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CASE REPORTS

Primary squamous cell carcinoma of the rectum: an atypical histology

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ABSTRACT

Squamous cell carcinoma of the rectum is one of the differential diagnoses of rectal tumors. It represents a low incidence in the population. The etiopathogenesis and the biology of these tumors are unclear, for this reason the gold standard treatment is difficult to establish. We present a 47-years-old woman who had a squamous cell carcinoma in medium rectum. She was treated with radiation therapy and chemotherapy and the treatment was followed by surgical excision.

Key words: Rectal cancer. Rectum. Squamous cell carcinoma. Surgery. Radiotherapy. Radiochemotheraphy.

INTRODUCTION

Squamous cell carcinoma of the rectum is a rarity within colorectal tumors entity. The incidence of this kind of tumors is estimated at 0.1-0.25 per 1,000 tumors (1). Due to the small number of cases of this disease, the pathogenesis is unclear and it is attributed to different assumptions about the available literature. Although surgery has been considered as the main route of approach, treatment is currently under discussion.

CASE REPORT

A 47-year-old woman presented with a history of uterine myoma of 10 years evolution and bilateral salpingectomy due to endometriosis. She was studied because of abdominal pain located in lower hemiabdomen, as well as hematochezia and diarrhea, these symptoms accompanied by weight loss during the last month. Physical examination showed a good overall appearance, although a rectal examination revealed a friable mass bleeding to the fingertip friction. The blood test showed hemoglobin levels at the lower limit of normal blood. A colonoscopy showed that the lesion was at 8 cm of the anal verge. It was an exophytic and stenotic tumor with malignant appearance. Biopsies revealed that the rectal mucosa was infiltrated by a squamous cell carcinoma. Immunohistochemistry samples showed CK7 positivity and CK20 negativity with overexpression of p16. HPV 16 was detected by PCR technique. At the cervical cytology and the biopsy by uterine curettage no pathological findings were identified. The computed tomography (CT) showed an irregular mass in the middle rectum as well as lymph nodes in the mesorectal fat with pathological appearance and other smaller unspecified periaortic nodes (Fig. 1). The magnetic resonance imaging revealed a bulky mass of 8 cm in length in the middle rectum with infiltrative appearance which invaded the mesorectal fat and fornix vaginal without cleavage plane (T4CRM+N+) (Fig. 2). The case was discussed by a multidisciplinary committee in our center that decided to perform neoadjuvant chemotherapy with cisplatin and neoadjuvant radiotherapy. After 4 months of treatment, the revaluation clinical tests showed a poor response and surgery was planned. The patient underwent a posterior pelvic exenteration with pelvic peritonectomy and intraoperative radiotherapy. The postoperative histopathological findings were a squamous cell carcinoma of rectum moderately differentiated infiltrating the radial margin pT3N1. Immunohistochemistry tests revealed positivity for AE1, AE3, CK7 and overexpression of p16 and p63. The postoperative period was uncomplicated. She was treated with adjuvant cisplatin and fluouracil. Nine months after the treatment the patient showed local relapse in the imaging tests and she has been treated until the present day with chemotherapy with little response. At the time this report was written, the patient had 24 months of follow-up.

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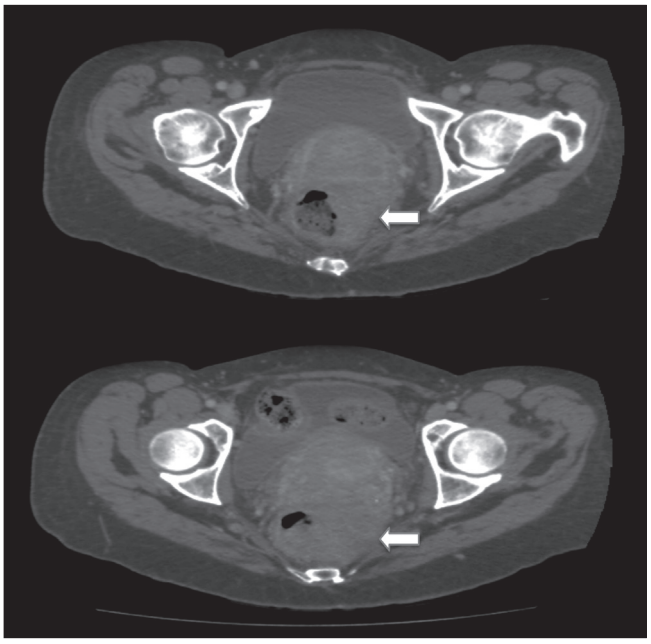

Fig. 1. Pelvic computed tomography.

