

# Case Report: A Case of Hematuria Exfoliative Cytological Examination Easily Misdiagnosed as Malignant Tumor

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## Case Report

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# Abstract

## Background

The incidence of urogenital fistula, whose typical manifestations are cyclic hematuria, absence of urinary incontinence and no vaginal bleeding, is on the rise due to gynecological surgery. Those patients who often present to the urologist for hematuriae are prone to be misdiagnosed as urogenital disorders.

## Case presentation

This article reports a case of vesicouterine fistula patient whose three regular urine exfoliative cytology examinations all found a large number of nest-like cell clusters. After a comprehensive understanding of the patient's medical history and auxiliary examination, exfoliated cells were identified as the endometrial glands and mesenchymal cells and the probability of malignant tumors was excluded finally.

## Conclusions

For pathological diagnosis, a thorough acquirement of the patient's medical history and relevant auxiliary examinations are extremely significant for the accuracy of pathological diagnosis.

# Introduction

The incidence of urogenital fistula, is on the rise due to gynecological surgery. Its urinary exfoliative cells having similarities to tumor cells can easily be misdiagnosed as tumor cells by pathologists, when they are unaware of the patient's clinical history.

# Case Report

A 43-year-old female was admitted to the Hospital of Chengdu University of Traditional Chinese Medicine on March 13<sup>th</sup> 2018 due to hematuria for 6 days and inability to urinate spontaneously for 1 day. 6 days ago, the patient discharged visible hematuria without any obvious cause and she denied frequent and urgent micturition, dysuria, lumbago, fever, nausea and vomiting. 1 day ago, the patient presented at a grade three A hospital emergency department for catheterization; the urinary system ultrasound revealed that there was an echo mass measured 6.5cmx3.0cm (considering blood clots) around the urinary catheter. She had a history of a myomectomy (the details were not available). At admission, the indwelling catheter was in the right place and the patient manifested with dark red urine, occasional bilateral lumbago and lower abdominal dull pain. At that time, she was in her period without chills, fever, nausea and vomiting. The physical examination showed stable vital signs with suspicious positive percussion pain in two kidney regions and mild percussion pain in the bladder region. Preliminary diagnoses were cause of hematuria to be investigated: (1) urinary tract infection (2) urinary tumors (3) other. Relevant examinations after admission were conducted. Urinalysis (clean midstream urine) were: erythrocytes 2189.2/uL, leukocytes 121.4/uL, and leukocyte esterase 1+. No abnormalities were found in coagulation

tests. Hepatic and renal function showed uric acid 373umol/L with no other abnormalities. There was no abnormality of tumor markers CA125:78.6U/ml, AFP, CEA, FERRITIN, pro- grp, nse, cefra21-1, ca72-4, ca15-3, ca19-9, ca50, CA242, SCCA, HE4, pro ROME, and post ROME. 3 times of urine exfoliative cytology smear examinations were listed as follows: a large number of exfoliative urinary tract epithelial cells were found and some nuclear heterogeneity were shown at the first time; tumor cells were found, which tended to be tumor cells at the second time(Figure 1) and specific types of cell blocks was to be made (Figure2) for immunocytochemical testing; a small number of degenerated heterogeneous epithelial cell clusters, and more neutrophils were seen at the third time. The immunophenotype of the cell blocks slides revealed tumor cells Ki-67 (+, <1%), EMA (+), CK7 (+), vimentin (+) (Figure 3), CD10 (+) (Figure 4) , P40 (-), P63 (-), S100P (-), suggesting endometrial glands and stromal cells, excluding malignant tumor cells. Besides, pathological section of prolapsed tissue in the bladder showed that there were scattered small and heterotypic cell clusters in blood clots and degenerative necrotic tissues. Immunophenotype: Ki-67 (+, <2%), EMA (+), Vimentin (+), CK7(+), CD10(+), ER(+), PR(+), Syn(-), CD56(-), S-100(-), CD99(-), CD117(-) , P63 (-), P40 (-), suggested degenerated endometrial glands and stroma. CT urography (CTU) indicated that there were few low-density filling defects in the bladder in the delayed phase, and the shape was irregular, considering the possibility of blood clots. Cystoscopy revealed a depressed change at the posterior wall of the bladder at its filling state, which seems to be connected to the peritoneum, and the surrounding bladder mucosa and the other bladder walls in the bladder triangle area were normal. Hematuria disappeared at the end of menstruation, and the urine routine re-examination revealed occult blood 1+Ca25cell/uL. Taking medical history and pathological examination into consideration, the cause of hematuria may be vesicouterine fistula (VUF).

