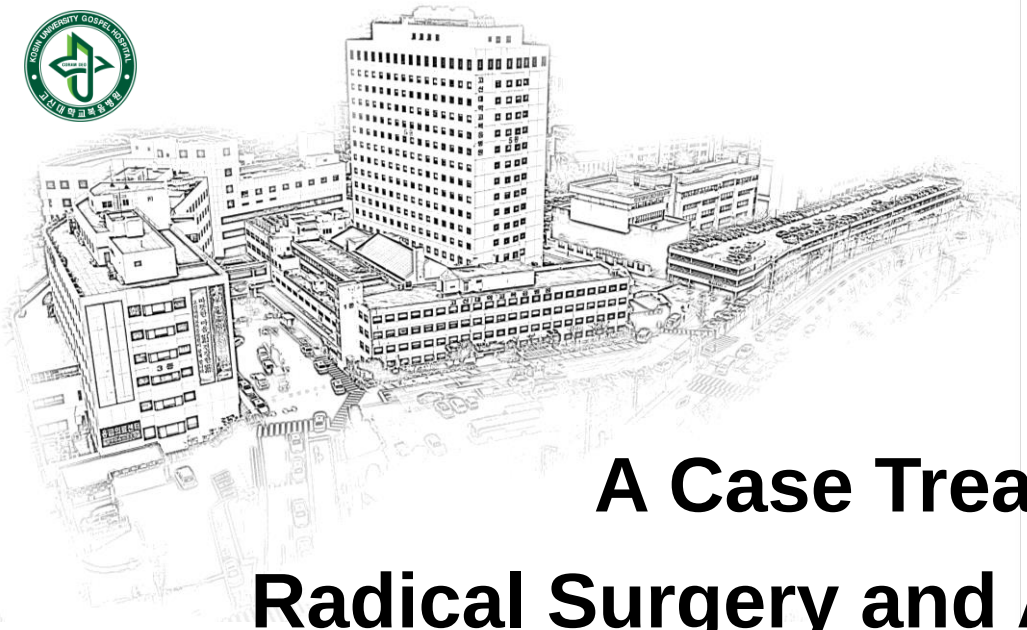


A Case Treated with Radical Surgery and Adjuvant Therapy for Advanced Gastirc Cancer Metastasis to Ovaries and Rectum

고신대학교 복음병원 소화기내과

이명훈, 박선자, 박무인, 문원, 김성은, 김재현, 정경원

Patient Information

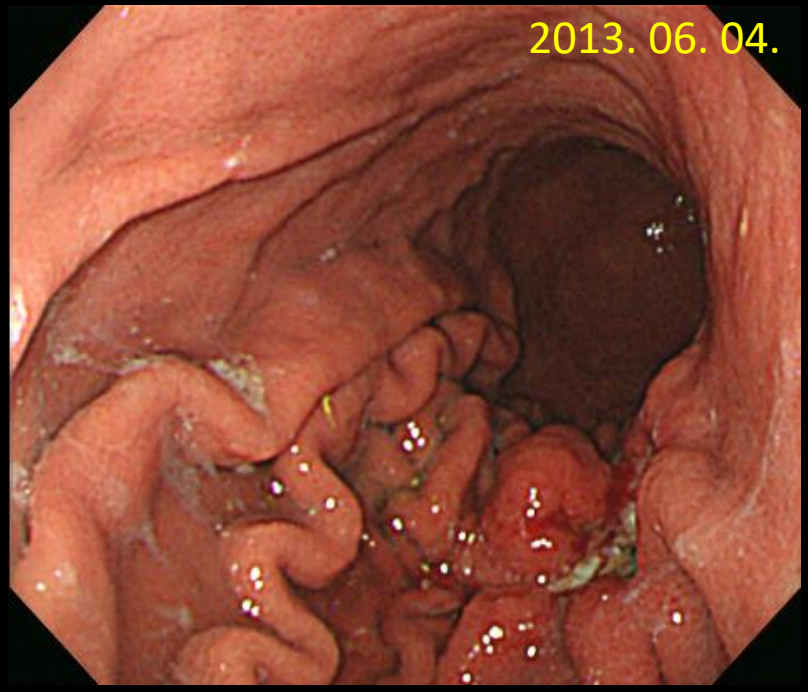
- 44-year-old female

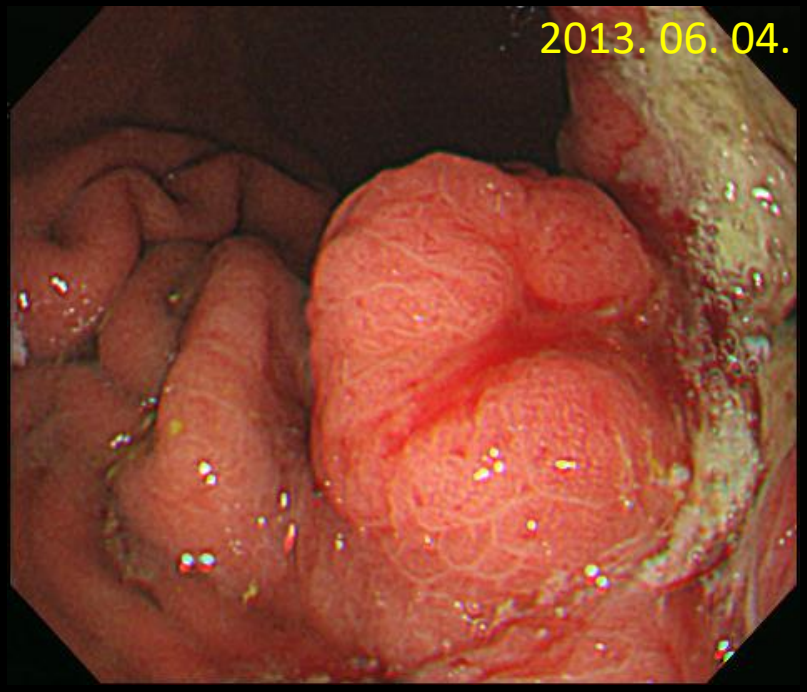
- Chief complain
  - ✓Epigastric discomfort (since 1 month ago)

- Present illness
  - ✓ 특별한 과거력 및 약물 복용력 없던 자로, 내원 1달 전부터 시작된 심와부 불편감을 주소로 시행한 상부위장관내시경 검사에서 관찰된 이상소견에 대하여 추가 검사 위해 내원함.

Patient Information

- **Past History**
  - ✓ DM(-)/HTN(-)
  - ✓ Pul. Tbc(-)/hepatitis(-)/cancer(-)
  - ✓ Hyperlipidemia(-)
- **Family History**
  - ✓ 모 – lung cancer
- **Review of System**
  - ✓ Nausea (-) Vomiting (-)
  - ✓ Diarrhea (-) Constipation (-)
  - ✓ Abdominal pain (-)
  - ✓ Melena (-) Hematochezia (-)
- **Physical examination**
  - ✓ V/S 110/80-65-18-36.5
  - ✓ Abdomen
    - ✓ Soft and mild distension
    - ✓ No rebound
- **Lab**
  - ✓ **Hb**/WBC/PLT **12.5**/7080/182k
  - ✓ BUN/Cr/Na/K 10/0.7/138/4.3
  - ✓ AST/ALT/CRP 10/10/0.06
  - ✓ **Tumor markers**
    - ✓ CEA : 2.95 ng/mL
    - ✓ CA : 19-9 26.4 U/mL
    - ✓ CA-125 : 17.18 U/mL


