

## Anatomipatology: PT1 Nomo High Grade Clinical Case

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### Abstract

### Case Report

**Summary:** The first publication dates back to the years 1841 by RAYES then the first histological description in 1875 by WINSIG t BLIX. .... Tumors of the upper excretory tract are rare but not exceptional tumors and represent 5 to 10% of UC. Their incidence is estimated at 2/100,000 hts. The natural history differs slightly from that of VT, we note 60% of VTEUS which are infiltrating against 15% of VT. The contributing factors are: occupational exposure to certain industrial dyes, aromatic amines, aristolochic acid (inducing nephropathy with Chinese herbs or Balkan wheat flour=Balkan nephropathy), lynch syndrome or HNCC (hereditary non polyposis colonic cancer). The factors indicating a possible tumor falling within a lynch syndrome are age less than 60 years, a family history of cancer or a personal history of other cancers linked to an HNCC (colorectal, endometrium). The diagnosis is based on uroscanner or uro-MRI, in situ urinary cytology, URRS plus biopsy. They can be of pyelo-calicielles or ureteral location, the prognostic factor are the stage, the tumor grade, but also the location which can thus influence the treatment. NUT remains the reference treatment with a collar on a case-by-case basis without forgetting conservative treatment: end urology and segmental resection in certain lesions classified as low risk. Thanks to more recent endourology and imaging studies, clinical and new treatment options, lead to an extension of therapeutic tools. We report a clinical case at the Mohammed V Raba military instruction hospital.

**Keywords:** tumors, histological description, nephropathy, pyelo-calicielles, Neoadjuvant chemotherapy.

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## INTRODUCTION

TVEUS are tumors developed at the upper urinary tract level (calices, renal pelvis, ureter).

These are rare but not exceptional tumors and represent 5% to 10% of UC [1]. The etiological factors remain discussed but professional explosion and tobacco are strongly incriminated.

Hematuria is the main revealing sign and the diagnostic work-up includes conventional investigation methods, morphological examinations, endoscopic maneuvers and Biological explorations. NUT plus resection of the bladder collar remains the standard oncological intervention.

Despite the technical progress observed in this field, conservative treatment, whether endoscopic or surgical, is not routine. Neoadjuvant chemotherapy also provides benefit, chemotherapy or PIPO is sometimes necessary after surgery. Then strict monitoring is

necessary even after surgery. Metastatic stages may benefit from chemotherapy.

We report a clinical case in a 65-year-old chronic smoking patient who weaned 20 years ago, hospitalized in the urology department of the Mohammed V Rabat military instruction hospital on 08/2021.

## OBSERVATION

Mr. TAI, 65 years old with a history marked by type 2 diabetes on oral antidiabetics, hypertension on amnlodipine 5mg chronic smoking weaned 45 packets per year is admitted to the emergency room for hematuria with left low back pain.

As a little story, the onset dates back to 5 days with the installation of low back pain accompanied by moderate macroscopic hematuria. Given the exacerbation of the aforementioned signs, the patient consults the emergency room for treatment.

On admission, Glasgow score was 15/15, well oriented in time and space, hemodynamically unstable with euphemistic BP 80/60mmh with good ambient air saturation.

On physical examination, there is lumbar contact and renal sloshing plus excusable pain in the left flank. The patient received a blood transfusion of two red blood cells then a biological assessment including an ionogram, NFS, an ECBU, (urea at 0.33mmol / l, creatine at 12mg / l, GFR at 62ml / min /, Reserve Alkaline at 23mmol/l, hemoglobin at 8g/dl, platelets at 234000, GB at 5700).

The patient returned with an MRI which was done externally on 10/11/2020 in favor of a left pyelo-ureteral tissue process measuring 80x30x30mm with hydronephrosis upstream of a 9mm left renal hilar ganglion fig. 1.

A pre-anaesthetic consultation is made in a short time, a decision to operate on the outcome of a medical staff. The patient has benefited from a digestive preparation the wish of the surgical intervention. The patient is thus operated on 10/08/2021. Part of NUT (nephro -ureterectomy fig. 2) Under general anesthesia.