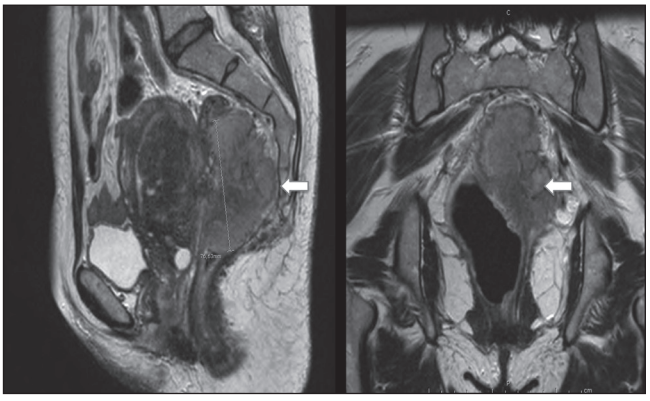

Fig. 2. Pelvic magnetic resonance imaging.

DISCUSSION

Squamous cell carcinoma of the rectum is an extremely rare finding. Its incidence is estimated around 0.1-0.25 per 1,000 colorectal tumors (1). It has been described in the literature in about one hundred cases (case reports and series of cases). The first reported case of this kind of colon neoplasm was made in 1919 (2). Later, in 1933, the first primary squamous cell carcinoma of the rectum was described by Raiford (3).

The pathogenesis is still uncertain. Several hypotheses have been proposed, such as the appearance of a squamous metaplasia due to an inflammation secondary to an infection (4), chronic irritation by radiotherapy exposure (5) or by intestinal inflammatory bowel disease (6). It has also been described the possibility of stem cells being able to differentiate into squamous tissue (7) or the probability of a transformation of adenomas or adenocarcinomas to this type of tumors (8).

In our patient, it was concluded that a persistent inflammation in the pelvis due to endometriosis may have influenced in the pathogenesis. There were no other demonstrated factors or unsafe sex that would affect the tumor progression.

At present the predisposing risk factors cannot be established with certainty. Interrelation with the HPV infection has not been demonstrated (9) although it has been associated with another type of infections as the colitis by *Entamoeba histolytica* or schistosomiasis (4). According to publications and the review of the literature by Kassir et al.**,** it appears more frequently in female form cases (66% women/34% males) and along the 5th-6th decade of life, as in this case (10).

The symptoms of rectal epidermoid are similar to those of an adenocarcinoma: abdominal pain, alteration in bowel habit, tenesmus and rectal bleeding (1).

Diagnosis may be delayed until the symptoms are not evident. In 1979 Williams et al. established the diagnostic criteria for colorectal epidermoid carcinoma (11): absence of extension of the lesion from the anal epithelium, absence of tumor epidermoid in another primary site, absence of squamous fistula tract within inflammatory bowel disease and, finally, histological confirmation.

In our patient, any gynecological involvement or any other cause that could have caused a local infiltration to the rectum was discarded. Histology confirmed it.

Magnetic resonance imaging (MRI) and endo-rectal ultrasound are necessary for any diagnosis of rectal tumors. They provide information about the loco-regional involvement.

Immunohistochemistry differentiates the anal or rectal squamous cell carcinoma origin through cytokeratin analysis, being AE1/AE3, 34bE12 and CK5 the most frequent ones (1).

There is no consensus on the staging of these tumors. Some authors staged TNM classification according to the rectal adenocarcinoma and others prefer TNM classification according to anal squamous cell carcinomas due to their common histology (12).

No treatment guidelines have been described due to the low incidence of these kinds of tumors and poor knowledge of their biology. Treatment is extrapolated from rectal adenocarcinoma and anal squamous cell carcinomas guidelines.

It has long been believed that surgery is the main option based on retrospective series and observational studies. However, it has recently been published that when chemo-radiotherapy is used alone or as a neoadjuvant treatment, complete clinical and pathological response is achieved in many cases.

