

## Chemotherapy Induced Renal Failure

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### Case 1

상기 56세 여환은 특이 내과적 과거력 없는 분으로, 2014년 6월 우상복부 통증을 주소로 시행한 복부컴퓨터단층촬영에서 담낭암 및 간, 대장 전이 소견 보여 본원 내원 후 시행한 조직 검사에서 adenocarcinoma with neuroendocrine differentiation으로 담낭암 확진하였고, Gemcitabine + Cisplatin 항암치료 시작하였다.

10차까지 항암치료 시행하였고, 항암치료에 대해서는 stable disease 소견 보였으나, 정상이던 신 기능(eGFR > 90 ml/min) 항암치료 중 eGFR 38 ml/min까지 감소하며 고칼륨혈증 보여, 2달 간 항암치료 중단 및 보존적 치료 후 환자 신기능 호전되어 11차 항암치료 시행하였다. 11차 항암치료 시행 후 신부전 반복되어, 추가 항암치료 없이 보존적 치료 유지하기로 결정하였고, 추적관찰 중 시행한 복부컴퓨터단층촬영에서 cancer progression 보였다.

### Case 2

상기 70세 남환은 2014년 9월 횡달로 본원 내원하여 시행한 복부컴퓨터단층촬영에서 간내담관암 및 간전이 보였고, 간 조직 검사에서 adenocarcinoma with moderately differentiation으로 확진 후, Gemcitabine + Cisplatin 항암치료 시작하였다.

8차까지 항암치료 시행 후, response evaluation 위해 시행한 복부 컴퓨터단층촬영에서 stable disease로 항암치료에 반응 보였으나, 정상이던 신기능(eGFR >90 m/min)이 eGFR 35 ml/min까지 감소하며, 신기능 악화 보여, 항암치료 중단 후 보존적 치료하며 경과관찰 하였다. 이후 신기능은 다시 호전 보였으나, 환자 general condition 악화 및 disease progression으로 추가 항암치료 시행하지 못하고 보존적 치료 유지 중이다.

**Key Words:** Gallbladder cancer, Cholangiocarcinoma, Renal failure, Chemotherapy induced renal failure

### REFERENCES

1. Boesler B, Czock D, Keller F, et al. Clinical course of haemodialysis patients with malignancies and dose-adjusted chemotherapy. Nephrol Dial Transplant 2005;20:1187.
2. Launay-Vacher V, Oudard S, Janus N, et al. Prevalence of Renal Insufficiency in cancer patients and implications for anticancer drug management: the renal insufficiency and anticancer medications (IRMA) study. Cancer 2007; 110:1376.
3. Launay-Vacher V, Chatelut E, Lichtman SM, et al. Renal insufficiency in elderly cancer patients: International Society of Geriatric Oncology clinical practice recommendations. Ann Oncol 2007;18:1314.

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### Case. 7881213 윤 O 옥 F/57

- ✓ PI: 상기 56세 여환 2014년 6월 1달간 지속되는 우상복부 통증을 주소로 외부 병원에서 시행한 복부 CT상 담낭 종괴 및 간, 대장 침범 소견 보여, 추가 검사 및 치료 위해 본원 내원함.
- ✓ Past History: HTN/DM/Pul.Tbc/Hepatitis (-/-/-/-)
- ✓ Social History: Smoking/Alcohol (-/-)

✓ Review of System

General weakness (-)	Anorexia /Nausea/Vomiting (-/-/-)
Easy fatigue (-/-)	Abdominal pain (+)
Fever/chill (-/-)	Abdominal discomfort (+)
Headache/Dizziness (-/-)	Constipation /Diarrhea (-/-)
Insomnia (-)	Hematochezia/Melena (-/-)
Cough/Sputum (-/-)	Wt. Loss (-)
Dyspnea /D.O.E. (-/-)	

✓ Physical exam

BP 117/80 mmHg PR 70회/min	CBS without rale
RR 16회/min BT 36.4 °C	RHB without murmur
	Soft and flat abdomen
Not so ill-looking appearance	Normoactive bowel sound
Alert mental status	Abdominal DT/RT (+/-)
Not Icteric sclera	Not palpable liver, spleen
Not Pale conjunctiva	Pitting edema (-/-)