First stage Exploratory cystoscopy: with the aim of looking for a synchronous tumor at the expense of the bladder.

The Patient is placed in the pruning, brushing and draping position. a urethro-cystoscopy performed without particularity.

Second time; Laparoscopic NUT after change of position:

The patient is installed in the left lateral decubitus position, we proceeded to washing and then draping the patient's patient followed by probing in the operating field, Creation of pneumoperitoneum on a veress needle.

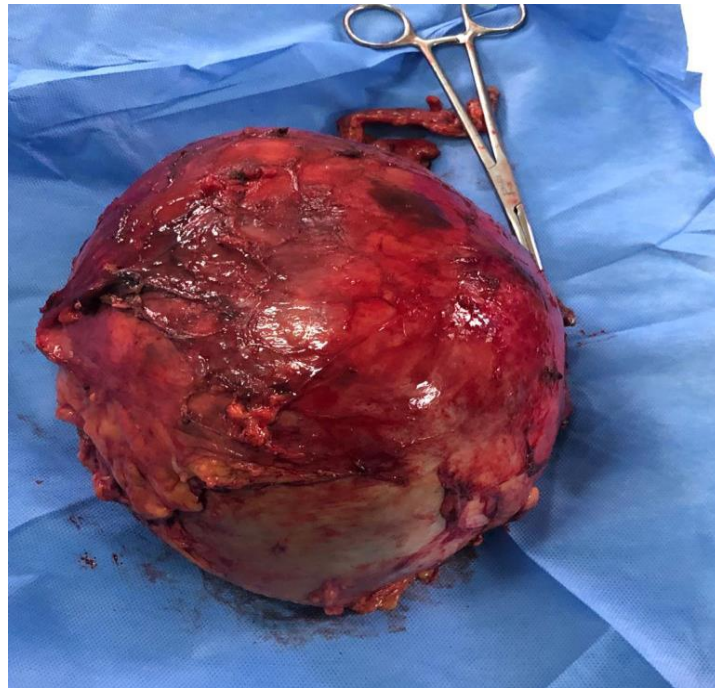
Four trocars are inserted respecting the triangulation including two of 5mm, a 10mm trocar and a 12mm trocar;

- A nephro-ureterectomy plus laparoscopic adrenalectomy is performed: as a first step within the framework of respecting the principle of oncological rules according to the recommendation of the AFU (installation of a Hemo-lock clip and respecting the integrity of the kidney and urinary tract.
- In the second step, the resection of the collar is performed by the open way (patient is reinstalled in the supine position, performance of an incision under the umbilical and access to the bladder after filling with 300cc saline serum, exposure of the collar) figure 11.
- In the third gesture it was the left lumbo-aortic dissection passed without incident.
- CCAFU recommendations; Installation of a Redon drain on the left.

### Trocar positions



**2.6 kg surgical specimen Plus ureter measured 20 cm from our patient**



**Operative part of another patient operated at the same period as our patient (just to show the management of the collarette, the ureter and kidney)**



- The duration of the laparoscopic surgery intervention is 3 hours 45 minutes, the bleeding is 200cc, the patient got up the next day as part of rehabilitation, the diet the next day, the intestinal transit restores 24 hours later, ablation of the Redon drain 48 hours after his intervention (quantity brought back was less than or equal to 5ml before its ablation), the ablation of the bladder catheter on D2 of his intervention. The patient was discharged on the fourth day of his intervention, the removal of the threads on the tenth day.

Referring to Clavien and Dindo no complications were observed, marked by a good evolution;

- Surveillance: as part of follow-up, the thoraco-abdomino-pelvic scanners seen at the various onco-urology consultations are unremarkable.
- Biological assessment: We currently note good renal function: DFG: 90ml/min. 173 m2, urea: 0.30g/l, creatinine at 12mg/l, k at 3.7 mmom/l, alkaline reserve 26mmom/ l. It should be noted that we had found a slight disturbance of the renal function just the surgery which was recovered immediately.
- REPORT OF THE ANATOMO-PATHOLOGY: regretfully, we were unable to recover the histological image of the operating room on those, we apologize the operating

