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Case report

# Adenocarcinoma mucinosum of extrophy bladder: A rare case report

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ABSTRACT

*Introduction:* Bladder exstrophy is a rare congenital anomaly while, bladder adenocarcinoma mucinous type is a rare type of bladder cancer, with aggressive behavior and inadequate response to radiation and chemotherapy. In extremely rare cases, untreated bladder exstrophy could transform into bladder mucinous adenocarcinoma.
*Case presentation:* We report a case of a 41-year-old male with untreated bladder exstrophy that transformed into mucinous adenocarcinoma. The patient also had epispadias and a right inguinal hernia. Joint procedures were conducted to perform radical cystectomy, total penectomy and W-Pouch continent urostomy, inguinal hernia repair, osteotomy, and keystone and scrotal flap by split-thickness skin graft (STSG) for wound closure. The patient progressed well after surgery, two months after initial procedure, nephrostomies were conducted due to pouches stenosis. Due to the government's limited transportation and lockdown policy, as the Covid-19 pandemic occurred, the patient could not come to the hospital for routine follow-up and died nine-month after surgery.
*Clinical discussion:* Bladder exstrophy is one of the risk factors of bladder cancer. Transformation of bladder exstrophy into mucinous adenocarcinoma is extremely rare, as the case is the first case to be discovered in Indonesia. Surgery, followed with a strict follow-up regime, is mainstay of treatment in this type of malignancy.
*Conclusion:* Adenocarcinoma of mucinous type is a scarce type of bladder exstrophy malignancies. A multidiscipline approach is mandatory in these cases. Strict and regular follow up are suggested for these cases.

## 1. Introduction

Being one of a rare congenital anomaly with an incidence of one per 50,000 newborns, neglected cases of bladder exstrophy is even more rare, with known total number of reported cases less than 90 cases [1–3]. One of the most common types of malignancy in bladder exstrophy is adenocarcinoma (80%). Of all cases, mucinous type was quite rare, comprising only two cases reported to date [4]. We reported a case of mucinous adenocarcinoma in an untreated bladder exstrophy. We proposed that the pathogenesis of malignancy is neglection and progression from chronic severe inflammation. Previous studies have also shown that severe inflammation led to progressive changes from mucinous metaplasia to mucinous adenoma to mucinous adenocarcinoma [4,5].

## 2. Case presentation

We report a case of 41-year-old male, in compliance with SCARE Guidelines [6], who has lived with bladder exstrophy without notable prior medical history or family illness. No procedure had been performed for the bladder exstrophy. The patient initially sought medical treatment for enlarged lump in his right inguinal region. By the time patient came to our hospital, the bladder was already ulcerated and infected. During physical examination, there were bladder exstrophy and epispadias complex in suprapubic region measuring 10 × 9 cm in size. The mass was granulated, easily bleeding on all surfaces of the bladder (Fig. 1). Penile epispadias was present with both testes were normally descended.

There was a well-defined lump in the right inguinal area with incarcerated type hernia. Other physical examinations were within the normal limit. There was no comorbid illness known. Excisional biopsy

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under anesthesia was conducted with mucinous adenocarcinoma were found. CT scan of the whole abdomen showed lobulated undefined mass in the suprapubic area and hernia in the right inguinal, and there were no lymph nodes involved nor other organ metastasis (Fig. 1). The mass-caused obstruction in both kidneys caused moderate hydronephrosis and hydroureter in the right kidney and mild hydronephrosis in the left kidney. Chest x-ray was normal. In pelvic X-ray, 6,8-cm symphyseal diastasis was found. During surgery preparation, the creatinine level was increased with worsen hydronephrosis found in ultrasonography.

A multidisciplinary team board meeting was conducted with the digestive, plastic, and orthopedic departments and concluded to hold a joint surgery from respective departments, after the diverted urine with nephrostomies placed by urologist. Wide excision with a two-cm margin of resection was done along with the distal of ureter, prostate, seminal vesica, followed by lymph node dissection of both obturator nodes. There was a proof of penile skin infiltration, resulting in continuing the procedure to total penectomy. The digestive department evaluated the digestive system, and there was no proof of infiltration; the operation then continued to appendectomy and preparation of ileal section for W-pouch. The osteotomy and plate-screw reconstruction with fibular graft was done by the orthopedic. Continent urinary diversion (W-shaped ileal reservoir) was conducted using a 40-cm long ileal segment. At last, the defect closure was done using scrotal flap and keystone flap-type 4 with split-thickness skin graft (STSG) from the right femoral (Fig. 2).

