

Session II

## A Case of Gemcitabine Induced Thrombotic Microangiopathy

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### 1. Case presentation

68세 남자가 담도암 간내전이로 진단된 이후 gemcitabine-cisplatin chemotherapy를 시행하였다. 첫번째 항암 이후 5일 뒤 환자는 좌측편마비를 주소로 내원하였고, 내원하여 Rt. ICA의 occlusion 및 brain에 multiple infarction이 확인되었다. 입원 치료 중 진행되는 anemia, thrombocytopenia, serum creatinin 및 LDH 증가가 확인되었으며, PBS에서 schistocyte가 확인되었다.

### 2. Diagnosis

r/o gemcitabine induced Thrombotic microangiopathy

### 3. Therapy and Clinical course

Thrombotic microangiopathy로 진단하여 plasmapheresis를 6차례 시행하였으며, 이후 serum creatinine은 감소되는 추이를 확인할 수 있었다. PLT 및 Hb도 추가적인 감소는 없었다.

### 4. Conclusion

췌장담도암에서 가장 많이 사용되어지는 gemcitabine의 드문 합병증으로서 thrombotic microangiopathy가 있으며, 이를 plasmapheresis를 시행함으로써 치료할 수 있었다.

**Key words:** Gemcitabine, Thrombotic microangiopathy

## REFERENCES

1. Hong, Junshik. Differential diagnosis and treatment of thrombotic microangiopathy syndrome. The Korean Journal of Medicine 94(1):83-88, 2019
2. Izzedine, Hassane, et al. Gemcitabine-induced thrombotic microangiopathy: a systematic review. (2006): 3038-3045.