Surgery resection for T1 tumors (mucosa and submucosa) and T2 tumors (muscularis propria) was the first option

with 20% tumor recurrence (1,13). In advanced local tumors, node-positive or poorly differentiated tumors, neoadjuvant chemo radiotherapy is preferred.

The total dose of radiation is similar to rectal adenocarcinomas chemotherapy treatments and chemotherapy is based on anal squamous cell carcinomas guidelines (fluorouracil and Mitomycin C) (12).

Musio et al. (12) published a small series (8 patients) which were treated with a radiotherapy (total radiation from 45 to 76.5 Gy) and chemotherapy (fluorouracil and Mitomycin C most cases) combination, and they reported only one recurrence that finally needed surgical resection. They concluded that high doses of chemo-radiotherapy could be enough for an adequate tumor control without surgical resection.

Péron et al. (14) treated ten patients with chemo-radiotherapy and only one with radiotherapy. They described a partial response in four of them and a complete response in seven with no tumor evidence. The patients with partial clinical response underwent surgical resection, two of them achieving complete pathological response. Two patients developed tumor recurrence. The median follow-up was 42 months. Thereby these authors suggest that chemo-radiation can be used as a healing technique and only in cases of local recurrence or no response surgery could be the best option.

Nahas et al. (15) presented nine patients treated with chemo-radiotherapy, and only two of them were healed with this treatment. Seven of them underwent surgical resection, six of them presenting a complete pathological response.

Authors, as previously published in the literature, defend the use of high-dose radiotherapy and chemotherapy for squamous cell carcinoma of the rectum. They found complete responses in 60% of cases. Only surgery will perform in recurrence or no clinical response.

Nowadays, there is no evidence or guidelines for this kind of tumors, so that it is necessary to individualize each case and evaluate surgical risk as well as that of chemotherapy or radiation therapy.

A literature review has been performed and 103 cases of rectum squamous cell carcinomas have been found. All of them were published in the Spanish or English language. Fifteen authors have published series of cases (Table I) and nineteen authors have described case reports (Table II). There is a lot of variability regarding surgical treatment, survival and oncological results.

The most important prognostic factor is the TNM classification. It is worse for rectal squamous cell carcinomas than for colon squamous cell carcinoma and rectum adenocarcinoma, with increased mortality (1).

In conclusion, rectal squamous cell carcinoma is a rare neoplasm, with unknown tumor biology and pathogenesis. In fact, it is necessary to individualize the optimal treatment for each tumor and patient.

Table I. Series of cases of squamous cell carcinoma of the rectum

Author	*Date*	*Cases*	*Age*	*Gender*	*Location*	*Clinical stage*	*Treatment*	*Outcome*	*Follow-up (days/ months)*
1. LeBlanc (16)	1950	5	56 (48-71)	2 M, 3 F					
			60	M	Low rectum	Dukes C	Surgery	LR & DOD	72 m
			54	M	Low rectum	Dukes B	Surgery	DOD	24 m
			48	F	Low rectum	Dukes C	RT + surgery	DOD	24 m
			56	F	Low rectum	Dukes C	Surgery	NED	24 m
			71	F	Low rectum	Dukes C	Surgery	NED	3 m
2. Hohm (17)	1964	2		2 F					
			34	F	8 cm	pT4N0M0	Surgery	NED	156 m
			51	F	Low rectum	pT4N0M0	Surgery	NED	252 m
3. Vezeredis (18)	1983	5	61 (44-66)	2 M, 3 F					
			44	M	3-4 cm	pT1N0M0	Surgery	Dead (others$_1$)	9 d
			56	M	7 cm	PT4N1M1(c)	Surgery	Dead (others$_2$)	0 d
			61	F	4 cm	M1(a)	CT	DOD	4 m
			66	F	5 cm	TxNxMx	RTCT	DE & DOD	15 m
			62	F	4-5 cm	pT4N2M0	Surgery + CTADJ	DE & DOD	3 m
4. Gelas (19)	2002	6	55 (43-93)	2 M, 4 F					
			47	F	8 cm	M0	RT + surgery	NED	192 m
			63	M	7 cm	M1(a)	Surgery + RTCTADJ	DOD	14 m
			70	F	9 cm	M0	Surgery + RTADJ	LR & DOD	18 m
			93	M	8 cm	T3N0M0	RT	DE & DOD	4 m
			45	F	12 cm	T3N+M0	RTCT + surgery + CTADJ	NED	6 m
			43	F	7 cm	M0	RTCT + surgery	NED	24 m
5. Nahas (15)	2007	12	58 (40-80)	2 M, 10 F					31 (6-192) m
			-	-	6 cm	I	RTCT	NED	-
			-	-	7 cm	II	RTCT	NED	-
			-	-	5 cm	II	RTCT	ICR→ Surgery: NED	-
			-	-	5 cm	II	RTCT	ICR→ Surgery: NED	-
			-	-	7 cm	IIIA	RTCT	ICR→ Surgery: NED	-
			-	-	8 cm	IIIA	RTCT	ICR→ Surgery: NED	-
			-	-	6 cm	IIIA	RTCT	ICR→ Surgery: NED	-
			-	-	8 cm	IIIA	RTCT	ICR→ Surgery: NED	-
			-	-	6 cm	IIIB	RTCT	ICR→ Surgery: NED	-
			-	-	8 cm	II	Surgery + RTCTADJ	NED	-
			-	-	7 cm	IIIA	Surgery + RTCTADJ	NED	-
			-	-	5 cm	IIIB	CT	NED	-

