

## INTRODUCTION

Encephalopathy is a rare serious side effect related with 5-Fluorouracil. Pathophysiology is unclear. Manifestation included alteration of consciousness, confusion, and seizure. We reported a 10-case serie of 5-FU induced encephalopathy.

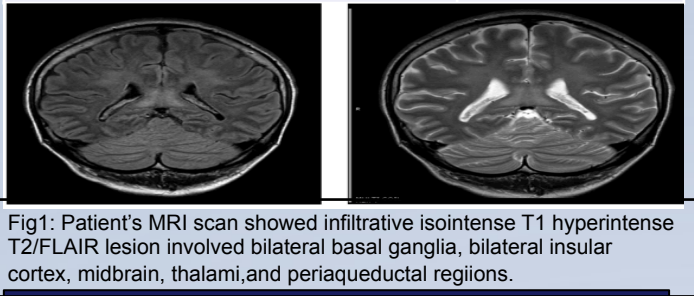
## METHODS

This is a retrospective report that were reviewed between January 2015 to January 2017 from medical record.

## RESULT

Four patients presented with severe neurological symptoms such as status epilepticus, left hemiparesis or lost of consciousness. All patients developed wide gap acidosis (median anion gap = 20.93 mmol/L) with declining of kidney function. Median time presenting symptoms was 2 days. At the time of presenting symptom, 7 out of 10 patients developed hyperammonemia (median NH<sub>3</sub> = 252 μmol/L ) normal thiamine level in 2 patients. All patients completely recovered in 1 day. Eight patients were treated with thiamine injection and 5 patients treated with lactulose. Ammonia level was decreased to normal level at the time of recovery. Rechallenging 5-FU was performed in 5 patients, only one patient had the recurrent symptoms, then the physicians decided to change the chemotherapy regimen afterward. Three patients had the MRI brain scan showed the characteristics of encephalopathy.

PATIENT CHARACTERISTIC	
Characteristic	N=10 ( % )
Median age	61.5
Range	14–78
Female Sex	5( 50 )
Median BSA ( mg / m <sup>2</sup> )	1.63
Cancer type	
Colon cancer	4 ( 40 )
Gastric cancer	3 ( 30 )
Nasopharyngeal cancer	3 ( 30 )
Stage	
II	1 ( 10 )
III	3 ( 30 )
IV	6 ( 60 )
Setting	
Adjuvant	4( 40 )
Palliative	6( 60 )
Chemotherapy regimen	
mFOLFLOX6	7 ( 70 )
Cis+5FU	3 ( 30 )
Mean 5FU dose at event( mg / m2 ) +SD	2507



## CONCLUSIONS

This is a huge serie report of 5-FU induced encephalopathy. Hyperammonemia, wide gap acidosis, and declining of kidney function in every patient which might happen from abnormal drug metabolism. Polymorphisms of drug transporter genes needed to be explored.

Fluorouracil induced encephalopathy: List of reported cases												
Case	Sex, Age (yr)	U/D Cancer	Chemotherapy regimen	Onset: cycle, day	Time to resolve	HCO3	Scr, Delta Cr	NH3 (mcg/dl)	Thiam aime	Clinical manifestation	Treatment	Rechallenge, Outcome
1	F, 59	Gastric	mFOLFOX6	5,2	3	16.2	0.73, +0.27	381	N/A	Alteration of consciousness, hippus, left gaze preference	Vit.B12 Lactulose	No
2	M, 42	NPC	Cisplatin + 5-FU	1,5	2	19.5	1.04, +0.31	25	1.07	Alteration of consciousness, slurred speech, agitation	Vit.B12	Yes Successful
3	M, 63	NPC	Cisplatin + 5-FU	1,5	1	15.8	1.7, +0.52	252	1.12	Confusion	Vit.B12 Lactulose	Yes Successful
4	M, 14	CRC	mFOLFOX6	1,2	2	14.3	0.91, +0.5	129	N/A	Status epilepticus	Vit.B12	No
5	F, 55	NPC	Cisplatin + 5-FU	3,5	1	14	3.18, +1.83	N/A	N/A	Alteration of consciousness, left hemiparesis	Vit.B12	No
6	F, 65	CRC	mFOLFOX6	3,2	1	21.1	1.19, +0.4	588	N/A	Alteration of consciousness, confusion, left hemiparesis	Vit.B12 Lactulose	Yes Successful
7	M, 78	CRC	mFOLFOX6	1,2	1	8.7	2.13, +0.54	N/A	N/A	Confusion, flapping tremor	No tx	Yes Failed
8	M, 60	Gastric	mFOLFOX6	1,2	1	18.6	1.27, +0.39	316	N/A	Oral automatism, inattention, slow speech, disorientation	Vit.B12 Lactulose	Change to Capecitabine, Successful
9	F, 77	Gastric	mFOLFOX6	1,3	1	12.7	0.85, +0.13	49	N/A	Loss of consciousness	Lactulose	No
10	F, 71	CRC	mFOLFOX6	1,2	1	7.7	1.15, +0.12	N/A	N/A	Confusion, slow response	Vit.B12	Yes Successful

## REFERENCES

1.Yi HJ, Hong KS, Moon N, et al. Acute Hyperammonemia Encephalopathy after 5-Fluorouracil based Chemotherapy. Ann Surg Treat Res. 2016;90(3): 179-182.

2. Kwon KA, Kwon H-C, Kim MC, et al. A Case of 5-Fluorouracil Induced Encephalopathy. Cancer Res Treat. 2010;42(2): 119-120.