A Case of Cholangiocellular Carcinoma with Partial Response to Gemcitabine Plus Cisplatin

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Introduction: Cholangiocellular carcinoma (CCC) is the second-most common hepatic malignancy, and one thirds of CCC arise as intra-hepatic lesion. CCC commonly disseminate through the lympha tic system to lymph nodes and hematogenous dissemination is less frequent and results in dissemination to the liver, peritoneum, and lung. We report a case of CCC with partial response to gemcitabine plus cisplatin combination therapy.

Case: A 69 years old female visited our hospital with a complaint of right upper quadrant abdominal pain for 7 days. Patient had a medical history of papillary thyroid carcinoma treated by laser, 3 years ago and was on medication with thyroid hormone due to hypothyroidism. On review of system, the patient had general weakness, easy fatigue, febrile sensation, nausea, and abdominal pain. CA 125 tumor marker was at 7546 U/mL. Abdominal computed tomography showed multiple masses in both lobes of liver and lymph node enlargement at hepatic hilum and para-aortic area. Primary origin of cancer was not found in examination with esophagogastroduodenoscopy, colonoscopy, and transvaginal sonography. Positron emission tomography showed multiple FDG uptake at liver and portocaval, porta hepatis, and paraaortic lymph node. Liver biopsy was done and histologic examination showed poorly differentiated adenocarcinoma and immunohistochemical stain was positive for cytokeratin 7 and 19, and negative for cytokeratin 20, suggesting intrahepatic CCC. Final diagnosis of the patient was CCC with intrahepatic and lymph node metastasis, TNM stage IV. Chemotherapy was started and the regimen was as follows: gemcitabine (1,000 mg/m^2 per day on 1, 8 days), cisplatin (25 mg/m^2 per day on 1, 8 days) every 3 weeks. After 7 cycles of chemotherapy, positron emission tomography demonstrated marked decrease in FDG uptake at liver and lymph node, suggesting partial response. CA 125 tumor marker dropped to 257 U/mL after 8 cycles of chemotherapy. Patient is still on chemotherapy without progression of cancer.

Conclusion: Combination therapy with gemcitabine and cisplatin has been recommended as the first line chemotherapy for patients with advanced CCC. Further studies are needed to make criteria for deciding when to cease chemotherapy in CCC patients with good response.

- **Chief complaint**

  Right upper quadrant abdominal pain for 7 days

- **Present illness**

  RUQ abdominal pain, febrile sensation for 7 days

  Local medical center visit and evaluation

  Multiple hepatic mass found in abdominal CT, PET CT

- **Past medical history**
  - Treatment history of papillary thyroid carcinoma, left, 3 yrs ago → on thyroid hormone PO medication
  - On hormonal replacement therapy, stopped 2 weeks ago

- **Social history**
  - Smoking: No
  - Alcohol intake: No
  - Occupation: housewife

- **Review of system**
  - General weakness (+)
  - Easy fatigue (+)
  - Febrile sensation (+)
  - Nausea (+)
  - Abdominal pain(+)

- Height: 154.9, Weight: 54.9 kg
- Body mass index: 22.88

- **Vital signs**
  - Blood pressure: 130/80 mmHg
  - Body temperature: 36.6
  - Pulse rate: 82
  - Respiration rate 20

- **Physical examination**
  - Soft and mildly distended
  - Normo-active bowel sound
  - No abdominal tenderness

Impression

- Multiple liver mass
  - r/o Multiple hepatic metastasis from unknown origin
  - r/o Primary hepatic malignancy