Histopathological examination revealed mucinous adenocarcinoma type of bladder infiltrated to prostate (shown in Fig. 3). There was no lymph node involvement. The penis and the ureter margin were free of tumor. No adjuvant therapy was given. 2 months after the surgery, bilateral nephrostomies were conducted by urologist due to stenosis of the W-pouch. Subsequent follow-up examinations were altered because of difficulty in accessing our institution due to lockdown policy. The patient died nine months after surgery with unknown causes.

## 3. Discussion

Epidemiologically, the global data have shown that bladder exstrophy occurs approximately in 2 every 100,000 stillbirths [1,3,7]. In Indonesia, the data are not well documented. In neglected cases of bladder exstrophy, malignancy incidence happens in the third to the fourth quarter of life. Patients with bladder exstrophy have 700-fold incidence of bladder cancer than the general population at the same age [8]. Such cases are reported both in developed and developing countries. Surgery is usually advised in early age in such condition to repair exstrophy. However, in this case, the patient's parents had chosen not to have the surgery due to the family's economic condition. Later, when the patient reached adolescence, the patient felt that he already accepted his condition and was again did not consider the surgery because he did not have any complaint. This case shows that patients with untreated exstrophy bladder can live healthily until other conditions emerged. In this case, the patient sought help for his hernia.

Grignon, et al. identified five subtypes of bladder adenocarcinoma: Papillary, mucinous, signet-ring cell, adenocarcinoma not otherwise specified, and mixed [9]. Currently, there was only one case been reported in the literature suggesting extreme rarity of this variant. The risk factor of carcinoma in untreated bladder exstrophy was male, with average cases in the fourth quarter of life, with around 80% were adenocarcinoma, 12.5% were squamous cell carcinoma, and 5% were unknown [4,5]. In contrast, the adenocarcinoma of bladder cancer is only 0,5–2% of the average population. In normal bladder population, the 5-year survival rate of this type of cancer is 35–55% [4].

The pathogenesis of these cases has been proposed, but the exact cause was difficult to determined due to the rarity of cases. Smeulders et al. describe that chronic inflammation and infection caused the metaplastic transformation of the urothelium [4]. McIntosh et al. concluded that recurrent infection and environment exposure resulted in glandular metaplasia that produce the protective mucus. However, overtime, malignant changes occur [5].

Surgery becomes the leading choice of treatment due to the ineffectiveness of systemic chemotherapy for non-urothelial carcinoma cases. To date, no comprehensive survival data after treatment have been published. Biopsy to distinguish the tumor followed by radical cystectomy with neobladder could be chosen, and permanently nephrostomy is another option if the strict follow up could not be done because of any condition. Multidisciplinary approaches are recommended as abdominal defects are also an issue because unprecise repair can lead to tension wounds and accompanying morbidity. In our cases, the abdominal defect is corrected with scrotal and keystone flap-type four and STSG from the right femoral with help from plastic surgeon colleagues. Other choices are tensor facia Lata flap as suggested by Bango et al.

We did an extensive search and came across about 90 cases of adenocarcinoma of neglected bladder exstrophy patients, none of which was from Indonesia. There was only 1 case from India with the same type. In 2016 Abhishek et al. report the same case in India of a 63-year-old male, who never sought help for her condition, and came for other complain that his left flank pain and after holistic exam found mucinous type bladder cancer [2]. The patient then underwent radical cystectomy, lymph node excision and, wide local excision with 1 cm margin of resection of skin with ileal conduit for urinary diversion. For surgery wound closure, the rectus abdominis rotation flap was done due to a significant defect. The patient was not given adjuvant therapy, and until the case was reported, the patient was followed up for one year without any complaint.

