

## Clinicopathological conference

วันที่ 7 มิถุนายน 2555

อายุรแพทย์ อ.พญ. สุนิสา พัชรตระกูล

รังสีแพทย์ อ.พญ. น้ำผึ้ง นาการุณอรุณโรจน์

Diagnostician: to be announced

ผู้ป่วยหญิงไทยคู่ อายุ 62 ปี อาชีพทำสวนผลไม้ ภูมิลำเนาอำเภอเมือง จังหวัดนครศรีธรรมราช ปัจจุบันกรุงเทพมหานคร

ครั้งนี้เป็น 1<sup>st</sup> admission ที่โรงพยาบาลจุฬาลงกรณ์

ประวัติได้จากผู้ป่วย,ญาติ และเวชระเบียน เชื้อถือได้

**Chief complaint:** ท้องบวมโตมากขึ้น 6 เดือนก่อนมาโรงพยาบาล

### Present illness

12 เดือนก่อนมาโรงพยาบาล เริ่มมีอาการแน่นท้องบริเวณลิ้นปี่ ไม่ร่าวไปไหน รับประทานอาหารได้น้อยลง รู้สึกอึดเร็ว อ่อนเพลีย ไม่มีไข้ ไม่มีตัวตาเหลือง มีอาการชาที่ขาทั้งสองข้างบริเวณใต้เข่าและฝ่ามือทั้งสองข้างถึงข้อมือ มีอาการชาหน้าขา ไม่มีอาการอ่อนแรง อาการเป็นตลอด ไม่ปวด เดินเองได้

7 เดือนก่อนมาโรงพยาบาล อาการแน่นท้องเป็นมากขึ้น น้ำหนักลด ไปตรวจที่ รพ.เอกชน ได้ทำ

CT –whole abdomen with contrast

Findings: The study reveals normal size and attenuation of the liver. There is a small cyst at segment 2, diameter about 0.9cm. The portal vein is patent. No dilatation of the IHD and CBD in noted. The gall bladder shows thin wall with tiny gallstones. The pancreas and both adrenal glands appear normal. Multiple enhancing lymphadenopathies at periportal and pancreatic head are found. The two largest nodes are diameter about 1.7 and 2.7 cm. Spleen is length about 15.4cm. Both kidneys appear normal in shape and size with no stones or hydronephrosis. The stomach and visualized bowel loops appear normal. There are subcentimeter para-aortic and inguinal lymph nodes. No ascites is detected. The urinary bladder and uterus appear normal. No basal lung nodules are observed. Multiple bone density spots within visualized spine are seen.

IMP: Splenomegaly with periportal and pancreatic lymphadenopathies. Hematologic malignancy cannot be excluded. Small liver cyst. Multiple bone density spots within visualized spine.

ญาติจึงพามาตรวจเพิ่มเติมที่โรงพยาบาลจุฬาฯ

6 เดือนก่อนมาโรงพยาบาล เริ่มมีอาการท้องโตขึ้นเล็กน้อย ขาบวมกดบุ๋ม เป็นตลอดทั้งวัน น้ำหนักลด 10 กิโลกรัมใน 6 เดือน มาตรวจที่โรงพยาบาลจุฬาลงกรณ์ พบต่อมน้ำเหลืองขาหนีบขาโต แพทย์ส่งกล้องทางเดินอาหารส่วนบน และตัดต่อมน้ำเหลืองไปตรวจ

PE: HEENT: not pale, no jaundice

Heart: SEM grade II at AVA, apical impulse at 5<sup>th</sup> intercostals space, mid clavicular line

Lung: normal breath sound

Abdomen: liver span 14cm, splenic dullness on percussion –positive

Shifting dullness – negative

Neurological examination: full EOM. Motor grade V all except hip flexion grade IV both