2013. 06. 04.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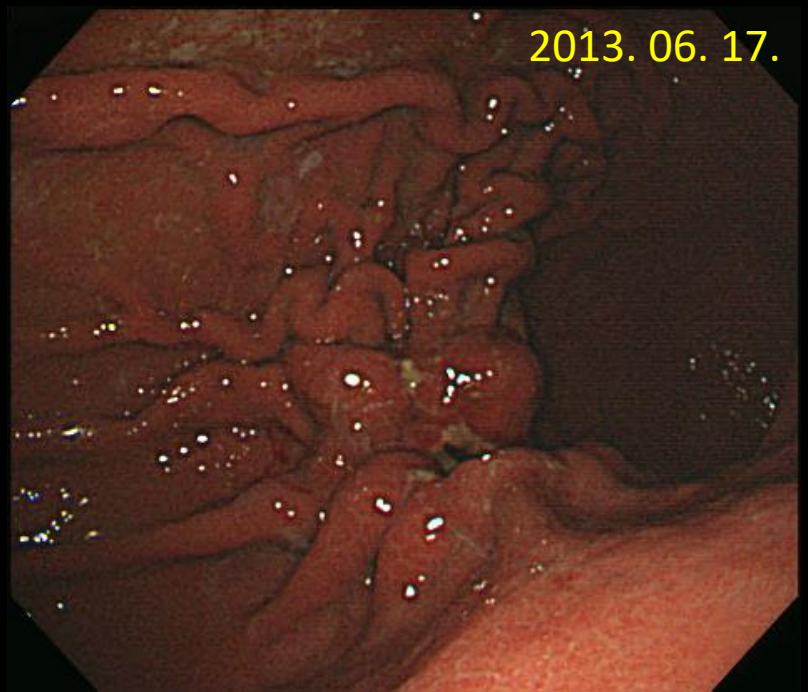
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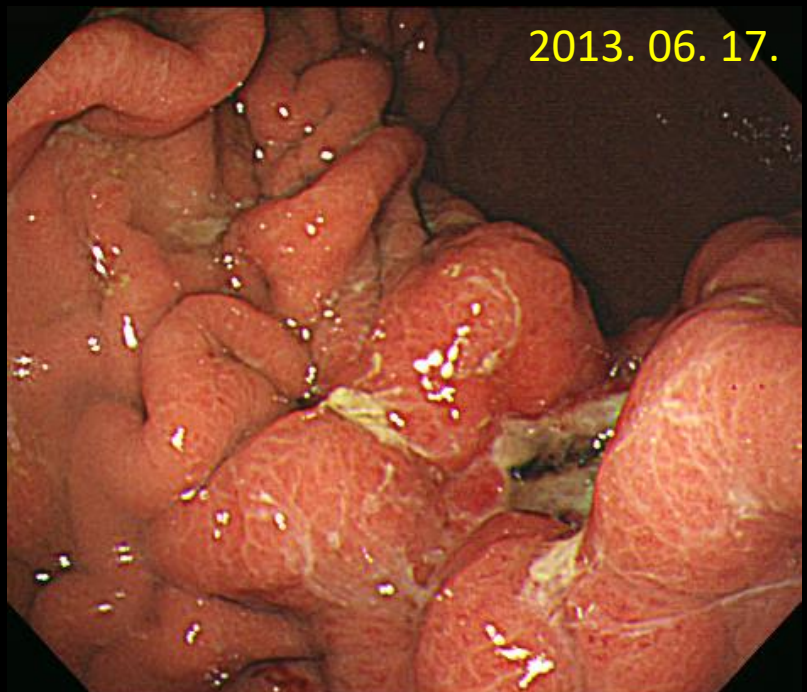
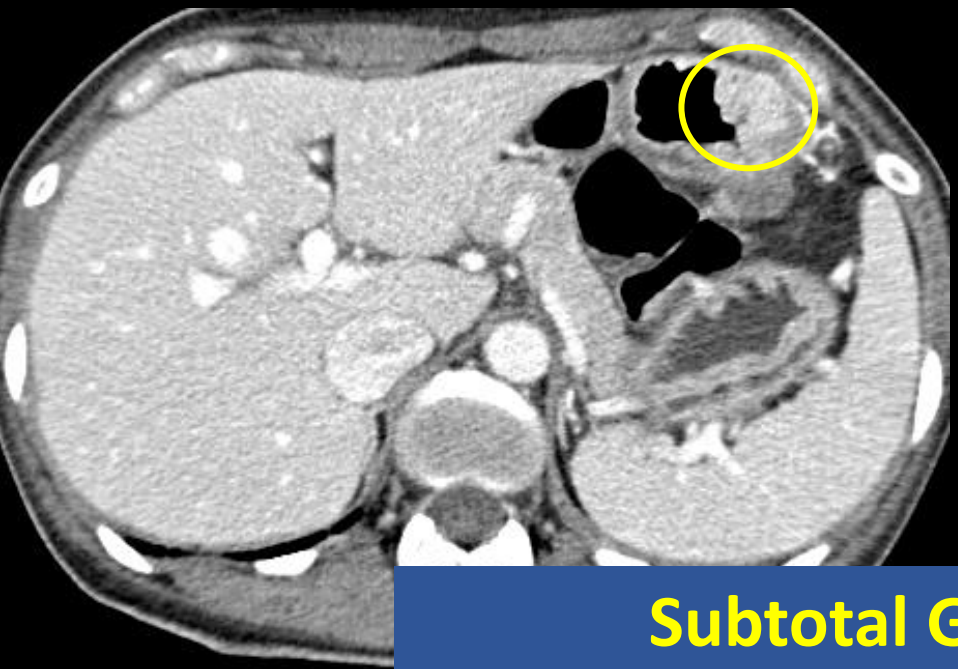
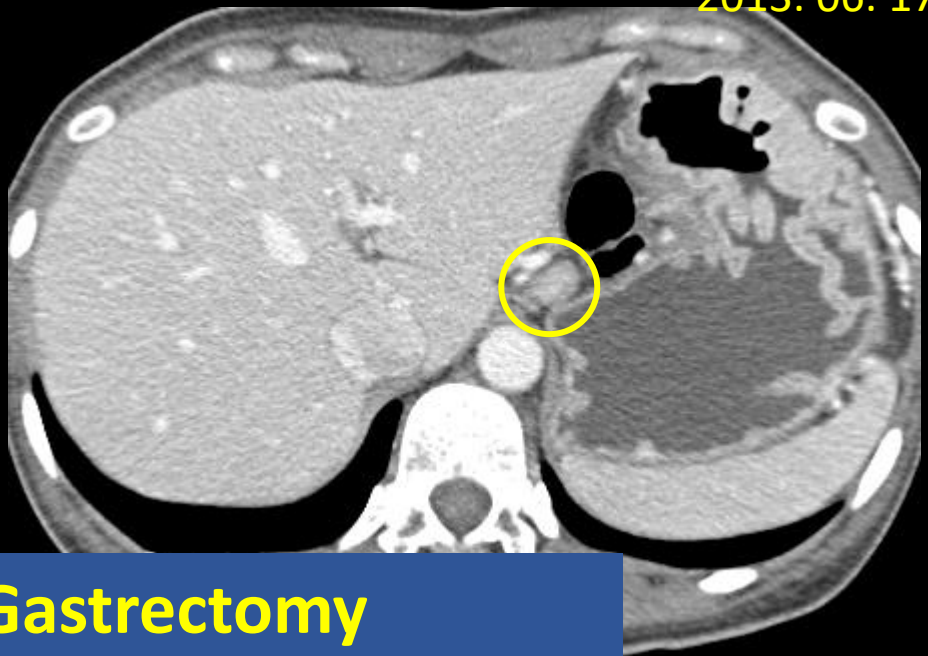
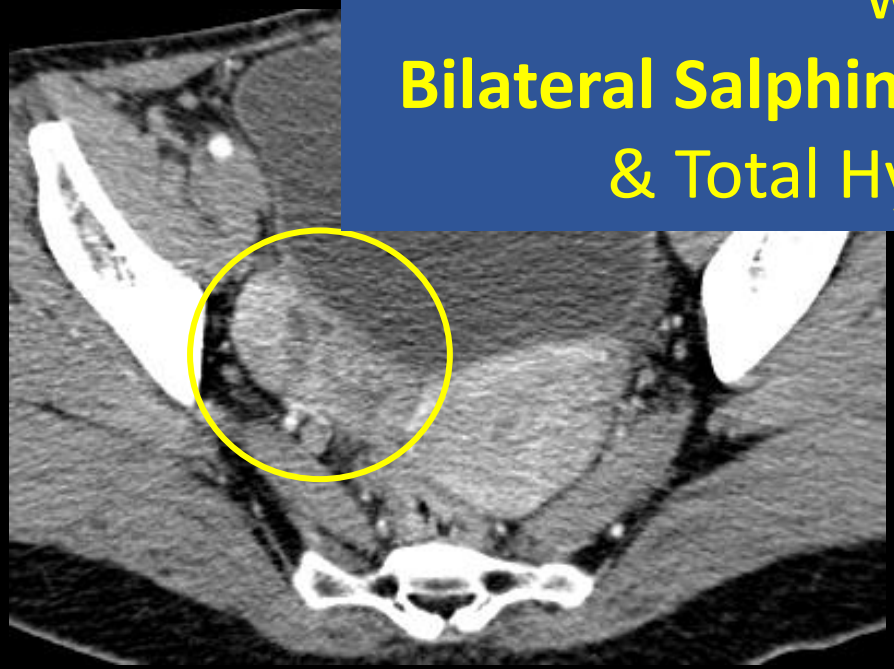

2013. 06. 17.

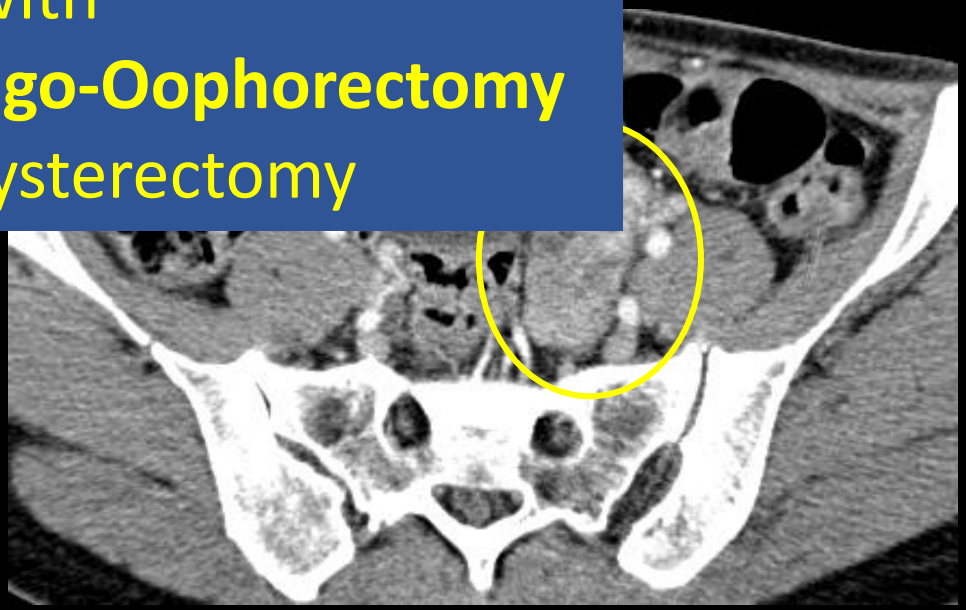
2013. 06. 17.