## M/68

### C.C) Abdominal pain

**P.I)** 지속되는 복통으로 시행한 타병원 복부 CT에서 hepatic mass가 확인되어  
내원함

**P.Hx)** HT / DM / Hepa / Tbc - / - / CHC (치료력 없음) / -

**S.Hx)** Smoking : 1갑/day, 50갑년

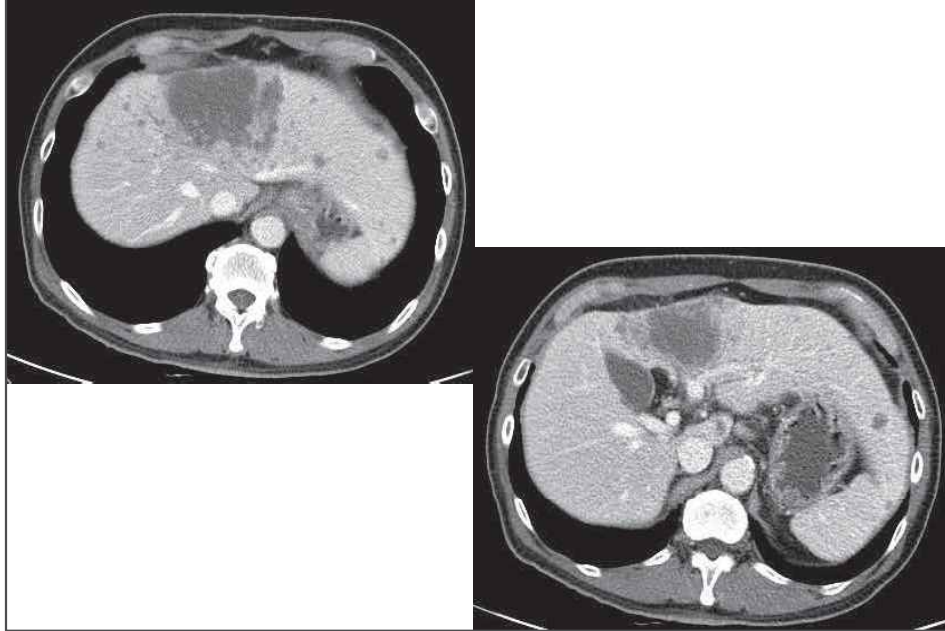
Alcohol : 1병, 주2회, 20년

**F.Hx)** N-S

### Lab finding (19.5.6)

CBC			Biochemistry		
WBC	7,800	/mm <sup>3</sup>	AST/ALT	49/35	IU/L
neutrophil	74.0	%	ALP/LDH	138/420	IU/L
Hb	12.3	g/dL	TB/DB	0.46/0.30	mg/DI
PLT	191	10 <sup>3</sup> /mm <sup>3</sup>	TP/Alb	6.85/3.82	gm/dL
GGT	140	IU/L	BUN/Cr	20.2/0.96	gm/dL
CRP	5.96	mg/dL	TC/UA	125/25.4	gm/dL
PT(INR) /aPTT	12.7(1.07) /26.5	sec	Ca/P	9.63/3.02	gm/dL
CA19-9	6,003	IU/mL	Na/K	136.0/4.72	mEq/L

### 19.4.16 CT abdomen



### 19.5.7 liver biopsy

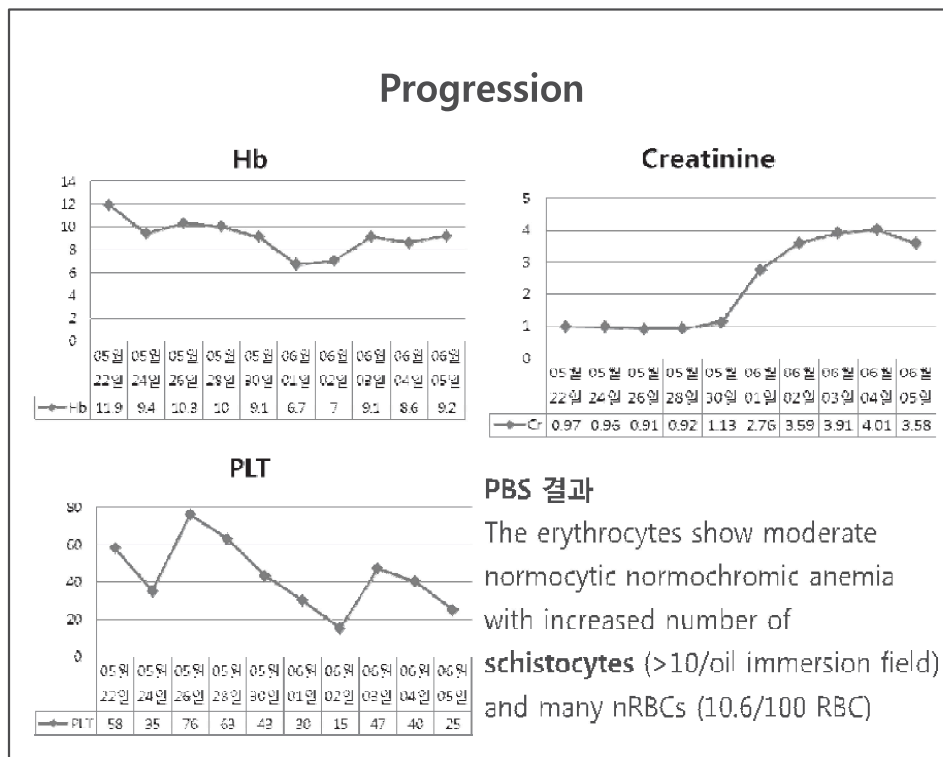
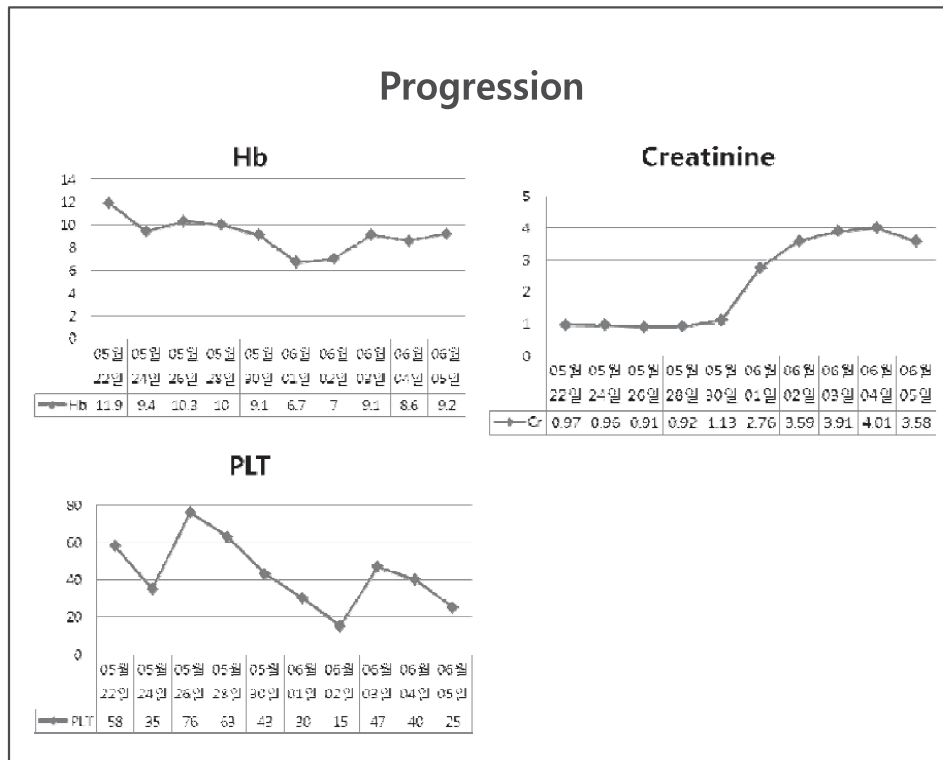
- Liver, site not specified, biopsy :
  - **Adenocarcinoma, moderately differentiated in sclerotic stroma**
  - 1) presence of necrosis: about 50% of tissue.
- # Immunohistochemistry: CK7 - positive in tumor cells
- # Special stain: MT, PAS, RT
- << Addendum 2019.05.23 >>
- # PD-L1 SP263 (Ventana)\* Tumor Expression: 20%

