Clinical Pathologic Conference
2013-03-02

General information:	Presented by: 長庚大學醫學生 陳昱廷 66832、廖晉億 66864、方琬云 66976、呂庭毅 66884
Gender: female	Discussed by:
Age: 19 y/o	血液腫瘤科　湯崇志醫師 68105
Occupation: student	胸腔內科　高國晉醫師 68070
Race: Taiwanese	胃腸肝膽科　黃建豪醫師 66128
Marriage: single	腎臟科　阮國彰醫師 66147
	感染醫學科　劉仕偉醫師 66160
	一般外科　詹昆明醫師 68197
	影像診療科　陳煥武醫師 65762
	病理科　莊文郁醫師 65832
	Moderator: 解剖病理科 孫建峰醫師 65837

Date of admission: 2102-Dec-01

Chief complaint: Right upper quadrant pain of abdomen for 4 days

Brief history:

The 19 year-old female who was quite well without active systemic disease presented with gradually onset but progressive RUQ pain for 4 days. Fever up to 38°C with chills accompanied nausea, vomiting and icteric appearance were also noted at that time. But there was no association with diarrhea. She visited Keelung emergency department due to progressive RUQ pain, and acute cholecystitis was impressed by the findings of physical examination and laboratory data. An abdominal CT scan was arranged which disclosed a distended and thicken gall bladder without stone inside, prominent lymphadenopathies and marked splenomegaly with multiple hypodense lesions. The patient underwent laparoscopic cholecystectomy and lymph node biopsy on 02-Dec-2012 and admitted to ward after operation. During admission, her fever and jaundice was in progression, and renal function as well as hemogram (pancytopenia) deteriorated. She was intubated due to respiratory failure and unstable hemodynamic status, and she underwent hemodialysis (CVVHD) due to severe metabolic acidosis induced by acute kidney injury. Hypofibrinogenemia, hyperferritinemia and hypertriglyceridemia were also detected in biochemistry examination. Bone marrow examination showed overt hemophagocytic features. Viral serology examination showed positive result for EBV and Rota virus but negative result for CMV, HAV, HBV and HCV. Based on above findings that the diagnosis of EBV-associated hemophagocytic lymphohistiocytosis (HLH) was made, intravenous immunoglobulin (IVIG) was administered to the patient. Because of rapidly downhill clinical condition, she then was transferred to Linko CGMH on 15-Dec-2012.

Past history:
Recent travel history: nil
Smoking: nil
Alcohol: nil
Operation history: nil
Current medication: nil
Systemic disease:
1. Hyperthyroidism diagnosed 5 years ago. OPD followed.
2. HTN: nil
3. DM: nil

Allergy: Methimazole

Family history: Identical twin sister- hyperthyroidism

Physical examination:

T: 36°C, P: 105/min, R: 16/min, BP: 98/55 mmHg

General appearance: ill-looking

Consciousness: E4V5M6

HEENT: Sclera: icteric
Conjunctiva: not pale
Oral: no ulcer, no thrush

Neck: supple, no lymphadenopathy, no jugular vein engorgement, no enlarged thyroid

Heart: regular heart beat without audible murmur

Chest: Smooth pattern and symmetric expansion
No use of accessory muscle
Clear breathing sounds

Abdomen: soft and flat, no superficial vein
Liver: impalpable. Spleen: 4 fb below LCM
Tenderness at RUQ. Murphy's sign (+)

Extermities: freely movable, no edema

Skin: no petechial or ecchymoses

Date	Hb	Hct	MCV	PLT	WBC	Seg	Lym	Mono	Eos	Baso	a-lym
12/01	13.8	41.4	85.2	46	2800	64	26	9	0	0	1
12/17	9.1	27.0	81.3	21	2800	44	6	3	1	0	33

Laboratory data:

12/01 PT: 12.4/10.8, INR 1.1. APTT: 37.1/28.3

12/15 PT: 16.4/11.2, INR 1.5 APTT: 48.5/27.4. Fibrinogen: 70 mg/dl

Date	Cr	ALT	AST	Bil-T	Bil-D	ALKP	R-GT	Ca	Na	K	UA	Sugar
12/01	0.75	137	60	9.0	4.9	179	-	-	132	3.9	6.8	109
12/15	2.08	182	350	21.7	10.4	463	325	7.9	140	3.1	10.2	-

12/07 TG: 635 mg/dl. Ferritin: 4303.9 ng/ml. LDH: 1183 U/L

12/05 EBEA Ab: (+), EBNA Ab: (+), EB VCA IgG: (+), EB VCAM: (+)

12/17 HTLV-1: negative

Date	12/17	12/31	1/21
EBV-DNA (copies/ml)	>2000000	4860	4300

12/27: Blood culture: Candida krusei

Sputum culture: Acinetobacter sp-MDR strain

12/30: Tip culture: Enterococcus faecium-VRE

Course and treatment:

Steroid (dexamethasone) was promptly initiated when the patient transferred to ACU (Linko) and etoposide was subsequently given on 18-Dec-2012 for treatment of HLH. In addition, 4 cycles of plasma exchange was arranged since 17-Dec-2013. After the final diagnosis was confirmed, chemotherapy with CVOP (cyclophosphamide, etoposide, vincristine and prednisone) was started on 09-Jan-2013. The patient developed tumor lysis syndrome and was treated with Rasburicase twice. The patients got temporary improvement in hepatic, renal, hematological and pulmonary function but also had various infection episodes after treatment. Although she was aggressively treated and supported by blood transfusion, G-CSF, antibiotics, mechanical ventilator and hemodialysis, she died on 29-Jan-2013 due to disease progression.

Image study: to be presented

Pathology: to be presented

Points for discussion:

1. How to diagnose and treat HLH?
2. What is the role of EBV in pathophysiology of this patient's disease?