## Discussion

Hematuria is a common clinical phenomenon, whose prevalence under microscope ranges from 1% to 18%. It is often caused by diseases of the urinary system<sup>[1]</sup> such as, infections, non-infectious inflammations, stones, and tumors. The diagnosis can be confirmed by patient's clinical symptoms, urinalysis, urobacterial testing, urinary Doppler ultrasound, abdominal plain film, intravenous pyelography, cystoscopy, urine exfoliated cytology, etc. Generally speaking, there are few cells in urine centrifugal smears, however, three urine exfoliated cytology examinations of the patient reveal large number of nest-like cells, which contributes to the misdiagnosis of tumor under the circumstance of clinical history absence. The patient's urine smear shows small and degenerated cells, and the nucleoplasm ratio is difficult to interpret accurately, which is initially diagnosed with nuclear heterogeneous cells. Therefore, when the doctor reads the film, he or she often thinks of tumor cells, especially the urinary tumor. From this case, a very important conclusion can be drawn that it is extremely essential to acquire the clinical history for pathology doctors, which is conducive to reducing the misdiagnosis rate and unnecessary doctor-patient conflicts. The second urine exfoliation cytology report of this case attracts the attention of clinicians and obtains feedback of clinical information. Through inquiring imaging data, clinical operation history, morphology and immunophenotype, it is finally determined that the exfoliated cells are the endometrial glands cells and stromal cells, which is caused by vesicouterine fistula .

The main cause of genital fistula is gynecological surgery injury. The incidence of urinary system injury during gynecological surgery is about 0.4%~2.5%<sup>[2]</sup>. According to its location of genitourinary tract lesion, it can be divided into vesicovaginal fistula, urethrovaginal fistula, ureterovaginal fistula and vesicouterine fistula. Among them, vesicouterine fistula is rare accounting for 1% to 4% of urogenital fistula<sup>[3]</sup>, and its typical manifestation is trilogy of cyclic hematuria, no vaginal bleeding and absence of urinary incontinence (Youssef's syndrome). Patients often go to the urology department for hematuria as the chief complaint and the incidence of vesicouterine fistula is relatively low, which results in the misdiagnosis of urologic diseases, especially the urinary tumor. Furthermore, it increases the psychological burden of patients and intensifies the contradiction between doctors and patients. Therefore, past history and current medical history are indispensable for pathological diagnosis. Clinicians should strengthen communication with pathologists; information should be accessible to the involved doctors, which is significant for improving the correct rate of pathological diagnosis.

## Abbreviations

Not applicable.

## Declarations

Ethics approval and consent to participate We got approval from EC of the Teaching hospital of Chengdu university of TCM.

Consent for publication All authors read and approved the final manuscript.

