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RESEARCH ARTICLE

RADIATION INDUCED SUBACUTE SPONTANEOUS BLADDER RUPTURE IN CERVICAL CANCER PATIENT: A CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Cervical cancer is the fourth most common cancer among women worldwide, with locally advanced cases often necessitating multimodal treatment, in which radiation therapy remains the mainstay. Although effective, radiation therapy can lead to severe, albeit rare, complications such as spontaneous bladder rupture (SBR). This report presents a case of a 47-year-old woman with FIGO Stage IVa cervical adenocarcinoma who developed SBR following external beam radiation therapy (EBRT) without the inclusion of brachytherapy due to the tumor's size. Initially managed with conservative treatment, her condition progressed to septic shock, necessitating urgent surgical intervention. Histopathological analysis of the partial resection of the bladder revealed radiation-induced bladder wall inflammation and necrosis without tumor infiltration. The patient ultimately succumbed to septic complications, underscoring the high morbidity associated with radiation-induced SBR. A literature review was conducted to contextualize this case, identifying 14 other reported cases of SBR in cervical cancer patients. This report aims to raise awareness of SBR as a rare but life-threatening complication, stressing the need for early detection, intervention, and optimized treatment strategies.

Introduction:-

Cervical cancer is the fourth most common cancer in women worldwide (1). Treatment options include surgery, chemotherapy,and radiation therapy. Locally advanced cervical cancer, classified as FIGO Stage IB3 to IVA, is predominantly treated with a combination of pelvic radiotherapy, with concomitant cisplatin-based chemotherapy, and intracavitary brachytherapy (2,3). The incorporation of cisplatin with radiation therapy, along with advancements in modern radiation techniques, has led to significant improvements in survival rates and pelvic disease control (2,4). While radiation therapy is effective, it can cause complications such as bladder damage due to its proximity to the cervix. Radiation-induced bladder rupture, though rare, poses a significant risk due to potential for severe morbidity and mortality. This case report aims to highlight the clinical presentation, radiological

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diagnosis, and management of this rare complication, emphasizing the need for vigilance in patients undergoing radiation therapy.

Case Report

We present the case of a 47-year-old woman, with 3 pregnancies and 3 births, admitted for the management of cervical adenocarcinoma Stage IVa according to the FIGO 2018 classification, with bladder involvement. She had no prior medical or surgical history. She was diagnosed in September 2023 following an admission for acute urinary retention that was managed promptly with bladder drainage to relieve the obstruction and prevent complications. A Foley catheter was inserted via urethral catheterization to effectively drain the bladder and restore normal urinary flow.

On initial clinical examination, the vaginal examination revealed a 7 cm ulcerative and exophytic cervical tumor that invades the anterior vaginal wall up to the lower third, with involvement of the parametria; no inguinal lymphadenopathy was detected.

An abdomino-pelvic CT scan revealed left ureterohydronephrosis caused by a tumoral obstruction of the anterior cervical wall measuring 48x37 mm, invading the left posterolateral bladder wall and the left ureteral meatus. left uretero-hydronephrosis. A cervical biopsy revealed a moderately differentiated infiltrating adenocarcinoma. Pelvic MRI was performed showing a cervico-isthmic tumor measuring 34x32 mm invading the bladder, vaginal wall and parameters, sparing the anterior rectal wall and posterior vaginal wall, causing left ureterohydronephrosis and bilateral external iliac lymph nodes. In October 2023, she underwent bilateral nephrostomy.

The decision of the multidisciplinary team meeting was to proceed with concurrent chemoradiotherapy with curative intent, followed by brachytherapy.

Initial radiation plan

The initial irradiation plan included whole pelvic irradiation using intensity-modulated external beam radiation therapy at a dose of 46 Gy in 23 fractions.

The clinical target volumes (CTV) were delineated following the guidelines of the Radiation Therapy Oncology Group (RTOG) and the Gyn IMRT consortium:

- **CTV-T**: Encompasses the gross tumor volume (GTV), cervix, entire uterus, and extends 2 cm beyond the most inferior extent of vaginal involvement.
- **CTV-N**: Includes the common, external, and internal iliac lymph nodes with a 7 mm margin around the vessels, the presacral lymph nodes (extending up to the superior border of the S3 vertebral body) with a 10 mm margin, and the obturator lymph nodes with an 18 mm margin.

PTV-T and PTV-N were generated by expanding CTV-T and CTV-N with margins of 10 mm and 7 mm, respectively.

The two planning target volumes (PTVs) were combined to create a unified **PTV-Sum** which received 46 Gy in 23 fractions.

Any lymphadenopathy was contoured separately with a 7 mm margin to receive a boost dose of 20 Gy, completing a total of 66 Gy following the pelvic irradiation.