Postoperative course:

specimen (NUT plus collar plus left dissection) is sent to the anatomopathology at the anatomy-pathology laboratory of the ESSAADA office, fax0537705938/ E-mail : essaada.anapath@gmail.com

In the report of the anatomo-pathology we retain this

- \* Operating specimen of excellent quality, significant interpretation,
- \* UC of the excretory tract (remaining perennial at the level of the renal pelvis and ureter whose perennial part measures 6cm in length, essentially papillary architecture of high grade

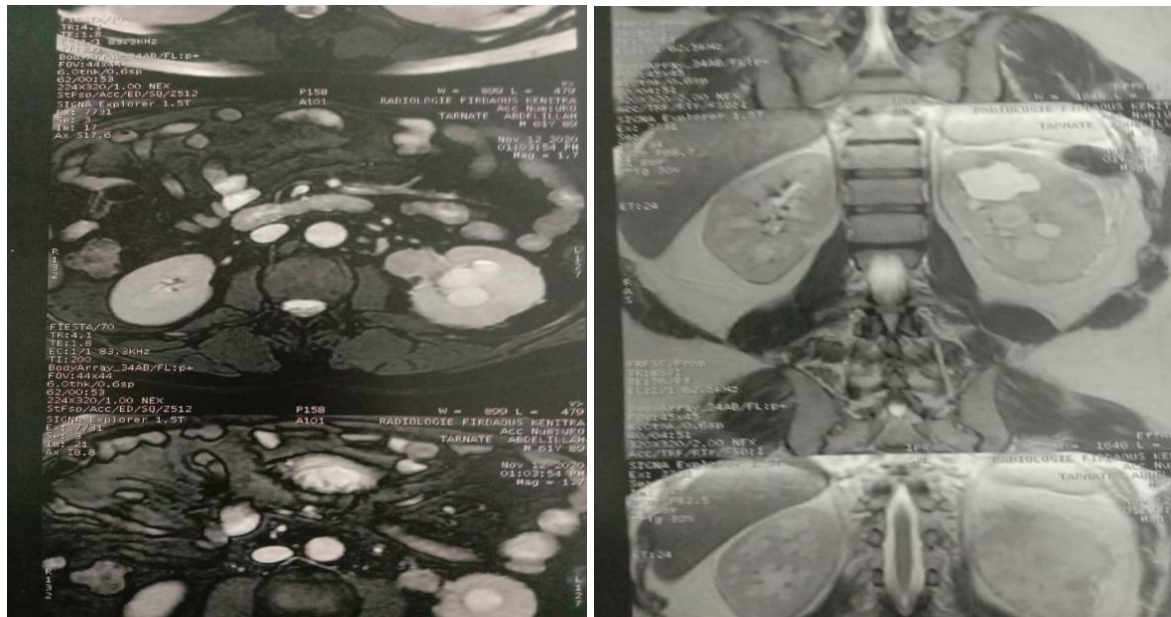
(WHO classification 2016), grade2 (WHO1974), Stage T1 (TNM 2017 UICC).

- Absence of muscle infiltration,
- \* Absence of CIS,
- \* Absence of vascular embolism,
- \* Kidney reduced to a multi-cystic pouch.