### Progression

- 19.5.17 **Gemcitabine – Cisplatin** (1,000 mg/m<sup>2</sup>, 25 mg/m<sup>2</sup>) C1D1
- 19.5.22 의식저하, 좌측상하지 마비 있어 ER 내원(fever 동반 38.8)
  - CT angiography Brain : **Rt. ICA total occlusion**
  - MR brain : **Multiple infarctions**
    - Rt. MCA territory and left ACA-MCA-PCA border zone, cerebellum
  - **Rt. ICA thrombectomy was done**

### Lab finding (19.5.22)

CBC			Biochemistry		
WBC	2,840	/mm <sup>3</sup>	AST/ALT	48/38	IU/L
neutrophil	66.0	%	ALP	165	IU/L
Hb	12.5	g/dL	TB/DB	0.47/0.35	mg/DI
PLT	58	10 <sup>3</sup> /mm <sup>3</sup>	TP/Alb	6.34/3.29	gm/dL
			BUN/Cr	31.0/0.97	gm/dL
CRP	7.22	mg/dL	TC/UA	89/5.24	gm/dL
PT(INR) /aPTT	12.8(1.07)/ 26.5	sec	Ca/P	8.79/3.51	gm/dL
D-dimer	33.98	ug/mL	Na/K	131.2/4.40	mEq/L
Hematuria	2+		LDH	481	IU/L



