

## Ectopic Prostatic Tissue in Uterine Cervix: A Case Report

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Received: 29 Mar 2022

Accepted: 14 Apr 2022

Published: 20 Apr 2022

J Short Name: AJSCCR

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### Citation:

Rubens J. Ectopic Prostatic Tissue in Uterine Cervix: A Case Report. *Ame J Surg Clin Case Rep.* 2022; 4(10): 1-5

### Keywords:

Prostatic tissue in uterine cervix;  
Immunohistochemistry; PSA; CKHMW

### Abbreviations:

H-SIL: High-grade Squamous Intraepithelial Lesion; L-CGIN: Low-grade Cervical Glandular Intraepithelial Neoplasia; PSA: Prostate Specific Antigen; CKHMW: Cytokeratin high molecular weight

## 1. Abstract

Speaking about prostate in the context of a female patient would sound rather odd to the vast majority of interlocutors. We describe a case of ectopic prostatic tissue in the uterine cervix in a 30 years old patient. The microscopic analysis of the cervical cone biopsy showed H-SIL in the lower-left quadrant, diffuse foci of L-SIL, as well as a focus of low-grade cervical glandular intraepithelial neoplasia in the lower-left quadrant. Tubulo-alveolar glands were incorporated deeply in the cervical stroma were identified in the lower right quadrant, lined with two-layered, cuboidal to columnar, secretory epithelium, resting on a basal cell layer. The immunohistochemical analysis showed strong and diffuse PSA positivity in the superficial secretory cells, while the basal cells were CKHMW positive, as well as a partial positivity of Smooth muscle actin. Diagnosis of H-SIL accompanied by LCGIN and aberrant prostatic glands in the cervical stroma was made. In almost all reported cases, ectopic prostatic tissue in the female genital tract is a benign condition, although a further follow-up of the patients is required. Possible theories of histogenesis include a developmental anomaly, metaplasia of pre-existing endocervical glands, and derivation from mesonephric remnants. It is important that pathologists be aware of this condition and to take it into account in the differential diagnosis.

## 2. Introduction

The discovery of normal tissue in an ectopic location is easily one of the most interesting discoveries a pathologist can encounter. In most circumstances speaking about the prostate in the context of

female patients would sound rather odd to the vast majority of interlocutors. Ectopic prostatic tissue can be frequently found along different locations in the male genital tract, mostly located in the urinary bladder of males. However, although probably extremely rare, prostatic tissue in various stages of differentiation and shapes may be found along the lower female genital tract [1-10]. From 1997, when according to the authors the first case of ectopic prostate in the uterine cervix [EPIUC] was published by Larraza-Henandez et al., until 2012, less than 70 cases have been reported [1]. According to a review published in 2015, ectopic prostate in the uterine cervix is most frequently found as an incidental finding while examining a loop biopsy or a cone biopsy taken for high-grade dysplasia, as well as in hysterectomy specimens [1]. The women's age varied, ranging between 21 and 82 years old according to Venyo. Venyo summarized the results from 17 previous publications and an extensive literature search through several internet search engines, and came up with 39 published cases of prostatic tissue in uterine cervix, another 27 cases presenting as vaginal mass or vaginal polyps, 3 cases in vulva and 1 case of prostatic tissue differentiation in Skene's gland hyperplasia, bearing in mind the possibility that few of the cases might have been reported separately and again as part of series. Ectopic prostate tissue has been included as an entity in the 5th edition of the WHO classification of female genital tumours in the chapter Tumours of the uterine cervix [11]. To the best of our knowledge, there were no additional published cases from the above-mentioned review until the present. We report a case of an incidental finding of ectopic

prostatic tissue in the uterine cervix in a 30 years old female.