✓ Lab

CBC 8540 (70.9%) > 10.8 < 324k

PT/aPTT 0.97(INR) / 36.4 sec

BUN/Cr 24.5/0.81 mg/dL

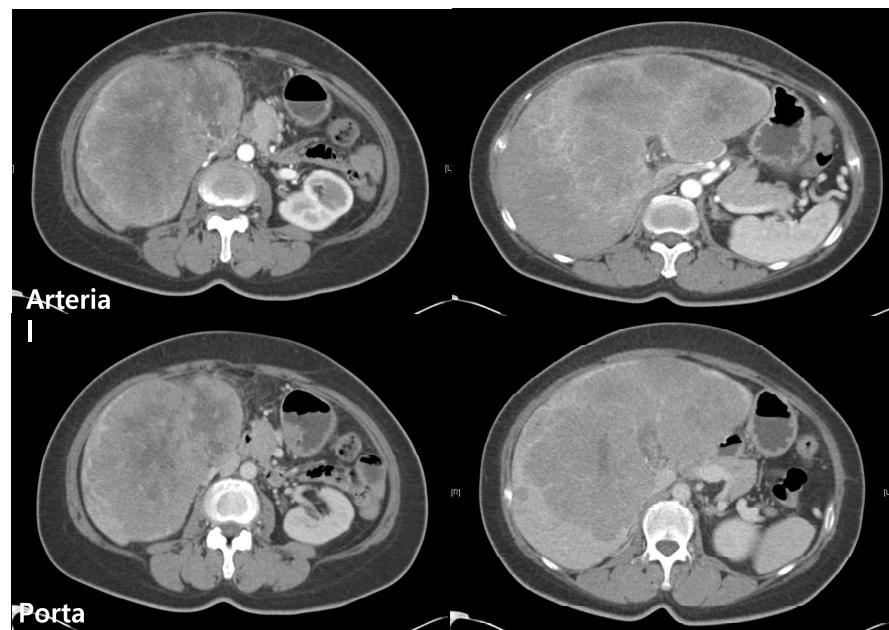
AST/ALT 45/21 IU/L, T.bil 0.5 mg/dL

T. Protein/Albumin 7.9/4.2 g/dL

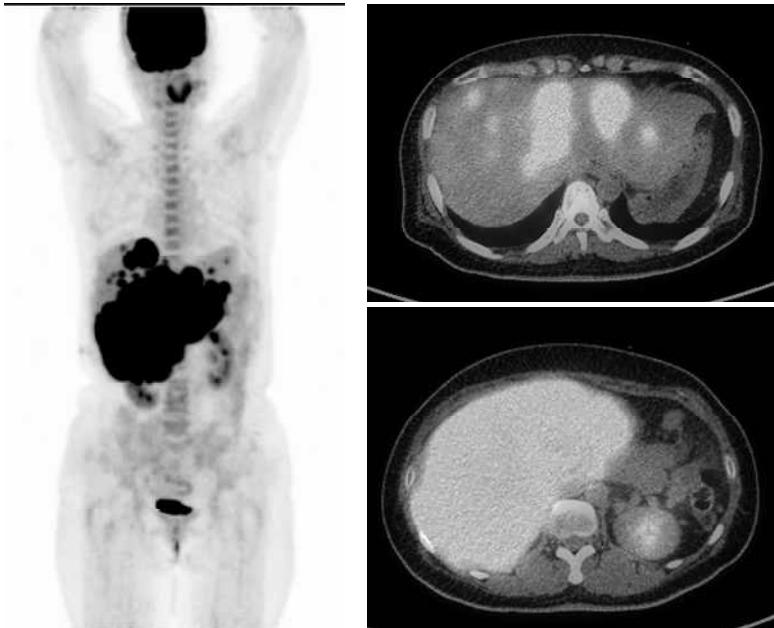
CEA 46.35 ng/mL (NL < 5.0)

CA 19-9 192.0 U/mL (NL < 37.0)