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Table I (Cont.). Series of cases of squamous cell carcinoma of the rectum

Author	*Date*	*Cases*	*Age*	*Gender*	*Location*	*Clinical stage*	*Treatment*	*Outcome*	*Follow-up (days/ months)*
6. Clark (29)	2008	7	70 (42-75)	2 M, 5 F					
			75	M	4 cm	T3N1M0	RTCT	NED	20 m
			71	F	6 cm	T4N1M0	RTCT	NED	31 m
			42	F	8 cm	T4NIM1(a)	RTCT	Surgery M1: CPR	13 m
			70	M	4 cm	T4N2M1(d)	RTCT	NED	14 m
			55	F	5 cm	T4N2M0	RTCT	ICR→Surgery: CPR	19 m
			45	F	5 cm	T4N1M0	RTCT	NED	23 m
			71	F	5 cm	T3N0M0	RTCT	NED	5 m
7. Rasheed (21)	2009	6	57 (41-69)	3 M, 3 F					
			55	F	2 cm	T2N0M0	RTCT	NED	132 m
			50	M	2 cm	T3N1M1(a)	RTCT	NED	84 m
			69	F	5,5 cm	T2N1M0	RTCT	NED	48 m
			61	M	6 cm	T3N1MO	RTCT	ICR→ Surgery: CPR	48 m
			58	M	4-5 cm	T3N1M0	RTCT	LR→ Surgery: NED	34 m
			41	F	2 cm	T4N1M0	RTCT	NED	24 m
8. Tronconi (22)	2010	6	54 (44-79)	1 M, 5 F					
			50	F	8 cm	T3N0M0	RTCT + surgery	CPR & NED	39 m
			45	F	2 cm	T3N0M0	RTCT	NED	41 m
			44	F	4 cm	T3N0M0	RTCT	NED	40 m
			66	M	1 cm	T4N1M0	RTCT	NED	26 m
			58	F	5 cm	T3N1M0	RTCT	ICR→ Surgery: NED	24 m
			79	F	1 cm	T3N2M1(a+b)	RTCT	ICR→ Paliative surgery & DOD	10 m
9. Yeh (23)	2012	6	59 (55-68)	1 M, 5 F	6 (4-9)				
			-	-	-	T3N1M0	RTCT	NED	24 m
			-	-	-	T3N0M0	RTCT	LR→ Surgery; DE→ DOD	67 m
			-	-	-	T3N0M0	RTCT		54 m
			-	-	-	T3N1M0	RTCT	NED	25 m
			-	-	-	T4N0M0	RTCT	NED	84 m
			-	-	-	T3N2M0	Surgery	ICR→ Surgery: NED DE & DOD	7 m
10. Jeong (24)	2013	4	59 (45-71)	4F					
			66	F	4 cm	T3N2M0	RTCT	NED	99 m
			45	F	5 cm	T3N1MO	RTCT	NED	84 m
			71	F	8 cm	T3N2M0	RTCT	Dead (others 1)	2 m
			52	F	4 cm	T3N0M0	RTCT	NED	53 m

