Granular cell tumor of the urethra: a case report and literature review

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Dear Editor,

Granular cell tumors (GCTs) are uncommon soft tissue neoplasms of unclear origin that most often occur in head and neck regions particularly the tongue. Until now, GCTs of the male genitalia are extremely rare with <20 cases reported in the English literature. Although GCTs of the penis, including prepuce, shaft, glans, corona, and corpus cavernosum, have been reported, this report describes a case of GCT originating from the urethra. To the best of our knowledge, this is the first report of a urethral case in man.

A 51-year-old man presented with a 5-month history of penile nodule. The patient denied any subjective symptoms related to the nodule except for slight difficulty in micturition, but he had noticed a gradual increase in size. Ultrasound study revealed a 2.0 cm × 1.5 cm solid hypoechoic nodule with some internal Doppler flow. Contrast-enhanced computed tomography (CT) of the male genitalia was performed and further demonstrated a 2.5 cm × 1.5 cm round mass with significant enhancement which had close associations with urethra (Figure 1). On physical examination, the patient was found to have a nodule (approximately 2.0 cm × 1.5 cm) at the left base of the penis. The mass was ill-defined, nontender, and firm with no fixation to the skin of the penis. The lymph nodes were not swollen, and no other lesions were identified.

Owing to progression in the size of the lesions and urinary symptom, we decided to proceed with open surgery. Preoperatively, we tried to insert a Foley catheter into the urethra, but it failed. On exploration, the penile nodule was located in the urethrocrotal junction and densely adherent to the urethra, thus it was impossible to separate the urethra from the tumor (Figure 2a). Subsequently, the patient underwent complete excision of the tumor including the involved urethra and simultaneous urethra reconstruction.

The excised specimen showed an ill-defined, yellow-white, firm tumor (Figure 2b). Histologically, the tumor was composed of large polygonal cells with eosinophilic granular cytoplasm and small round central nuclei (Figure 3a). Immunohistochemical staining for S-100 protein, neuron-specific enolase (NSE), smooth muscle actin (SMA), and cluster of differentiation 68 (CD68) was positive, indicating that it was compatible with GCTs (Figure 3b). The patient was followed up for approximately 12 months without evidence of tumor recurrence and metastasis. Dysuria and erectile dysfunction was not detected during the follow-up period except for ventral curvature of the penis for 15°.

GCTs are uncommon, generally benign, slow-growing tumors of unclear origin first described by Abrikossoff in 1926. More and more studies via immunohistochemistry and electronic microscope revealed that these tumors seemed to be derived from Schwann cells because of the close association with the peripheral nerves. In general, GCTs more commonly occur in the head and neck region with tongue being considered the most common site. However, GCTs of the male external genitalia, especially the penis (Table 1), have been rarely reported. Here, we report the first case of a GCT of the urethra in man.

It is difficult to diagnose GCTs preoperatively. In this case, we decided to proceed with open surgery mainly because the lesion had been slowly increasing in size and his difficulty in micturition got worse. On the one hand, the histological specimens could be got through surgery, but, on the other hand, the micturition symptoms could also be relieved. Compared with surgical excision, fine needle aspiration (FNA) remains to be a simple, critical, minimally-invasive diagnostic tool in preoperative recognition. However, histologic sections of GCTs show relatively consistent morphology while the cytologic appearance of GCTs on FNA is variable, for GCTs can mimic many different lesions from benign histiocytes to malignant cells. With this in mind, recognition of the cytomorphic features of GCTs on FNA specimens and their distinction from other commonly encountered conditions is important for making a preoperative diagnosis. In difficult cases, judicious use of relevant markers will be contributory to its final diagnosis.
Ancillary immunostaining is extremely valuable for rendering the specific diagnosis, especially for GCTs with an atypical cytomorphology. As shown in our case, GCTs immunohistochemically express S-100, NSE, SMA, and CD68 indicating their neural origin. Due to this, a concept of neural derivation is widely accepted; some investigators have advocated the idea that only S-100 immunohistochemical stain is necessary for confirmation of the diagnosis of GCTs. This immunohistochemical feature helps distinguish GCTs from other soft tissue tumors. However, not all reports have been in agreement with these findings. S-100-negative atypical GCTs were reported in the literature. Recently, Gurzu et al. proposed that the GCTs cannot be considered a purely neural tumor. An immunohistochemical profile study of 2250 soft tissue tumors suggested that the GCTs seemed to have an endomesenchymal origin.