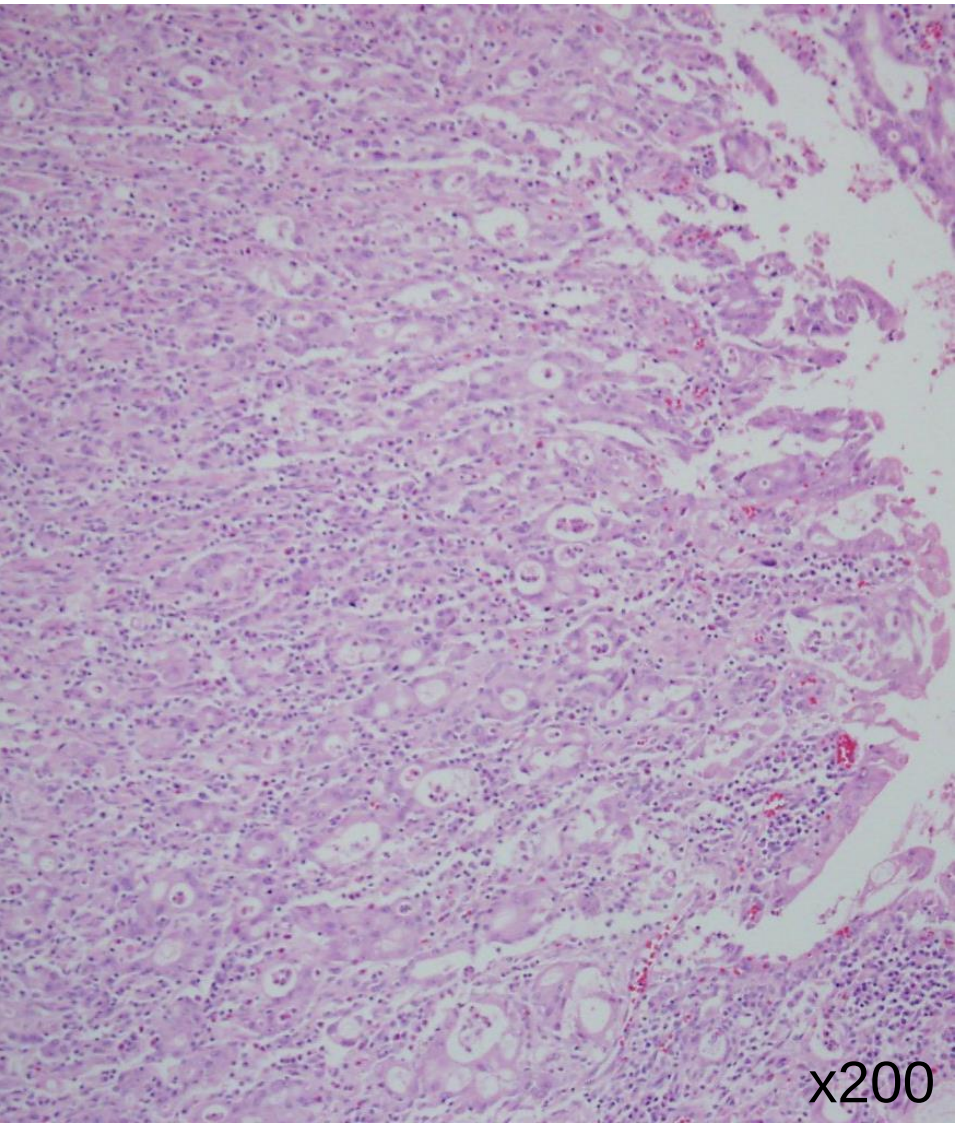


Subtotal Gastrectomy
with
Bilateral Salphingo-Oophorectomy
& Total Hysterectomy

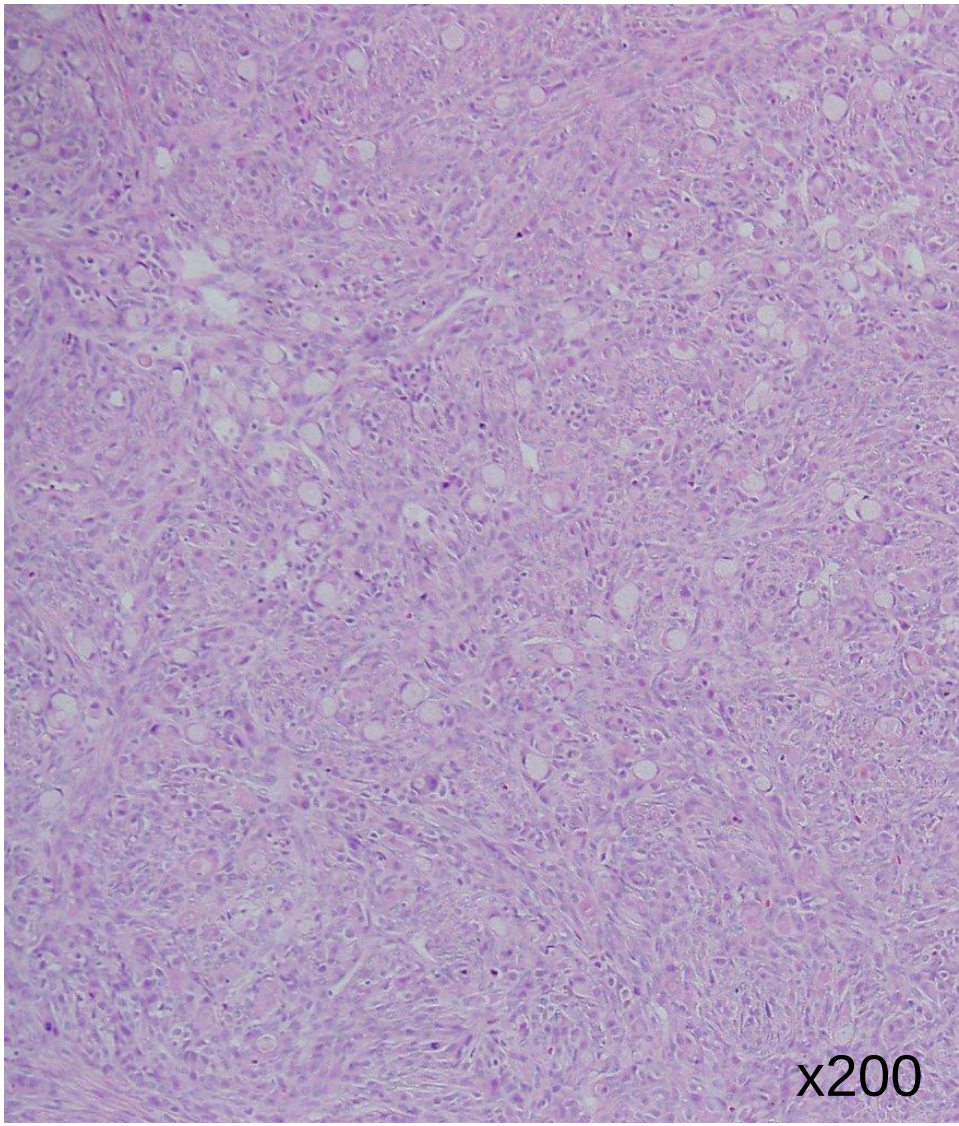




Pathologic Findings



- Stomach



- Ovary

Pathologic Findings

- **Stomach :**

  1) Location : middle third, center at body, posterior wall

  2) Gross type : Borrmann type II

  3) Histologic type : tubular adenocarcinoma, moderate differentiated (type by Lauren : **intestinal**)

  4) Size : 3.0 x 3.0 x 1.0 cm

  5) Depth of invasion : penetrate to subserosa w/o invasion of visceral peritoneum or adjacent structure (**pT3**)

  6) Resection margin : **free** (distal 11.5cm, proximal 3.9cm)

  7) LN meta : **4**/46 (3, 4d, 4s, mesentery)

  8) lymphatic invasion -/venous /perineural invasion +

  IHC :
  p53 +(51%), **C-erb-B2** 3+, Muc2 -, Muc 5Ac and 6 +

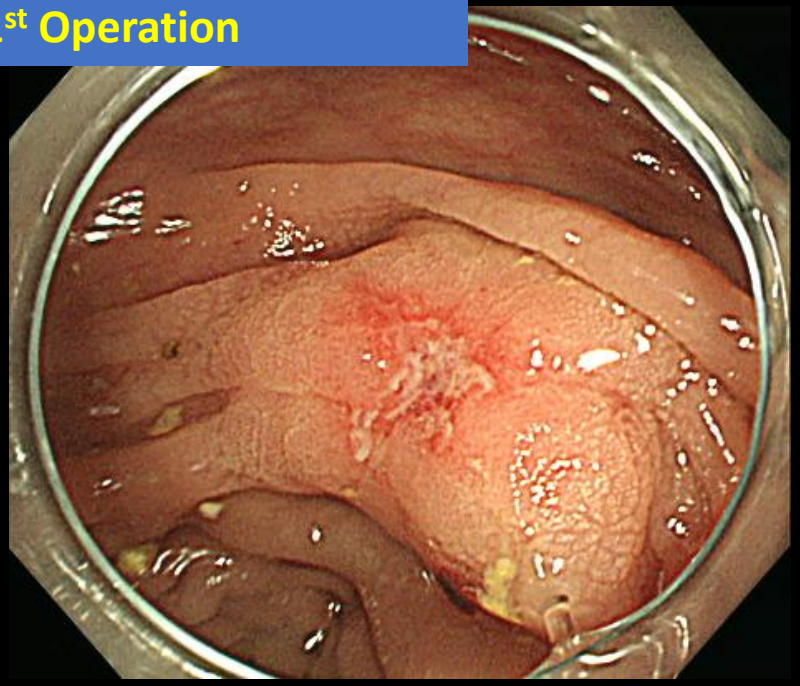
- **Ovary :**
  - Rt 6.5cm, Lt 3.3cm,
  - **Adenoca. m/d**. and **signet ring cell**
  - **CK 7 diffuse, CK 20 focal** Ki67 50% p53 1-2%
  - Stomach origin is favored

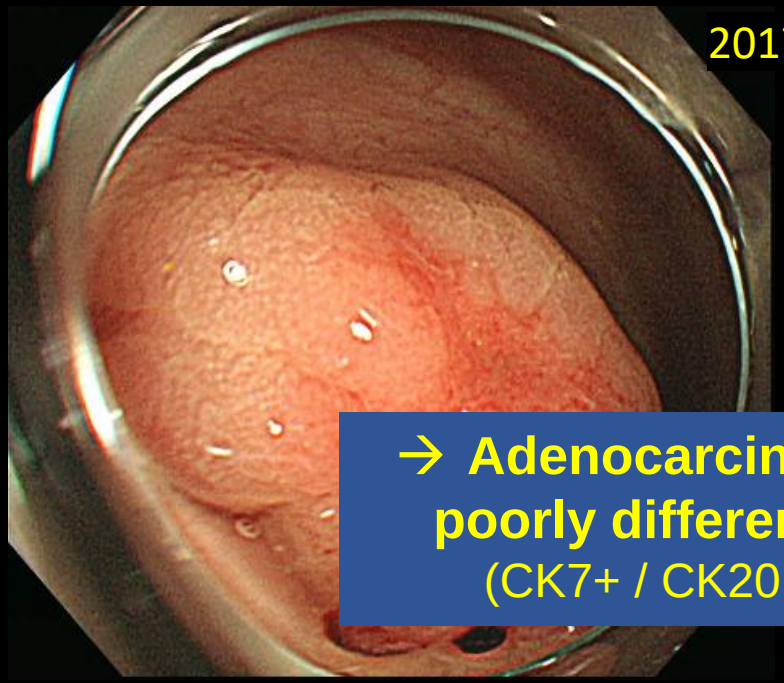
- **Salphyx, Uterus :**

  negative for malignancy

Adjuvant Chemotherapy :
Capecitabine plus Oxaliplatin #1~13('13.8.~'14.4.)

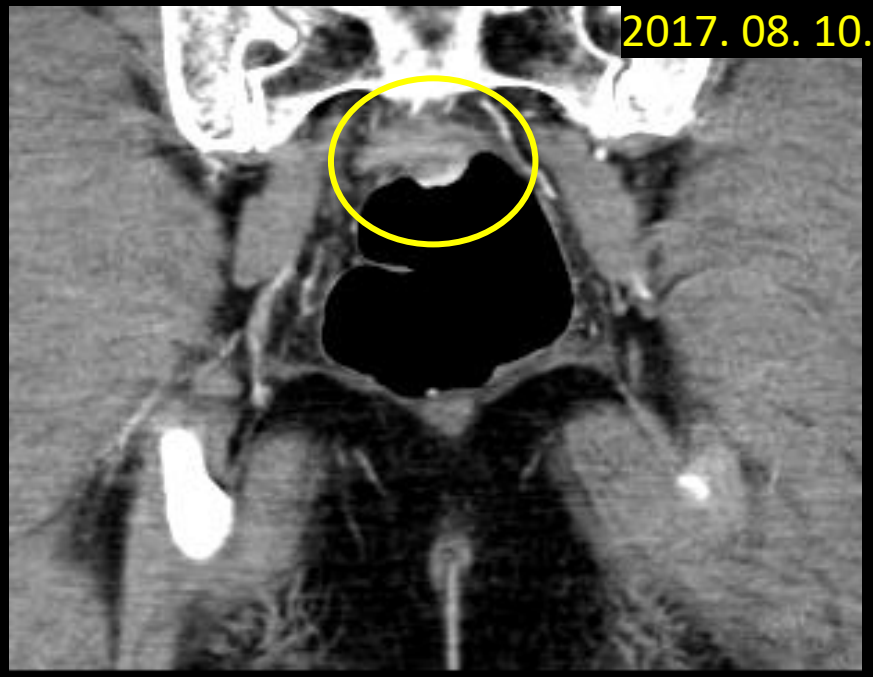
Clinical Course : 4 years later after 1st Operation



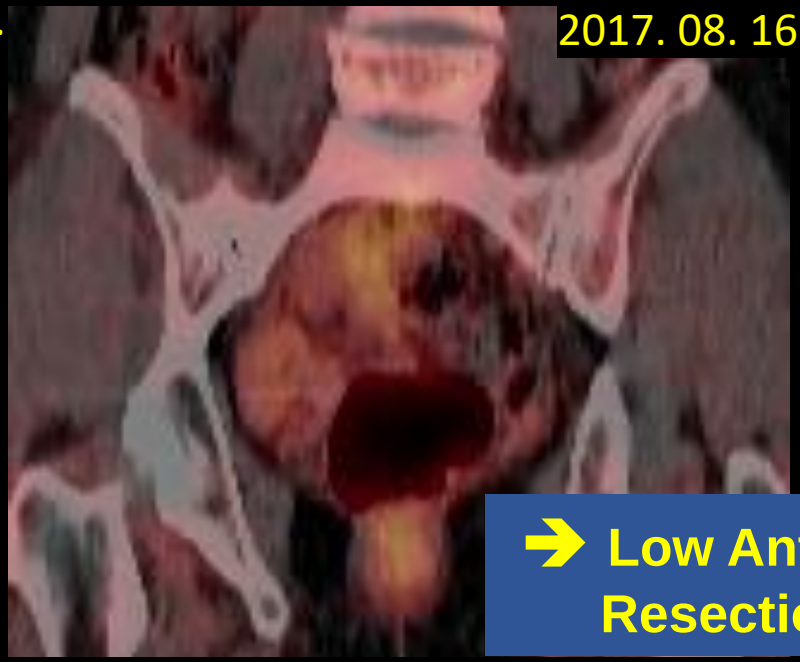


2017. 08. 10.