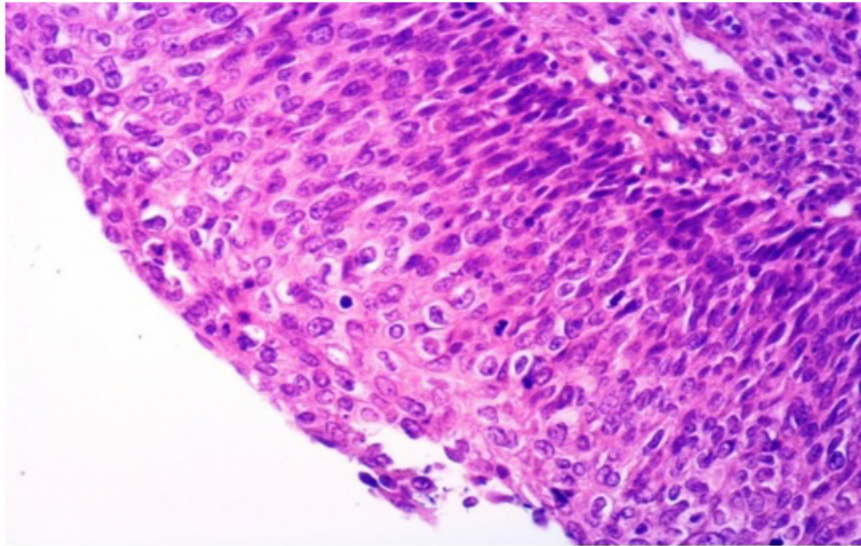
### 3. Case presentation

A 30-years old female, unipara-unigravida, was admitted at the University Clinic for Gynaecology and Obstetrics [UCGO] for cervical cone biopsy. Six months earlier she's had a positive PAP-smear interpreted as CIN2, followed by cervical biopsy which revealed HSIL of the cervical epithelium. HPV genotyping revealed HPV type 16. She had no specific complaints or symptoms, nor relevant conditions in her medical history. A cervical cone biopsy was performed.

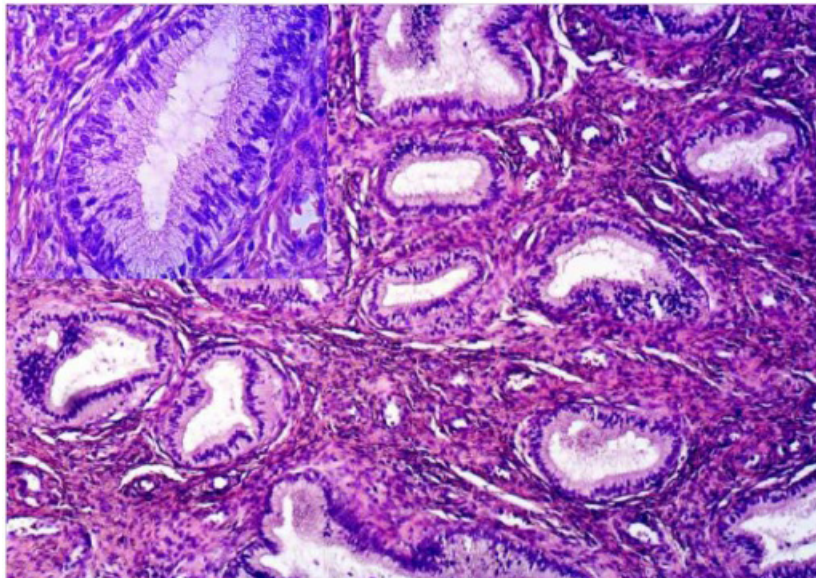
#### 3.1. Pathological findings

Cervical cone biopsy with epithelial surface measuring 1.6x2.5cm, 2.2 cm long/high, serially dissected, and completely paraffin-embedded in 16 blocks. Microscopic analysis showed H-SIL in the

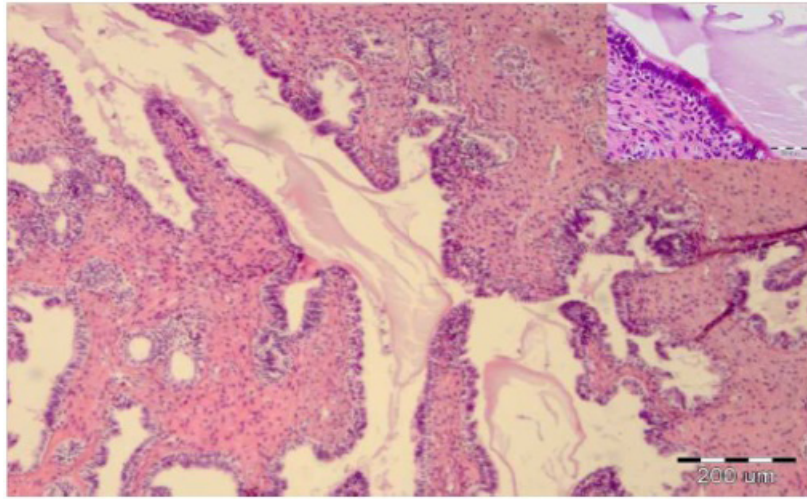
lower-left quadrant (Figure 1), diffusely distributed foci of L-SIL, as well as a focus of L-CGIN in the lower-left quadrant (Figure 2). At 7-10 o'clock of the cone biopsy, tubuloalveolar glands were incorporated deeply in the cervical stroma, lined with two-layered, cuboidal to columnar, benign-looking secretory epithelium, resting on a basal cell layer (Figure 3a-c). (Figure 3). Tubulo-alveolar prostatic glands incorporated in the cervical stroma. A: H&E 40x [Inset H&E; 200x]; B: Prostatic glands lined with basal and secretory cells. H&E; 400x. Immunohistochemical analysis showed strong and diffuse PSA staining in the superficial secretory cells (figure 4). The basal cells were positive for CKHMW (Figure 5) and partially for Smooth muscle actin. Diagnosis of H-SIL accompanied by LCGIN and aberrant prostatic glands in the cervical stroma was made. Papanicolaou cervical smear three years after the procedure again showed HPV infection. Serum PSA level fol-



