Obstructive Uropathy in Gynecologic Malignancy and Value of Percutaneous Nephrostomy

Pariseema S. Dave*, Bijal M. Patel**, Himanshu Patel***, Meeta H. Mankad****

Abstract :

Aims and Objectives : To assess whether percutaneous nephrostomy (PCN) placement in patients having obstructive uropathy due to gynecological malignancy can provide further tumor specific treatment or improvement in quality of life. **Material and Methods :** This is a prospective study conducted at the Department of Gynecologic Oncology, Gujarat Cancer and Research Institute, Ahmedabad from June 2010 to April 2012. Patients having malignant ureteric obstruction presenting with uremia underwent PCN placement after workup. **Results :** A total of 25 patients fulfilled the criteria for PCN placement. Out of 25 patients, 20(80%) were of cervical cancer, 3(12%) of ovarian cancer and 2(8%) of cancer vault. 44% patients presented with symptoms of uremia. All patients showed improvement in renal function parameters after PCN placement. Infection was the most common complication. After PCN 19 patients received tumor specific treatment in form of palliative or curative radiotherapy or palliative chemotherapy. **Conclusion :** PCN is an excellent initial procedure for relieving the malignant ureteral obstruction with minimal complications. In treating naive patients, percutaneous nephrostomy was effective to improve renal function and allowed definitive treatment in many cases. Patients treated for primary neoplasia, who can still be treated with other therapeutic modalities can also benefit from PCN.

Key words : Cervical cancer, Obstructive uropathy, Percutaneous nephrostomy, Quality of life.

Introduction :

In many forms of gynecological cancer, the malignant disease itself may extend to involve the lower urinary tract and complicate the overall plan of management. Cervical cancer is the most common female cancer in the developing countries and its incidence in India is about 32 per 100,000 women. [1] Worldwide 3,70,000 cases are diagnosed annually leading to approximately 1,90,000 deaths. [2] Overall uterine cancer is the most common female cancer in the developed countries. Invasive cancer of cervix is a preventable disease because it has a long pre invasive state which can be detected by cervical cytology, but due to less awareness, over 70% of the cases present in advanced stage of the disease with associated poor prognosis and high mortality rates. [3] In many of them, it is difficult to offer definitive treatment as they present in uremia due to associated obstructive uropathy. This is due to either external compression or malignant involvement of lower ureters. These patients may have large primary advanced/recurrent/post treatment progressive residual disease. Uremia is the most common cause of death in cervical cancer patients. Obstructive uropathy was also sometimes observed in previously treated patients who had no evidence of recurrent disease, but developed hydronephrosis due to entrapment of ureters in pelvic fibrosis. Patients may be symptomatic or asymptomatic with high blood urea nitrogen (BUN), serum creatinine and electrolytes. Urinary diversion by percutaneous nephrostomy (PCN) is the commonly practiced method, not only to improve renal function, but also to improve quality of life and enable the patient to accept tumor specific palliative treatment in most and curative treatment in some. There are no clear-cut guidelines for management of obstructive uropathy in patients of advanced gynecologic cancer. The results are unpredictable in terms of recovery of renal functions and benefit attained to administer subsequent radiotherapy or surgery or chemotherapy.

Therefore, we evaluated our experience with PCN in the management of gynecologic cancer patients presenting with obstructive uropathy. Our aim was to offer symptom relief and avoid complications from renal insufficiency. After PCN insertion we wanted to

* Professor, **Associate Professor, ***Ex Resident,
**** Professor and Head, Department of Gynecologic Oncology, Gujarat Cancer & Research Institute. Ahmedabad, Gujarat, India.
Correspondance : drpariseema@gmail.com

determine definitive treatment for primary gynecological malignancy that can still be treated with therapeutic modalities like radiotherapy or chemotherapy and to evaluate the complications of percutaneous nephrostomy and improvement in quality of life.

Material and Methods :

This is a prospective study which consists of 25 cases of gynecological malignancy with obstructive uropathy. They underwent PCN insertion at Gynecologic Oncology department, Gujarat Cancer and Research Institute, Ahmedabad from June 2010 to April 2012.