There is no specific guideline for follow-up cases of such cases, and we applied the general bladder cancer follow-up plan. Slaton et al. recommended that evaluation of physical examination, serum chemistry indexes, and computed topography depends on the stage can be done annually or in a shorter time [10]. Austen et al. propose an annual endoscopy from the 3rd postoperative year due to mixed urinary and fecal stream use as a diversion [11]. In this case, periodic, routine

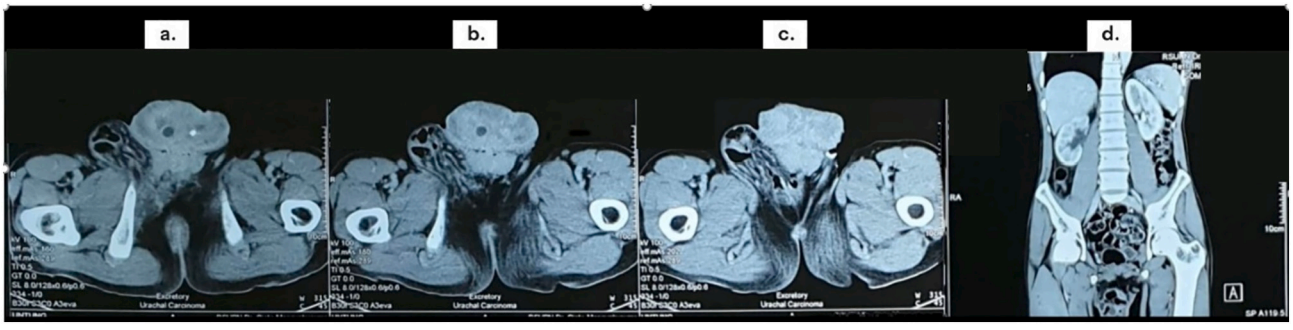


**Fig. 1.** Contrast-enhanced computed tomography of whole abdomen a-c: lobulated undefine mass with right inguinal hernia, d: moderate hydronephrosis and hydroureter in right kidney and mild hydronephrosis in left kidney.

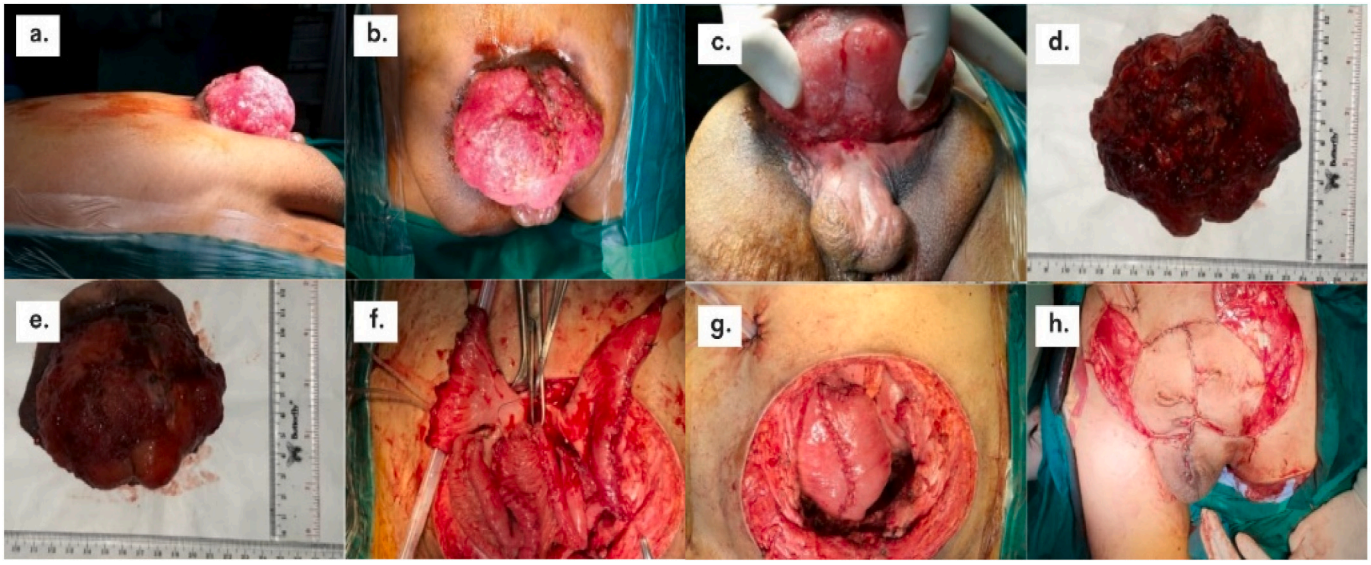


**Fig. 2.** Intraoperative photograph. Appearance of the bladder exstrophy with tumor; (d-e): macroscopical appearance of the specimen after surgery, (d) shows base of tumor view, (e) shows superficial of tumor view; (f-g): Ileal continent urinary diversion; (h): defect closure.