The irradiation was delivered concurrently to weekly Cisplatin at a dose of 40mg/m².

The patient completed her initial plan with good tolerance of radiation therapy and she received 2 cycles of weekly Cisplatin complicated by hypokaliemia and anemia.

High-dose brachytherapy was not feasible for this patient because of the significant size of the residual tumor; so a complementary 4-field treatment of 10 Gy for the parameters (56 Gy) in 5 fractions and 20 Gy over 10 fractions for the residual tumor and lymph nodes (66 Gy) was initiated using intensity-modulated external beam radiation therapy (Figure 2).

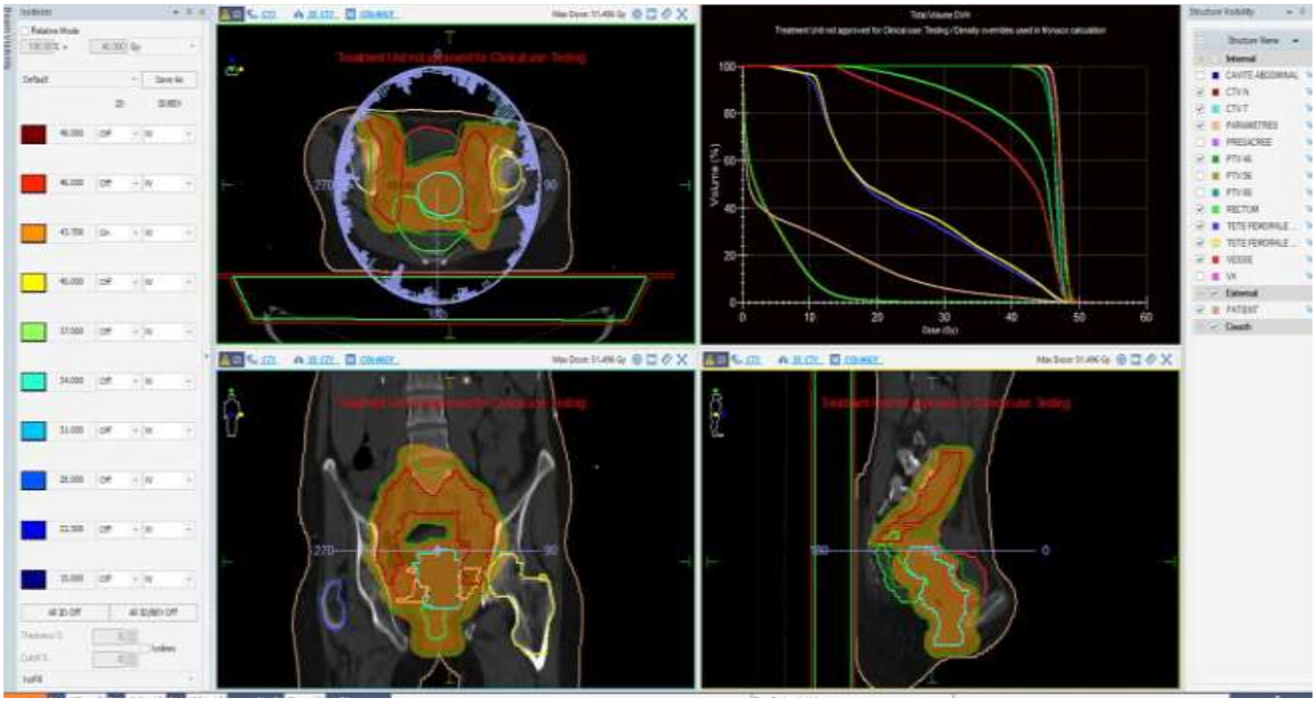

Figure 1:- Initial radiation Plan of the pelvis (46 Gy).

Figure 2:- Radiation plan of the complementary 4 field treatment showing the isodose of 66 Gy (in yellow); bladder on red and the residual tumor on blue.