→ **Adenocarcinoma, poorly differentiated**
(CK7+ / CK20 -)



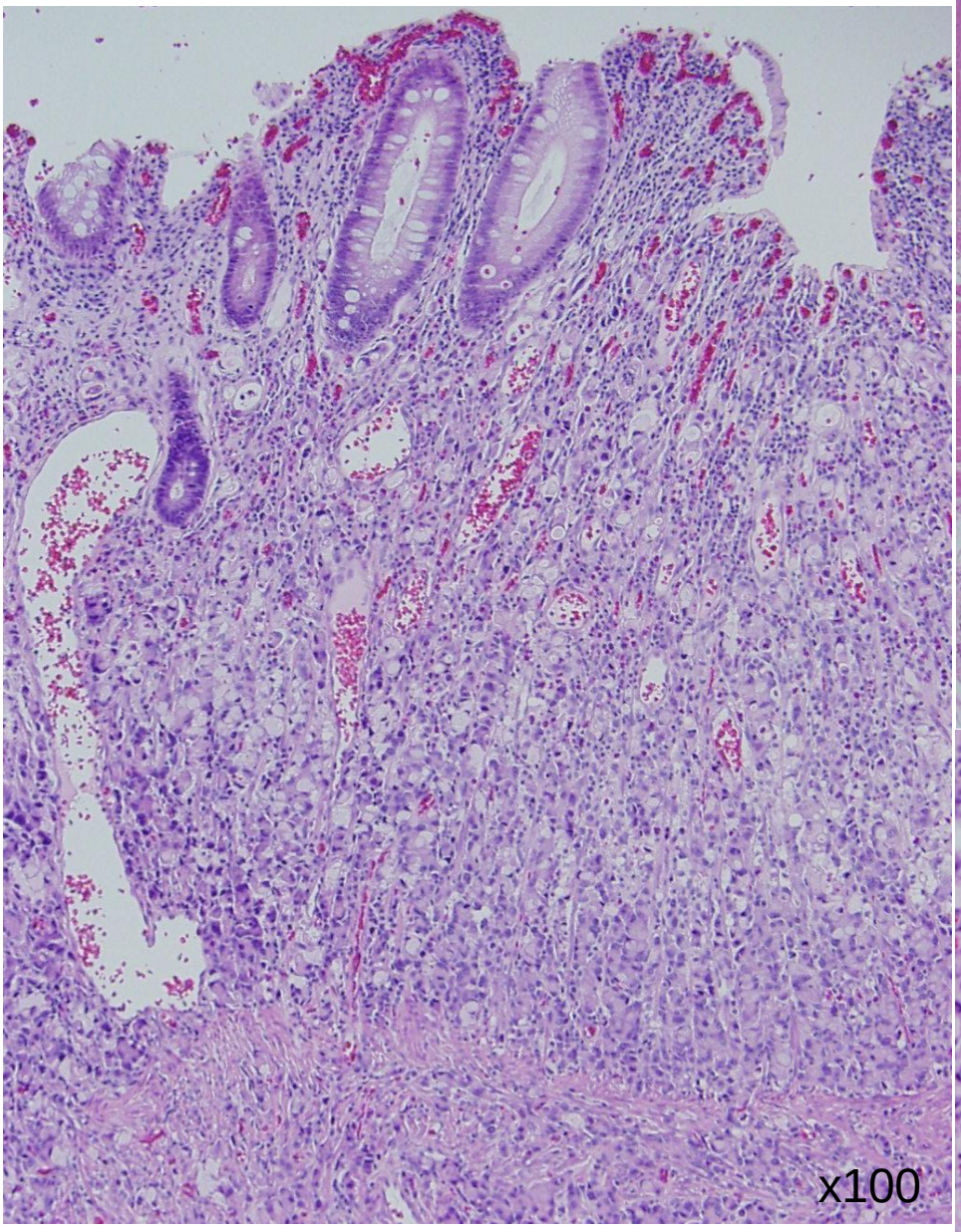
2017. 08. 10.

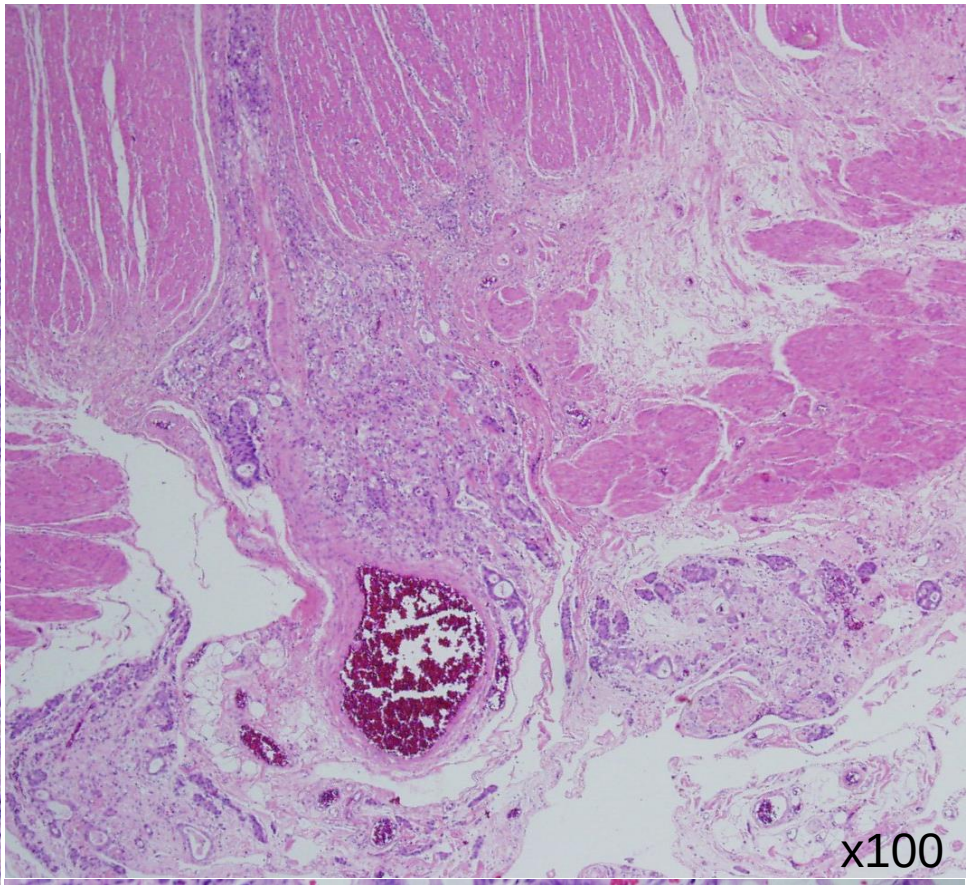


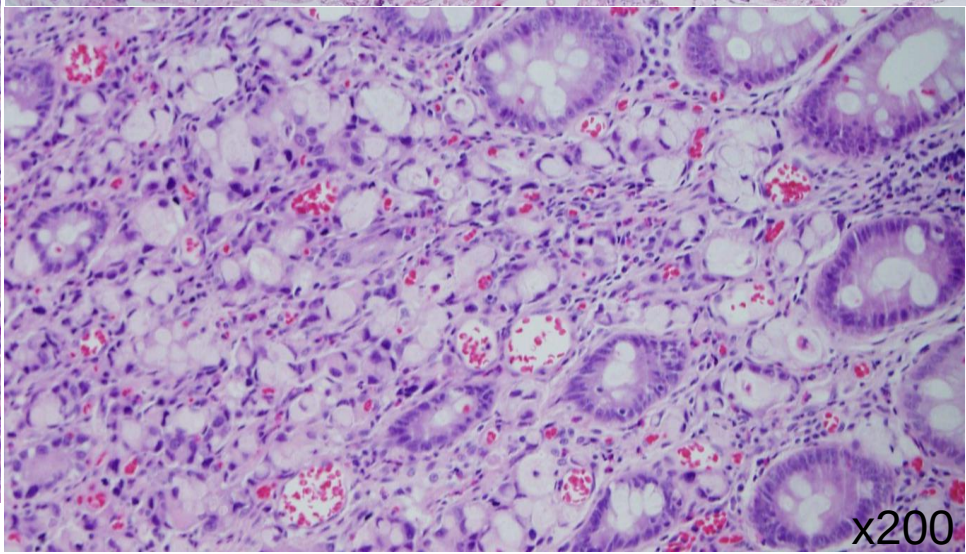
2017. 08. 16.

➔ **Low Anterior Resection**

Pathologic Findings







Pathologic Findings

- **Rectum, Low Anterior Resection :**
  - **Adenocarcinoma, signet-ring cell carcinoma, metastatic**
  - **IHC : CK7 + / CK20 - /** LCA +

1) Location : rectum
2) Gross type : fungating
3) Size : 1.6 x 1.0 x 0.5 cm
4) Depth of invasion : tumor invasion serosa to mucosa
5) Resection margin :

   Distal margin – involved carcinoma (tumor cells are seen in serosa, focally)

   Distal post margin – negative for malignancy

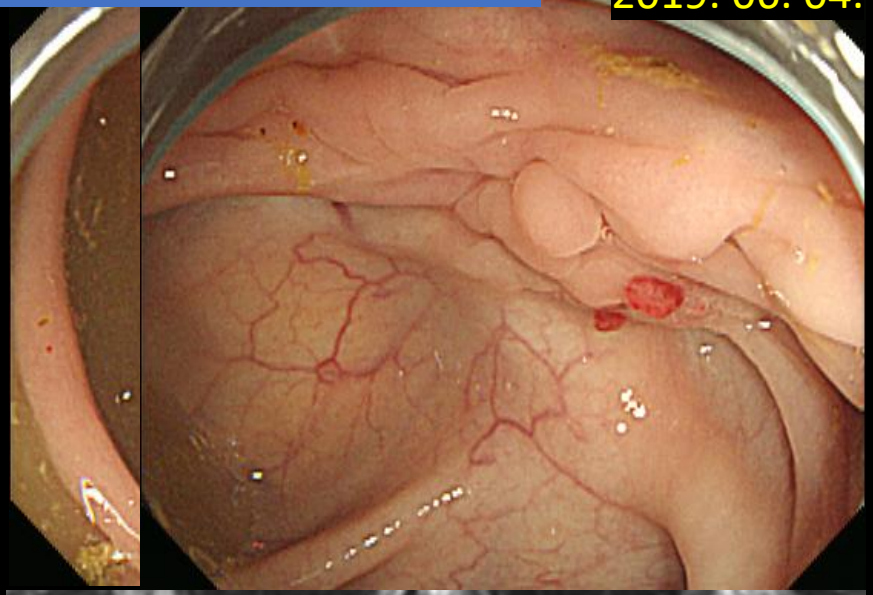
6) LN meta : 3/22 (perirectal 3/16)
7) lymphatic invasion + / venous invation - / perin

Stomach origin is favored

Adjuvant Chemotherapy :
with **Trastuzumab, Cisplatin, and Fluorouracil**
#1~13('13.8.~'14.4.)

Clinical Course : 2 years later after 2nd operation(LAR)

2019. 06. 04.



