Content available at: https://www.ipinnovative.com/open-access-journals

IP Archives of Cytology and Histopathology Research

Journal homepage: https://www.achr.co.in/

Case Report

Clear cell adenocarcinoma of posterior urethra- A rare histological subtype of female genitourinary cancer

Prachi[1,*], **Hema Malini Aiyer**[1]

[1]*Dept. of Pathology, Dharamshila Narayana Superspeciality Hospital, New Delhi, Delhi, India*

ARTICLE INFO

Article history:
Received 14-01-2023
Accepted 28-01-2023
Available online 11-03-2023

Keywords:
Uretheral clear cell adenocarcinoma
Urethrectomy
Immunohistochemistry
Histology

ABSTRACT

Urethral Clear cell adenocarcinoma is a very rare variant of lower urinary tract malignancy. We present a 62-year old lady who complained of hematuria, obstructive urinary symptoms and pain abdomen. Her MRI pelvis revealed a mass in the posterior urethra measuring 30x20x15mm. Further she underwent total urethrectomy with regional lymph node dissection. Histology demonstrated features consistent with clear cell adenocarcinoma with 8/29 positive lymph nodes. Immunohistochemically cells were positive for CK7(+4), CD10(+4), HMWCK(+2) and PAX-8(+3). Whilst it was non- immunoreactive for GATA3, CK20, uroplakin and p-63. Subsequent PET scans have demonstrated lymphatic disease progression, and later on, the patient succumbed to disease after one year of diagnosis.

1. Introduction

Primary malignancies of female urethra are infrequent, unlike other genito-urinary malignancies. Though urethral malignancies are more common in female as compared to male population[1] accounting to less than 1% of all malignant tumor and <5% of all malignant tumors of urinary system.[2]

Squamous cell carcinoma (70%) constitutes the vast majority of all the urethral cancers, followed by transitional cell carcinomas (20%) and then adenocarcinomas.(10%).

The prognosis of urethral carcinoma is extremely poor and they often presents with extensive metastasis. Distal tumors, i.e., squamous cell carcinoma tends to have better prognosis, as compared to proximal tumors, i.e. urothelial carcinoma and adenocarcinoma.

Rare variants of adenocarcinoma are mucinous and clear cell variant. Primary clear cell carcinoma is even more rarer, and histo-morphologically it resembles clear cell carcinoma of female genital tract.

Due to its rarity of this carcinoma, the histogenesis remains unclear. It was postulated that, it can be either diverticular, Mullerian or glandular differentiation of urothelial cancer.

Immunohistochemistry work-up helps in knowing the origin of the tumour.

Hereby, we present a rare case of clear cell uretheral carcinoma with involvement of the vaginal wall, presented with history of haematuria and obstructive symptoms since 3-4 months. Detailed immunohistochemistry follow- up was done to achieve a definitive diagnosis of primary clear cell urethral carcinoma of posterior urethra.

2. Case Details

A 62-year old female presented with obstructive urinary symptoms, pain abdomen and hematuria. Her MRI pelvis with contrast showed multiple nodular areas seen in inguinal region (left>right) and pelvis side wall on left side, size ranging from 9 to 15mm in axial plane. A mass seen

* *Corresponding author*.
E-mail address: prachipath123@gmail.com (Prachi).

https://doi.org/10.18231/j.achr.2023.012

posterior to urethrameasuring 30x20x15mm in size.

PET scan revealed malrotated bilateral renal pelvis appears prominent. Bilateral kidneys are normal. FDG avid enhancing predominantly hypodense mass lesion measuring 39x29 mm along the periurethral region, more marked along left side and is seen in posterior aspect. FDG avid left external iliac lymph node measuring 20x13mm and few left inguinal lymph nodes measuring 12x7mm.

Her initial histopathology report revealed Malignant mesenchymal tumor suggestive of urethral soft tissue sarcoma, examined at other laboratory centre.

Following the radiological investigation, patient underwent urethral resection along with anterior vaginal wall mucosa adherent to it posteriorly.

Grossly, total urethrectomy specimen with attached vaginal wall measures 5x4.5x2.0 cm.

A grey white growth measuring 4.5x2.5x1.0cm was seen extending from proximal to distal part of urethra. Anterior vaginal wall was unremarkable grossly.

Microscopically, the tumor growth showed diffuse arrangement of round to oval cells, having hyperchromatic, pleomorphic nuclei with eosinophilic cytoplasm with few cells showing clear cytoplasm and hob nail pattern. The tumor was invading the periurethral fibromuscular and adipose tissue along with the vaginal muscle invasion. But the vaginal epithelium is free of tumor. [Figure 1A,B]

IHC study done to find out origin of the tumour, and the tumour cells showed immunoreactivity CK7(+4), CD10(+4), HMWCK(+2) and PAX-8(+3). Whilst it was non- immunoreactive for GATA3, CK20, uroplakin and p-63. There was multiple regional lymph node metastasis in the inguinal region, perivesical, hypogastric, obturator, internal and external iliac lymph nodes (8/29). Considering the morphology and immunohistochemistry, the final diagnosis of Urethral Clear cell was rendered with pT3N2 (pTNM AJCC 8^{th} edition). Follow up of the patient was uneventful. [Figure 1C,D].