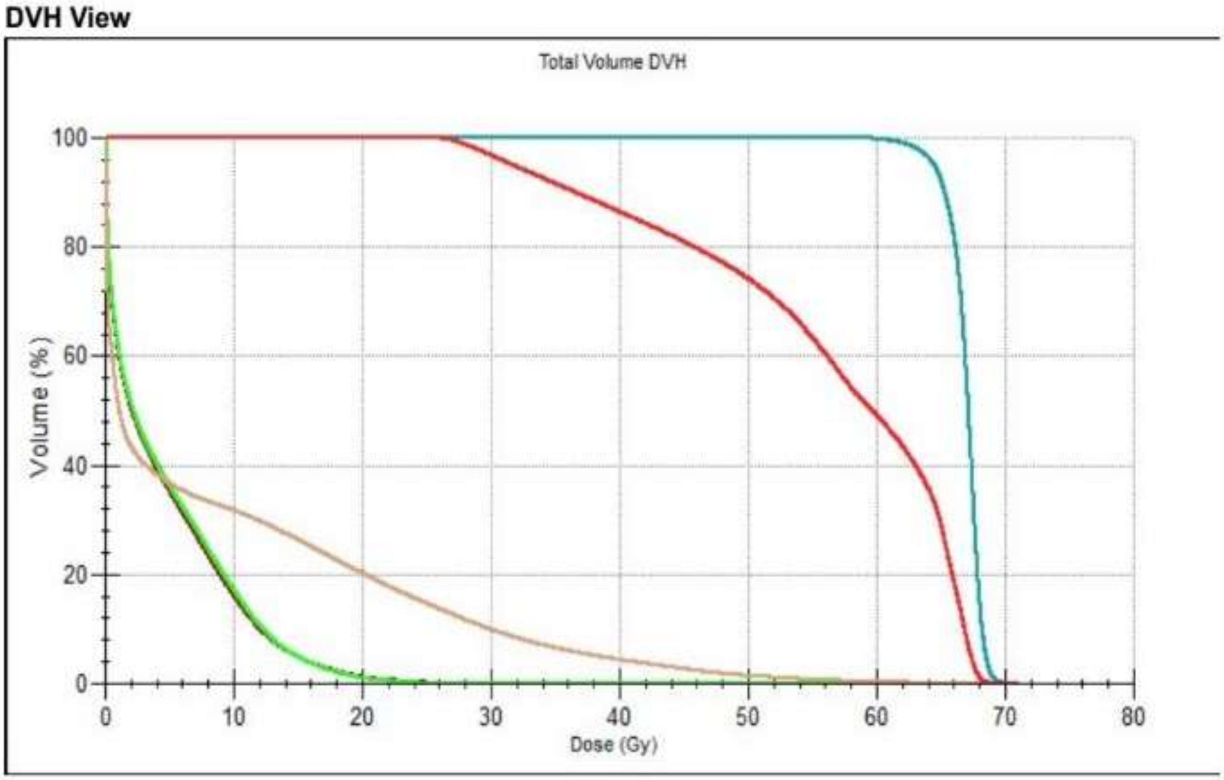

Figure 3:- DVH of the bladder in red in 66 Gy.

At the third session of the second planner complementary 4-field treatment, she reported abdominal pain, fever, nausea and vomiting. She exhibited tachycardia but was otherwise hemodynamically stable, with widespread abdominal tenderness. Laboratory results (Table 1) showed hyperkalemia with a potassium level of 7 mmol/L, a C-reactive protein level at 151.30 mg/L, and no evidence of kidney injury, as indicated by a creatinine level of 8.2 mg/L. Radiation therapy was suspended and she was admitted.

Table 1:- Laboratory Findings on Admission.

Peripheral Blood	Blood Chemistry
Red Blood cells 3.1 x 10^{6}/µl	**Na** 135 mEq/L
Hemoglobin 9.3 g/dL	**K** >7 mEq/L
Hematocrit 26.3%	**Cl** 114 mEq/L
White Blood Cells 4.9x10^{3}/µl	**Urea** 0.20 g/l
Neutrophils 4.4x10^{3}/µl	**Creatinine** 8.2 mg/L
Lymphocytes 0.3x10^{3}/µl	**Ca** 58 mg/L
Monocytes 0.2x10^{3}/µl	**C-reactive protein** 151.30 mg/L
Platelets 132x10^{3}/µl	**Total protein** 53.00 g/L
	Albumin 17.36 g/L

A CT abdominal Scan (Figure 4) identify a breach in the anterior wall of the bladder communicating with a supravesical formation containing both liquid and air, measuring 35x82x61mm with a late extravasation of contrast medium into the peritoneal cavity suggesting an infected supravesical urinoma causing a reflex ileus and resulting in peritonitis.