Intact pinprick sensation. Finger to nose test –positive

Lymph node: right groin node 3 cm, rubbery, not tender

CBC: Hb 15.3 g/dl, HCT 47.2%, MCV 81.1 fl, RDW 15.3%, WBC 7,490 cells/mm<sup>3</sup> (N 67.5%, L 21%)

Platelet 596,000 cells/mm<sup>3</sup>

Prothrombin time 13.20 sec (control 12.2 sec), INR 1.08

Activated partial thromboplastin time 27.4 sec (control 27.0sec)

LFT: Total protein 8.2 g/dL, albumin 2.9 g/dL, total bilirubin 0.35 mg/dL, direct bilirubin

0.13 mg/dL, SGOT 12 U/L, SGPT 8 U/L, ALP 135 U/L

BUN 25 mg/dl, Cr 0.97 mg/dl

UA: yellow, Sp.gr 1.010, PH 6.0, protein 2+, glucose –negative, ketone – negative, WBC 0-1 cells/HPF,

RBC 2-3 cells/HPF

24hr protein urine 998.3 mg/24hr, 24hr urine creatinine 0.61 g/24hr, volume 1490.0 ml

#### Lymph node biopsy

Gross Examination: Two pieces of fibrofatty tissue measure 2.5x2x1 and 2.8x0.7x0.6 cm.

Microscopic examination: Section unveils the enlarged lymph node exhibiting sinus histiocytic hyperplasia and plasma cell hyperplasia forming medullary hyperplasia with some lymphoid follicles and monocytoid hyperplasia. The perinodal adipose tissue shows focal foreign-body granulomas and focal fibrosis with an organizing hematoma. The histiocytes in the sinuses show erythrophagocytosis.

Pathological diagnosis: reactive lymphoid, plasmacytic and histiocytic hyperplasia of the lymph nodes. Focal fibrosis and organizing hematoma with foreign body inflammatory reaction. No malignancy seen.

EGD: stomach, U-tern, pylorus, duodenal bulb: normal

4 เดือนก่อนมาโรงพยาบาล มาตรวจตามนัด มีอาการท้องบวมโตมากขึ้น ชาบวมกดบุ๋ม ตรวจร่างกายพบ ascites

FT4 0.79 ng/dl (0.8-1.8), FT3 1.55 pg/ml (1.6-4.0), TSH 5.84 uIU/ml (0.3-4.1), morning cortisol 2.4 ug%

Repeat lab: FT4 0.94 ng/dl, TSH 5.05 uLI/ml, morning cortisol 19.8 ug%, ACTH 93.9 pg/ml (0-71), FSH 23.6 IU/l (1.6-9.3), LH 30.2 IU/l (2.4-9.3), prolactin 21.9 ng/ml (3.0-25.0)

Colonoscopy: Anus: Internal hemorrhoids without any evidence of active bleeding

Rectum: normal

Sigmoid colon: one diverticulum at sigmoid colon without evidence of bleeding or inflammation

Descending, transverse and ascending colon: normal

Cecum: normal

Terminal ileum: normal

CBC: Hb 14.3 g/dl, HCT 44.2%, MCV 82.6 fl, RDW 15.7%, WBC 8,710 cells/mm<sup>3</sup> (N 72.6%, L 19.3%)

Platelet 477,500 cells/mm<sup>3</sup>

Prothrombin time 14.50 sec (control 11.8 sec), INR 1.22

Activated partial thromboplastin time 30.30 sec (control 28.6 sec)

เนื่องจากมี Hepatosplenomegaly with thrombocytosis จึงมีการตรวจ investigations เพิ่มเติม