Availability of data and materials The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

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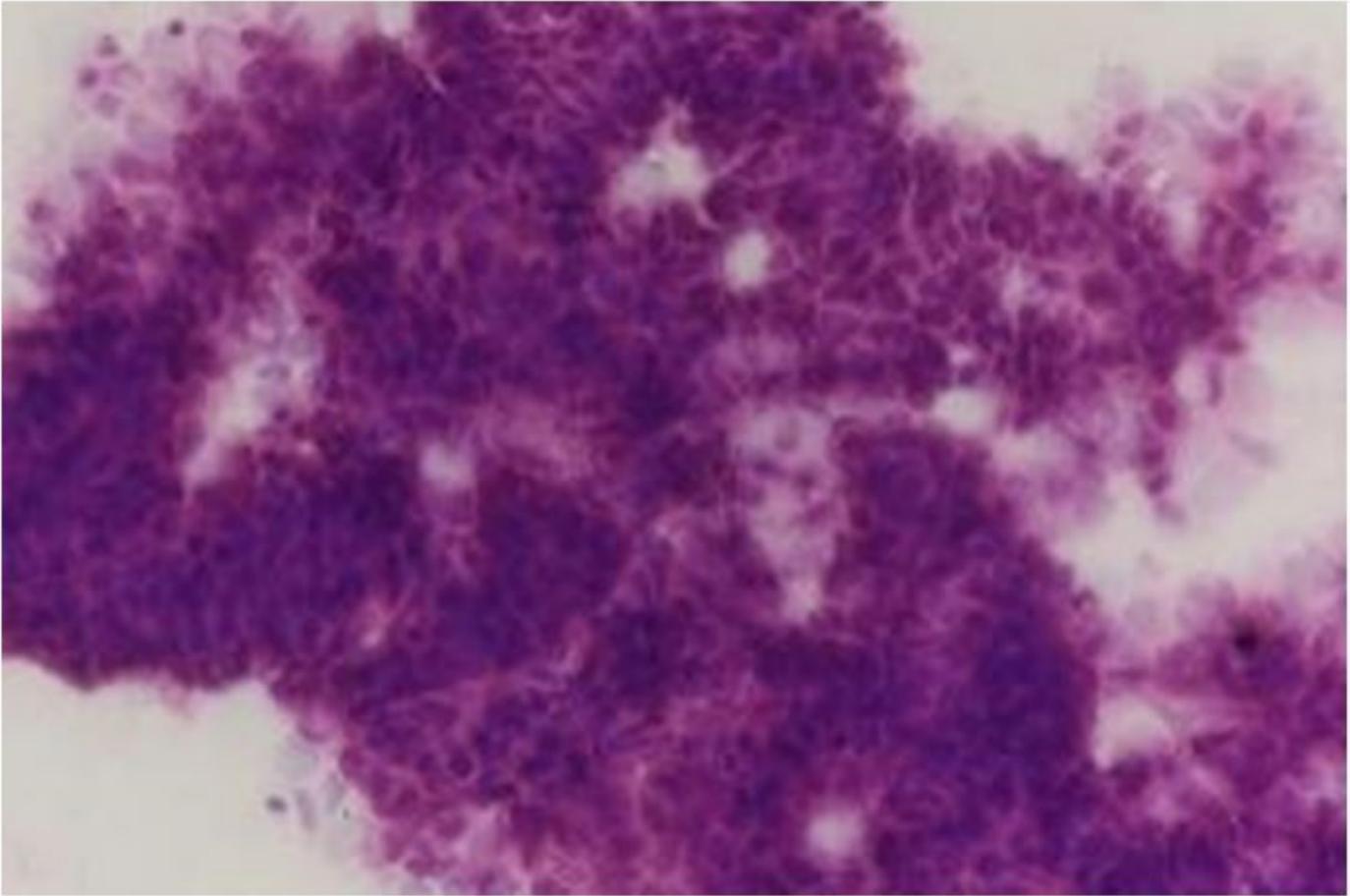