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Table I (Cont.). Series of cases of squamous cell carcinoma of the rectum

Author	*Date*	*Cases*	*Age*	*Gender*	*Location*	*Clinical stage*	*Treatment*	*Outcome*	*Follow-up (days/ months)*
11. Sturgeon (25)	2014	14	66 (44-81)	14F					
			55	F	12 cm	T4N0M0	RTCT	LR→ Surgery: NED	197 m
			47	F	7 cm	T3N0M0	RTCT	NED	158 m
			60	F	13 cm	T3N1M0	RTCT	Dead (others 4)	22 m
			67	F	9 cm	T2N0M0	RTCT	NED	103 m
			61	F	5 cm	T2N0M0	RTCT	DE→ Surgery: NED	67 m
			53	F	4 cm	T4N0M0	RTCT	DE & DOD	52 m
			60	F	5 cm	T2N0M0	RTCT	NED	94 m
			53	F	7 cm	T3N1M0	RTCT	NED	74 m
			48	F	6 cm	T4N0M0	RTCT	NED	58 m
			57	F	7 cm	T4N1M0	RTCT	NED	46 m
			48	F	10 cm	T1N3M0	RTCT	NED	38 m
			54	F	8 cm	T2N1M0	RTCT	NED	34 m
			59	F	4,5 cm	T2N1M0	RTCT	NED	34 m
			61	M	4 cm	T2N0M0	RTCT	NED	25 m
12. Péron (14)	2015	11	67 (59-82)	2 M, 9 F					
			-	-	4 cm	T2N1Mx	RTCT	ICR→ Surgery: NED	133 m
			-	-	5 cm	T3N0Mx	RT	CCR; LR→ Surgery	40 m
			-	-	4 cm	T3N1Mx	RTCT	ICR→ Surgery: NED	127 m
			-	-	4 cm	T3N1Mx	RTCT	ICR→ Surgery:NED	107 m
			-	-	10 cm	T3N1Mx	RTCT	ICR→ Surgery: NED	24 m
			-	-	6 cm	T4N1Mx	RTCT	DE→ CT: NED	28 m
			-	-	4 cm	T3N1Mx	RTCT	NED	51 m
			-	-	5 cm	T3N1Mx	RTCT	NED	41 m
			-	-	6 cm	T4N0Mx	RTCT	NED	17 m
			-	-	4 cm	T4N1Mx	RTCT	NED	16 m
			-	-	7 cm	T3N2Mx	RTCT	NED	6 m
13. Ozuner (26)	2015	8*							
			-	-	Rectum	IA	Surgery	NED	-
			-	-	Rectum	IIA	Surgery + RTCTADJ	DE	-
			-	-	Rectum	IIA	Surgery + RTCTADJ	DE	-
			-	-	Rectum	IIA	Surgery	NED	-
			-	-	Rectum	IIIA	Surgery + CTADJ	DE	-
			-	-	Rectum	IIIA	Surgery + CTADJ	NED	-
			-	-	Rectum	IV	Paliative Surgery + RT	DE	-
			-	-	Rectum	IV	Paliative Surgery + CTADJ	DE	-

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Table I (Cont.). Series of cases of squamous cell carcinoma of the rectum

Author	*Date*	*Cases*	*Age*	*Gender*	*Location*	*Clinical stage*	*Treatment*	*Outcome*	*Follow-up (days/ months)*
14. Funahashi	2015	3	64 (54-84)	3 F					
(27)			54	F	Low rectum	T3N2aM0	RTCT	NED	44 m
			84	F	Low rectum	T3N0M0	RTCT	NED	25 m
			64	F	Low rectum	T4bN2bM0	RTCT	ICR→ Surgery: CPR; DE→ RT & DOD	14 m
15. Musio (12)	2015	8	66 (44-81)	4 M, 4 F					
			78	F	5 cm	T2N1M0	RTCT	NED	48 m
			62	F	6 cm	T3N1M0	RTCT	NR→ Surgery	6 m
			77	F	5 cm	T2N1M0	RTCT	NED	15 m
			52	M	5 cm	T3N0M0	RTCT	NED	8 m
			44	M	8 cm	T3N3M0	RTCT	NED	164 m
			56	M	4 cm	T4N1M0	RTCT	NED	72 m
			69	F	4 cm	T2N0M0	RTCT	NED	20 m
			81	M	4 cm	T4N1M0	RTCT	ICR→ Surgery: NED	1 m

