

# Diabetes Insipidus in Young Women with Cervical Cancer

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## **Abstract**

*A 25 year old, unmarried, Indonesian woman came to the emergency department Cipto Mangunkusumo Hospital with shock condition. Initially assessed as septic condition, the patient was then diagnosed as diabetes insipidus (DI). It was concurrently found that the patient also had several sexual intercourse before and not until later that the patient diagnosed with stage IB cervical cancer. Cervical cancer (CC) is the third most common cancer in women worldwide and primarily affects young adult women, with consequences not only individually but also socially. DI is a rare disease that causes frequent urination that is not frequently related with CC. Concurrent incidence of DI with CC can only be seen in several case reports. It has not yet been established whether these two conditions are concurrent or having a cause-effect relationship. DI is not a common case, hence knowing its clinical sign and symptoms are very important. In fund limited setting in third world countries, the laboratory examination can be simplified by examining the osmolality of the serum and urine condition. These low level of serum can be very helpful in diagnosing DI with treatment can be as simple as fluid restriction. Regarding the CC, radical trachelectomy can be done with surveillance must be done every 3-6 month for 2 years and every 6-12 month for 3-5 years with cytology.*

**Keywords:** CC, diabetes insipidus

## **Diabetes Insipidus pada Perempuan Muda dengan Kanker Serviks**

## **Abstrak**

*Seorang perempuan Indonesia, 25 tahun, belum menikah datang ke IGD RSCM dengan keadaan syok. Awalnya dinilai sebagai keadaan sepsis namun akhirnya didiagnosis sebagai diabetes insipidus (DI). Didapatkan riwayat berhubungan seksual sebelumnya dan kemudian diketahui menderita kanker serviks stadium IB. Kanker serviks merupakan kanker ketiga tersering pada perempuan di seluruh dunia dan terutama menyerang dewasa muda, dengan konsekuensi individual dan sosial. DI merupakan penyakit yang menyebabkan sering berkemih dan jarang berhubungan dengan kanker serviks. Kejadian bersamaan antara DI dan kanker serviks hanya ditemukan pada beberapa laporan kasus. Belum dipastikan bahwa kedua kondisi tersebut terjadi bersamaan atau memiliki hubungan sebab-akibat. DI bukan kasus yang sering sehingga mengetahui tanda dan gejala klinis menjadi penting. Di wilayah dunia ketiga dengan keterbatasan dana, pemeriksaan laboratorium dapat disederhanakan dengan memeriksa osmolalitas serum dan urin. Apabila didapatkan kadar yang rendah maka diagnosis DI dapat ditegakkan dengan tatalaksana sederhana seperti pembatasan cairan. Mengenai kanker serviks, trakelektomi radikal dapat dilakukan dengan pengawasan tiap 3-6 bulan untuk 2 tahun dan tiap 6-12 bulan untuk 3-5 tahun dengan sitologi.*

**Kata Kunci:** kanker serviks, diabetes insipidus

## Introduction

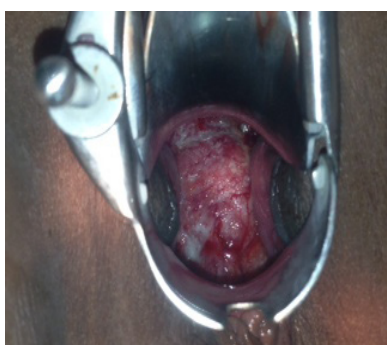
Cervical cancer (CC) is the third most common cancer in women worldwide after breast and colorectal cancer.<sup>1</sup> More than 85% of the global incidences occur in less developed regions, where it accounts for 13% of all female cancers.<sup>2</sup> CC primarily affects young adult women, with consequences not only individually but also socially in terms of child care and labor force.<sup>3</sup> CC takes a toll on young women from the poorest countries and the most disadvantaged populations. Diabetes insipidus (DI) is a rare disease that causes frequent urination that is not frequently related with CC. Concurrent incidence of DI with CC can only be seen in several case reports.

## Case Illustration

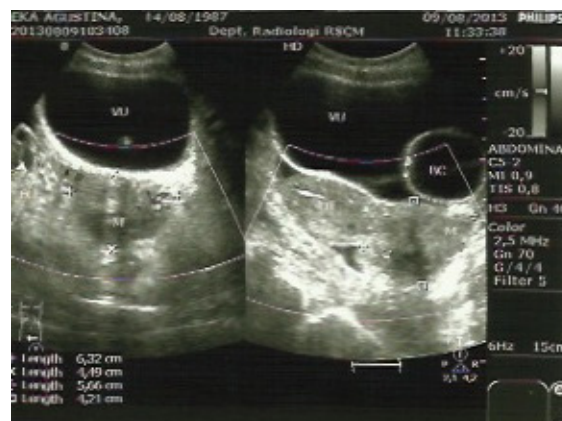
### History, examination and management

We are reporting a case of a 25 year old Indonesian woman who came to the Emergency Department Cipto Mangunkusumo Hospital with chief complaint of fever since the previous month referred by a nearby hospital. Fever is felt especially at night time. Patient didn't complain of any vaginal bleeding and post coital bleeding and felt whitish discharge since 6 month ago. She had a history of multiple sexual partner eventhough have not married yet with no complaint of micturition and defecation. There are also a weight loss up until 10 kg in these past 2-3 months.