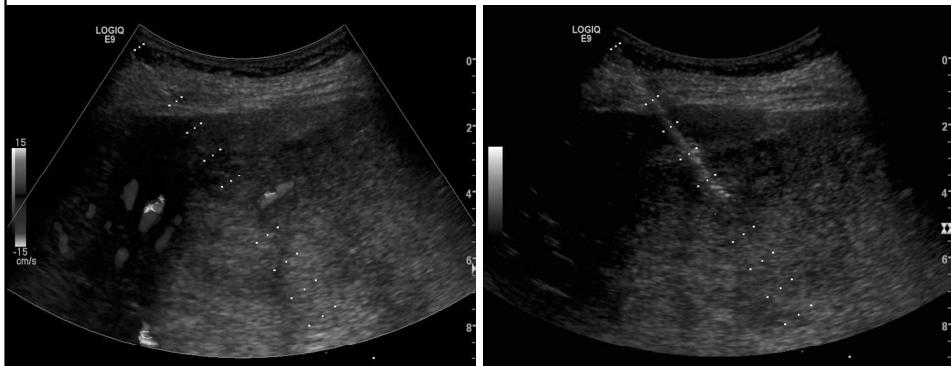
### Abdomen & Pelvic CT (2014.06.13)



**<sup>18</sup>FDG-PET CT scan (2014.06.24)**



**US-guided Liver biopsy (2014.06.24)**



Adenocarcinoma with neuroendocrine differentiation, either metstatic or primary

CD56: positive in tumor cells

CK19: focal positive in tumor cells