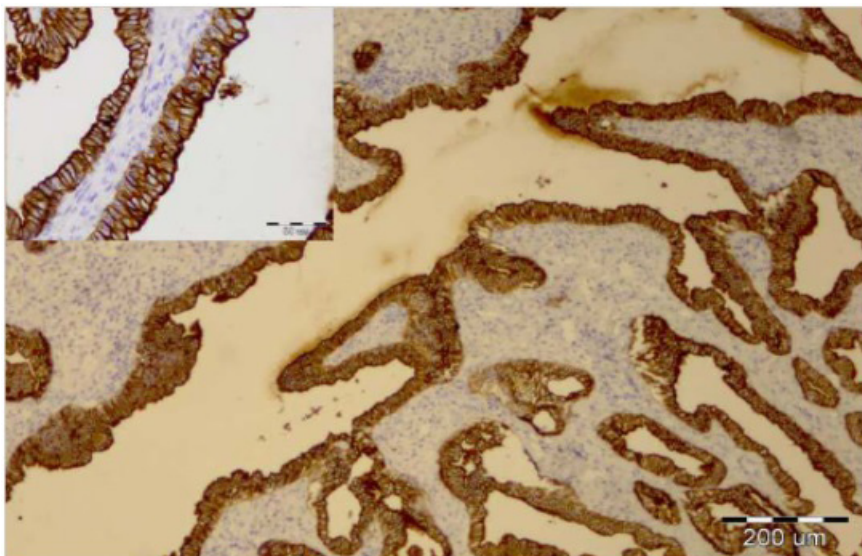
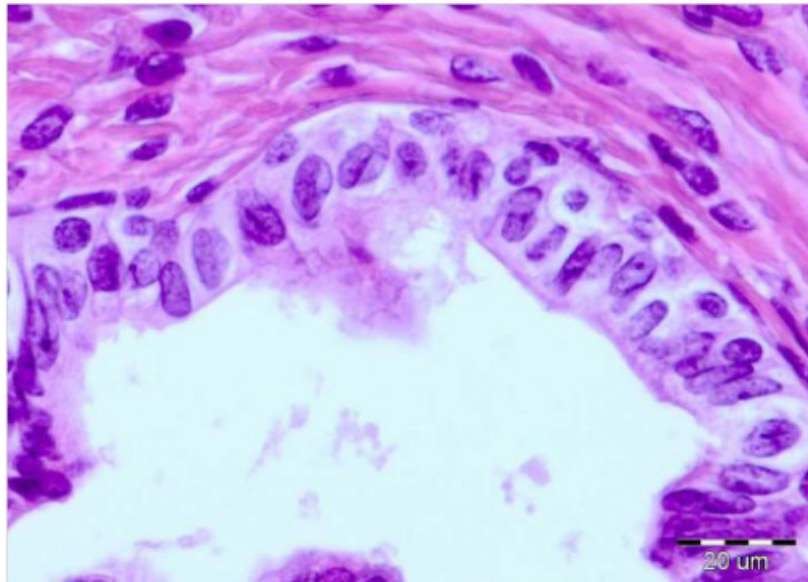
**Figure 1:** High-grade squamous intraepithelial lesion (H-SIL). H&E; 100x.



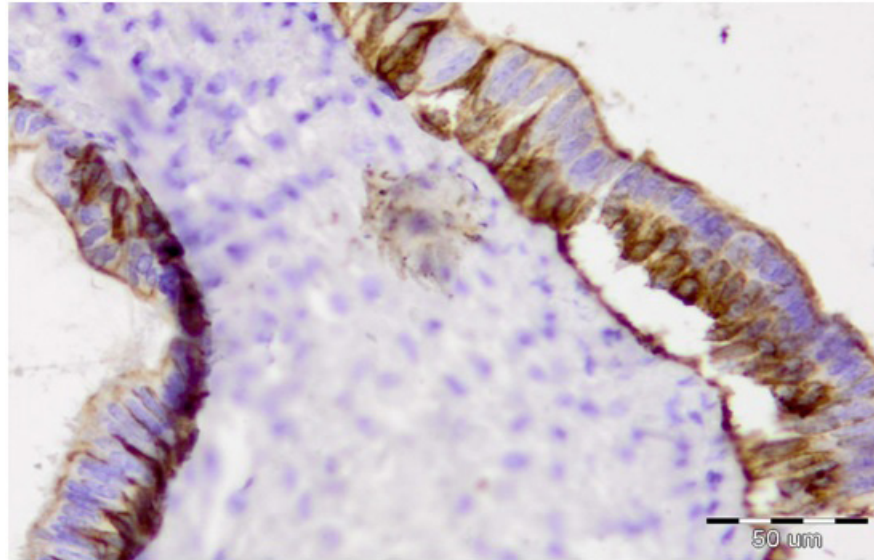
**Figure 2:** Low-grade cervical glandular intraepithelial neoplasia (L-CGIN) in the lower-left quadrant. H&E; 40x (Inset H&E; 200x)