The treatment of choice for GCTs is surgical excision, regardless of whether the lesion is benign or malignant. In addition to conventional excision, Mohs Micrographic Surgery (MMS) has been applied for the excision of GCTs in selected cases. MMS is almost exclusively used for skin cancers of the head and neck region where tissue preservation is essential. This method aims to ensure the most appropriate and complete excision by microscopic examination of the specimen at the

**Table 1: Clinical features of the reported series of granular cell tumor of penis**

| Authors          | Number of patients | Age (year) | Race | Presentation | Medical history (month) | Location      | Diameter (mm) | Treatment          | Outcome/follow-up interval (month) |
|------------------|--------------------|------------|------|--------------|-------------------------|---------------|---------------|--------------------|------------------------------------|
| Bulstrode et al.1 | 1                  | 17         | W    | Painless nodule | 72                      | Glans         | 25            | Simple excision    | NER/12                             |
| Tanaka et al.2    | 1                  | 8          | O    | Painless nodule | NA                     | Corpus cavernosum | 3             | Simple excision    | NER/27                             |
| Laskin et al.3    | 9                  | 20–60 (median, 40) | W (8) B (1) | Painless nodule (8) Painless nodule with ulceration (1) | 0.2–24 months (median, 6 months) | Prepuce (3) Shaft (4) Corona (2) | 6–25 (mean, 15) | Simple excision    | NER/6–336 (6) NA (3)                  |
| Bryant7           | 1                  | 42         | W    | Simple excision | 6                      | Shaft         | 3             | Simple excision    | NER/24                             |
| Yang et al.8      | 1                  | 9          | NA   | Painless nodule | 5                      | Glans         | 8             | Simple excision    | NA                                 |
| Grotas et al.9    | 1                  | 5          | W    | Painless nodule | 4                      | Corona        | 7             | Simple excision    | NER/1                              |
| Carver et al.10   | 1                  | 53         | W    | Painless nodule | 6                      | Shaft         | 25            | Simple excision    | NER/12                             |
| Dema et al.11     | 1                  | 31         | NA   | Painless nodule | NA                     | Shaft         | 20            | Simple excision    | NER/6                              |
| Suarez and Lewis12 | 1                  | 29         | B    | Painless nodule | NA                     | Glans         | 2             | Simple excision    | NA                                 |
| Stone et al.13    | 1                  | 33         | B    | Simple excision | NA                     | Shaft         | 1.5           | Simple excision    | NER/12                             |
| Dehner and Smith14 | 1                | 24         | W    | Simple excision | NA                     | Prepuce       | 4             | Simple excision    | Circumcision NER/96                |
| Gardner and Goldberg15 | 1            | 47         | W    | Simple excision | 3                      | Corona        | 9             | MMS                 | NER/6                              |

W: white; B: black; O: oriental; NER: no evidence of recurrence at documented follow-up; MMS: Mohs micrographic surgery; NA: not available.
time of the operation. Based on our experience, it makes little sense to perform MMS in this case, owing to the small size and clinically low aggressive behavior of the lesion. However, further studies are required for better elucidate the efficacy and superiority of extirpate for MMS versus conventional excision.

AUTHOR CONTRIBUTIONS
PH designed the study and revised the manuscript; LG and YJB collected the clinical information and pathological data; and CXP drafted the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS
The authors declared no competing interests.

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