Synaptophysin, chromogranin A, CEA, alcian-blue and mucicarmine:  
negative

## Diagnosis & Treatment

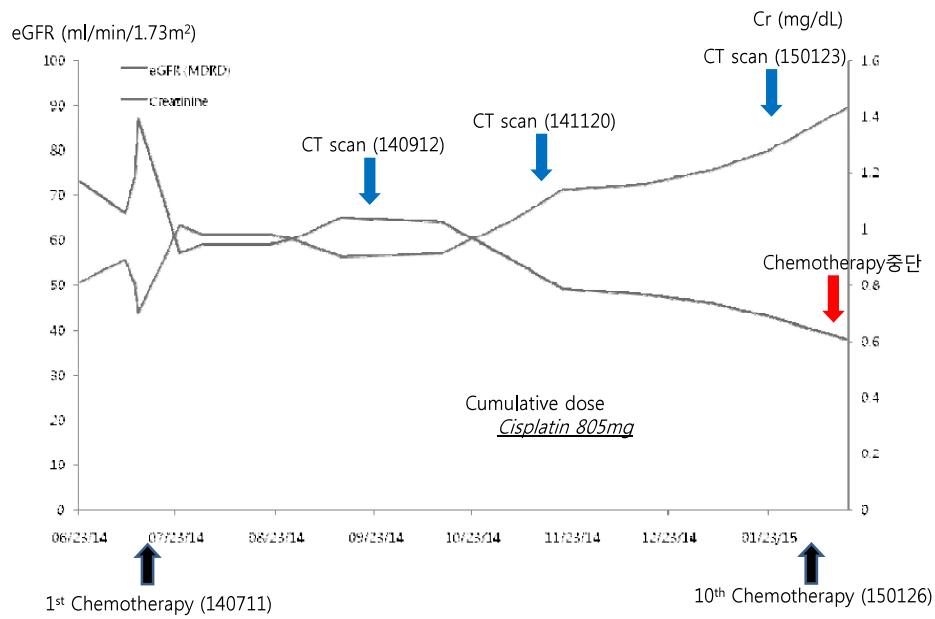
### ✓ Diagnosis

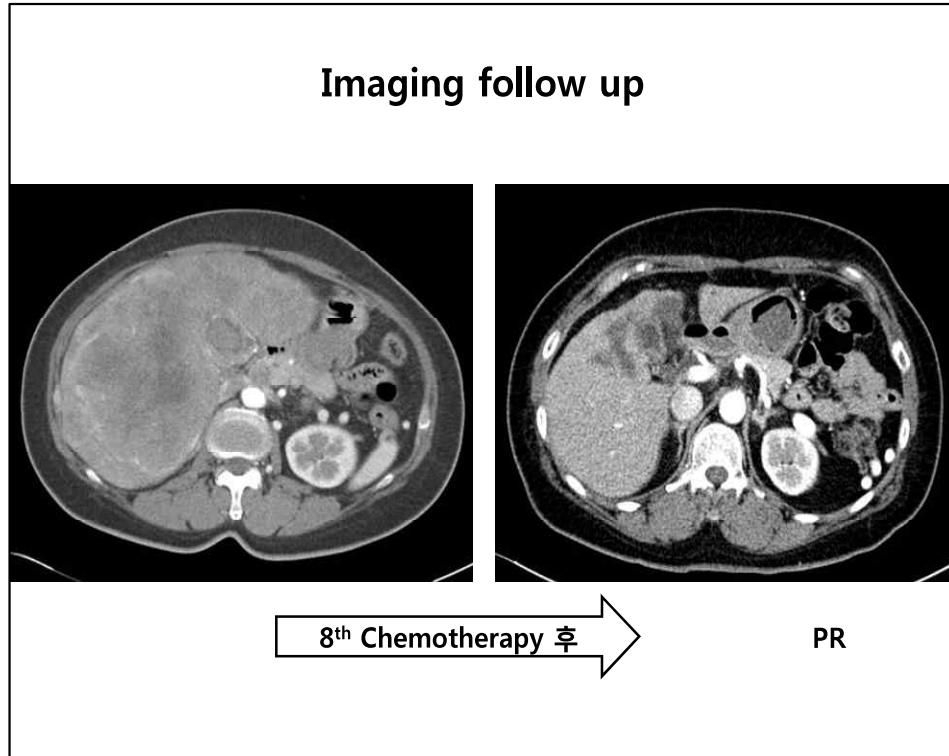
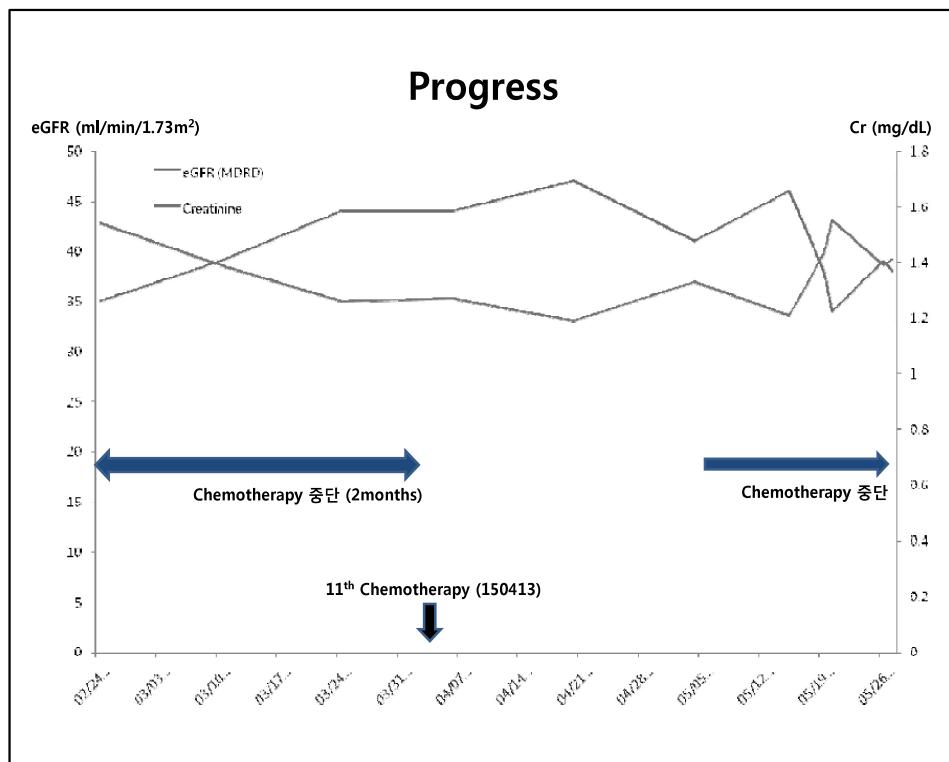
- ✓ GB cancer with liver and LN metastasis
- ✓ cT4N1M0, Stage IVa