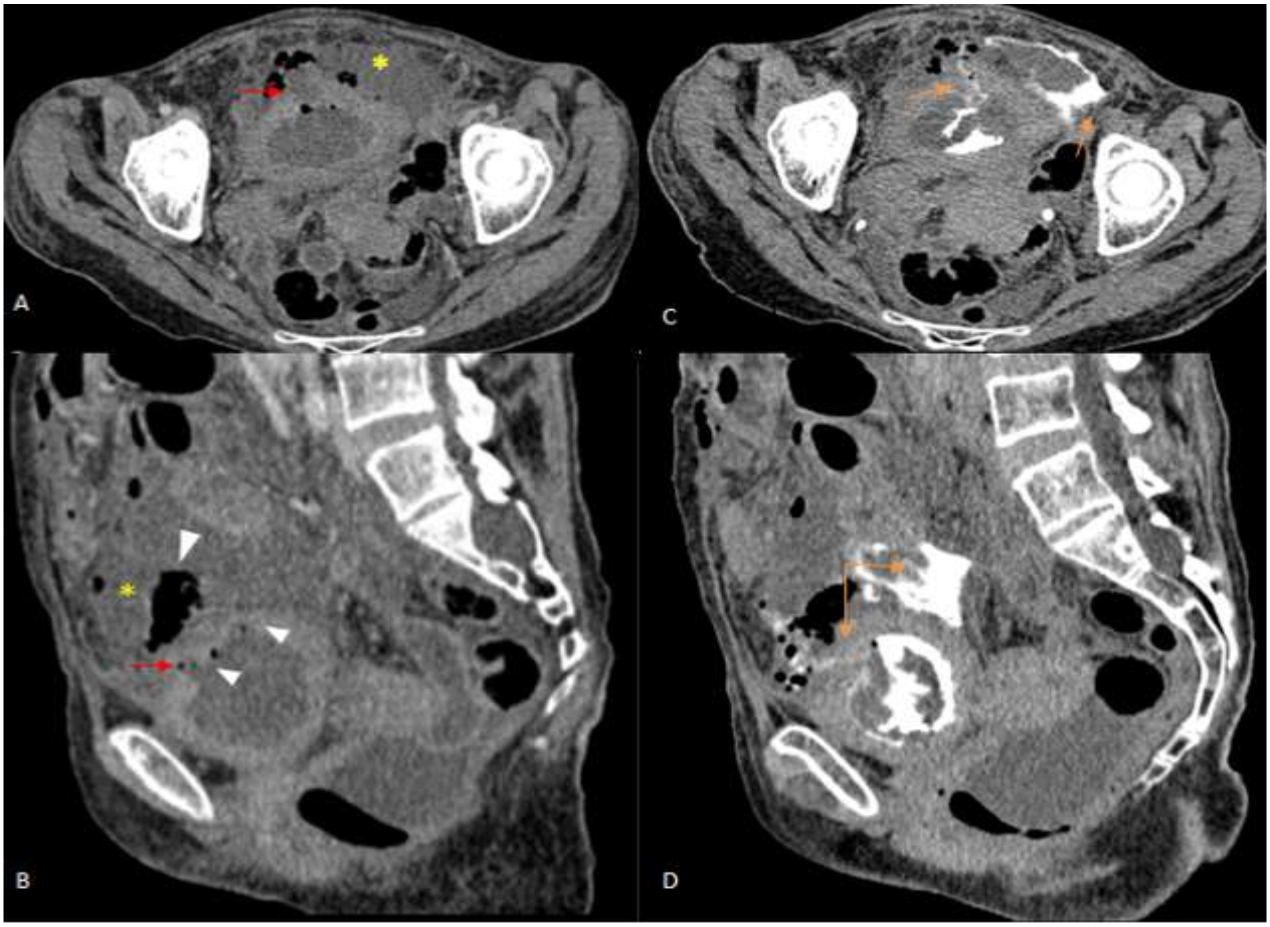

Figure 4:- Abdominal Ct Scan.
A-B : Abdominal CT in axial (A) and sagittal (B) reconstruction , prior to contrastinjection demonstrates a complete rupture of the bladder wall (red arrow) in addition to airbubbles within the inner side of the walls as well as air inside the peritoneum cavity (whitearrow heads) delineating a diffuse liquid masse forming anteriorly to the bladder(yellowasterisks). **C- D:** CT urogram with contrast demonstrating extra-peritoneal leak (orange arrow). White arrows shows contrast extravasation into extra peritoneal space.

The patient was admitted to the ICU with urinary peritonitis complicated by septic shock caused by a bladder breach. She underwent peritoneal lavage and drainage. During the laparotomy, two large bladder breaches, approximately 3 cm each and communicating with each other, were identified, with aspiration of 3 liters of peritoneal pus. Bladder drainage was performed using a Foley catheter. She was administered broad-spectrum antibiotics and started on norepinephrine. Seven days later, she underwent a second surgery for a supratrigonal cystectomy with bilateral ureterostomy due to a necrotic and severely infected bladder. The histopathological examination revealed that the bladder wall had acute suppurative inflammatory changes with no evidence of tumor infiltration.

The course in the ICU was characterized by persistent septic shock with increasing norepinephrine requirements and failed extubation, leading to a tracheostomy. The patient died on day 47 of admission to the ICU from cardiac arrest due to septic shock secondary to the urinary peritonitis.