Plan

- Abdominal CT
- GFS, CFS
- Check viral hepatitis serology
- Check tumor marker

Laboratory findings

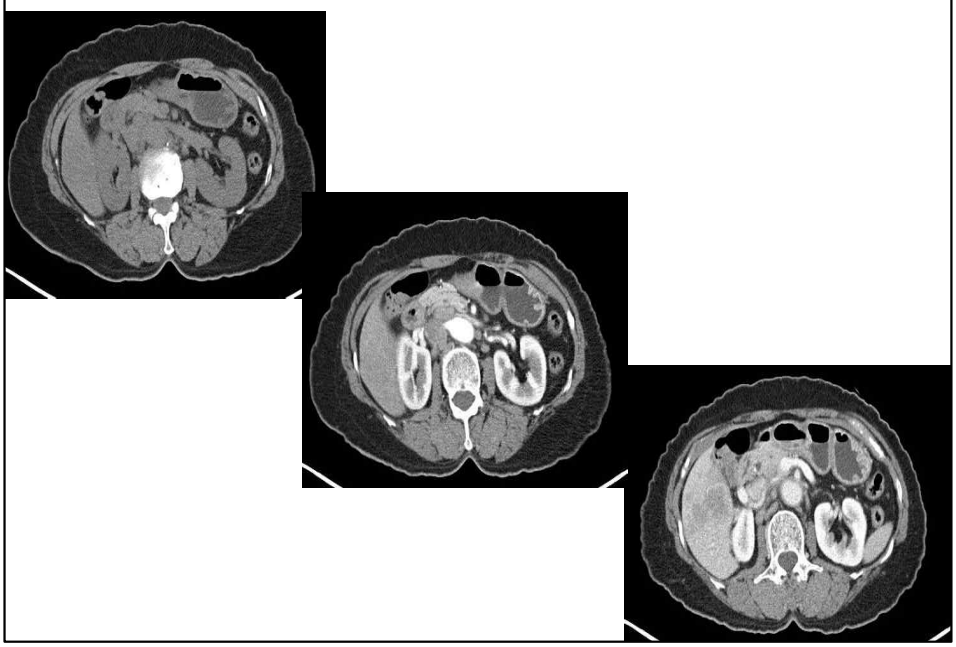
WBC (/uL)	Hb (g/dL)	Plt (/uL)
5660	13.4	262000

TP	Albumin	T-bil	D-bil	AST	ALT	ALP	GGT	LDH
7.3	4.14	0.61	0.13	50	38	309	142	480

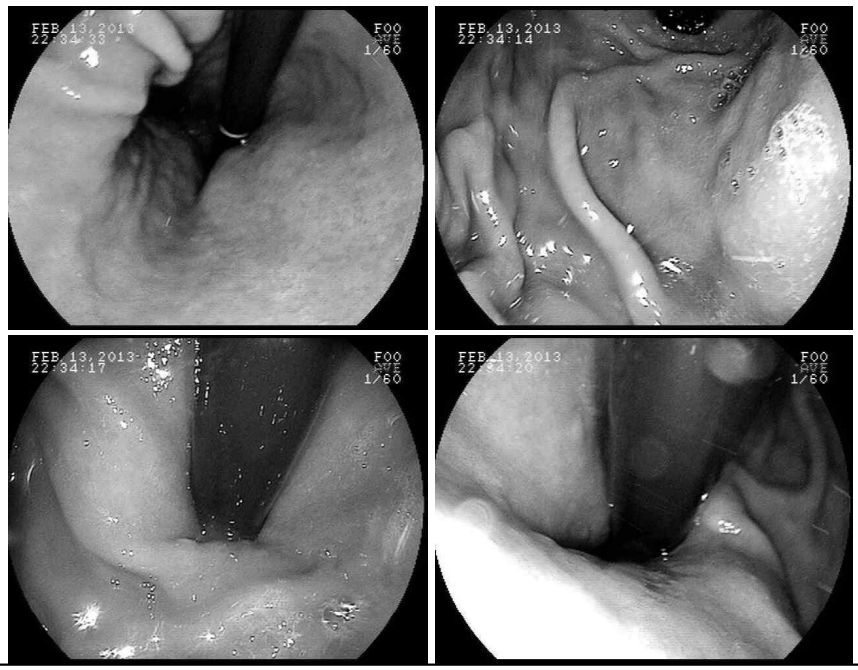
Tumor marker		
CA19-9 (U/mL)	CEA (ng/mL)	CA125 (U/mL)
6.88	1.3	7546