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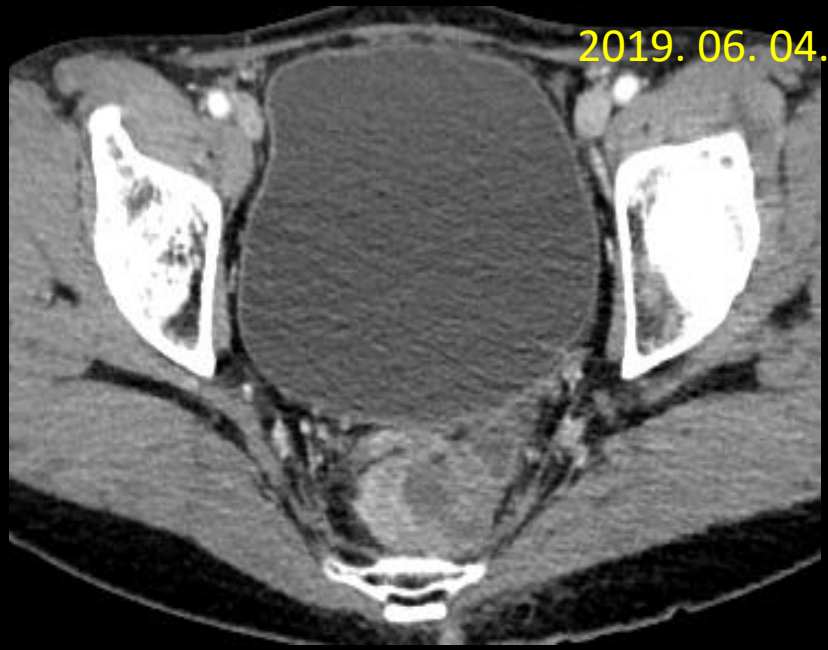
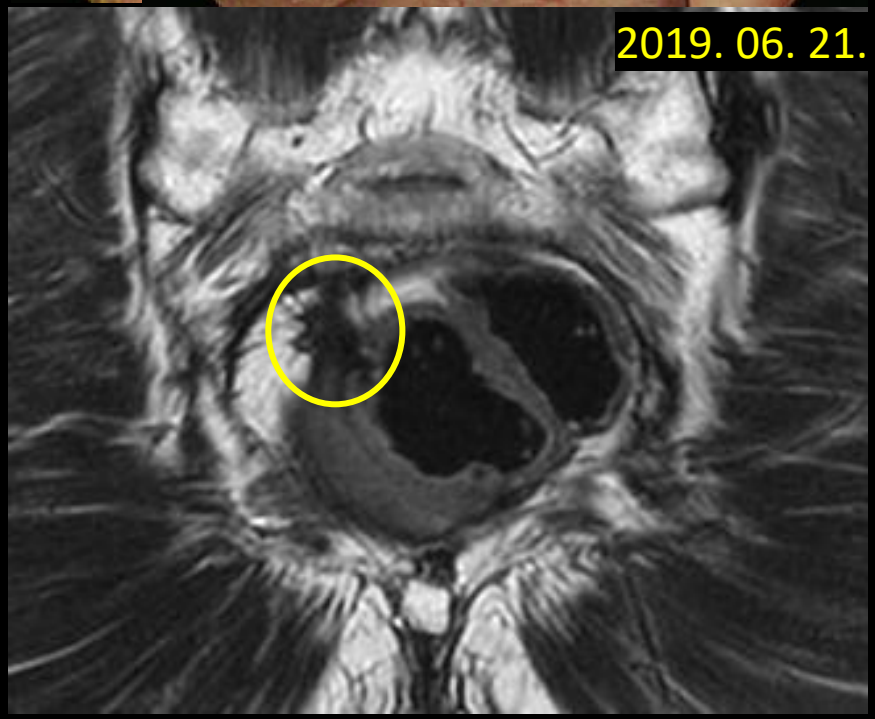


2019. 06. 21.



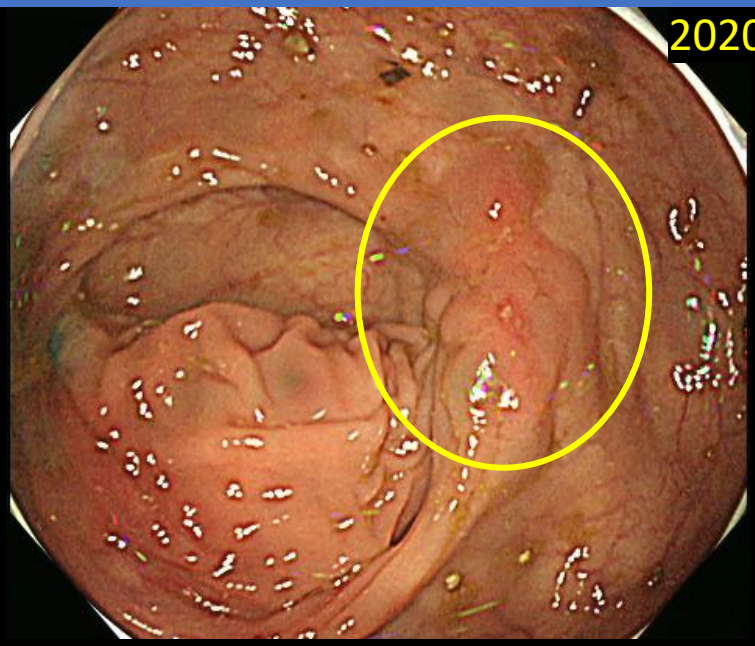
2019. 06. 21.

Clinical Course

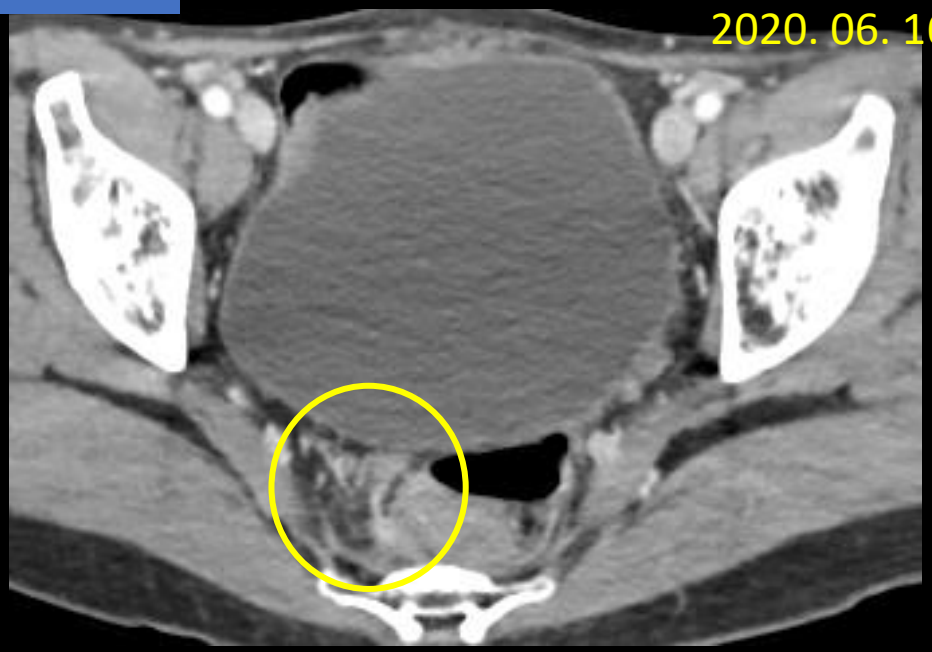
- Follow-up of **tumor markers** for 1 year:

	2019.06.03	2019.06.20.	2019.09.17.	2019.12.16.	2020.03.16.	2020.06.15.
CEA (ng/mL)	3.26	3.23	3.25	2.92	3.42	3.67
CA 19-9 (U/mL)	<2.0	<2.0	<2.0	<2.0	<2.0	<2.0

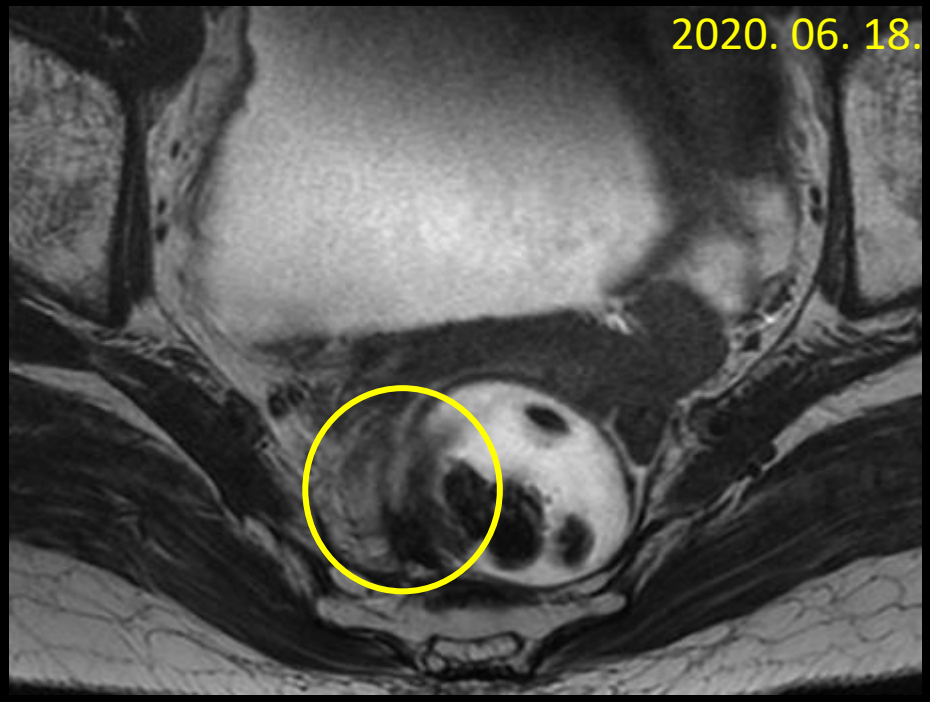
Clinical Course : 1 years later (3 years later after 2nd op.)



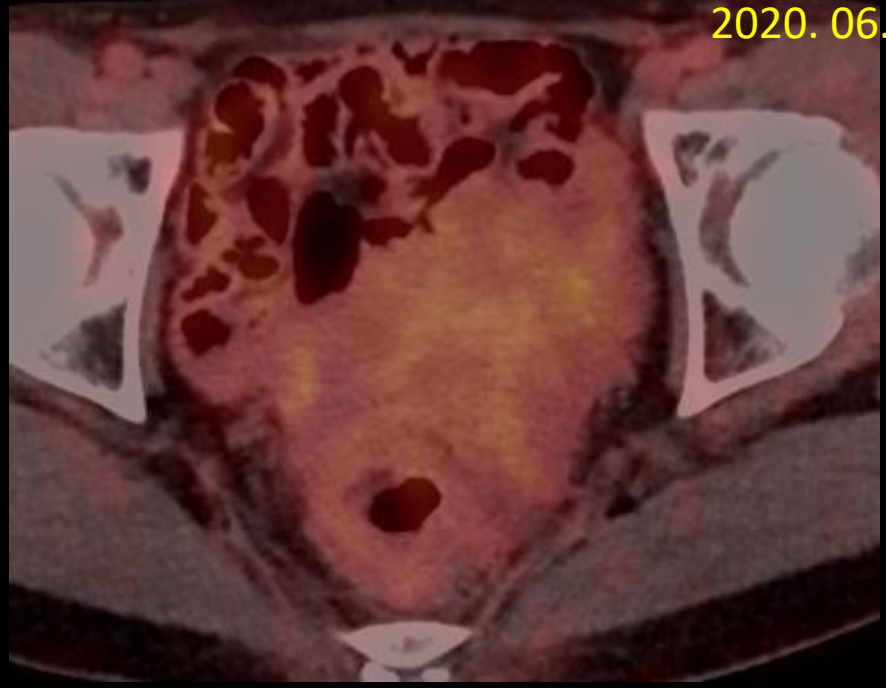
2020. 06. 16.



2020. 06. 16.



2020. 06. 18.