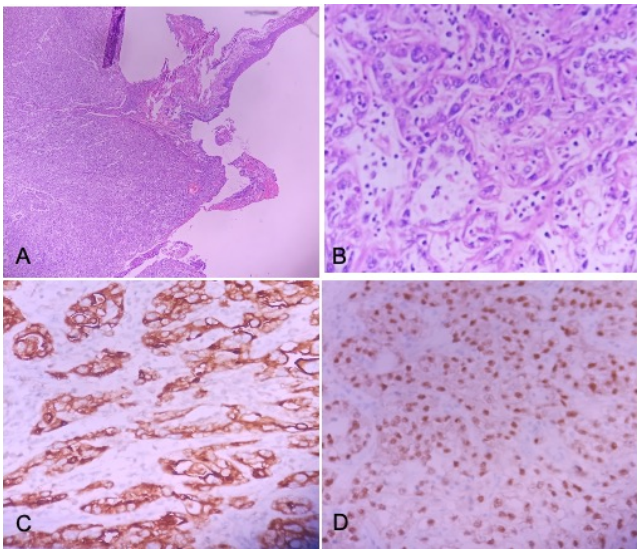

Fig. 1: A-B: Diffuse sheets of neoplastic cells with clear cytoplasm and hob nailing (H &E X100); **C:** Immunohistochemistry for CK7 (score 4+) in neoplastic cells (IHC STAIN- CK x400); **D:** immunohistochemistry for PAX-8 (score 3+) in neoplastic cells. (IHC STAIN -PAX 8 x400)

3. Discussion

Primary urethral cancer is exceedingly rare, resulting in a limitation in clinical and surgical practice and an accurate diagnosis is often delayed due to non specific clinical condition.

Clear cell adenocarcinoma accounts for 0.003% of malignant tumours occurring in female urogenital tract, with the average age of occurrence in females being 58 years.[3,4]

According to Clayton M et al., and Evans KJ et al., 46-56% of the urethral diverticulum associated carcinomas are adenocarcinoma and only 15-18% is squamous cell carcinoma.[5,6]

The origin and development of clear cell carcinoma remains undetermined, having more than one tissue of origin, as studied and reported in literature.

Many theories of its origin from paraurethral ducts/glands (Skene's gland) or mullerian rest/urothelial metaplasia have been suggested.[7,8]

The microscopic examination revealed that the classic triad of tubulocystic, papillary, and diffuse patterns of clear cell showing hobnail pattern, flattened cells, and cells with abundant clear cytoplasm which characterizes the tumour. Immunohistochemically, they show positivity for CK7, CD10, HMWCK, PAX-8 and non- immunoreactivity for uroplakin, p-63, GATA-3 and CK-20, as in our case too.

Due to its non- specificity, immunohistochemical evaluation is mandatory for its definitive diagnosis. Clear cell adenocarcinoma carries poor prognosis with statistically significantly lower cause specific survival and recurrence free survival rates.

Despite only having case studies and very small case series, it has been shown that surgical resection for localised disease has been curative. Surgical options have ranged from localised transurethral resection (TUR) through to anterior exenteration depending on anatomical considerations with varying success rates. Further the decision to use chemoradiotherapy is a multidisciplinary team approach, with the patient fully informed of risks and benefits.

4. Conclusion

Urethral clear cell carcinoma is very rare and diagnosis is often delayed due to non- specific symptoms. Its diagnosis, staging and treatment is very much essential, as it carries poor prognosis and have chances to recur. Hence, the

histopathology and immunohistochemistry plays a very important role in its diagnosis, treatment aspect and to create awareness amongst the clinicians and radiologists.

5. Conflict of Interest

None.

6. Source of Funding

None.

Acknowledgements

The Entire lab staff and technician of Department of Pathology, Dharamshila Narayana Superspeciality Hospital.

References

1. Amin MB, Young RH. Primary carcinomas of the urethra. *Semin Diagn Pathol*. 1997;14(2):147–60.
2. Gakis G, Morgan TM, Efstathiou JA. Prognostic factors and outcomes in primary urethral cancer: results from the international collaboration on primary urethral carcinoma. *World J Urol*. 2016;34(1):97–103.
3. Satyanarayan A, Redd L, Dyer A, Wright A, Walker J. Adenocarcinoma of the urethra with mucinous features. *Rev Urol*. 2015;17(1):38–41.
4. Venyo AKG. Clear cell adenocarcinoma of the urethra: Review of the literature. *Int J Surg Oncol*. 2015;p. 790235. doi:10.1155/2015/790235.
5. Clayton M, Siami P, Guinan P. Urethral diverticular carcinoma. *Cancer*. 1992;70(3):665–70. doi:10.1002/1097-0142(19920801)70:3<665::aid-cncr2820700321>3.0.co;2-h.
6. Evans KJ, Mccarthy MP, Sands JP. Adenocarcinoma of a female urethral diverticulum: case report and review of the literature. *J Urol*. 1981;126(1):124–6. doi:10.1016/s0022-5347(17)54408-0.
7. Kato H, Ogihara S, Kobayashi Y, Toguri AG, Igawa Y, Nishizawa O, et al. Carcinoembryonic antigen positive adenocarcinoma of a female urethral diverticulum: case report and review of the literature. *Int J Urol*. 1998;5(3):291–3.
8. Young R, Scully RE. Clear cell adenocarcinoma of the bladder and urethra. A report of three cases and review of the literature. *Am J Surg Pathol*. 1985;9(11):816–26.

Author biography

Prachi, Junior Consultant https://orcid.org/0000-0002-6069-5559

Hema Malini Aiyer, HOD

Cite this article: Prachi, Aiyer HM. Clear cell adenocarcinoma of posterior urethra- A rare histological subtype of female genitourinary cancer. *IP Arch Cytol Histopathology Res* 2023;8(1):53-55.