Viral hepatitis serology			
HBsAg	HBsAb	HBcAb	Anti-HCV
-	+	+	-

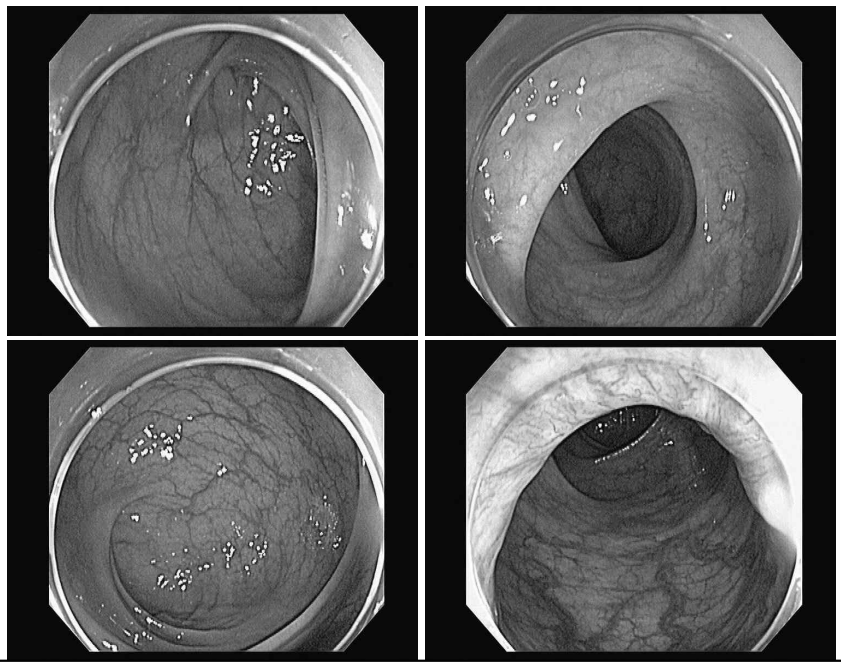
Abdominal CT



Esophagogastroduodenoscopy



Colonoscopy



Transvaginal Sonography

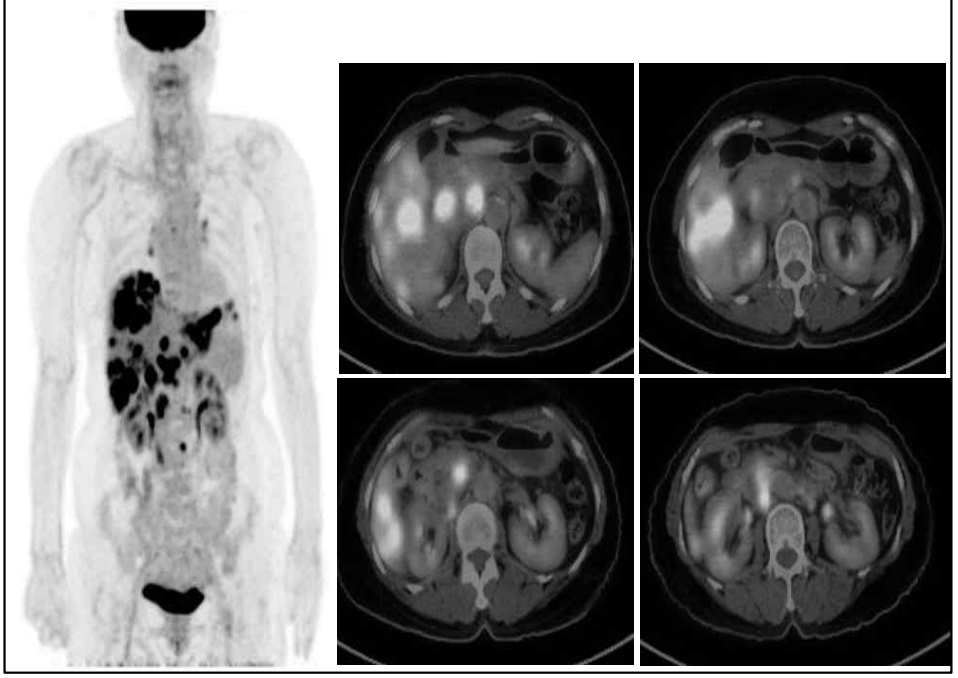
- Uterine venous engorgement
- Thin Endometrium
- Both adnexa: not visible
- Visible focal mass was not seen