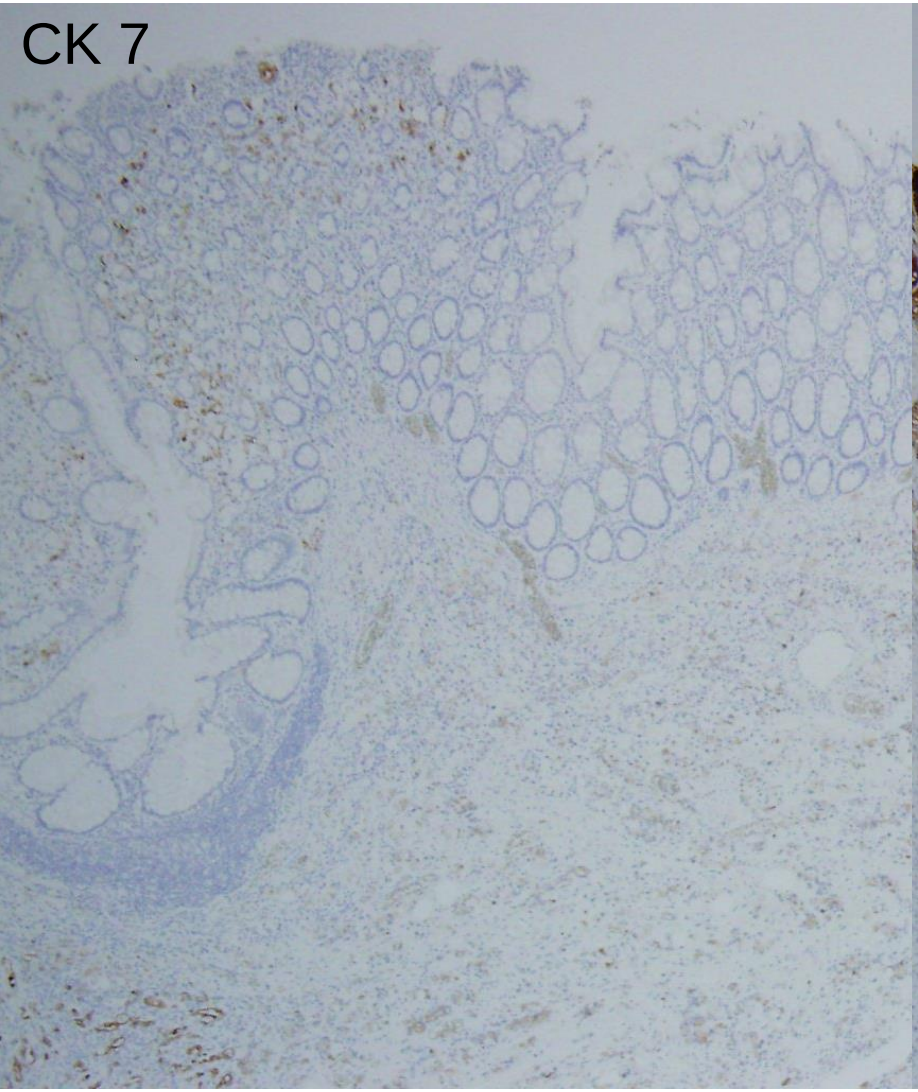


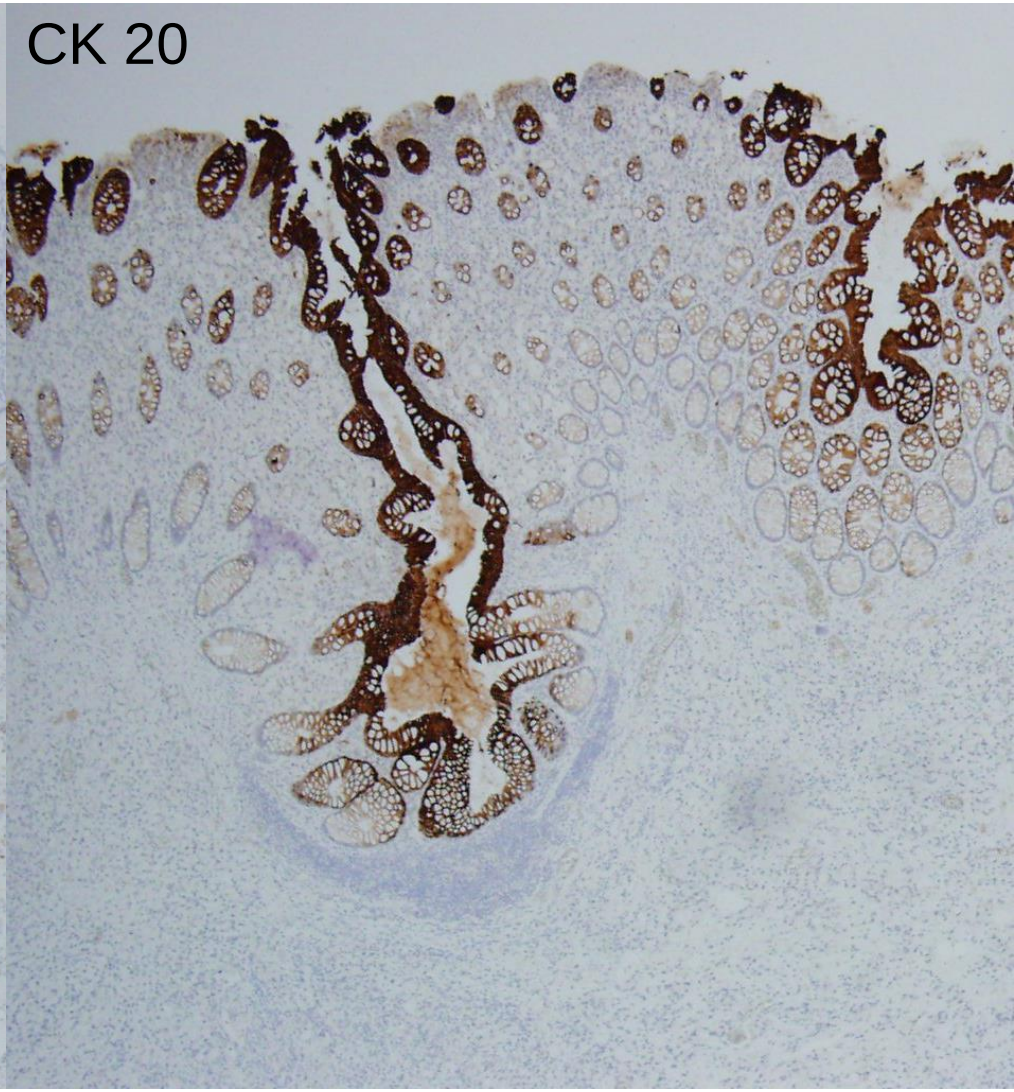
2020. 06. 18.