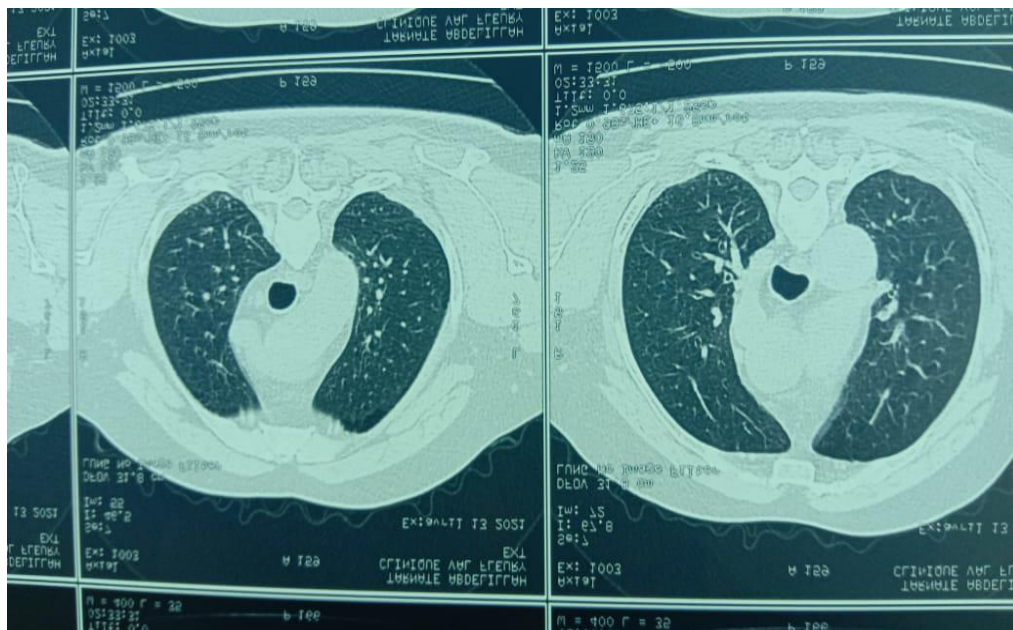
The rest no particularity

- \* Healthy collarette and ureter,
- \* Healthy adrenal.

Cleaning, we note 6N- /6N



**Fig. 1: MRI 80mm tissue mass**



**Fig. 2: THORACIC CT with 9mm nodule**

## DISCUSSION

*Our patient is classified stage pt1 NOM0 High grade.* The first observation on TVEUS was reported in 1841 by RAYER in his treatise on kidney disease.

It took until 1878 to find a histological description of it which was made by WINSING and BLIX.

In 1905, ALBARRAN again described this cancer by visualizing during a cystoscopy a ureteral tumor proceeding at the level of the ureteric meatus and he detailed his observation in 1909 in his treatise on operative medicine. Publications remain quite rare until the report by MELTZER in 1926, 181 tumors of the excretory tract, the renal pelvis [1]. The characterization of TVEUS then gradually multiplied thanks to the advent of uro-radiology and endourology, which caused the disease to lose its exceptional character. Several important reviews have taken place.

Noted including that of MAZEMAN (1972) at the 66th congress of the AFU, 737 cases of pyelocalicielle tumors and 381 ureteral tumors.

TVEUS represent 5% of UC with an incidence of approximately 1/100,000 inhabitants/year. The peak incidence is between 70 and 90 years. A ratio of 1.5 to 2.8 [3]. The pyelo-calicielles location is 50 to 59%, the multifocal is found in 7 to 23% [3].

VTES are diagnosed at an invasive stage in 60% of cases with an increasing incidence of high-grade forms.

A history of bladder injury is found in 12 to 30% of patients [4-6]. Recurrences in the form of bladder tumors are found in 30%; conversely recurrence in the bladder after radical treatment is low 2 to 5%.

Histologically, we distinguish 95% UC, epidermoid contingents, sarcomatoid contingents (5%). The 2009 TNM classification makes it possible to determine the infiltrating or non-infiltrating forms.

\* **We distinguish the common risk factors with TV:** Tobacco which was the only risk factor, occupational exposure to aromatic amines and polycyclic aromatic hydrocarbons and chlorinated solvents. Genetic polymorphism of detoxifying enzyme systems. Chronic exposure to acrolein is a risk factor. Lunch syndrome is a familial form of colorectal cancer that exposes to the development of TVEUS which increases the risk by 14 to 22% whose positive diagnosis requires molecular confirmation [3].

\* **The risk factors specific to TVEUS:** Namely aristolochic acid (AA) is the active ingredient of aristolochia herbaceous plants whose accidental ingestion can cause Balkan nephropathy, regular and prolonged consumption of phenacetin contained in analgesics [4].

The clinic is marked by macroscopic hematuria in 68 to 82% of cases [3]. Pain in the flanks and lumbar pits are revealing in 20 to 30%. The diagnosis is fortuitous in 10 to 16%.

Morphological assessments are based on Uro-CT / Uro-MRI [7].

\* **The multi-detector scanner:** Constitutes the reference imaging modality for the diagnostic work-up of TVEUS in patients with a creatine clearance greater than 45ml/min [3].