Bone marrow biopsy: cell: fat = 50:50, myeloid: erythroid ratio= 2:1

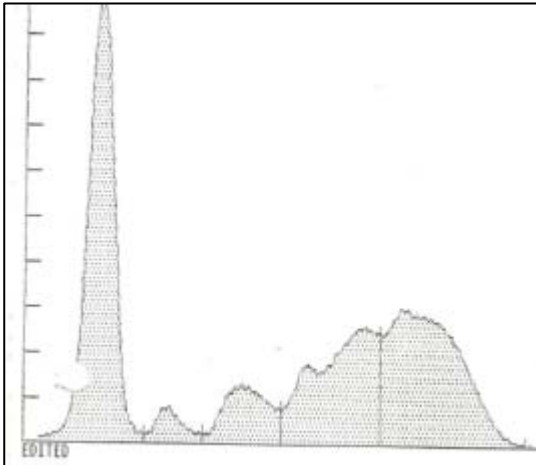
Erythroid morphology: unremarkable; myeloid morphology: unremarkable

Megakaryocyte: mildly increased; megakaryocyte morphology: unremarkable

Diagnosis: Normocellular trilineage marrow. No histological evidence of myeloproliferative neoplasm and dysplasia

Chromosome study: Karyotype: 46, XX[20], interpretation: normal female karyotype

Serum electrophoresis:



| Fraction  | %    | g/dl | g/dl | Range   |
|-----------|------|------|------|---------|
| ALBUMIN   | 36.2 | 2.7  | lo   | 3.2 5.0 |
| ALPHA 1   | 3.0  | 0.2  |      | 0.1 0.4 |
| ALPHA 2   | 8.2  | 0.6  |      | 0.6 1.0 |
| BETA      | 22.2 | 1.7  | hi   | 0.6 1.3 |
| GAMMA     | 30.3 | 2.3  | hi   | 0.7 1.5 |
| Total SPE |      | 7.5  |      |         |

JAK2 V-167F mutation: positive

วินิจฉัยโรคเป็น Essential thrombocytosis R/O hepatic vein thrombosis ได้ยา hydroxyurea (500) 1tab po OD และทำ

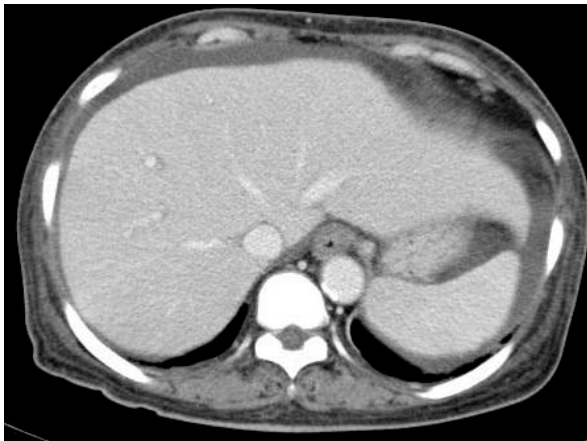
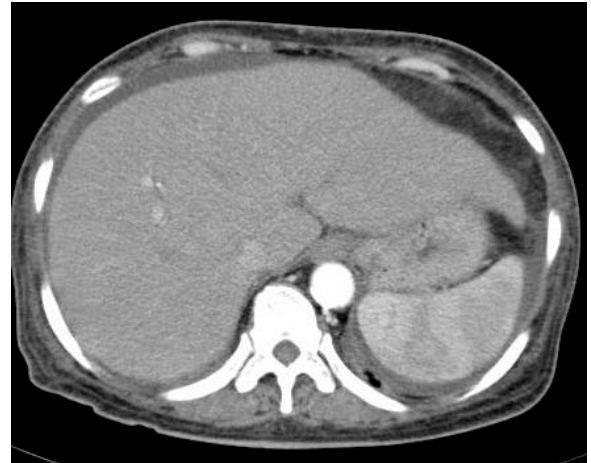
CT whole abdomen

