina, and less evidence of epithelia with active secretion.'[4] In the 1940s, Huffman described Skene's glands as located primarily along the distal half of the urethra. Additionally, he stated the 'female periurethral glands are homologous with only that portion of the male prostate arising cephalad to the urogenital sinus.' Huffman also recognized the importance of the Skene's gland and diverse pathologies that can arise from them. He noticed that inflammation and irritation of the glands might result in cystic enlargement. This could lead to obstruction and abscess formation of the anterior vaginal wall and urethra while creating urethra-vaginal fistulas.[5,6]

2. Aim

To readdress the focus to Skene's glands and recall the overlooked historical perspective, embryology, anatomy, histology, and current role of prostatic specific antigen (PSA) as a tumor marker of lesions which develop from the Skene's glands 'female prostate.'

3. Material and methods

Medline searches were performed to review the current literature regarding skene's glands, pathology, clinical manifestations, diagnosis, and treatment options.

4. Discussion

4.1. *Embryology, anatomy, and histology of Skene's glands and their ducts*

The Skene's glands and ducts are normally located on the distal third of the female urethra, emptying approximately of an eighth of an inch from the outer edge of the meatus.[1] According to Huffman who performed serial sections and wax model reconstructions of the paraurethral glands, no ducts were found to be larger than 4 cm. Additionally, they extend aligned along the urethra's lateral, ventral, and to a lesser extent, the dorsal side. The glands themselves are described as 'branched tubular glands, with straight or slightly curved branches, which empty into the paraurethral ducts.' Furthermore, the glands are limited to the urethra with no evidence of vestibular or vaginal mucosa involvement.[5,6] Johnson described that Skene's glands are structurally similar to the male prostatic glands as they are solid, round, directed toward the bladder, and extend into the surrounding mesenchyme. They differ because there are fewer of them, they are dispersed, and do not exhibit active secretions.[4] Regarding embryological aspects, Johnson described the appearance of Skene's glands in a 60-mm female fetus, which originate from the urogenital sinus.[4] Histologically, they are composed of columnar epithelium and contain pale staining cytoplasm. The nucleus is described as being a large rounded structure that is located centrally or basally. Furthermore, within the columnar epithelium, the mucous secreting cells are stained for mucicarmine.[5] The lumen of a Skene's gland is composed of tall cylindrical secretory cells with short microvilli. Ample secretory granules and vacuoles are noted, in addition to numerous mitochondria and Golgi complexes. Dispersed throughout the secretory cells are basal cells, referred to as 'reserve cells,' which play a role in the regeneration of cells in the Skene's glands. The nucleoli of the basal cells contain dense chromatin.[7] Zaviacic et al. describes expression of human protein 1 in the prostatic tissues of both males and females. Human protein 1 can be found in the secretory cells of the Skene's glands which may function to protect the urothelium from the harsh urinary environment.[8]

4.2. *Presence of PSA in Skene's glands and tumors arising from Skene's glands*

Like the male prostate, the female prostate Skene glands have been shown to stain for PSA. Tepper et al. examined 18 female urethras with paraurethral glands by staining tissues for antibodies to PSA and prostate-specific acid phosphatase (PSAcPH). In total, 83% were positive for PSA and 67% positive for PSAcPH. This study thus proved the homology between the female paraurethral glands and male prostate.[9] It should be noted that the total PSA level in a female arises from the combination of female prostatic tissues such as diseased breast tissue.[10] Sloboda et al. described a case of a 46-year-old female with adenocarcinoma of the paraurethral glands that stained positive for PSA and PSAcPH, therefore linking it to male prostatic carcinoma.[11] Further studies have produced similar results, correlating carcinoma of the Skene's gland to male prostatic carcinoma.[12] Additionally, just like males, PSA can be used as a reliable tumor marker, as levels correlate with responsiveness to treatment.[10,13] Korytko et al. described a case of a 71-year-old female diagnosed with a Skene's gland adenocarcinoma with an initial PSA of 54.42 ng/μL. Treatment consisted of 73.8 Gy of intensity-modulated radiotherapy in 41 fractions, after which her PSA was 0.65 ng/μL (32 months after treatment). Therefore, females presenting with periurethral adenocarcinomas should be evaluated to determine if they are Skene's glands in nature, which would allow PSA levels to assess for treatment response.[13] Dodson et al. further discuss the decline in PSA