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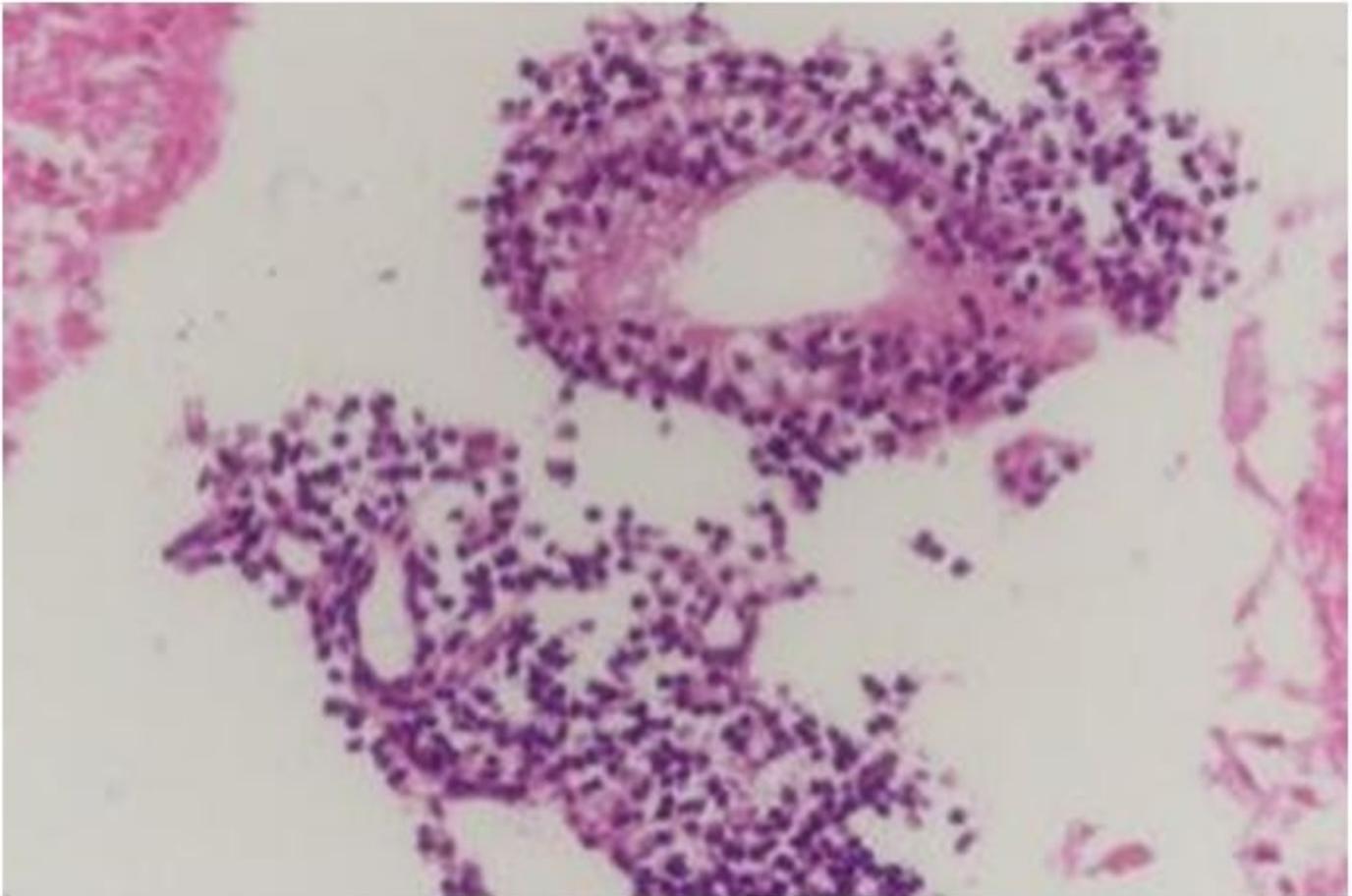
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## Figures