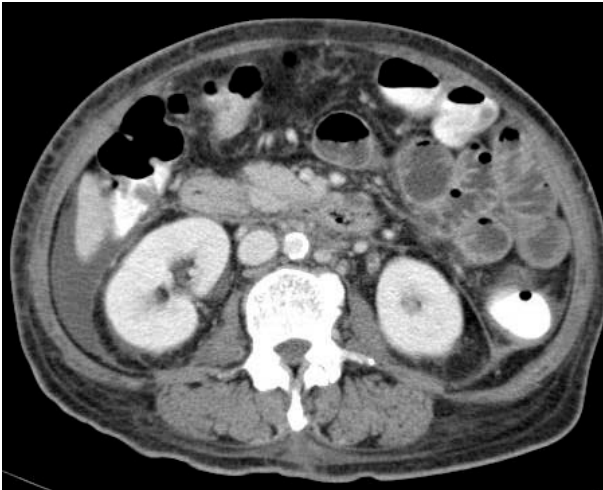
- Generalized subcutaneous edema.
- The liver is slightly enlarged. There is 1.3x0.9 cm non-enhanced hypodense nodule at the superolateral segment of left lobe liver. Bile duct not dilated. Portal veins, hepatic veins and IVC appear normal. Few small gall stones are noted.
- The spleen is slightly enlarged.
- The pancreas, adrenal glands, kidneys, urinary bladder, uterus and ovary appear normal.
- Massive amount of ascites. Bilateral minimal perinephric fluid.
- There are numerous enlarged lymph nodes at the bilateral superior anterior diaphragmatic, right superior posterior diaphragmatic, gastrohepatic, perisplenic, peripancreatic, periportal, gastroduodenal, celiac, aortocaval, para-aortic, retrocaval, bilateral inguinal lymph regions. The sizes of nodes are subcentimeter up to 2.5 cm in short axis.
- There is diffuse osteoblastic bone change at the sternum, bilateral ribs, thoracolumbar vertebrae, bilateral pelvic bone, sacral and bilateral proximal femurs.
- The included basal lungs reveal minimal amount of bilateral pleural fluid

IMP

- generalized subcutaneous edema

- slight hepatosplenomegaly, massive ascites
- numerous enlarged anterior and posterior superior diaphragmatic, abdominal retroperitoneal, bilateral iliac and bilateral inguinal lymph nodes
- diffuse osteoblastic change





#### Echocardiogram

- Normal LV size and systolic function. LVEF = 84% by Teicholtz's method. No RWMA. Mitral inflow study showed pseudonormalized pattern with mildly elevated LV filling pressure; E/e'=13. Medial e'=5.1cm/s.
- Normal RV size and systolic function. Mildly thickened AV without restricted opening. No AS/AR.
- Structurally normal TV and PV. Mild TR and mild PR. Mildly dilated NPA. No evidence of portal hypertension. Estimate PAP = 38/15 mmHg
- No exaggerate respiratory variation of MV and TV inflow. No septal bouncing. No diastolic reversal flow of hepatic vein.
- No pericardial effusion. No intracardiac thrombus.

IMP: Good LV systolic function. Moderate diastolic dysfunction. Mild TR. No evidence of constrictive pericarditis.

#### Work up abdominal paracentesis

Body fluid: protein 4.2 g/dl, Albumin 1.8 g/dl (SAAG 3-1.8 =1.2)

WBC 70 cells/mm<sup>3</sup> (PMN 3%, Mo 97%, RBC 11,800cell/mm<sup>3</sup>)

PCR TB – negative, cytology: negative for malignancy cells

2 สัปดาห์ก่อนมาโรงพยาบาล มาตรวจตามนัดที่แผนกผู้ป่วยนอก ยังมีอาการท้องบวมโต ชาหน้าบริเวณเท้าและมือ ทั้งสองข้าง ตรวจร่างกายพบ ต่อม้ำเหลืองโตที่บริเวณ รักแร้ด้านซ้ายขนาด 3เซนติเมตร

#### Axillary lymph node biopsy

Microscopic examination: Section exhibiting sinus histiocytosis, increase plasma cells and lymphoid follicles with Castleman's disease like features.