In these cases detailed history was taken about chief complaints, menstrual history, obstetric history, past history, family history. In history, more care was taken to rule out symptoms of uremia and site of malignancy. General examination followed by systemic examination was done to confirm the diagnosis and to rule out any other coexisting abnormality. Routine blood investigations including Renal Function Test (RFT), X-Ray chest, Ultrasonography (USG)/ Computed Tomography (CT scan), Biopsy etc. were done.

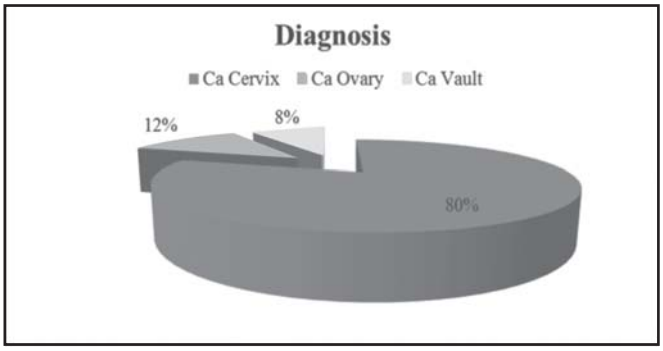
Inclusion criteria for this study were the patient should have any gynecological malignancy and obstructive uropathy, high Blood Urea Nitrogen (BUN) and S. creatinine level and USG findings suggestive of hydroureter and hydronephrosis. Patients fulfilling the criteria underwent percutaneous nephrostomy tube insertion after explanation of prognosis, subsequent treatment possibilities and expected results. Unilateral/ bilateral PCN was done according to USG by the urologist under ultrasound guidance under local anesthesia. Positions of catheters were confirmed with X-ray KUB after the procedures. Urine analysis and cultures from both PCN sites were performed at regular intervals and antibiotics were administered according to report. Serum creatinine and BUN were measured on Day 1, 7, and 14 of PCN insertion. In case of non-functioning PCN, a nephrostomogram was done to confirm the position of the catheter in the renal pelvis. Patients were monitored also by measuring daily urine output through PCN tubes. Monitoring for developing complication of PCN was also done. After normalization of Renal Function Test (RFT), patients underwent definitive treatment of the existing gynecological malignancy.

Results :

A total of twenty five (25) patients fulfilled the criteria for initial PCN placement for obstructive uropathy in patients with gynecological cancer. Majority of patients (68%) were between the 40 – 59 years of age which is the common age group for invasive gynecological cancer. Only 12% of patients were above 60 years of age. Mean age was 46.8 years. 80% of patients were multigravida; only 1 patient was nulligravida. Being multigravida is one of the risk factors for the cervical cancer.

80% of patients with obstructive uropathy were of cervical cancer, 12 % of ovarian cancer and 8% of vault cancer (Figure: 1)

Figure 1: Percentage of patients of gynecological malignancy presenting with uremia



Majority of patients (80%) presented with complaints of bleeding per vaginum (P/V). 44% of patients were presented with symptoms of uremia. 9 patients (36%) had complaints of anuria or oliguria (Table. 1).

Table 1: Presenting complaints of patients with uremia and gynecological malignancy

Complaints of Patients	No of Patients	Percentage
Bleeding per vaginum	20	80%
Abdominal pain	10	40%
Discharge per vaginum	9	36%
Symptoms of uremia	11	44%
Anuria	9	36%

Cervical growth was present in 80% of patients and 8% of patients had vault growth. All of them had parametrial involvement which was the cause for lower ureteric obstruction. Around 44% patients had