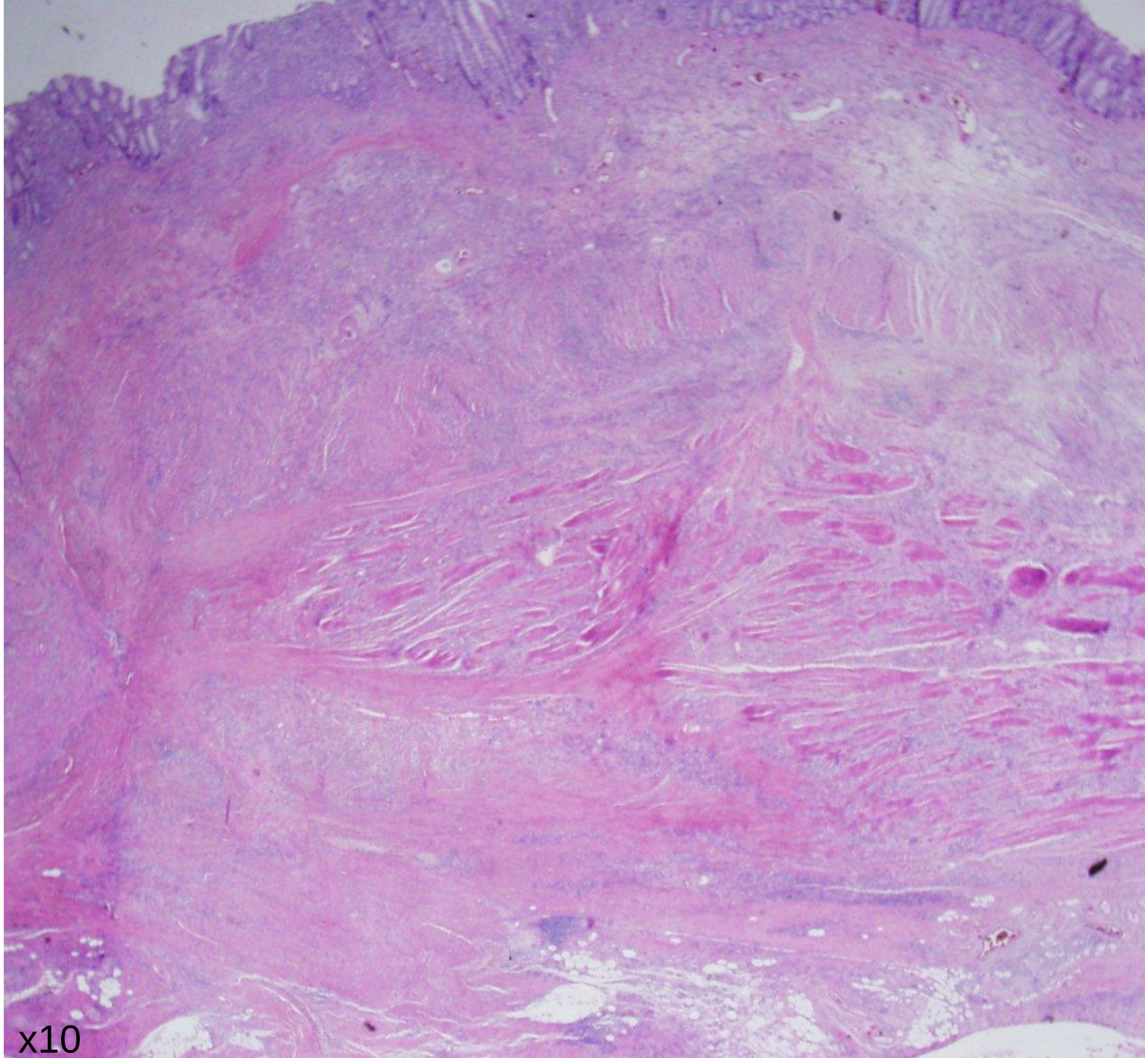
Operative Findings

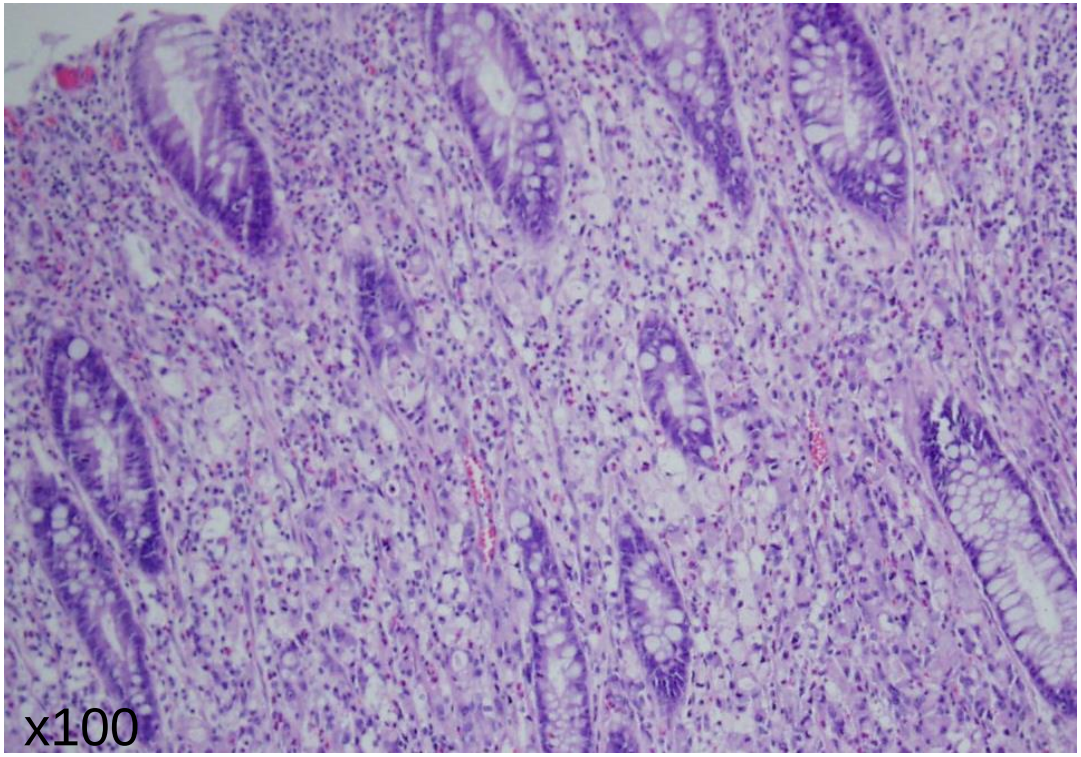
- Additional **Low Anterior Resction** (2020.07.10.)
  - Radicality : R0 Resection
  - explored any metastasis, no meta at liver, small bowel & mesentery, peritoneum.
  - ascites 100cc 있어서 10cc sampling.
  - 이전 문합부는 항문연에서 7cm 높이
  - 문합부에서 두꺼워진 흔적(encirclig)을 외부에서 촉지하였고, **하부 2cm 절제연**을 포함하여 하단을 절제 하였고 근위부는 종양에서 10cm 더 올라가 절단하였다.
  - 근위부 절제연 근처의 5mm 림프절은 동결 생검에서 음성.
  - 유착이 심한 right sacral fascia에 2개의 clips(방사선 치료 가능성)

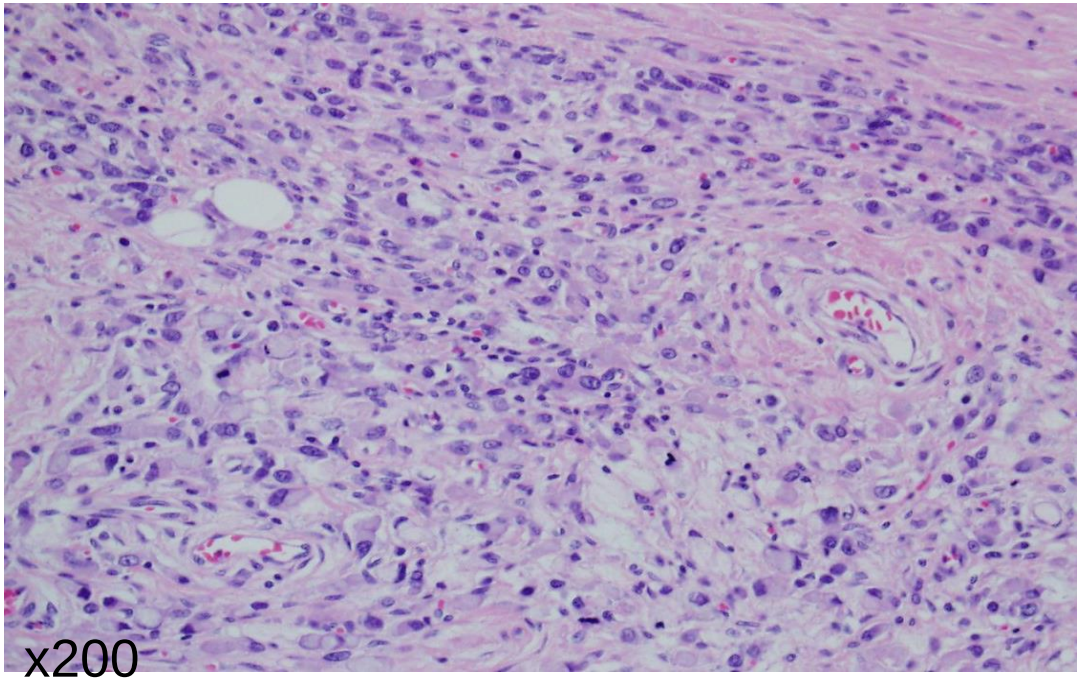
Pathologic Findings






x10


x100


x200

Pathologic Findings

- **Rectum, Low Anterior Resection :**
  - **Adenocarcinoma, signet-ring cell carcinoma, metastatic**
  - **IHC : CK7 + / CK20 - / CDX -**

Stomach origin is favored

1) Location : rectum
2) Gross type : elevated
3) Size : 1.4 x 1.1 x 0.8 cm
4) Tumor invade serosa to mucosa
5) Resection margin : free from the carcinoma

   (Safety margin : distal 1.6cm, proximal 7.5cm)

6) LN meta : 0/11

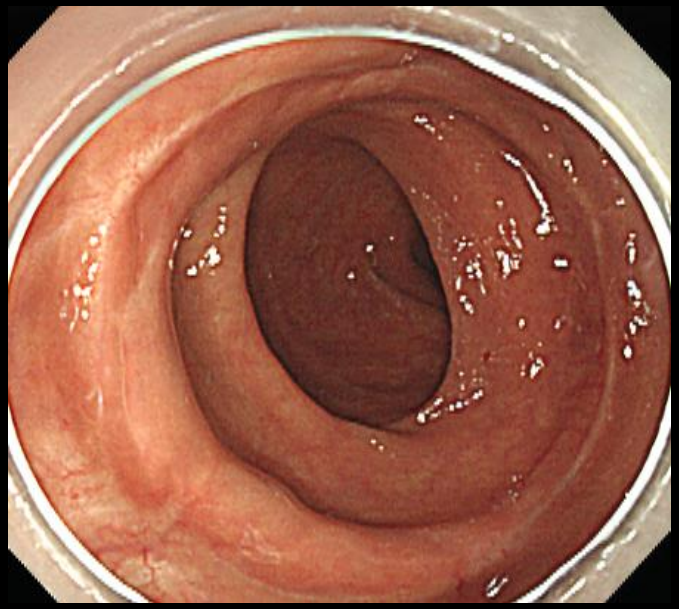
Multidisciplinary Discussion

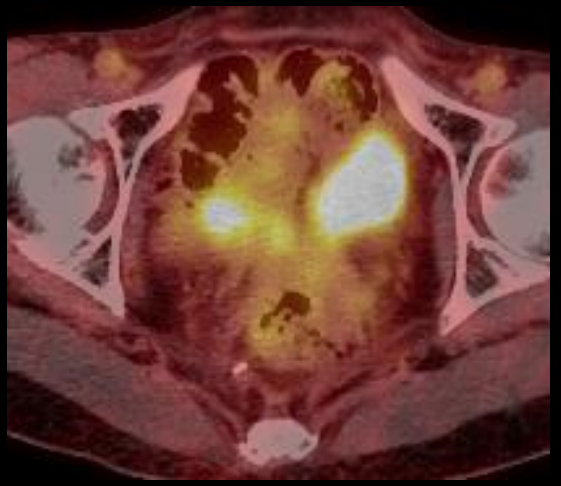
7) lymphatic invasion + / venous invation - / perineural invasion -

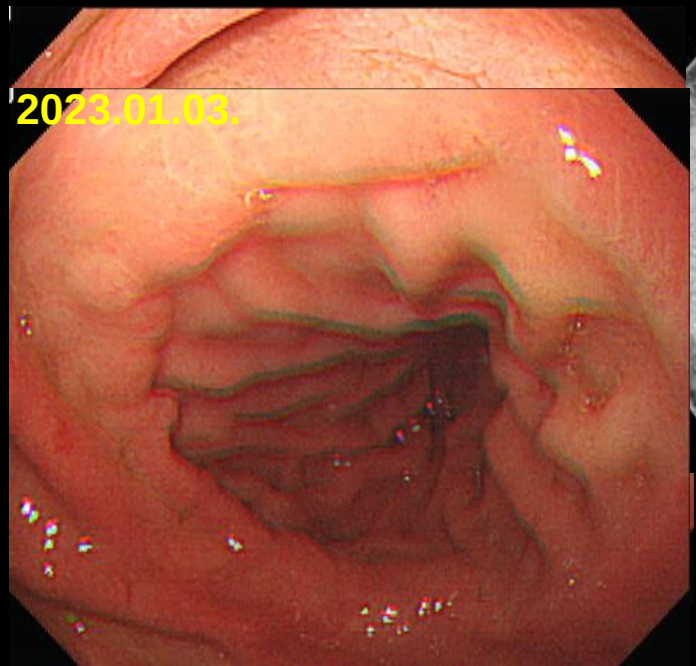
Clinical Course

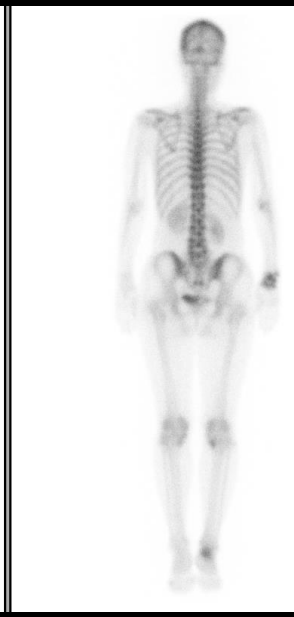
- **Multidisciplinary Discussion**
  - the lesion was radically resected but the extent was insufficient
  - further systemic chemotherapy was unlikey to be beneficial
  - 28 cycles of **adjuvant radiotherapy** were performed.

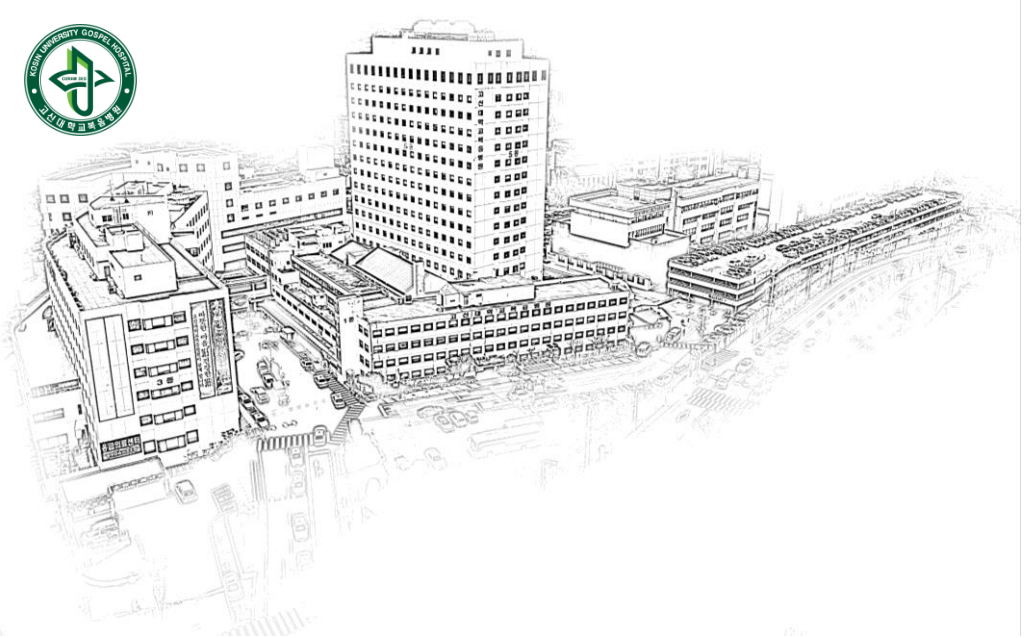
Clinical Course (2022.07.05., 2023.01.03.)