Diagnosis: reactive lymphoid hyperplasia of the lymph node with Castleman's disease like features (mixed Hyaline vascular type and plasma cell type). No malignancy. No granuloma.

Nerve conduction velocity

**NCS:** Prolonged DLS, low SNAP amplitude and marked slow SNCV of all median, ulnar and sural nerves

Prolonged DML, low CMAP amplitude with wide duration of waveform and marked slow MNCV of both median, ulnar, common peroneal and tibial nerves.

**Needle EMG:** Increased insertional activity and spontaneous discharges was found in both Gastrocnemius and left FDI muscles.

Reduced recruitment pattern was found in all tested muscles.

**Conclusion:** There is electrophysiological evidence of symmetrical sensory-motor, myelin greater than axon, polyneuropathy of both lower and upper extremities.

| Nerve / Sites                  | Onset ms | Pk-Pk Amp $\mu$ V | Peak Amp. $\mu$ V | Distance cm | Velocity m/s | Lat. 2 ms |
|--------------------------------|----------|-------------------|-------------------|-------------|--------------|-----------|
| <b>R MEDIAN - Digit II</b>     |          |                   |                   |             |              |           |
| Wrist                          | 4.5      | 14.3              | 9.8               |             |              | 6.20      |
| Elbow                          | 10.9     | 9.7               | 6.5               | 19          | 30.2         | 12.95     |
| <b>L MEDIAN - Digit II</b>     |          |                   |                   |             |              |           |
| Wrist                          | 4.1      | 19.8              | 11.7              |             |              | 5.15      |
| Elbow                          | 9.9      | 6.0               | 6.3               | 18          | 31.0         | 11.55     |
| <b>R ULNAR - Digit V</b>       |          |                   |                   |             |              |           |
| Wrist                          | 3.2      | 34.1              | 21.0              |             |              | 4.20      |
| B.Elbow                        | 8.8      | 14.8              | 7.6               | 21          | 36.8         | 10.05     |
| <b>L ULNAR - Digit V</b>       |          |                   |                   |             |              |           |
| Wrist                          | 3.2      | 28.0              | 17.3              |             |              | 4.20      |
| B.Elbow                        | 8.5      | 19.8              | 9.4               | 21.5        | 40.2         | 10.15     |
| <b>R SURAL - Lat Malleolus</b> |          |                   |                   |             |              |           |
| Calf                           | 3.5      | 5.2               | 10.6              | 10          | 28.6         | 4.40      |
| <b>L SURAL - Lat Malleolus</b> |          |                   |                   |             |              |           |
| Calf                           | 3.2      | 1.2               | 7.9               | 10          | 31.7         | 3.90      |

| Nerve / Sites                | OnsetLat ms | Peak Amp mV | Area mVms | Distance cm | Cond.Vel m/s |
|------------------------------|-------------|-------------|-----------|-------------|--------------|
| <b>R MEDIAN - APB</b>        |             |             |           |             |              |
| Wrist                        | 7.30        | 4.9         | 29.1      |             |              |
| Elbow                        | 13.70       | 3.0         | 19.9      | 19          | 29.7         |
| <b>L MEDIAN - APB</b>        |             |             |           |             |              |
| Wrist                        | 5.70        | 6.7         | 30.4      |             |              |
| Elbow                        | 11.45       | 5.3         | 27.4      | 18          | 31.3         |
| <b>R ULNAR - ADM</b>         |             |             |           |             |              |
| Wrist                        | 4.25        | 4.4         | 20.4      |             |              |
| B.Elbow                      | 10.30       | 3.4         | 21.0      | 21          | 34.7         |
| <b>L ULNAR - ADM</b>         |             |             |           |             |              |
| Wrist                        | 4.00        | 5.0         | 22.4      |             |              |
| B.Elbow                      | 9.40        | 4.0         | 22.5      | 20          | 37.0         |
| <b>L COMM PERONEAL - EDB</b> |             |             |           |             |              |
| Ankle                        | 5.85        | 1.4         | 6.7       |             |              |
| Fib Head                     | 19.60       | 1.0         | 5.7       | 31          | 22.5         |
| <b>R COMM PERONEAL - EDB</b> |             |             |           |             |              |
| Ankle                        | 6.55        | 1.4         | 6.7       |             |              |
| Fib Head                     | 18.80       | 1.3         | 7.3       | 31          | 25.3         |
| <b>L TIBIAL (KNEE) - AH</b>  |             |             |           |             |              |
| Ankle                        | 6.30        | 1.2         | 4.8       |             |              |
| Knee                         | 20.85       | 0.7         | 2.1       | 34          | 23.4         |
| <b>R TIBIAL (KNEE) - AH</b>  |             |             |           |             |              |
| Ankle                        | 7.35        | 1.9         | 6.5       |             |              |
| Knee                         | 18.70       | 0.6         | 2.7       | 32          | 28.2         |