- P/E Cervix – no erosion

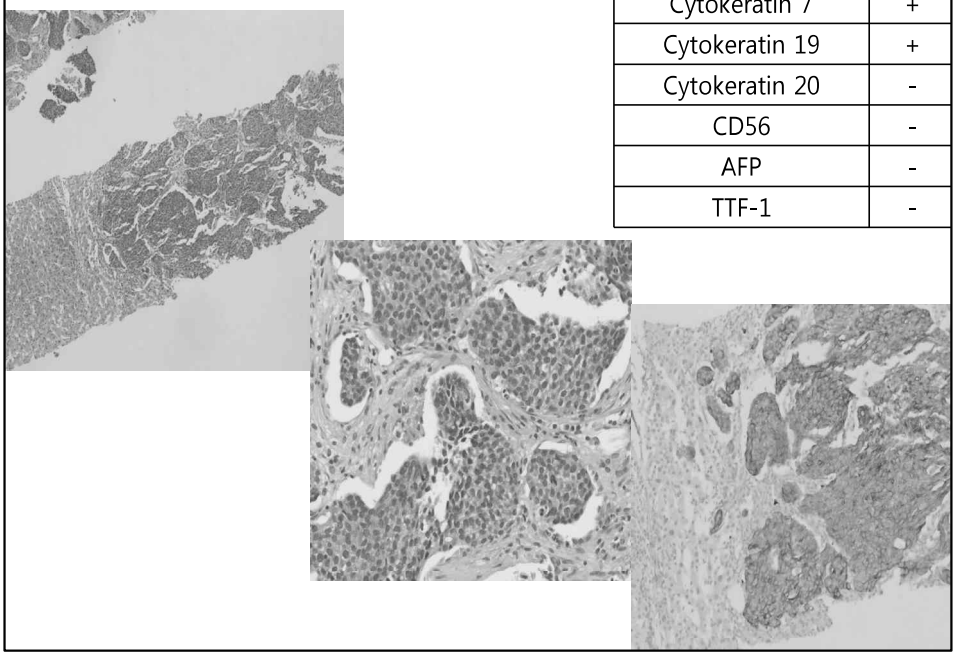
no tenderness

smear: negative for intraepithelial lesion or malignancy

PET CT



Liver biopsy

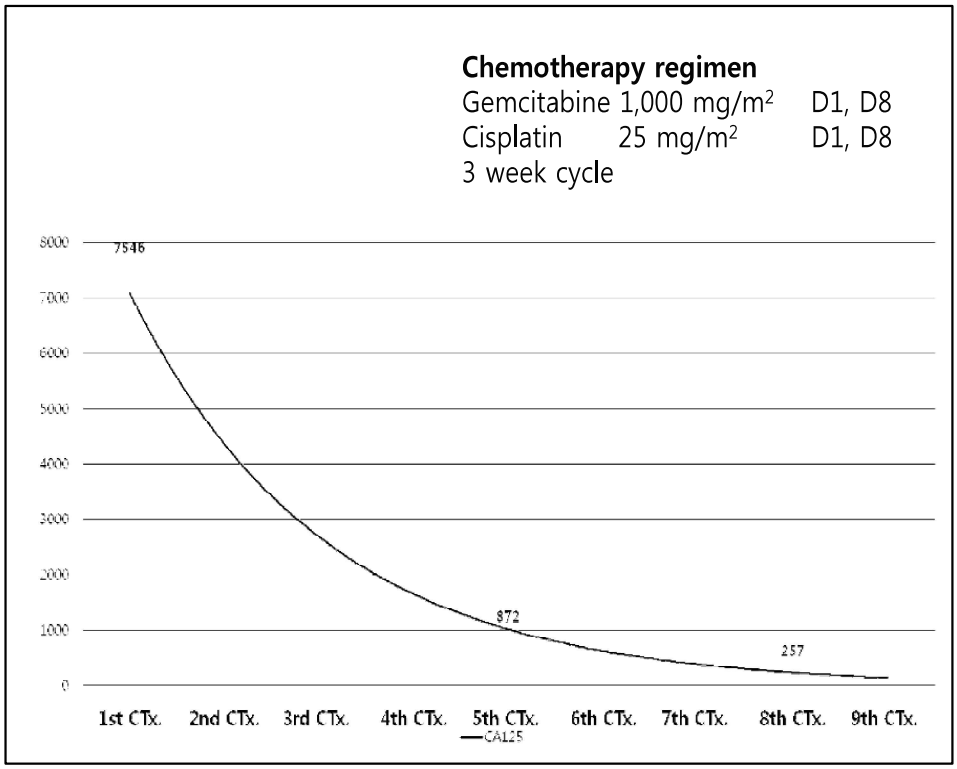


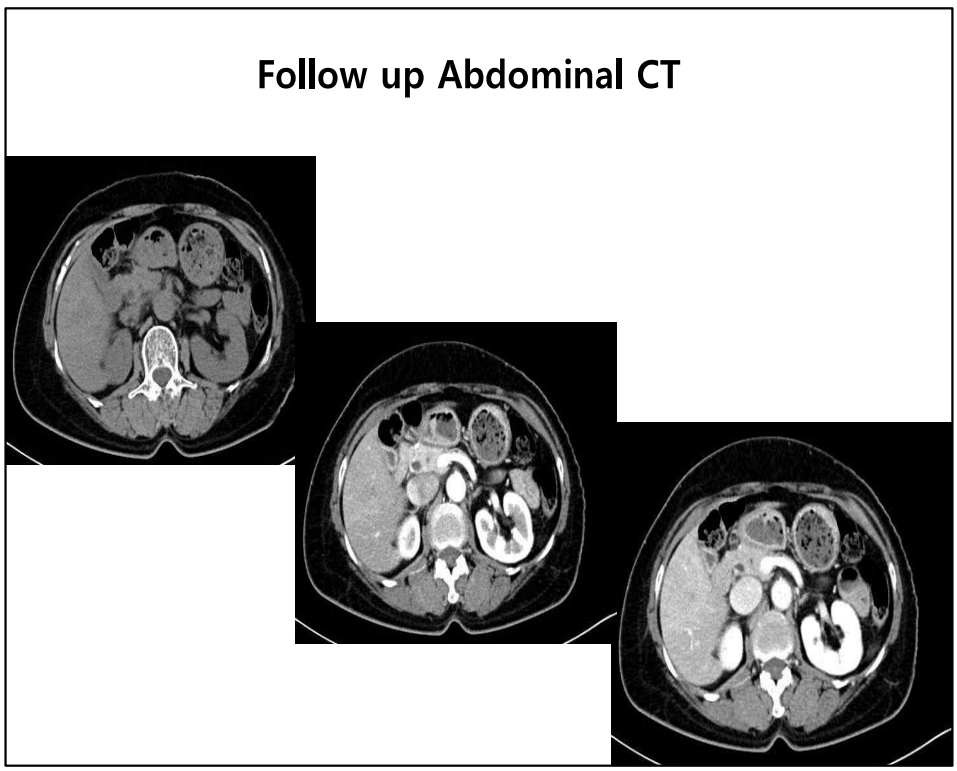
Immunohistochemical stain	
Cytokeratin 7	+
Cytokeratin 19	+
Cytokeratin 20	-
CD56	-
AFP	-
TTF-1	-

Final diagnosis

Cholangiocellular carcinoma with nodal metastasis

- AJCC TNM stage IV A
- Histologic grade G3 (poorly differentiated)


Chemotherapy regimen
Gemcitabine 1,000 mg/m2 D1, D8
Cisplatin 25 mg/m2 D1, D8
3 week cycle
8000
7000
6000
5000
4000
3000
2000
1000
0
7546
872
257
1st CTx.
2nd CTx.
3rd CTx.
4th CTx.
5th CTx.
6th CTx.
7th CTx.
8th CTx.
9th CTx.
CA125