Case Review

Statement 32-2: Radical gastrectomy, oophorectomy and perioperative chemotherapy could be considered for selected gastric cancer patients with oligometastases in the ovary (evidence: very low, recommendation: conditional for).

For ovarian metastasis, 3 retrospective studies were analyzed in the meta-analysis, and there was better survival in the metastasectomy group (HR, 0.45; 95% CI, 0.34 to 0.59; P<0.001) [432-434] (**Fig. 26**). Cheong et al. [435] reported that Krukenberg tumors were frequently accompanied by peritoneal dissemination with a significantly worse prognosis (HR, 1.74; 95% CI, 1.28 to 2.36; P<0.001), and only when curative resection was obtained was the median OS time longer in the resection group than in the nonresection group (17 vs. 3 months, P<0.001).

Regarding para-aortic LNs, only 3 prospective nonrandomized studies evaluated the response rate of preoperative chemotherapy and the efficacy of subsequent D2 LND plus para-aortic LN dissection; they did not show favorable survival outcomes [436-438].

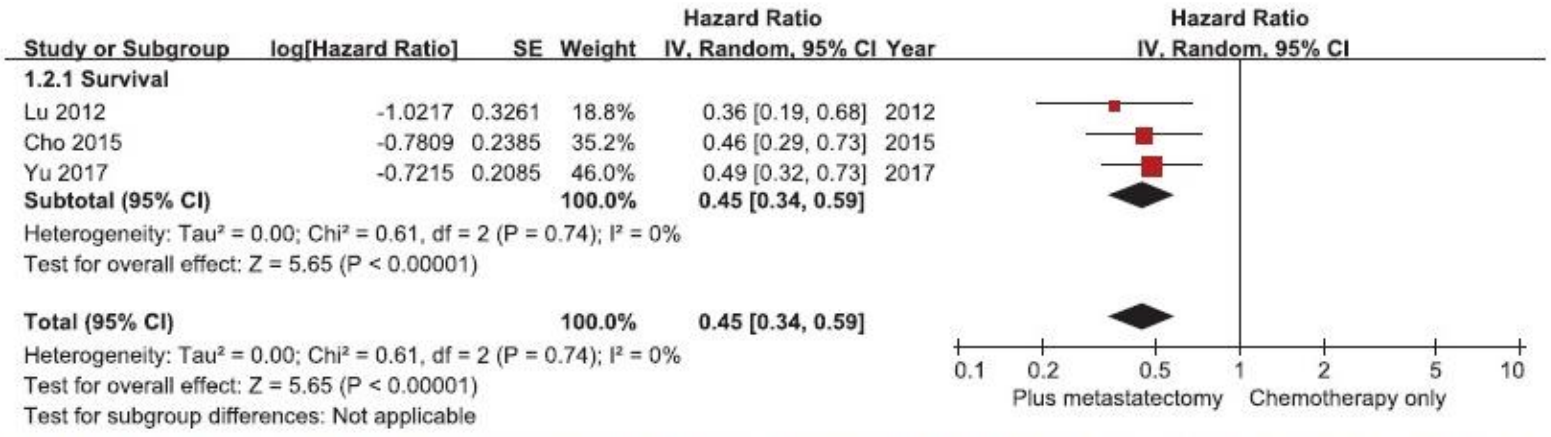


Fig. 26. Forest plot for comparison of overall survival between (oophorectomy and gastrectomy with chemotherapy) vs. (chemotherapy only) in gastric cancer with oligometastasis confined to ovary in observational studies.
SE – standard error; IV – interval variable; CI – confidence interval.

Kim TH et al., Korean Practice Guidelines for Gastric Cancer 2022: An Evidence-based, Multidisciplinary Approach, J Gastric Cancer. 2023 Jan; 23(1): 3–106.

Case Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
49(5) 1–8

DOI: 10.1177/03000605211018420
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SAGE

Gastric cancer with repeated metastasis in the colonic lumen: a case report and multi-surgical experience

Yi Wang[1], Peiqing Ma[2], Kan Liu[3], Dongkui Xu[1] and Qian Liu[4]

No:	Year	First author	Age (years)	Sex	Primary tumor	Stage of GC*	Chemotherapy after gastrectomy	Disease-free interval	Recurrent lesion	Operation for colorectal lesion(s)	Outcome
1	2014	Noji et al[6]	61	M	Por, Mod	IIA	No	110 M	T, D, S	Lht, Tsc	125 M, alive
2	2014	Noji et al[6]	46	F	Por	IIIA	Yes	106 M	R	LAR	144 M, alive
3	2018	Su et al[7]	78	M	Por	IIIB	Yes	18 M	T	Tsc	24 M, died
4	2016	Fujimoto et al[8]	58	F	Por, Sig	IA	Yes	28 M	S	Sdt,	59 M, alive
5	2018	Uemura et al[9]	60	M	Well	IA	No	24 M	R	LAR	79 M, alive
6	2020	Yang et al[10]	57	M	Por, Sig Muc	IIIA	Yes	30 M	A, C	Rht	39 M, died
7	2021	Our case	42	F	Por, Sig	IIIA	Yes	30 M	A, T, S	Rht, Sdt	154 M, died

*According to the 7th edition of the American Joint Committee on Cancer (AJCC).
Sex (M/F: male/female); GC, gastric cancer; C: cecum; A: ascending colon; T: transverse colon; D: descending colon; S: sigmoid colon; R: rectum; Por: poorly differentiated adenocarcinoma; Sig: signet ring cell adenocarcinoma; Muc: mucinous adenocarcinoma; Mod: moderately differentiated adenocarcinoma; Well: well-differentiated adenocarcinoma; LAR: low anterior resection; Rht: right hemicolectomy; Lht: left hemicolectomy; Tsc: transverse colectomy; Sdt: sigmoidectomy; M: month.

1) poorly differentiated adenocarcinoma containing signet ring cell carcinoma
2) Lymph node metastasis
3) Intestinal metastases - multiple, scattered polyp-like lesions
4) Tumor marker(CEA, CA 19-9, and CA724) - within normal ranges

Wang Y et al., Gastric cancer with repeated metastasis in the colonic lumen: a case report and multi-surgical experience, J Int Med Res. 2021 May; 49(5): 03000605211018420.

Contents lists available at ScienceDirect

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journal homepage: www.casereports.com

Surgical resection of colorectal recurrence of gastric cancer more than 5 years after primary resection

Takehiro Noji[a,b,*], Yoshiyuki Yamamura[a,1], Jun Muto[a,1], Aki Kuroda[a,1], Junkichi Koinuma[a,1], Tatsuya Yoshioka[a,1], Katsuhiko Murakawa[a,1], Setsuyuki Otake[a,1], Satoshi Hirano[b,2], Koichi Ono[a,1]

[a] Department of Surgery, Obihiro Kosei General Hospital, W7 S8, Obihiro City, Hokkaido 080-0016, Japan
[b] Department of Gastroenterological Surgery II, Graduate School of Medicine, Hokkaido University, N15W7, Kita-ku, Sapporo, Hokkaido 060-8638, Japan

- Resection of late-onset colorectal recurrence appears worthwhile for selected patients because of potential gains in long-term survival.
- Surgical margins is needed
  - Likelihood of lymph node metastases and the intra-muscular spread of tumor cells

Noji T et al., Surgical resection of colorectal recurrence of gastric cancer more than5 years after primary resection, International Journal of Surgery Case Reports 5 (2014) 954–957

Literature reports of late onset colorectal recurrence of gastric cancer >5 years after primary resection.

Year	Author	Age	Gender	Recurrent lesion	LNM	Primary tumor	DFI (month)	Outcome
1988	Okabe[8]	49	F	C, A	Unknown	Por	60	Unknown
1988	Ohta[7]	57	M	C	Yes	Por	68	42M died
	Ohta	51	F	A, T, D, S	Yes	Por	69	22M died
	Ohta	44	F	R	Yes	Por	106	27M died[a]
1991	Yamada[9]	61	M	T	Unknown	Por	64	3M alive
1994	Ogiwara[3]	53	F	D	Yes	Por	660	Unknown
2001	Man-i[12]	58	M	T, D, S, R	Yes	Sig	84	10M alive
2001	Kim[11]	75	M	T	Unknown	Well	77	26M alive
	Kim	70	M	C	Unknown	Well	68	44M alive
2001	Hase[10]	44	F	T	Unknown	Por, Sig	68	Unknown
2006	Hiraki[13]	68	F	A	Yes	Por, Sig	60	7M alive
2008	Shiokawa[4]	69	F	T	Yes	Por	156	4M alive
2009	Takahashi[14]	76	M	R	Unknown	Por	66	6M alive
2010	Iwakawa[15]	75	F	R	Yes	Por	83	25M died
	Iwakawa	76	F	R	Yes	Por	82	22M died
2011	Arai[17]	62	M	A, D, R	Unknown	Por, Mode	180	Unknown[a]
2011	Murakami[16]	60	M	D	Unknown	Mode, Por	72	2M alive
2012	Watanabe[2]	58	M	T	Unknown	Por, Sig	77	27M died
2013	Yamamura[4]	79	M	T	Yes	Por, Sig	132	19M died
–	Our Case 1	61	M	T, D, S	Yes	Por, Mode	110	17M alive
–	Our Case 2	46	F	R	Yes	Por	106	24M alive

LNM: lymph node metastasis; DFI: disease free interval; Gender (M/F: male/female); C: cecum; A: ascending colon; T: transverse colon; D: descending colon; S: sigmoid colon; R: rectum; Por: poorly differentiated adenocarcinoma; Sig: signet ring cell adenocarcinoma; Mode: moderately differentiated adenocarcinoma; Well: well-differentiated adenocarcinoma; M: month.

[a] This patient was not resected; the only treatment was chemotherapy.

- Median disease-free interval : **74** months.
- Most frequent site of metastasis : **Transverse** colon

versus peritoneal seeding

(direct extent via mesenteric reflection)

- The majority originated : **poorly** differentiated
- Regional lymph node metastasis : **11**/21 cases
- Median survival after surgery for metastatic colon ca. : 26 months

2/19 cases survived **>3** years

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Multidisciplinary Treatment (MDT)

- The **advantages** :
  - Correct diagnosis (18.4%–26.9%)
  - Change into better treatment plan (23.0%–76.81%)
  - Shorter decision-making time and survival benefit
- **Include** - Surgeons, Gastroenterologists, medical and radiation Oncologists, Radiologists, Pathologists, Nuclear medicine experts, and Others.
  - nutritional services, social workers, nurses, and palliative care specialists
- Increasing proportions of patients with very old ages and comorbidities
  - development of diverse treatment options

Kim TH et al., Korean Practice Guidelines for Gastric Cancer 2022: An Evidence-based, Multidisciplinary Approach, J Gastric Cancer. 2023 Jan; 23(1): 3–106.

Take Home Massage

- Could not ignore colonic examinations after gastric ca. treatment during regular follow-up.
- Early detection of metastasis and radical surgery and/or adjuvant treatment → could achieve survival benefit.
- Multidisciplinary Treatment