| EMG Summary Table   | Spontaneous |      |      |      |      | MUAP |      |     | Recruitment |
|---------------------|-------------|------|------|------|------|------|------|-----|-------------|
|                     | IA          | Fib  | PSW  | Fasc | H.F. | Amp  | Dur. | PPP | Pattern     |
| L. TIB ANTERIOR     | N           | None | None | None | None | N    | N    | N   | Reduced     |
| L. GASTROCN (MED)   | 2+          | None | None | None | None | N    | N    | N   | Reduced     |
| R. GASTROCN (MED)   | 2+          | 1+   | 1+   | None | None | N    | N    | N   | Reduced     |
| L. FIRST D INTEROSS | 1+          | None | 1+   | None | None | N    | N    | N   | Reduced     |

Today แพทย์นัดมานอนโรงพยาบาลเพื่อทำ peritoneoscope, intra-abdominal lymph node biopsy

#### Past history

- DM type2 no diabetic retinopathy (ตรวจ 2550)เป็นมานาน 20 ปี, good control FBS 140, HbA1C 6.4%
- Hypertension: blood pressure SBP 130-150 mmHg, DBP 70-90 mmHg  
รักษาที่ โรงพยาบาลรัฐบาล
- C- spondylosis c myofascial pain syndrome (วินิจฉัยมา 5เดือน)มีอาการปวดไหล่บริเวณ สะบักสองข้าง
- Herniated Nucleus Pulposus s/p surgery 2552 ที่ รพ.เอกชน หลังผ่าตัดไม่ปวดหลังอีก

#### Personal and social history

- ไม่สูบบุหรี่
- ไม่ดื่มเหล้า
- ปฏิเสธประวัติยาเสพติด/ยาหม้อ/ยาสูกกลอน ปฏิเสธการซื้อยากินเอง

#### Current medications

- Glipizide (5) 2x1 po ac.
- Simvastatin (20) 1x1 po pc.
- Metformin (500) 1x1 po pc.
- Pioglitazone (30) 1x1 po pc.
- Bisoprolol fumarate (5) 1x1 po pc.
- Manidipine (10) 1x1 po pc.
- Amitryptiline (25) 1x1 po hs.
- Furosemide (40) 1x1 po pc.
- Spironolactone (100) 1x1 po pc.
- Vit B1-6-12 1x1 po pc.

#### Physical examination

General appearance: An elderly Thai female patient looked chronically ill.

Vital sign: BT 37.0°C, BP 130/80 mmHg, PR 90 beats/min regular, RR 20/min

HEENT: not pale conjunctiva, anicteric sclera, no neck vein engorge

Lymph node: Multiple subcentimetric posterior cervical lymph node enlargements.