Discussion:-

The occurrence of spontaneous bladder perforation following radiotherapy is an exceptionally rare complication, and to our knowledge, its incidence has not been specifically studied (5). Spontaneous bladder rupture was first documented by Altman and Horsburgh in 1966 as a case report(6). Since then, such occurrences have been extremely rare, and cases caused by radiotherapy are even more infrequent. Several factors have been identified as potential causes of spontaneous bladder perforation, including tuberculosis, schistosomiasis, bladder diverticulum, intravesical obstruction, and bladder carcinoma (5). .

Urological complications are more likely to occur decades after pelvic radiotherapy, including radiation cystitis, a defunctionalized bladder due to scarring, hemorrhagic cystitis, ureteral stricture, urethral stricture, and fistulas (7–9). Estimates suggest that high-grade adverse effects range from 5% to 13% in the long term(10). According to a report by Fujikawa et al., in a follow-up study of patients after radiotherapy for gynecological diseases, bladder rupture was observed in 2.1% of patients, indicating that it is not a rare occurrence (7). Additionally, Murata et al. investigated cases of bladder rupture due to radiation cystitis reported in Japan and found that the period from radiotherapy to the onset of symptoms ranged from 3 to 40 years, with an average of 14 years.

Regarding histological changes in the bladder wall caused by radiation, pathological findings have been reported, including abnormal dilation and obstructive changes in capillaries, scarring and fibrosis of the interstitial and muscular layers, and degeneration and detachment of the mucosal epithelium. These findings indicate that in the early stages of radiation exposure, congestion and dilation of submucosal capillaries occur with edema of the bladder mucosa. As the condition progresses, epithelial atrophy secondary to fibrosis of submucosal and intramuscular tissues and vascular occlusion occurs, leading to degenerative necrosis and sloughing (11).

In our case the histopathological examination showed that the surface lining of the bladder wall is completely ulcerated and replaced by a fibrinous and leukocytic coating. The remainder of the wall was extensively altered by a dense polymorphous inflammatory infiltrate rich in neutrophils, with large areas of necrosis suggesting a radiation induced lesion.

Historically, 2-dimensional (2-D) treatment planning using plain film X-rays was utilized in both postoperative and definitive treatment of cervical cancer, employing anteroposterior/ posteroanterior or 4-field techniques. With the advent of CT treatment planning, 3-dimensional (3-D) conformal radiation therapy has allowed for precise delineation of target volumes and organs at risk (OARs), enabling better protection of normal tissues through more accurate blocking while using standard beam configurations. Intensity-Modulated Radiation Therapy (IMRT) enhances this by using inverse planning, which modulates multiple treatment fields or arcs to achieve optimal target coverage while sparing OARs (14). IMRT has become widely adopted for many malignancies due to its ability to spare OARs, improve dose conformity, and deliver higher doses (14).

Technological advancements in radiotherapy, such as intensity-modulated radiotherapy (IMRT) and volumetric arc therapy (VMAT) have improved dose shaping and conformality, minimizing the exposure of surrounding organs at risk (OARs) to the prescribed radiation dose. In gynecologic cases, the RTOG 1203 trial demonstrated that IMRT reduces toxicities like diarrhea and has a less harmful effect on genitourinary and gastrointestinal outcomes in the postoperative setting compared to conformal radiotherapy (CRT) techniques (1)

The currently recommended parameters for bladder dose reporting in EMBRACE II Protocol for locally advanced cervical cancer are reported in Table 2 (15).

Table 3:- Bladder dose in our case.

Bladder dose	Unit	Current case
V40	%	61.35
V30	%	80.6
Dmax	Gy	49.85
Dmean	Gy	38.732

Table 2:- Planning aims for OAR in cervix cancer EMBRACE II.

OARs	Bowel	Dmax < 105% (47.3Gy)*	When no lymph node boost: • V40Gy < 100cm3** • V30Gy < 350cm3** When lymph node boost or para-aortic irradiation: • V40Gy < 250cm3** • V30Gy < 500cm3** Dmax < 57.5Gy
	Sigmoid	Dmax < 105% (47.3Gy)*	Dmax < 57.5Gy
	Bladder	Dmax < 105% (47.3Gy)*	V40Gy < 75%** V30Gy < 85%** Dmax < 57.5Gy
	Rectum	Dmax < 105% (47.3Gy)*	V40Gy < 85%** V30Gy < 95%** Dmax < 57.5Gy
	Spinal cord	Dmax < 48Gy	
	Femoral heads	Dmax < 50Gy	
	Kidney	Dmean < 15Gy	Dmean < 10Gy
	Body	Dmax < 107%*	
	Vagina PIBS-2cm		When vagina not involved: $D_{PIBS-2cm}$<5Gy