A CT scan or sometimes called it has 4 phases: a phase without preparation, a medio-cortical phase, a nephrogenic and an excretory phase is more and more frequently proposed. It has a sensitivity of 93.5-95.8% and a specificity of 94.8-100%.

Diagnostic performance decreases for flat tumors and tumors smaller than 5mm.

**UIV:** It is an examined which was carried out in time before the advent of the scanner: two images must retain the presence of a TVEUS which are the gap (endoluminal budding image), image of BERGUEMANN.

The IVU does not provide information on whether or not the lesion is infiltrating; it allows one to roughly assess the prognosis of a ureteral or pyelic lesion. It also makes it possible to assess the functional value of the contralateral and homolateral kidney. It is currently overlooked by the scanner.

Multifocal TVEUS seen at IVU: Shortcomings.



Uro-MRI is desired in case of mute kidney, local and locoregional extension assessment, distinction of tumor gaps from clots [4].

\* **Cystoscopy and UPR:** Performing a cystoscopy is recommended in the systematic assessment of a TVEUS because of the possibility of a synchronous

bladder lesion in 8 to 13% of cases (rank A recommendation [3]. Our patient underwent a primary cystoscopy, the result of which was unremarkable.

UPR can be performed in an emergency context or when optimal imaging of the upper urinary tract could not be achieved, it has a sensitivity of 97% and specificity 93% for the detection of TVEUS [4]. Our patient did not benefit from UPR.

- \* **Urinary cytology and biological markers** [1, 2, 5, 6]: Cytology of TVEUS is less sensitive than in VT, including for high-grade lesions and must be carried out selectively in situ during endoscopy before injection of contrast products: overall sensitivities are only around 40 to 60% [1, 2, 7]. No marker is recommended these days. Urinary cytology was negative in our patient.
- \* **Flexible ureteroscopy (USSR)** [1-3]: Allows the exploration of high apparatus in a macroscopic way in 95% and allows the realization of biopsy and cytology in situ; the biopsy establishes the diagnosis with a sensitivity of 89 to 95% with low reliability and an under-evaluation rate of 45%.

The biopsy grade is a good reflection of the definitive tumor grade in 61 to 91% of cases. There is a correlation between biopsy grade and definitive tumor stage [1, 2].

So a USSR must be performed in case of positive cytology while no lesion on cystoscopy and imaging, doubtful diagnosis on imaging, conservative treatment is considered.

- \* **Optional examinations:** A chest CT scan in the event of an infiltrating lesion. Secondary lesions are pulmonary in 52%, Hepatic 33%, Bone 26% (level of evidence 4) [4].
- \* **A bone scintigraphy** is performed in the event of a clinical sign of bone localization, a brain scan.
- \* **Pre and postoperative prognostic factors:** The preoperative prognosis is based on the low or the high risk, the question of the lower size of 1cm, the evolutionary stage, other pejorative prognoses are useful even if they have not been integrated directly into the preoperative stratification [4]: ureteral location, sessile tumor architecture, high CRP, polymorphonuclear/lymphocyte ratio greater than 3.0, operating time greater than 3 months, high or very high body IDM, deterioration in general health and performance status [5].
- \* **The specific postoperative survival prognostic factor:** Includes the stage and the tumor grade, level of evidence 2. Vascular embolism, lymph node invasion, presence a positive surgical margin, the CIS. Our patient presented among the postoperative prognostic factors the high grade G2.
- \* **Bladder recurrence [1, 2]:** Postoperative bladder recurrence is a factor of poor prognosis. There are

30 to 40% recurrences in the literature, observed especially in tumors classified as high grade G3. Our patient so far is free of any bladder recurrence.

**Lymphovascular invasion:** This is a poor prognostic factor.

Positive surgical margins [6, 8] is also a pejorative factor, correlated with local recurrence, sometimes with progression.

**NB: Three categories of risk factors have been identified:**

- Patient-dependent factor (male gender, history of bladder injury, preoperative IRC),
- Factors dependent on the tumor (preoperative positive urinary cytology, ureteral location, Pt2 stage, necrosis),
- Factors depending on the treatment : positive surgical margin, extra-vesical approach to the collar, laparoscopic approach.