Skin: no rash, no spider nevi, no palmar erythema

Chest: coarse crepitation both lungs, no wheezing, equal breath sounds

CVS: apical impulse at 5<sup>th</sup> ICS, MCL; no heave, no thrill

Normal S1S2, SEM grade II at left upper sternal border

Abdomen: mild distension, active bowel sound

Soft, not tender, no guarding, no rebound tenderness

Liver span 14cm, splenic dullness on percussion: positive

Fluid thrill and shifting dullness: positive

Extremities: pitting edema 3+ both legs, no clubbing of fingers

Neurological examination

Consciousness: E4M6V5

Motor:

Tone: normal tonicity of upper and lower limbs.

Power: Upper left grade III/V, right grade III/V

Lower left grade III/V, right grade III/V

Deep tendon reflex 1+ all

Babinski's sign: dorsiflexion both, Clonus – negative

Sensory: Decrease pinprick sensation at both hands to wrist level

Decrease pinprick sensation at both feet to knee level

Cerebella functions: normal

## Investigations

CBC: Hb 13.4 g/dl, HCT 41.8%, MCV 84.8 fl, RDW 20.6%, WBC 7,230 cells/mm<sup>3</sup> (N 65.3%, L 23.8%)

Platelet 407,000 cells/mm<sup>3</sup>

Prothrombin time 14.90 sec (control 11.8 sec), INR 1.26

Activated partial thromboplastin time 28.7 sec (control 28.6 sec)

Blood smear: normochromic normocytic red cells, anisopoikilocytosis 1+, few polychromosias, normal WBC count and differential, increased platelets with normal size and granularity

UA: Sp.gr. 1.015, PH 5.0, protein 1+, glucose: negative, ketone: negative, RBC 1-2 cells/HPF, WBC 3-5 cells/HPF, Squamous epithelium 3-5 cells/HPF

Iron study: Ferritin 93.4 ng/ml (15-50), Serum iron 35.0 ug/dl (37-145), TIBC 243 ug/dl (228-428)

Chemistry: BUN 34 mg/dl, Cr 1.19 mg/dl, Na 134 mmol/L, K 5 mmol/L, Cl 105 mmol/L, HCO<sub>3</sub> 26 mmol/L

LDH 297 U/L, Uric 9.6 mg/dl, Ca 8.0 mg/dl, PO<sub>4</sub> 4.6 mg/dl

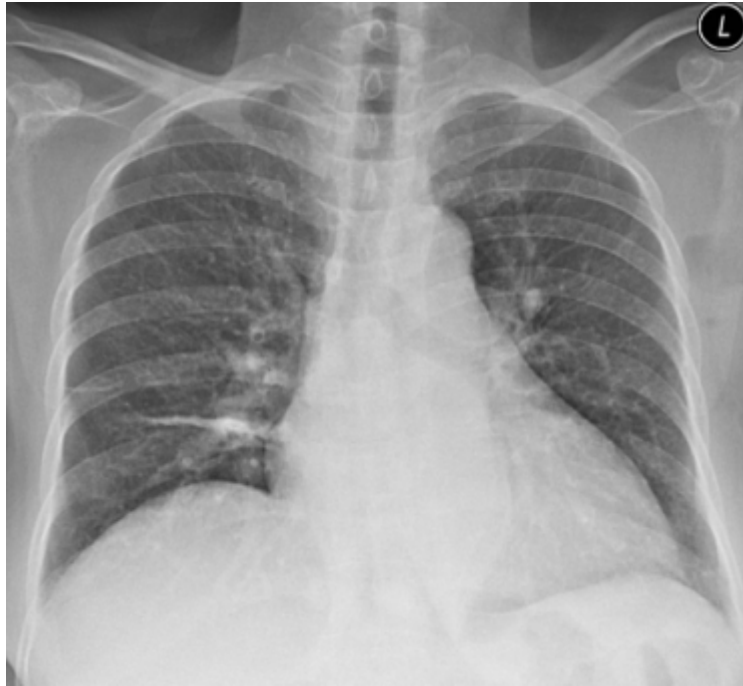
LFT: TP 8.1 g/dl, albumin 2.9 g/dl, TB 0.55 mg/dl, DB 0.22 mg/dl, SGOT 10 U/L, SGPT 6 U/L, ALP 197 U/L