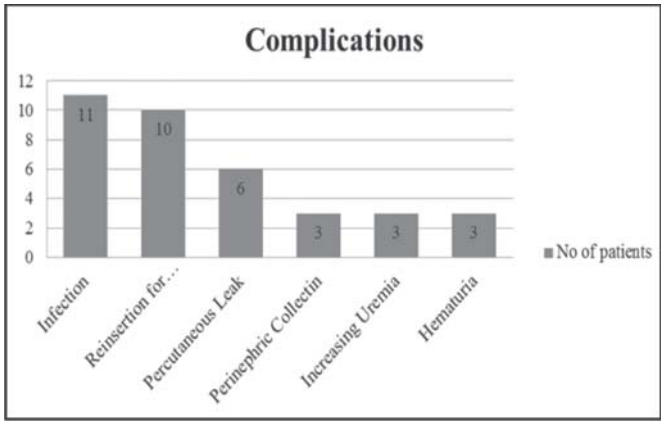
hemoglobin level of 8gm%. This was due to bleeding per vaginum(P/V) which is the most common symptom in the patients with cervical cancer. 52% patients had gross hydronephrosis on ultrasonography and 36% had moderate hydronephrosis and 12% had mild hydronephrosis. In the study, 92% of patients had bilateral ureteral obstruction and hence underwent bilateral PCN insertion. Only 8% patients had unilateral PCN insertion. Following PCN insertion there was significant fall in mean pretreatment creatinine level from 10.23 mg/dl to 2.1 mg/dl and BUN level from 79.20 mg/dl to 28 mg/dl (Table 2).

Table 2 : Renal Function Test in Patients of Gynecological Malignancy Presenting with Uremia

Renal Function	Pre PCN (mg/dl)	Post PCN (Day 7) (mg/dl)	Post PCN (Day 14) (mg/dl)
S. Creatinine	10.23	4.93	2.1
Blood Urea Nitrogen	79.20	45.52	28.0

Most common complication of PCN was infection (44%) followed by dislodgment requiring reinsertion in 40% patients, percutaneous leak was in 24% (Figure 2).

Figure 2 : Complications of Percutaneous Nephrostomy



84% patients primarily presented with uremia without previous cancer diagnosis. 4% patients underwent radical surgery followed by adjuvant RT for cervical cancer and 4% patients had taken complete radiotherapy or irregular radiotherapy (Table: 3)

Table 3 : Treatment status of patients of gynecological malignancy presenting with uremia at presentation.

Treatment Status	No. of Patients	Percentage
Primarily present with uremia	21	84%
Radical surgery followed by Adjuvant RT completed	2	8%
Palliative or Curative RT Completed	1	4%
Irregular, Incomplete RT	1	4%

Following PCN insertion after normalization of renal parameters, 15 patients received palliative radiotherapy, 2 patients received palliative chemotherapy and 3 patients received curative radiotherapy as definitive treatment for cancer itself. 5 patients had received only symptomatic treatment due to very advanced malignancy (Table: 4).

Table 4 : Treatment Received after PCN

Type of Treatment	Specific treatment received	No of Patients
Curative	Curative Radiotherapy	3
Palliative	Palliative Radiotherapy Palliative Chemotherapy	15 2
Only Symptomatic	No specific treatment	5

Discussion :

Percutaneous nephrostomy is an interventional procedure to divert urine from an obstructed collecting system.[4,5,6] Though it is an invasive procedure, it is very simple and feasible. In 1955, Goodwin described the technique for temporary drainage of the renal pelvis. [6] 400 BC, Hippocrates said that cervical cancer is incurable. Treatment of cervical cancer began in the sixteenth century. [5] In 1974, the first ultrasound guided percutaneous nephrostomy was reported. The cope loop catheter, which has a distal loop that is reformed in the renal pelvis with a loop shape, was introduced by Cope in 1980. [6]

Obstructive uropathy is a condition in which the flow of the urine is blocked, causing it to go back up and injure one or both kidneys. Common causes of obstructive uropathy in gynecologic malignancy are cervical cancer, uterine cancer, tumors of nearby organs (ovarian malignancy), retroperitoneal fibrosis etc. Lower ureteric obstruction can be due to parametrial involvement, radiation fibrosis and recurrent disease. Upper ureteric obstruction can be due to extrinsic ureteral obstruction by metastatic lymph nodes or peritoneal seedlings. The most important factors determining extent of recovery of renal function are extent and duration of obstruction.