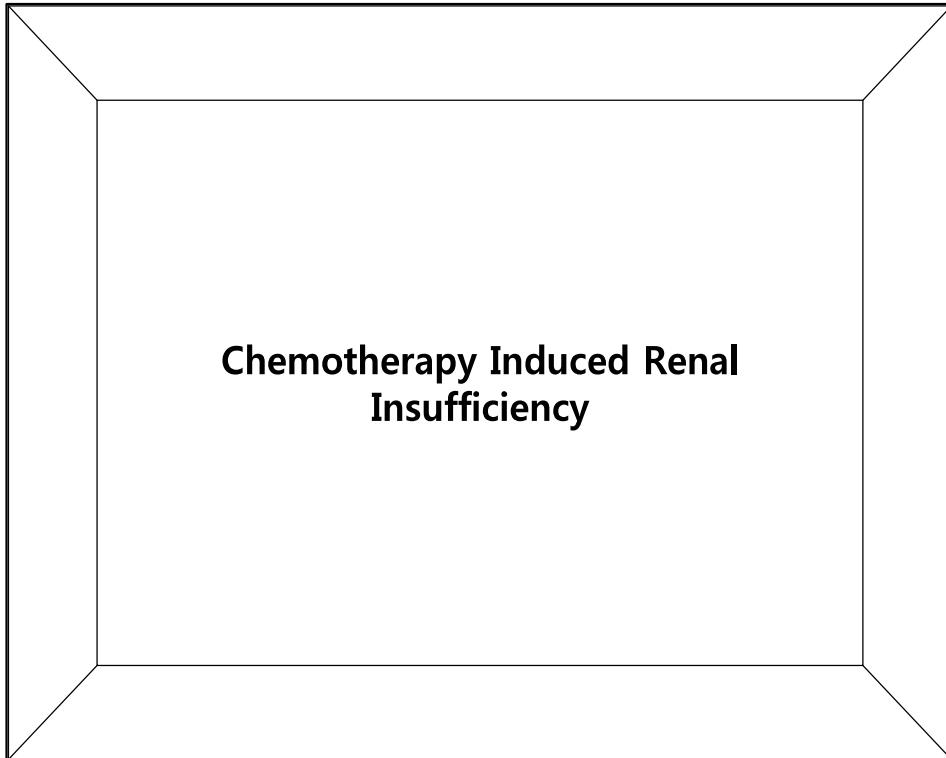
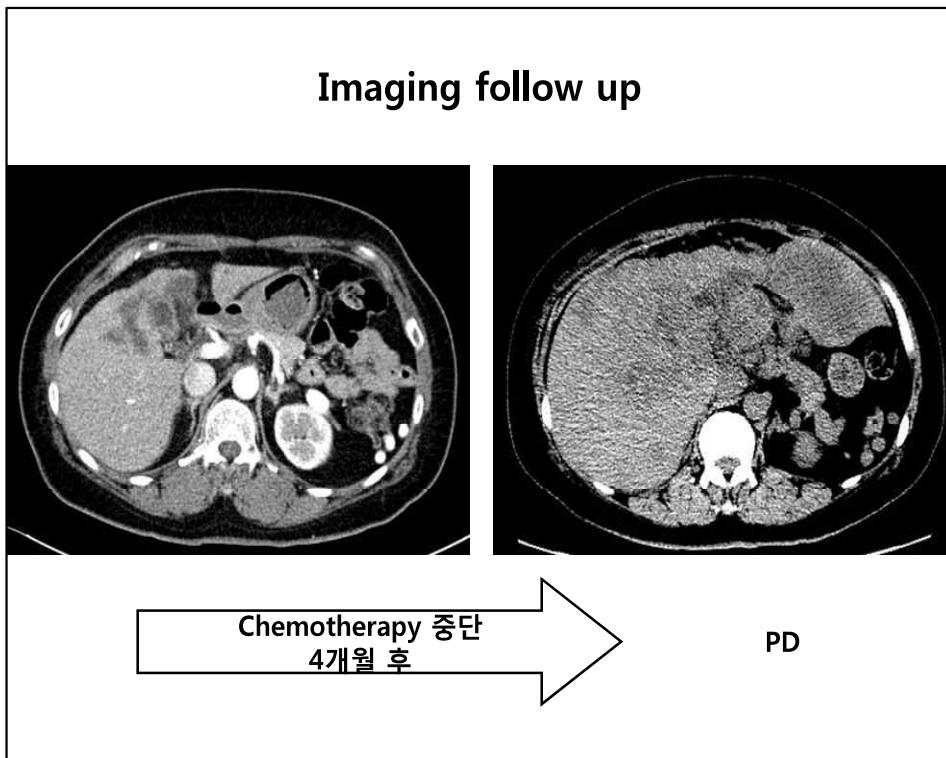
### ✓ Treatment Plan