Serology: ANA <80, Anti smooth muscle Ab –negative, HBsAg – negative, anti HBc –negative, anti-HBs –negative

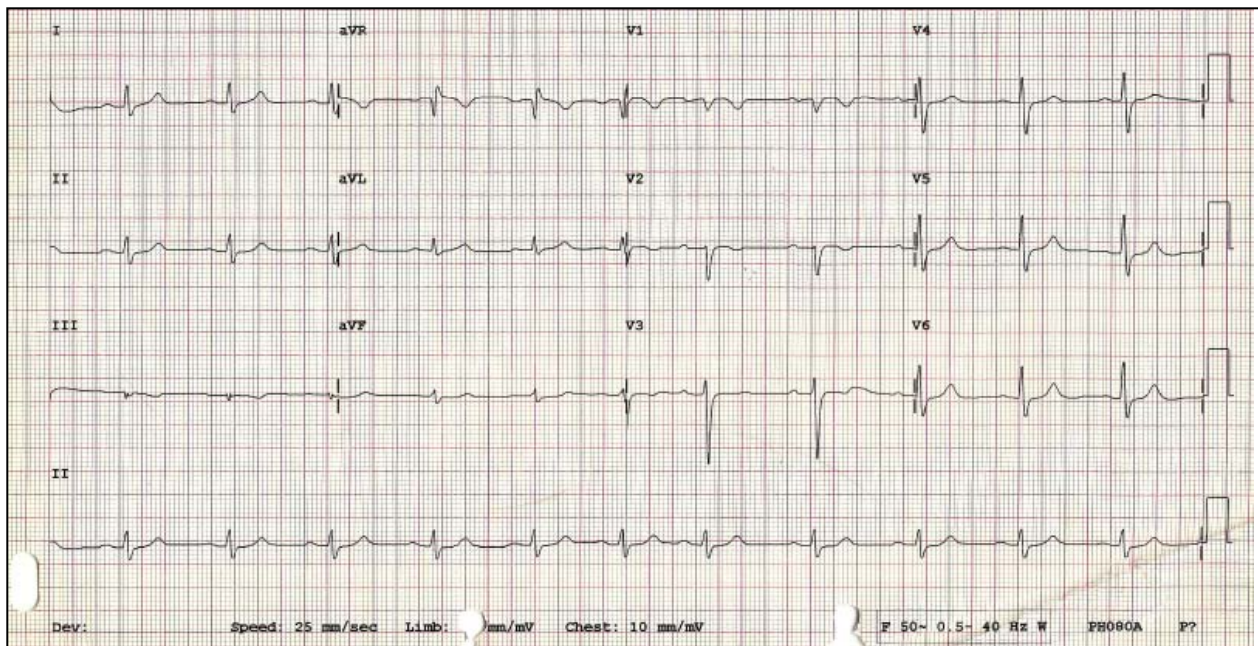
Anti HCV – negative, Anti-HIV – negative

Fibroscan: stiffness 42.8 KPa, IQR 3.4 KPa, success rate 100%

CXR



EKG



Peritoneoscope: no peritoneal nodule, no omental nodule. Macro nodular surface of liver

Normal anterior surface of stomach and small bowel

Normal uterus and ovary

Clear yellow ascites 1,500 ml

### Great omental biopsy

Gross examination: The specimen consists of a yellow omentum tissue measuring 4.2x2.5x0.6 cm sections show yellow brown cut surface.

Microscopic examination: Section show a fibroadipose tissue comprising mature adipocyte admixed with small amounts of inflammatory cell infiltrates. No malignancy is seen on the plane of examination.

Diagnosis: Fibroadipose tissue. No malignancy seen.

1. What are the diagnostic investigations leading to final diagnosis?
2. What is the most likely diagnosis?