**Figure 3:** Tubulo-alveolar prostatic glands incorporated in the cervical stroma. A: H&E 40x (Inset H&E; 200x); B: Prostatic glands lined with basal and secretory cells. H&E; 400x.



**Figure 4:** Strong and diffuse immunohistochemical staining of the secretory cells for PSA; 40x (Inset PSA; 200x)



**Figure 5:** CKHMW staining of the basal cells. (200x magnification)

lowing control examination was 0.01 ng/ml, suggesting that there was no residual aberrant prostatic tissue.

#### 4. Discussion

Since 2020, ectopic prostate tissue has been included as an entity in the Tumours of the uterine cervix chapter in WHO classification of female genital tumours, 5th edition [11]. It is classified as a benign condition, with a still unknown frequency. Several authors have previously published findings of ectopic prostatic tissue in the uterine cervix in women from 21-82 years of age. To the best of our knowledge, not more than 70 cases [with most loose criteria applied] have been reported in the literature. In most of the published cases the prostatic tissue was located in the uterine cervix [39 cases], followed by the vagina [27 cases] where prostatic tissue presented either as a mass in the vaginal wall or protruding as a polyp [1]. In 3 of the remaining 4 cases, prostatic tissue was found in the vulva, and in 1 case it was found as a peculiar prostatic differentiation in hyperplastic Skene glands. One of the cases of vaginal prostatic tissue was in fact myofibroblastoma, harboring aberrant prostatic glands [3]. From the available literature, it is evident that in some of the cases there was variable differentiation of the prostatic glands. In some of them, there were only morphologic features of prostatic glands lacking both PSA and PAP [Prostatic alkaline phosphatase] expression [4-6], others had either PSA or PAP expression [7], still, most of them had the complete morphologic and immunohistochemical features, including specific [high molecular weight keratin or p63] staining of the basal cell layer [8, 9]. Some of these differences might be attributed to the context in which prostatic glands were detected, also shedding light on the possible etiology.

Furthermore, McCluggage and Young reported 10 cases of a morphologically distinct vaginal polyp [i.e. tubulo-squamous polyps] ranging 1-3 cm in diameter composed of hypo-cellular fibrous

stroma containing expansile nests of squamous cells with glycogenated or non-glycogenated cytoplasm, with occasional central necrosis or central keratinization, as well as the presence of tubular structures unassociated with the squamous nests. In three of the cases, those tubular structures were PAP positive, and in 2 of the cases, PSA positivity was found also, while the squamous nests expressed estrogen and progesterone receptors [6]. The theories of possible histogenesis include intrauterine exposure to androgens as well as a developmental anomaly, metaplasia of pre-existing cervical glands, and mesonephric remnants derivation. Kim et al. reported a case of transitional cell metaplasia and ectopic prostatic tissue in the uterine cervix in a patient with adrenogenital syndrome and proposed the hypersecretion of adrenal androgens as the cause of both conditions, suggesting that prolonged androgen stimulation in utero could induce the development of prostatic tissue in the uterine cervix [13]. Another possible theory is proposed by Halat et al. suggesting the ectopic prostatic tissue has a mesonephric remnants derivation and consider it a developmental anomaly [14]. Furthermore Smith et al. hypothesised a metaplastic induction in the mesonephric remnants [15]. Still, there hasn't been published a fully comprehensive explanation for this phenomenon.

#### 5. Conclusion

Although an intriguing discovery for any pathologist, the importance of prostatic tissue in uterine cervix is mainly in its recognition and further follow-up. The diagnosis is dependent on the pathologists' awareness, recognizing the nature and behaviour of the prostatic tissue, and immunohistochemical confirmation. It is crucial for the pathologists to take into account its occurrence and to be able to properly diagnose it and include it in the differential diagnosis. Furthermore, although previously published cases, as well as ours, display only ectopic tissue with benign characteristics, one should take into account its dysplastic and malignant potential.

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