*We exclude the tumors when they were not in the rectum. F: Female; M: Male; d: Days; m: Months; M1(a): Hepatic; M1(b): Lung; M1(c): Malignant pleural effusion; M1(d): Paraaortic nodes; RT: Radiotherapy; CT: Chemotherapy; RTCT: Radiochemotherapy; IORT: Intraoperative radiotherapy; CTADJ: Adyuvant chemotherapy; RTADJ: Adjuvant radiotherapy; Others 1: Sepsis; Others 2: Intraoperative heart failure; Others 3: Pneumonia; Others 4: Other tumor; CCR: Complete clinical response; ICR: Incomplete clinical response; CPR: Complete pathological response; NR: Not response; LR: Local relapse; DE: Disease evolution; NED: No evidence of disease; DOD: Dead of disease.

Table II. Cases of squamous cell carcinoma of the rectum

Author	*Date*	*Age*	*Gender*	*Location*	*Clinical stage*	*Treatment*	*Outcome*	*Follow-up (months)*
1. Dixon (28)	1954	60	F	6 cm	-	Surgery	-	-
2. Wiener (4)	1962	52	F	9 cm	-	Surgery	DOD	10
3. Cabrera (29)	1967	62	F	4 cm	pT2N0M0	Surgery	NED	10
3. Higton (30)	1970	49	M	6-7 cm	pT1NxM0	Surgery	-	-
4. Williams (11)	1979	-	-	Rectum	-	-	-	-
5. Martínez-González (31)	1996	40	F	8 cm	T4N+M0	RTCT	ICR→ Surgery: NED	18
6. Sotlar (32)	2001	87	M	8 cm	pT3N1M0	Surgery	LR→ RTCT & DOD	21
7. Yurdakul (5)	2003	67	M	Rectum	T4N0M0	Surgery	-	-
8. Anagnostopoulos (33)	2005	75	M	9 cm	pT4N1M0	Surgery + CTADJ	NED	14
9. Theodosopoulos (34)	2006	39	F	8 cm	T4N0M0	RTCT + Surgery + CTADJ	DE→ Surgery M1(a) + CT	18
10. Leung (35)	2009	63	F	3 cm	M1(a & e)	Paliative surgery	-	-
11. Sameer (36)	2010	60	M	4 cm	T3N2M0	Surgery + CTADJ	NED	24
12. Iannacone (37)	2010	78	F	5 cm	T2N1M0	RTCT	NED	12
13. Al Hallak (38)	2010	49	M	2 cm	T2N1M0	RTCT	NED	30
14. Custodio (39)	2011	46	F	5 cm	T4N+M0	RTCT + surgery	CPR→ DE: CT & DOD	14
15. Hogan (40)	2013	61	M	6 cm	pT4N2-3M0	RTCT	ICR→ DE: RTCT	6
16. Wang (13)	2014	75	F	3 cm	pT4N0M0	Surgery + RTADJ	NED	43
17. Kassir (10)	2014	62	F	8 cm	T3N+M0	RTCT + surgery	IPR	-
18. Ferreira (41)	2014	52	F	5 cm	T1N1M0	RTCT	NED	40
19. Scaringi (42)	2015	73	M	7 cm	pT3N1M0	Surgery	LR & DE: DOD	4
20. Ballestero	2015	47	F	8 cm	pT3N1M0	RTCT + surgery + IORT+CTADJ	LR→CT	24

F: Female; M: Male; d: Days; m: Months; M1(a): Hepatic; M1(b): Lung; M1(c): Malignant pleural effusion; M1(d): Paraaortic nodes; RT: Radiotherapy; CT: Chemotherapy; RTCT: Radiochemotherapy; IORT: Intraoperative radiotherapy; CTADJ: Adyuvant chemotherapy; RTADJ: Adjuvant radiotherapy; Others 1: Sepsis, Others 2: Intraoperative heart failure; Others 3: Pneumonia; Others 4: Other tumor; CCR: Complete clinical response; ICR: Incomplete clinical response; CPR: Complete pathological response; NR: Not response; LR: Local relapse; DE: Disease evolution; NED: No evidence of disease; DOD: Dead of disease.

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