On physical examination we found that the patient is hypotensive with 80/50 mmHg and heart rate of 110x/minute. On speculum examination we found an exophytic mass that easily bleeds with diameter of 5x4x6 cm. The uterine size is within normal limit with palpable mass in the cervix and no involvement of the parametrium, the pelvic wall and the rectum. On ultrasonography we found that there is mass size 4.75x3.75x4.13 cm that thought to be originated from malignancy of the uterine cervix. The pathology anatomy result later showed as a CC with keratinized squamous cell carcinoma well differentiated with no lymphovascular invasion.



**Figure 1. Speculum Examination Results Show Easily Bleed Mass Size 5x4x6 cm**



**Figure 2. Ultrasonography Result Showing Mass Size 5,6x4.1 cm in The Cervix**

On laboratory findings we found an increase of the leucocyte up until 27.000/m<sup>3</sup>. Lactate with 2.0 mmol/L, procalcitonine 0.19 ng/ml with non reactive of any hepatitis and HIV marker. The patient was then treated as a shock septic patient and we performed early goal directed therapy of antibiotic, rehydration, vasoconstriction medication and supportive therapy.

The patient was not getting better in spite of our treatment and was still in a hypotensive condition. The echocardiography resulted in global normokinetic with dilatation of left atrium and moderate tricuspid and mitral valve regurgitation. There were also minimal pericardial effusion with ejection fraction 68%. It was that within our care that we realize a massive diuresis of patient until 7cc/kgBW/hour with urinary production 2000-3000 cc/24 hours. It was admitted by the patient that she had this complaint of micturition since 9 months before admission.

MRI of the head and ADH examination was planned but not done due to financial problems. Hence we checked her urine osmolality and serum osmolality. The osmolality of the urine is 133 mosm/kg with serum osmolality 260 mos/kg. The urinary electrolyte results are 314 mEq, 30 mEq and 274 mEq per 24 hours for Natrium, Kalium and Chlorida urine level respectively. The patient was then concluded as a diabetes insipidus and treated conservatively with fluid restriction. The patient was gradually recovered with less polyuria daily in our treatment and discharge with unremarkable condition 5 days afterwards.

## Discussion

Young age at first sexual intercourse (AFI) is an important risk factor for CC. The OR for invasive cervical carcinoma is approximately proportional to

the square of time since first intercourse up to age 45.<sup>4</sup> The CC risk was 2.4-fold among those having their first sexual intercourse less than 16 years of age compared with those more than 21 years.<sup>5</sup> Although the peak age at presentation is between 40 and 49 years, the incidence of CC is rising in women under 40; at a rate of 318.6 per 100,000 (25 – 29 year age group).<sup>2,6</sup> In 2004, the The National Health Service Cervical Screening Programme (NHSCSP) published revised guidelines for cervical screening. One of the recommendations was to raise the age of initiation of cervical screening from 20 to 25 years.<sup>7,8</sup>

Early diagnosis also resulted in adequate treatment with conservative surgery. Delayed screening may result in diagnosis at a more advanced stage. Case reports also reported cases with patient as young as 15 year old.<sup>9</sup> CC screening may not be effective at preventing invasive CC in women under the age of 40. This may be due to the rapid progression of the disease and misdiagnosis because CC is primarily thought to be a disease in older women and not considered a disease of young women.<sup>6</sup> This is one of the obstacles of diagnosing CC in very young age woman. The US Preventive Services Task Force (USPSTF) cites the Pap test as the most effective way to screen for CC in women who have been sexually active and have a cervix.<sup>10</sup>

DI is a condition caused by an abnormality of the pituitary gland which leads to a deficiency of the hormone vasopressin.<sup>11</sup> There are two types of DI which are central and nephrogenic DI. In the central DI, a deficiency of vasopressin, resulted in the kidneys not being given the signal to retain fluid, hence large quantities of fluid are lost as very dilute urine. In nephrogenic DI, the kidneys are not able to respond to the vasopressin stimulus. The symptoms of nephrogenic DI are similar to central DI; that is, excessive urination (polyuria) followed by excessive thirst (polydipsia). It has not yet been established whether these two conditions are concurrent or having a cause-effect.