Michael Hopkins reported hydronephrosis to have prognostic value in Stage IIIB cancer cervix patients. [1] In his study, 5 year survival rate in patients with normal IVP with no obstruction was 47%, with ureteric obstruction without renal failure was 29%. Contrary to this, all patients with ureteric obstruction with renal failure died within 16 months. Selective criteria for doing percutaneous nephrostomy were tumor stage, prognosis of primary cancer, further anticancer therapy, quality of life and age of patient (5 year survival is 40-50% in stage 3 cancer & 10% in stage 4 cancer). Its only contraindication is bleeding diathesis. In our study, total of twenty five (25) patients fulfilled the criteria for initial PCN placement for obstructive uropathy in patients with gynecological cancer.

Out of 25, majority of patients (68%) were between the 40 – 59 years of age, which is the common age group for invasive gynecological cancer. Only 12% of patients were above 60 years of age. Mean age was 46.8 years. In study conducted by K. Mishra, the mean age was 44.5 years [1] while in C. Emmert's study mean age was 45.9 years. [7]

Majority of patients with obstructive uropathy were of cervical cancer(80%), ovarian cancer (12%) and vault cancer(8%) (Figure: 1). In Jonathan Carter's study performed on 35 patients, 91% patients were of cervical cancer and 3% patients were of vaginal cancer.[8] In Malik Hussain's study performed on 40 patients, 88% patients were of cervical cancer and 12% patients were of ovarian cancer. [4]

Of the 25 patients, majority of patients (80%) presented with complaints of bleeding P/V. 44% of patients presented with symptoms of uremia (Table 1). Depending on ureteral obstruction either unilateral or bilateral, patient may have symptoms of uremia like flank pain(bilateral/unilateral), anorexia, nausea & vomiting, fever, weight gain or swelling (edema), urinary tract infection, hematuria and if untreated may lead to renal failure.9 patients (36%) had complaints of anuria or oliguria (Table 1). In Malik Hussain's study, 25% patients presented with anuria and 17.2% presented with symptoms of uremia. [4] Out of 25 patients, 80% of patients were multigravida only 1 patient was nulligravida. Multigravida status is one of the risk factors for the cervical cancer.

When cervical cancer extends in to the parametrium, the ureter can be encased by tumor and this leads to the hydroureteronephrosis and eventually renal failure. Such patients can be initially managed with ureteric stenting or PCN, to relieve the obstruction and then can be considered for tumor specific treatment. During systemic examination by per speculum and per vaginal examination, 80% of patients had cervical growth and 2% of patients had vault growth. All of them had parametrial involvement and that lead to lower ureteric obstruction and ultimately hydronephrosis and uremia. Most of the patients in this study had anemia. 44% patients had haemoglobin level of 8 gm%. This was due to bleeding per vaginum which is the most common symptom in the patients with cervical cancer. All those patients presented with anemia. It was corrected by blood transfusion, because best effect of radiotherapy can be achieved if the hemoglobin level is more than 8 gm%.

Out of 25 patients, 52% had gross hydronephrosis on ultrasonography, 36% had moderate hydronephrosis and 12% had mild hydronephrosis. Of them, 92% patients had bilateral ureteral obstruction and so underwent bilateral PCN insertion. Only 8% patients had unilateral PCN insertion. In Kalpesh Prajapati's study, 91.6% patients had bilateral ureteral obstruction and 8.4% had unilateral ureteral obstruction. [9] While in Malik Hussain's study, 50% patients had bilateral and 50% had unilateral ureteral obstruction. [4] Hyppolite Jean-Claude in his study of obstructive uropathy in gynecological malignancies found bilateral nephrostomy to be superior to unilateral nephrostomy and even to intraureteric stenting. [1] They suggested avoidance of intraureteric catheter placement in cervical cancer patients, as it was associated with 86% incidence of urosepsis, leading to death in 43%.