**TNM Classification 2016**

*T:* primary tumor

*Tx:* Primary tumor cannot be assessed

*T0:* no signs of primary tumor

*Ta:* Non-invasive papillary carcinoma.

*Tis:* carcinoma in situ.

*T1:* tumor invading the sub-epithelial connective tissue.

*T2:* Tumor invading the muscularis.

*T3:* renal pelvis and calyx: tumor extending beyond the muscle and invading the peri-pelvic fat or the renal parenchyma.

*Ureter:* tumor extending beyond the muscle and invading the peri - ureteral fat.

*T4:* tumor invading adjacent organs or extending through the kidney to the perirenal fat.

*N:* Regional lymph nodes

*Nx:* lymph nodes cannot be assessed.

*N0:* no involvement of regional lymph nodes.

*N1:* involvement of a single regional lymph node less than or equal to 2cm.

*N2:* involvement of a single lymph node larger than 2 cm.

*M:* Distant metastases

*M0:* absence of distant metastasis.

*M1:* Distant metastasis(ies).

**DEFINITIONS OF LOW GRADE AND HIGH GRADE**

**Low grade TVEUS:** are non-infiltrating, unifocal, small size and low grade pta according to (pathologist) no CIS, resectable in one piece

**High grade TVEUS:** are high grade pt1, pt2, pt3, pt4 multifocal or large size, non-resectable in one piece, infiltrating

**Treatments:** *The therapeutic options and methods depend on the evolutionary stage, tumor grade, sometimes the size, as well:*

**TVEUS classified as low grade:** for low-risk tumours, conservative treatment is systematic and theoretically makes it possible to avoid the morbidity of radical treatment without compromising overall survival or specific level 3 evidence [4]. The patient must be warned of the risk of recurrence and progression and must accept strict and close monitoring.

The USSR is preferred to the URR [1, 2], a laser generator with a biopsy is necessary for the treatment.

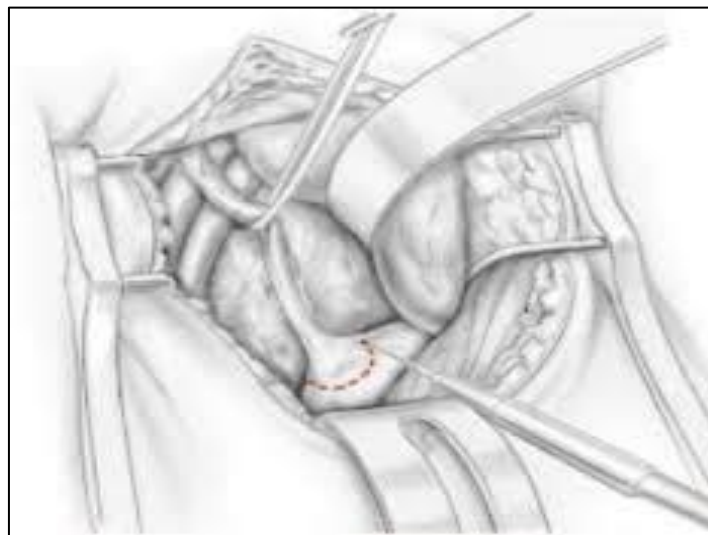
By percutaneous approach: the development of the USSR has reduced the use of this approach initially. It can be performed in the event of an inferior calicelles lesion inaccessible to treatment by USSR [3].

Instillation of topical adjuvant agents of BCG or mytomycin C has been reported for curative purposes for CIS lesions and as adjuvant therapy after conservative treatment of low-risk papillary lesions.

Instillations seem to decrease the frequency of local recurrences without improving survival only for CIS lesions (2% of all TVEUS) [6].