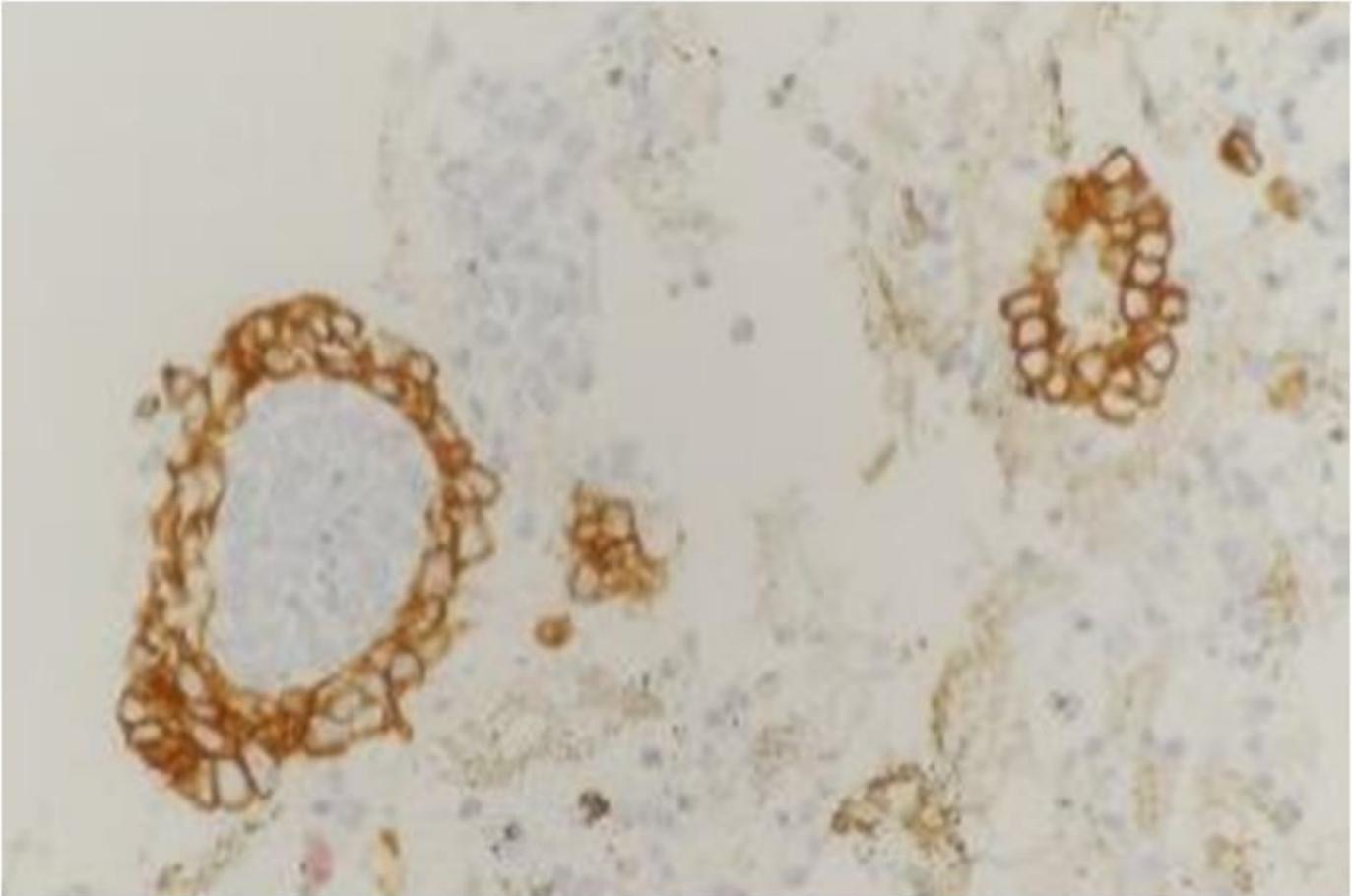
**Figure 1**

aggregated exfoliated cells, increased nuclearcytoplasmic ratio and obvious cell pleomorphism under HE staining and medium magnification.