All the patients showed improvement in their symptoms within 2-3 days with a decline in their renal function parameters. Two patients needed hemodialysis due to very high serum creatinine, BUN and serum potassium levels. Following PCN insertion there was significant fall in mean pretreatment creatinine levels from 10.23 mg/dl to 2.1 mg/dl and BUN levels from 79.20 mg/dl to 28 mg/dl (Table: 2). In K. Mishra's study, there was decrease in creatinine from 7.5 mg/dl to 0.9 mg/dl and for BUN 41.2 mg/dl to 14.36 mg/dl. [1] According to Malik Hussain's study, fall in creatinine was from 7.8 gm/dl to 1.4 gm/dl and for BUN from 148.1 mg/dl to 39.2 mg/dl. [4]

84% patients primarily presented with uremia without previous cancer treatment. 4% patients underwent radical surgery followed by adjuvant RT for cervical cancer and 4% patients had taken complete radiotherapy or irregular radiotherapy(Table: 3). In K. Mishra's study, 80% patients primarily presented with uremia and 20% with previous treatment received. [1] In Kalpesh Prajapati's study, 70.9% patients primarily presented with uremia and 29.1% with previous treatment received. [9]

Most common complication following PCN insertion was infection seen in 44%, followed by dislodgment requiring reinsertion in 40% patients and percutaneous leak in 24% (Figure 2) . In Kamlesh Mishra's study, infection (26%), reinsertion for dislodgement (53%), percutaneous leak (20%). [1] In C. Emmeret's study, increasing uremia in 8% and hematuria in 4%. [10] Following PCN insertion after normalization of renal parameters, 15 patients received palliative radiotherapy, 2 patients received palliative chemotherapy and 3 patients received curative radiotherapy as definitive treatment for cancer itself. This is one of the most important advantages of PCN insertion in which we can administer tumor specific treatment. 5 patients had received only symptomatic treatment due to very advanced malignancy (Table: 4). In Kamlesh Mishra's study, out of 15 patients 3 received curative RT, 5 palliative RT, 2 palliative CT and 5 only symptomatic treatment. [1, 11] In Kalpesh Prajapati's study, out of 24 patients 3 received curative RT, 8 palliative RT, 2 palliative CT and 11 only symptomatic treatment. [9]

According to this study, 80% of patients had satisfactory quality of life ≥2 months after PCN insertion in the form of improvement in symptoms of uremia like nausea, vomiting, anorexia and edema (Table: 5).

Table 5. Satisfactory Quality of Life after PCN (improved nausea, vomiting and anorexia)[9,12]

Duration	No of Patients	Percentage
<2 Months	5	20%
≥2 Months	20	80%

In C. Emmert's study, 55% patients had satisfactory quality of life ≥ 2 months after PCN insertion. [9, 12] Out 25 patients, 44% patients had required more than 20 days hospitalization. This was due to the period required for normalization of uremia after PCN insertion and to monitor complications of PCN after which patients got definitive treatment.

Conclusion :

Percutaneous nephrostomy is an excellent initial procedure for relieving the malignant urinary obstruction with minimal complications. In treated and cured patients with long life expectancy percutaneous nephrostomy was effective to save renal functions. In treating naive patients percutaneous nephrostomy was effective to improve renal function and allowed definitive treatment in many cases. Patients treated for primary neoplasia that can still be treated with other therapeutic modalities especially radiotherapy, chemotherapy and hormone therapy can also be benefitted from PCN. However, it is almost impossible to separate the relative benefits of nephrostomy from those achieved by further therapy. After PCN insertion there is definitive improvement in symptoms of uremia like nausea, vomiting, anorexia and edema and ultimately it leads to improvement in quality of the life.

However, majority of patients having advanced neoplasia whose progression is enough to cause ureteral obstruction and refractory to any other therapeutic modality are not good candidates for diversion. In patients who have recurrence after completing definitive treatment and who presented with uremia the only benefit of PCN is to prolong life. As no other definitive treatment could be offered even

after PCN, the role of PCN in such cases is controversial. Malignant ureteric obstruction with hydronephrosis and uremia is a severe complication of advanced cervical cancer. Percutaneous nephrostomy can improve uremia, but prognosis and outcome of the primary disease are not influenced and patients are forced to go through all the complications of terminal cancer.

Hence PCN is safe and feasible and should be done in carefully selected cases. It should be avoided in cases where it only serves to prolong suffering. Ultimately the wish of patient's need is to be respected.

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