Follow up Abdominal CT

Follow up PET-CT

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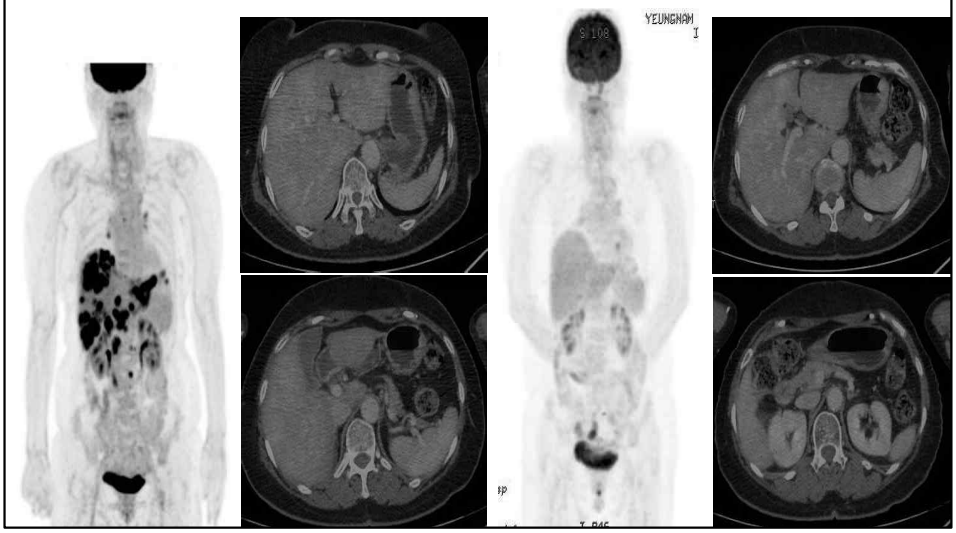
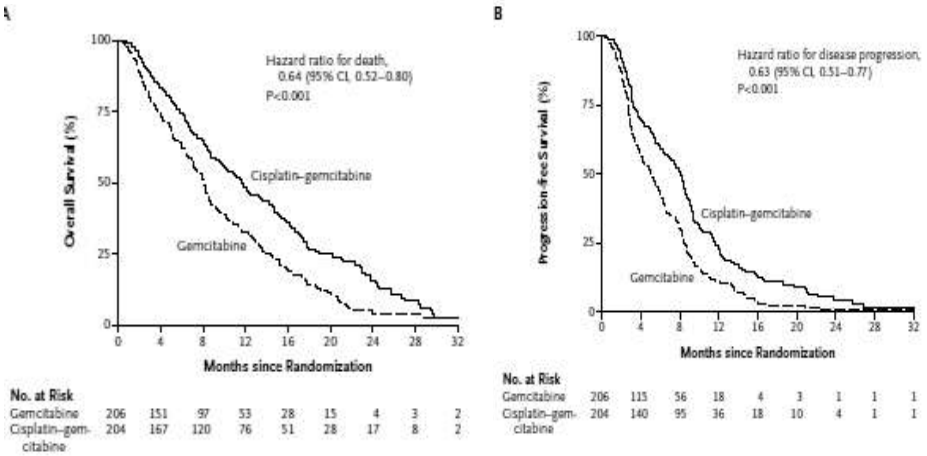


- When to stop chemotherapy ?
- What is the best regimen for 2nd line chemotherapy in CCC ?

Chemotherapy regimen

- **Cisplatin-Gemcitabine group**
  - Cisplatin 25 mg/m^2 + Gemcitabine 1,000 mg/m^2 for D1, 8: every 3 weeks
- **Gemcitabine alone group**
  - Gemcitabine 1,000 mg/m^2 D1, 8, 15: every 4 weeks



NEJM 2010;362(14):1273-1281

Chemotherapy regimen

- **Fluoropyrimidine based regimen**
  - 5-FU + Leucovorin
    Response rate: 32%, Overall survival: 6 months
  - 5-FU + Cisplatin
    Response rate: 10-40%, Overall survival: better than 5-FU alone
  - 5-FU + Capecitabine
    Response rate: 21% for CCC, 40% for GB cancer
    Overall survival: 9.1 months, 12.4 months
  - Combination of taxane, etoposide, streptozotocin, irinotecan
    → no superiority over 5-FU alone

The oncologist 2008;13:415-423