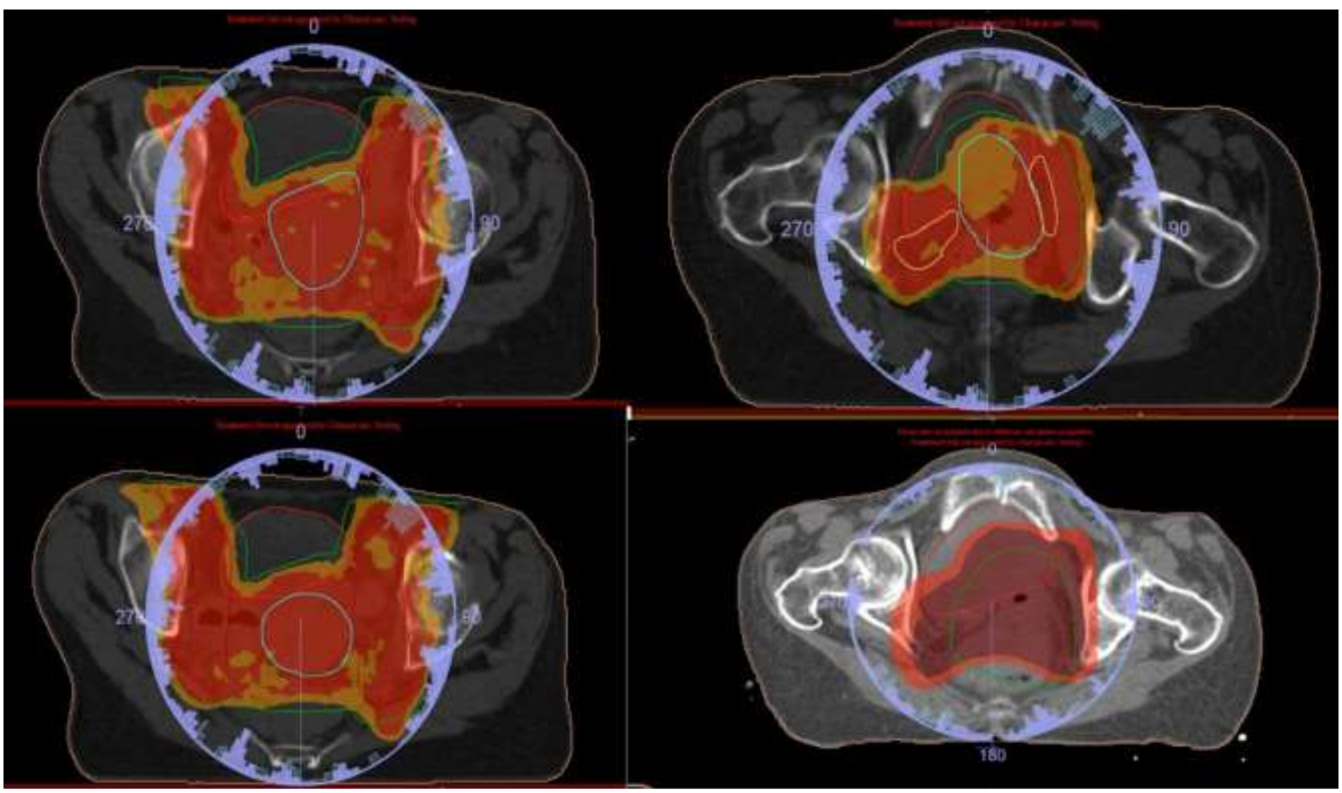

Figure 5:- Isodose plots of the 66 Gy dose distribution (in red) of the current case

Brachytherapy is a cornerstone in the management of locally advanced cervical cancer, particularly when combined with external beam radiotherapy (EBRT). Its primary advantage lies in the precise delivery of high-dose radiation directly to the tumor, limiting radiation exposure to nearby organs such as the bladder, rectum, and intestines. Brachytherapy allows for a rapid dose fall-off, meaning that the radiation dose is concentrated in the tumor with minimal spread to surrounding tissues, thus significantly reducing the risk of long-term complications. This precision is crucial in the pelvic region, where organs at risk are located in close proximity to the cervix. Studies by the **American Brachytherapy Society (ABS)** and others [30–32] have consistently shown that brachytherapy is integral to curative intent in cervical cancer, with its omission leading to poorer outcomes.In the absence of brachytherapy, achieving local tumor control with EBRT alone requires a higher radiation dose, leading to increased exposure of surrounding healthy tissues. This leads to a higher incidence of late toxicities such as radiation cystitis, fibrosis, and perforation of nearby organs like the bladder and rectum.