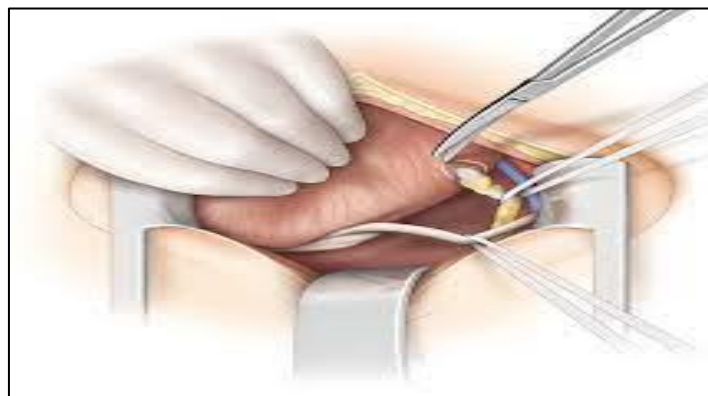
Segmental resection and end-to-end anastomosis in the event of distal ureteral involvement or uretero-vesical anastomosis in the event of lower involvement on the pelvic ureter.

\* **For high-risk TVEUS:** The reference indication is open NUT with excision of the perimeatic bladder collar, regardless of the location of the tumor [7]. Our patient underwent laparoscopy.



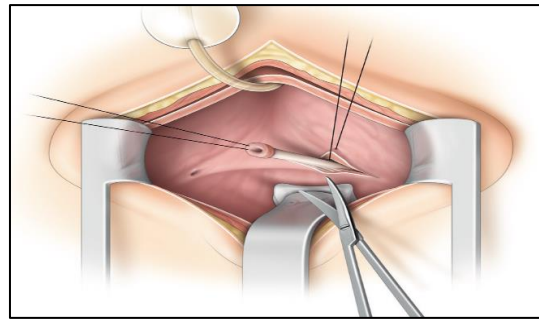
*Approach to the collar different surgical technique*

**Extra bladder approach [11]**



*Perimeal incision taking a collarette of bladder mucosa, then dissection and release of the intramural part of the ureter with Metzenbaum scissors. A gentle pull on the marker thread allows exposure. The ureter is then fully freed and retrieved extra-vesically [11]*

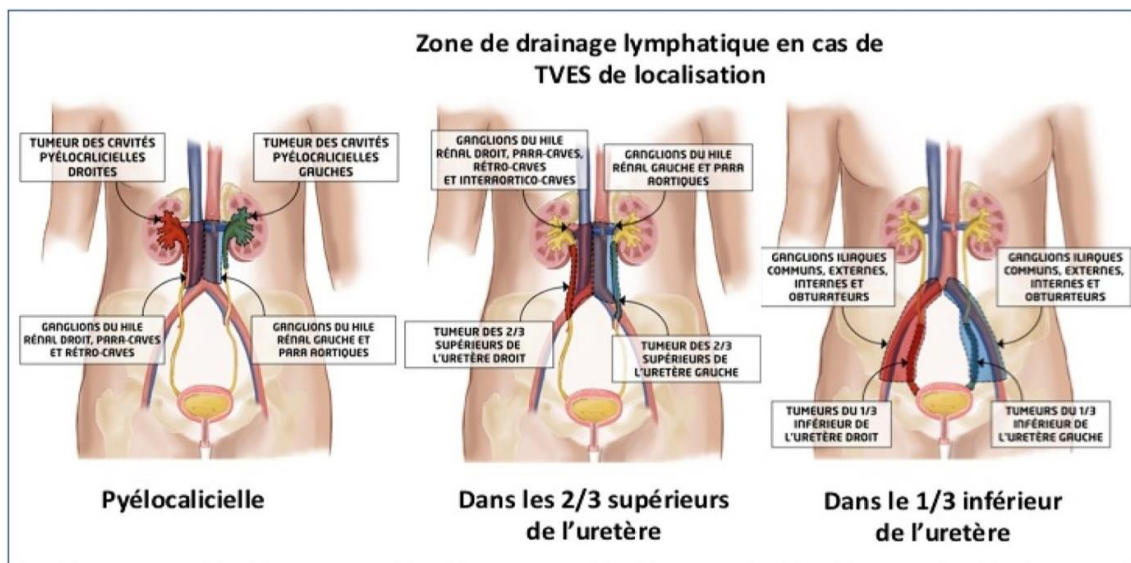
**Another procedure in intravesical approach**



**Lymph node dissection plus NUT:**

Allows better staging and guides subsequent therapeutic management (adjuvant chemotherapy and could improve survival level of evidence) [4, 6].