- ✓ Palliative Chemotherapy
- ✓ Regimen: Gemcitabine/Cisplatin every 3 weeks  
(Gemcitabine 1,000 mg/m<sup>2</sup>, Cisplatin 25 mg/m<sup>2</sup>, D1,8 each)

## Progress







## Prevalence of Renal Insufficiency

INN	No. of prescriptions	Percentage of all prescriptions	Need for dosage adjustment	Potential nephrotoxicity
5-FU	1182	16.46	No	No
Cyclophosphamide	701	9.76	Yes	No
Docetaxel	601	8.37	Yes	No
Epirubicin	556	7.74	No	Yes
Gemcitabine	428	5.96	No	Yes
Vinorelbine	390	5.43	Yes	No
Carboplatin	378	5.26	Yes	Yes
Doxorubicin	340	4.73	No	Yes
Paclitaxel	328	4.57	No	Yes
Cisplatin	313	4.36	Yes	Yes
Oxaliplatin	302	4.21	No	Yes
Irinotecan	258	3.59	No data available	Yes
Trastuzumab	256	3.56	No data available	Yes
Zoledronate	153	2.13	Yes	Yes
Etoposide	131	1.82	Yes	No
Capecitabine	92	1.28	Yes	No
Methotrexate	81	1.13	Yes	Yes
Total	9036			

Prevalence of Renal Insufficiency in Cancer Patients and Implications for Anticancer Drug Management;

The Renal Insufficiency and Anticancer Medications (IRMA) study. Vincent Launay-Vacher, Stephane Oudard, et al., *Cancer* 2007; 110:1376-84.

## Risk factors for Renal Insufficiency

### Repeated administrations and frequent courses

- ✓Cumulative dose >450 mg/m<sup>2</sup>
- ✓Pre-existing renal disease/abnormal renal function
- ✓Dehydration
- ✓Heart failure, edema, ascites, etc
- ✓Anemia
- ✓Coadministration of other nephrotoxic agents
- ✓Dosage not adjusted to the level of renal function

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## Renal toxicity associated with Weekly Gem/DDP Regimen

Variables	Cumulative dose of cisplatin (mg)					
	0	100	200	300	400	500
Sex	0.50	0.99	1.0	1.0 (0.082–12.5)		
Age ≥65 years	0.057	0.11	7.3	7.3 (0.65–83.0)		
ECOG performance status 1	1.0	0.30	0.39	0.39 (0.063–2.4)		
Presence of ascites	1.0	0.47	3.2	3.2 (0.14–73.7)		
Second-line chemotherapy	0.74	0.14	0.20	0.20 (0.023–1.7)		
Pretreatment creatinine level ≥0.7 mg/dl	0.033	0.52	2.0	2.0 (0.25–15.3)		
Pretreatment eGFR <80 ml/min	<0.001	0.011	58.2	58.2 (2.5–1334.0)		
Relative dose intensity of cisplatin ≥80%	1.0	0.79	1.3	1.3 (0.24–6.7)		
Total dose of cisplatin ≥400 mg	0.21	0.021	18.3	18.3 (1.6–215.5)		

Renal toxicity associated with weekly cisplatin and gemcitabine combination therapy for treatment of advanced biliary tract cancer.  
 Satoshi Kobayashi, Makoto Ueno, et al., *Oncology* 2014; 87: 30-39.

- ✓ Assessment and Optimization of **hydration status** as precise as possible
- ✓ Evaluation of renal function to establish any need for **dose adjustment is required; SCr alone is insufficient**
- ✓ Within each drug class, preference may be given to agents **less likely to be influenced by renal clearance and to be toxic to the kidneys**
- ✓ **Coadministration** of known nephrotoxic drugs such as **NSAIDs or Cox-2 inhibitors** should be **avoided or minimized**

**NCCN Guidelines  
International Society of Geriatric Oncology**