In our case, brachytherapy was not feasible due to the significant size of the residual tumor, and this limitation necessitated dose escalation using EBRT. As a result, the patient experienced severe bladder damage, ultimately leading to bladder perforation and urinary peritonitis—a rare but serious complication. This underscores a major risk associated with relying solely on EBRT when brachytherapy is not an option. The dose escalation required in EBRT to achieve tumor control often exceeds the tolerances of normal tissues, leading to adverse outcomes such as radiation cystitis and necrosis, which were observed in our patient. Conversely, brachytherapy provides the ability to deliver a much higher, tumor-specific radiation dose without such widespread exposure, significantly reducing the likelihood of complications.

Symptoms of spontaneous bladder rupture include sudden abdominal pain, hematuria, and urinary difficulty. However, if inflammation is localized due to adhesions or the omentum covering the perforation site, the symptoms may be milder.

Diagnosis is relatively difficult, with a low accuracy rate of 43.2%, and treatment is often initiated for peritonitis or ileus due to suspected gastrointestinal perforation(16). Diagnosis is usually made by cystography and cystoscopy, but in some cases, it remains elusive. Peters recommends that a cystogram of 250 ml or more be used, as the contrast injection amount of 100 ml in this case likely resulted in the failure to detect leakage (17). Other important diagnostic findings of intra-abdominal rupture include increases in blood urea nitrogen (BUN) and creatinine levels, thought to be due to transperitoneal reabsorption of urine (18).

Although CT diagnosis can be challenging, in this case, imaging shows a complete rupture of the bladder wall before contrast injection, with air bubbles present inside the bladder wall and air in the peritoneal cavity. This delineates a diffuse liquid mass forming anterior to the bladder. CT urogram with contrast reveals an extraperitoneal leak, with contrast extravasation into the extraperitoneal space.

Currently, no clinically validated guidelines exist for the treatment of spontaneous bladder rupture (SBR). Extraperitoneal ruptures are typically managed conservatively with antibiotics and prolonged catheterization, while intraperitoneal injuries generally require surgical repair due to the high risk of abdominal sepsis and peritonitis. However, in cases of small perforations or in patients with significant comorbidities unfit for general anesthesia, a conservative approach involving antibiotics, abdominal drainage, and catheterization may be a viable alternative.

Spontaneous bladder rupture can sometimes be managed by simply placing a bladder catheter in cases without severe peritonitis or bleeding, but recurrence is common. In cases of repeated recurrence, surgical repair of the ruptured area or urinary diversion surgery may be required. It is crucial to consider this condition when treating patients after radiotherapy (18).

Literature Review:-

A literature search on PubMed using the terms "spontaneous urinary bladder rupture," "radiotherapy," and "cervical cancer" revealed only 13 reported cases of SBR after radiotherapy, along with one case of SBR after hysterectomy. The information is summarized in Table 4. Previously reported cases involved 20 women aged 27 to 78 years (median: 59 years). The time between radiotherapy and SBR onset ranged from 0 days (SBR occurring during radiotherapy) to 31 years (median: 10 years), indicating that SBR often occurs long after radiotherapy. The diagnosis of SBR was initially confirmed in 7 cases and not confirmed in 13 cases, suggesting that SBR can be challenging to diagnose. SBR should be comprehensively diagnosed based on clinical symptoms and a history of pelvic radiation therapy. Each study provided insights into potential risk factors, delayed onset, and therapeutic approaches, emphasizing the critical need for vigilant monitoring in patients undergoing radiation therapy without brachytherapy.

This combined case study and literature review aims to enhance the understanding of SBR risks, diagnostic challenges, and management approaches in cervical cancer treatment.

Table 4:- Summary of reports of SBR developed in women with a history of cervical cancer.