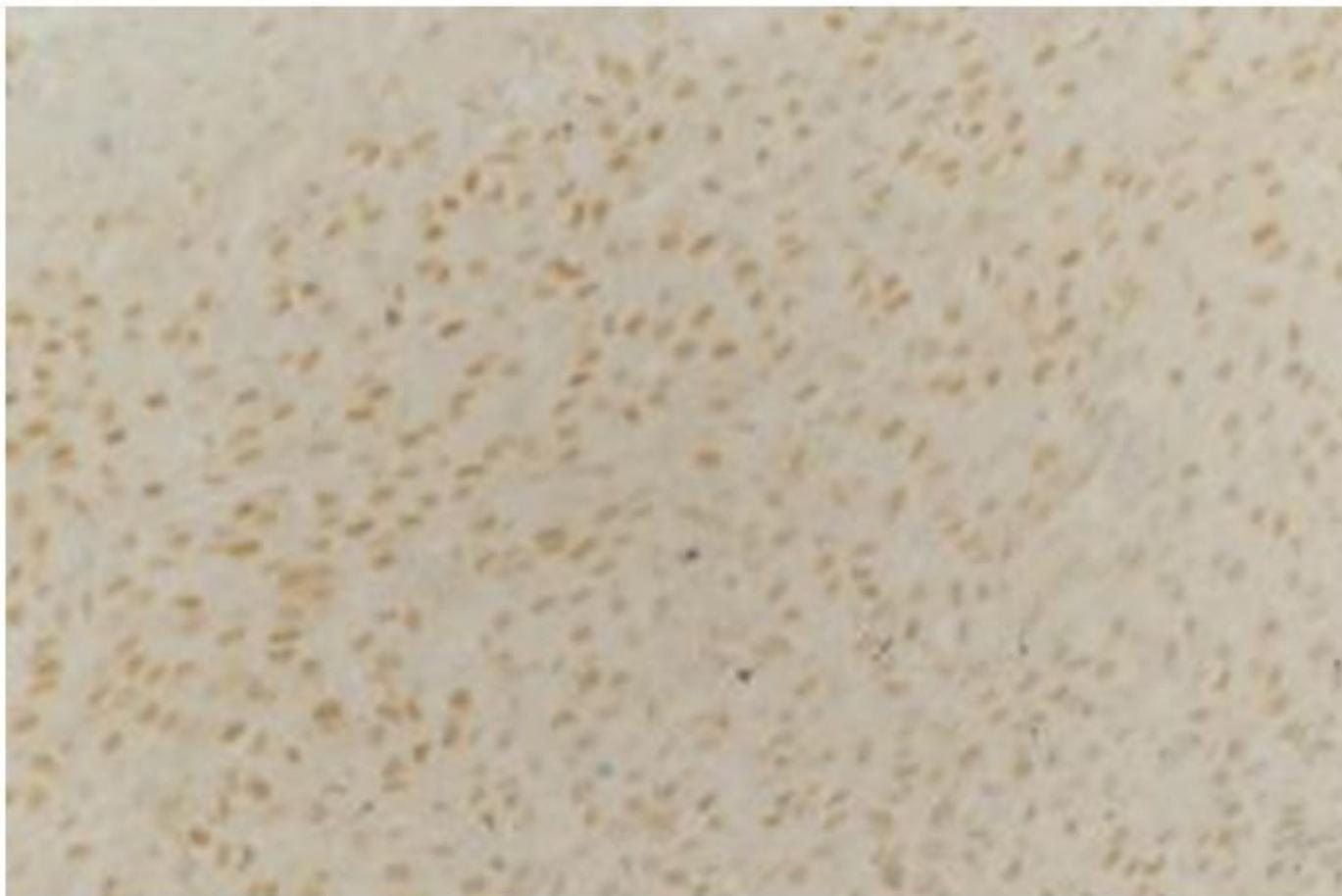
**Figure 2**

cell block: the cells were arranged in a glandular cavity-like pattern and surrounded by short fusiform cells under HE staining and high magnification.



**Figure 3**

Vimentin showed positive thyroid under enhance labeled polymer system and high magnification.



**Figure 4**

CD10 showed positive short fusiform exfoliated cells under enhance labeled polymer system and medium magnification.

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