The pituitary gland is a relatively uncommon site for malignant metastatic tumours. One case from Italy reported symptomatic pituitary metastasis from uterine CC that resulted in history of frontal headache, polyuria and polydipsia.<sup>12,13</sup> The patient undergone trans-sphenoidal surgery and partial removal of the lesion in an intra and suprasellar mass, extending into the right cavernous sinus and partially eroding the dorsum sellae and sella turcica.<sup>3</sup> Cases were reported from Brazil.<sup>13</sup>

Haematogenous spread depends on histological type of the tumor. Cerebral metastasis are more frequent in poorly differentiated tumors. Histological subtypes in decreasing frequency are squamous cells carcinoma, adenocarcinoma, carcinoid tumor and adenosquamous carcinoma.<sup>13</sup>

Treatment options for Central DI patients are desmopressin and carbamazepine. Desmopressin will be ineffective in nephrogenic DI. Instead, the diuretic hydrochlorothiazide (a thiazide diuretic) or indomethacin can improve nephrogenic DI. Thiazide diuretics are sometimes combined with amiloride to prevent hypokalemia. It seems paradoxical to treat an extreme diuresis with a diuretic, but the thiazide diuretics will decrease distal convoluted tubule reabsorption of sodium and water, thereby causing diuresis.<sup>11,14</sup> This decreases plasma volume, thus lowering GFR and enhancing the absorption of sodium and water in the proximal nephron. Less fluid reaches the distal nephron, so overall fluid conservation is obtained

DI is not a common case, hence knowing its clinical signs and symptoms are very important. The patient condition that were first thought as a septic condition turns out was hypovolemic because of severe DI. In fund limited setting in third world countries such as ours, the laboratory examination can be simplified by examining the osmolality of the serum and urine condition. These low level of serum can be very helpful in diagnosing DI. Its treatment can also be as simple as fluid restriction before we go into pharmaceutical approach. The bright side of these case are if its not due to its hypovolemia condition because of the DI, the patient would not been able to be diagnosed as early in its Ib stage.

The treatment of choice for stage IB CC that have no regard of fertility are radical hysterectomy with pelvic lymph node dissection and paraaortic lymph node sampling whereas in bulky tumor alternative such as pelvic radiotherapy with or without adjuvant hysterectomy can be performed.<sup>15</sup> Fertility sparing method that were the treatment of choice for our patient are radical trachelectomy that accompanied with pelvic lymph node dissection and paraaortic lymph node sampling. Surveillance must be done every 3-6 month for 2 years and every 6-12 month for 3-5 years with cytology must be taken annually. Laboratory and imaging examination must be performed based on symptoms or examinations that suspicious for recurrence.<sup>15</sup>

## References

1. Castellsagué X, Bruni L, Alemany L, Mireia Diaz, Sanjosé Sd, Bosch FX. The epidemiology of cervical cancer. HPV and cervical cancer: achievements in prevention and future prospects. 2012;63-83.
2. ACS. Cervical Cancer Overview. Booklet 2013.
3. Tidy J, Gillespie AM, Bright N, Radstone CR, Coleman RE, Hancock BW. Gestational trophoblastic disease: a study of mode of evacuation and subsequent need for treatment with chemotherapy. *Gynecol Oncol*. 2000;78:309-12.
4. Plummer M, Peto J, Franceschi S. Time since first sexual intercourse and the risk of cervical cancer. *Int J Cancer*. 2012;130:2638–44.
5. Louie K, Sanjose Sd, Diaz M, Castellsague X, Herrero R, Meijer C, et al. Early age at first sexual intercourse and early pregnancy are risk factors for cervical cancer in developing countries. *British Journal of Cancer*. 2009;100:1191-7.
6. Yu CK, Chiu C, McCormack M, Olaitan A. Delayed diagnosis of cervical cancer in young women. *Journal of Obstetrics and Gynaecology*. 2005;25(4):367-70.
7. Nair MS, Bhandari HM, Nordin AJ. Cervical cancer in women aged less than 25: East Kent experience. *Journal of Obstetrics and Gynaecology*. 2007;27(7):706-8.
8. Kaufman RH. Cancer screening in the young female. *Arch Pathol Lab Med*. 2011;135:296-7.
9. Majeed U, Jamshed A, Hameed S, Shah MA, Anwar N, Ahmed Q, et al. Invasive carcinoma of uterine cervix in young females under 20 years. *Journal of Obstetrics and Gynaecology*. 2009;29(3):269-70.
10. Warman J. Cervical Cancer screening in young women: saving lives with prevention and detection. *Oncology Nursing Forum*. 2010;37(1):33-8.
11. APEG. Hormones and me: DI. Booklet. 2011.
12. Salpietro FM, Romano A, Alafaci C, Tomasello. Pituitary metastasis from uterine cervical carcinoma: a case presenting as diabetes insipidus. *British Journal of Neurosurgery*. 1998:156-8.
13. Cordeiro JG, Prevedello DM-S, Ditzel LFdS, Pereira CU, Araújo JC. Cerebral metastasis of cervical uterine cancer. *Arq Neuropsiquiatr* 2006;64(2-A):300-2.
14. NIDDK. Diabetes insipidus. Booklet. 2008.
15. NCCN. Cervical cancer. NCCN Guidelines. 2013.