*Curing scheme adapted once indicated [1, 2].*



*Lymph node dissection areas if necessary*

**\*Perioperative treatments:**

**Neoadjuvant / adjuvant treatment:**

TVES are considered chemo-sensitive tumours. However, the level of proof of studies on the benefit of platinum-based chemotherapy in the perioperative period is low.

**Neo-adjuvant chemotherapy:**

Is the concept with the strongest rationale in the TVEUS once the patient is stratified and classified in fit for chemotherapy (PS, renal function and comorbidity) normal.

**Radiotherapy:**

Could improve local control of the disease but it does not influence the occurrence of metastases, nor specific or overall survivals [2-4].

**Adjuvant intravesical instillations:**

The rate of bladder recurrence after NUT is 40% [4], early instillation of intravesical chemotherapy (IPOP) reduces this risk. However, the time and type of chemotherapy (epirubicin, mytomyacin c) are

undetermined but it is necessary to retain 7 to 10 days after the NUT for mytomyacin.

**\*Metastatic disease [2-5]:**

Local treatment, whether surgery or radiotherapy, has no place in cases of metastatic disease outside of a symptomatic palliative context. Platinum-based chemotherapy is the reference treatment.

**\*Monitoring:**

Thanks to patient monitoring software from our onco-urology consultation service, our patients are well identified and are reviewed every three months with the results of biological and morphological explorations. Thus this patient presented through this clinical case is in good evolution.

After radical treatment: monitoring is necessary in order to detect bladder recurrence, local or distant [3]. After NUT, the risk of local recurrence is low, whereas the risk of distant recurrence depends directly on the prognostic factors; this monitoring is



based on urinary cytology, cystoscopy, uro-CT with a specific rhythm depending on the risk.

High invasive and non-invasive risk: cystoscopy and cytology at 3 months then annually.

Uro-CT extended monitoring over 5 years [6-8].

The infiltrating form; cystoscopy and cytology at 3 months then annually, Uro-CT and thoracic DTM (half-yearly for 2 years then annually for 5 years).

**-Low risk after conservative treatment [1-3]:** Cystoscopy, in situ cytology, uretero-endoscopy plus second look at 6 weeks – At 3 months, 6 months, then half-yearly for 2 years, then annually.

**-Uro-CT** 3 months, 6 months, then annual extended over 5 years.

After conservative treatment, the ipsilateral approach requires special monitoring because of the high risk of recurrence [3].

**-After management of a VT [8-10]:** The incidence of occurrence of a TVEUS is low (2 to 5%) in the case of TVNIM in this case the TVEUS is diagnosed at a stage at a stage symptomatic (hematuria).

A uro-CT is recommended for the diagnosis of intermediate and high risk VT (high grades) and during recurrence and trigonal, meatal location.

The risk of recurrence in the upper urinary tract after cystectomy is low -5% and 60% of cases the diagnosis is made at a symptomatic stage.

## CONCLUSION

TVEUS is a rare urothelial tumour, representing 5% of UC whose first publication dates back to 1841 by RAYES and the first histological description in 1875 by WINSSING and BLIX. A distinction is made between high-risk and low-risk forms guaranteeing treatment. The last decade has been marked by an improvement in care through the development of endourology, which has allowed macroscopic and microscopic diagnosis and the conservative treatment of low-risk lesions that were previously inaccessible. But the reference treatment remains the NUT plus a collar on a case-by-case basis with the possibility of mini-invasive or laparoscopy.

Through the progress of imaging, endourology as well as effective prognostic factors, we will allow the

multiple therapeutic options to be better adjusted over time.

## CONFLICTS OF INTEREST

All the authors participated in the context of the care of the patient preoperatively, intraoperatively, early and late postoperatively, research of references and writing of the manuscript and present no conflict.

## Contribution

This article recalls the main principles of the management of a tumor of the upper excretory tract through a clinical case, to recall the action to be taken in a case of TVEUS from reception to monitoring to improve overall survival and the specific survival, and also match the feasibility of a TVEUS by laparoscopy even if the size is sometimes important.

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