## Progression

\* low PLT, schistocytes, elevated LDH, AKI

=>TMA

- r/o gemzar induced

- r/o cancer related

Plan : ADAMTS 13 측정 및 Plasmapheresis 고려

## Progression

ADAMTS 13 activity

노 78

B2075

ADAMTS 13 activity: 51 %

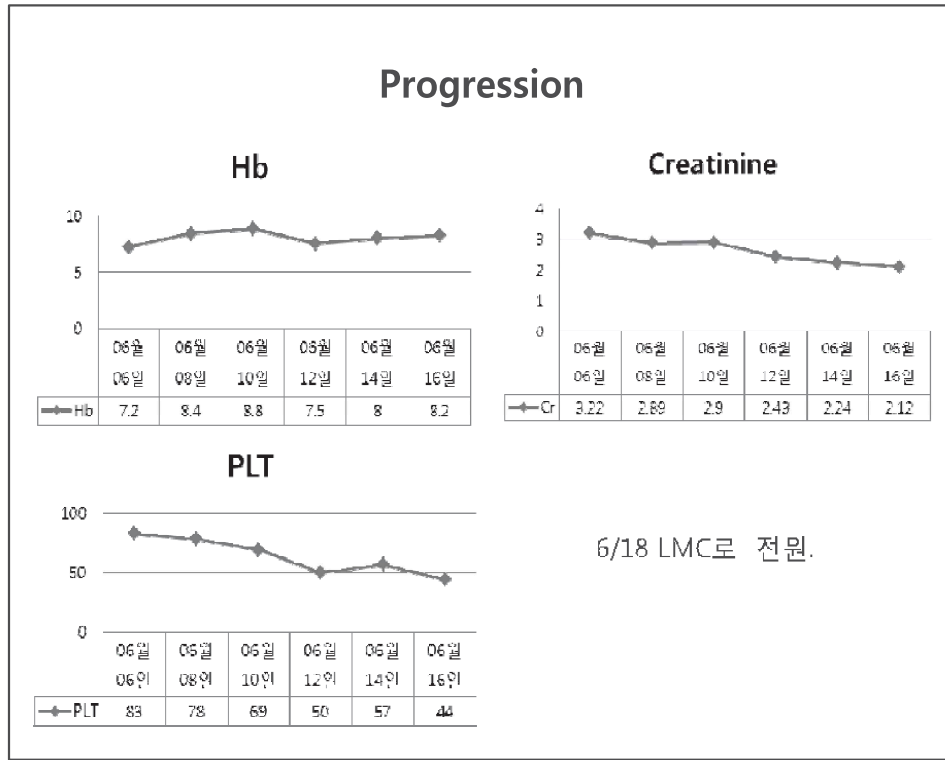
Inhibitor: ND BU/mL  
(Activity 10% 이하만 실시합니다.)

측정방법 : SDS-Agarose gel electrophoresis

Interpretation : severe deficiency <10%  
mild to moderate deficiency 10 ~ 49 %  
normal range 44 ~ 121 % (Ref. 8)

Severe ADAMTS13 deficiency is a specific feature of TTP but cannot exclude the possibility of TTP. Higher remission rate and lower TTP-associated mortality rate is associated with severe ADAMTS13 deficiency. Low ADAMTS13 activity and presence of high inhibitory anti-ADAMTS13 antibody titers after remission increase the risk of relapse of TTP.

Plasmapheresis 6차례: 19년 6월 4일, 5일, 7일, 11일, 13일, 15일



## Case Review

Gemcitabine Induced Thrombotic  
Microangiopathy (TMA)

## TMA

### 1> 정의 : MAHA + Thrombocytopenia

- 진행하는 빈혈 + Reticulocyte 증가 + LDH 증가 + Haptoglobin 감소
- Coombs test 음성
- PBS에서 분절적혈구 관찰

### 2> 분류

- TTP, STEC-HUS, Atypical HUS

- **Secondary TMA:** 악성종양, 약제(항암제(quinine계, gemcitabine, oxaliplatin), 항생제 및 면역억제제(cyclosporine, tacrolimus)), 임신, 고형장기이식, 조혈모세포이식, 각종 바이러스 감염이나 폐렴구균 감염 등.

### 3> 검사

- 분변 다중 PCR 검사(STEC-HUS), ADAMTS 13 activity (후천성 TTP), 보체 검사(aHUS)

## Gemcitabine-associated TMA

- 1994년에 처음 보고
- 유병률 : 0.015-0.4%
- 기전은 뚜렷하지 않고 종양에 의한 것인지 Gemcitabine에 의한 것인지 구분하기 어렵다.
- dose dependent, however, it can occur in first expose
- 1 day to several months, mean time 6-8 months
- 증상 : anemia, thrombocytopenia, LDH상승, proteinuria/hematuria , neurological signs, 혈압상승, dyspnea, 전신부종  
=> **careful evaluation, discontinuation of gemcitabine**
- 치료 : Gemcitabine 중단, Steroid, 투석, FFP, Plasmapheresis, Rituximab, Eculizumab
- mortality rates : 40-90%