Author (Year)	Age Clinical Stage	Cervical Cancer Treatment	Delay RT - SBR	Symptoms	Initial diagnosis	Treatment	Type SBR	Evolution
Addar MH, et al.(19) **1996**	40 IIB	Definitive RT	15 years	Abdominal pain Nausea/ Vomiting Hematuria	SBR	Laparotomy Bladder repair	Intraperitoneal	No recurence
Tabaru A, et al.(20) **(1996)**	74 IIIB	Definitive RT	10 years	Abdominal pain Nausea/ Vomiting Hematuria	SBR	Laparotomy Bladder repair	Intraperitoneal	No recurrence
Fujikawa K, et al.(7) **(1998)**	57 IIIB	Definitive RT	15 years	Abdominal pain	SBR	Laparotomy Bladder repair	Intraperitoneal	No recurrence
	67 IB	Definitive RT	12 years	Abdominal pain	Intestinal perforation	Laparotomy Bladder repair	Intraperitoneal	No recurrence
	60 IIB	Definitive RT	10 years	Abdominal pain	Intestinal perforation	Laparotomy Bladder repair	Intraperitoneal	1 year later (Bladder repair)
	48 NA	Definitive RT	10 years	Abdominal pain Oliguria	Peritonitis	Percutaneous drainage/Bladder repair	Intraperitoneal	1 week later (Bladder repair)
	68 NA	Definitive RT	13 years	Abdominal pain	Acute abdomen	NA	Intraperitoneal	5 month later(Ureterostomy)
	78 NA	Definitive RT	30 years	Abdominal pain	SBR	Indwelling catheter	Intraperitoneal	4 month later (Bladder repair)
Nishimura T, et al. (21) **2000[**	66 IIA	Hysterectomy + adjuvant RT	3 years	Abdominal pain	Acute abdomen	NA		1 year later (Bladder repair)
Kim MK, et al.(22) **(2009)**	70 NA	Hysterectomy + adjuvant RT	3 weeks	Abdominal pain Dysuria	SBR	Total cystectomy Ureterostomy	Intraperitoneal	No recurrence

T. Suzuki et al 2011	62 NA	Hysterectomy + adjuvant RT	17 years	Abdominal pain Fever	SBR	Conservative treatment/Bladder catheter	Intraperitoneal	No recurrence
Snauwaert C, et al.(23) **(2012)**	44 IB	RT followed by Hysterectomy	5 years	Abdominal pain	Ascite	Bladder repair+Antibiotics	Intraeritoneal	No recurrence
Shin JY, et al.(24) **(2014)**	55 NA	Hysterectomy + adjuvant RT	13 years	Abdominal pain Distension Oliguria	Acute abdomen	Hemodialysis Nephrostomy Bladder repair	Intraperitoneal	No recurrence
T.Wakamiya et al.(25) **2016**	45 NA 71 NA	Hysterectomy + adjuvant RT Hysterectomy + adjuvant RT	9 years 31 years	Abdominal pain and distension Fever Abdominal pain and fever	Peritonitis Peritonitis	Laparotomy/Bladder repair Laparotomy/ Bladder repair	Intraperitoneal Intraperitoneal	Death after 65 days postoperative No recurrence
Mizuhu Nagatal et al.(11) **2018**	49 IIA	Hysterectomy + adjuvant RT	10 years	Abdominal pain	Ascite	Conservative treatment/ Bladder catheter	Intraperitoneal	No recurrence
Welp A, e al.(26) **(2020)**	27 IIIC1	Definitive RT	0 days (last day of RT)	Abdominal pain Nausea/ Vomiting	SBR	Indwelling catheter	Extraperitoneal	No recurrence
Iwasaki H, et al.(27) **(2021)**	52 NA	Hysterectomy + adjuvant RT	7 years	Abdominal pain	Peritonitis	Antibiotics Indwelling catheter	Intraperitoneal	No recurrence
Salleh, et al.(28) **(2022)**	71 NA	Definitive RT	30 years	Abdominal pain Nausea	Peritonitis	Laparotomy Bladder reapair	Intraperitoneal	No recurrence
Hayashida et al (29) **2023**	74 IB3	Hysterectomy	-	Abdominal pain Fever	Peritonitis	Antibiotics Indwelling catheter followed by Ureterostomy	Intraperitoneal	No recurrence
Current case	47 IVa	Definitive RT	0 day (2nd session of 4 fields complement RT)	Abdominal pain Fever	Peritonitis SBR	Laparotomy Antibiotics Supra trigonal cystectomy with bilateral ureterostomy	Intraperitoneal	Death at 47 days postoperative

Conclusion:-

Spontaneous bladder rupture following radiotherapy is a rare but serious complication that requires heightened clinical awareness, especially in cervical cancer patients. This case underscores the importance of close monitoring and prompt intervention, as demonstrated by the patient's progression from acute urinary retention to bladder perforation. Radiation-induced histological changes, such as fibrosis and necrosis, considerably elevate the risk of bladder rupture, making early detection crucial. However, diagnosing SBR remains challenging due to its nonspecific symptoms and low diagnostic sensitivity, often requiring advanced imaging for confirmation.

Brachytherapy helps optimize radiation delivery by focusing high doses on the tumor while minimizing exposure to surrounding organs, reducing the risk of severe complications. Its absence necessitates higher EBRT doses, increasing bladder toxicity and rupture risk.

This case highlights the complexities of SBR management, showing that while conservative treatment may be feasible in select cases, surgical intervention is often necessary for severe ruptures. Given the high morbidity and recurrence risk, vigilant follow-up and optimized radiation techniques are essential to reduce this rare but potentially life-threatening complication.

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