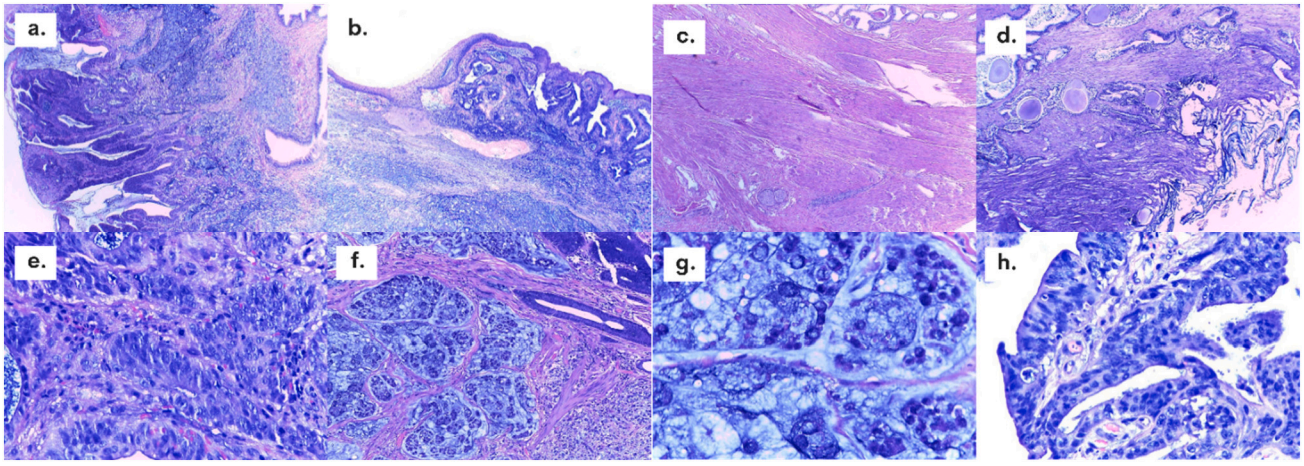


**Fig. 3.** Micrographs from the tumor. (a-d HE, 40× magnification) a. Papillary tumor mass, infiltrative, partially submerged in mucin pool, b. Tumor mass composed papillary, glandular, infiltrative. c. Tumor mass between the fibromuscular tissue of the prostate's left and right posterior edges. d. Tumor mass between the fibromuscular tissue of the prostate's left and right posterior edges. (e-f HE, 100× magnification) e. Tumor cells showing pleomorphic, hyperchromatic, partially eccentrically located nuclei. The cytoplasm is vacuolated. f. The tumor mass is inundated in the mucin pool. (g-h HE, 400× and 100× magnification) g. Pleomorphic nuclei with vacuolated cytoplasm. Mitotic figures are found. h. Area with intestinal-type epithelia.

follow-up examinations was not properly conducted, as there were difficulties to access our center and seek medical treatment due to COVID-19 lockdown policy. Subsequently, he died nine months after surgery.

## 4. Conclusion

Untreated extropy and primary adenocarcinoma bladder are rare cases. Adenocarcinoma is a more common type, however, mucinous type is less common in previous reports. Surgical treatment is the first choice for this case. Multidisciplinary approach followed by carefully planned management is important for better holistic care in such patient.

## Ethics approval and consent to participate

This case report has been exempted from ethical approval by Universitas Indonesia Ethical Committee.

## Availability of data and materials

The datasets generated during and/or analysed during the current study are available on demand.

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## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Declaration of competing interest

The authors declare that they have no competing interests.

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*Consent*

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

*Author contribution*

Agus Rizal Ardy Hariandy Hamid: Conceptualization, Methodology, Writing Original-Draft, Investigation, Resources.

Chaidir Arif Mochtar: Supervision, Methodology, Validation, Writing-Review and editing, Resources.

Lisnawati: Writing-Review and editing, Resources.

Meilania Saraswati: Writing-Review and editing, Resources.

Sahat Matondang: Writing-Review and editing, Resources.

Muhammad Isa Fuad Affan: Writing Original-Draft, Investigation.

*Research registration*

Not applicable.

*Guarantor*

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