Clinicopathological Conference

31 **มีนาคม** 2554

Clinician: ศ. นพ. ธีระวัฒน์ เหมะจุฑา

Radiologist: อ. พญน้ำผึ้ง นำการุณอรุณโรจน์ .

Diagnostician: To be announced

ผู้ป่วยชายไทยคู่อายุ 43 ปี อาชีพรับจ้างเชื่อมเหล็ก ภูมิลำเนาและที่อยู่ปัจจุบัน จ. ลพบุรี นับถือศาสนาพุทธ 1st admission ประวัติได้จากผู้ป่วย ญาติและเวชระเบียน

CC: กลืนลำบาก 2 สัปดาห์ก่อนมาโรงพยาบาล

PI: 15 เดือนก่อนมาโรงพยาบาล มีอาการปวดเมื่อยหลังตรงกลางบริเวณเอวส่วนล่างร้าวไปก้นกบ ปวดมากเวลาก้มหรือทำงานนาน ๆ ไม่มีจุดกดเจ็บ ไม่มีอาการอ่อนแรง ได้ยา piroxicam มาทานจากคลินิก อาการพอทุเลา

10 เดือนก่อนมาโรงพยาบาล อาการเมื่อยหลังยังไม่ดีขึ้น เริ่มมีอาการเมื่อยบริเวณต้นขาสองข้าง รู้สึกขาไม่ค่อยมีแรงทั้งสองข้าง ลุกขึ้นลำบากต้องใช้มือพยุงช่วย เดินได้รองเท้าไม่หลุด ไม่มีแขนอ่อนแรง ปัสสาวะอุจจาระได้ปกติ ยังคงไปทำงานได้ตามปกติ

7 เดือนก่อนมาโรงพยาบาล เริ่มมีอาการเหยียดแขนซ้ายเอื้อมหยิบของไม่ได้ ยกแขนหวีผมไม่ได้ ไม่มีอาการปวดต้นคอ ขายังคงอ่อนแรงเท่า ๆ เดิม กำของได้ไม่หล่น 2 สัปดาห์ต่อมาเริ่มมีแขนขวาอ่อนแรงยกไม่ขึ้น เริ่มเดินได้น้อยลงเพราะรู้สึกเมื่อยต้นขา

4 เดือนก่อนมาโรงพยาบาล มีขาซ้ายบวมตั้งแต่เข่าลงไปถึงปลายเท้า ปวด บวมกดบุ๋ม ไม่แดง เวลายกขาสูงอาการปวดลดลง แขนขาอ่อนแรงมากขึ้น เวลาลุกนั่งต้องมีคนช่วยพยุง ขึ้นบันไดได้ทีละขั้น

2 เดือนก่อนมาโรงพยาบาล ขาซ้ายยังคงบวมเท่า ๆ เดิม มีไข้ต่ำ ๆ เป็น ๆ หาย ๆ มีเหงื่อออกตอนกลางคืน

1 เดือนก่อนมาโรงพยาบาล เริ่มไปทำงานไม่ได้เพราะขาซ้ายบวมมากขึ้น อาการอ่อนแรงเป็นเท่า ๆ เดิม

2 สัปดาห์ก่อนมาโรงพยาบาล เริ่มมีอาการกลืนลำบาก กลืนของแข็งแล้วติด กลืนอาหารเหลว ๆ หรือน้ำได้ กลืนไม่เจ็บ ไม่มีปากเบี้ยว อาการแขนขาอ่อนแรงเท่า ๆ เดิม ไปตรวจที่โรงพยาบาลชัยบาดาล จึงส่งต่อมารักษาต่อที่โรงพยาบาลจุฬาลงกรณ์

น้ำหนักลดลง 13 kg ใน 10 เดือน (86 → 73 kg)

Past history:

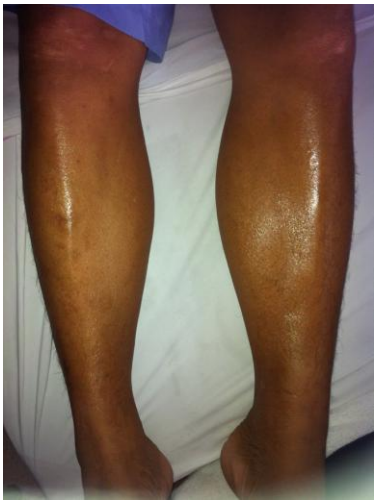
- 4 ปีก่อนมาโรงพยาบาล มีอาการเหนื่อยหอบ หายใจดังวี๊ด ๆ ไปตรวจที่โรงพยาบาล ได้พ่นยาอาการดีขึ้น

Current medications: diclofenac (25) 1 tab po tid pc, Norgesic 1 tab po tid pc, theophyline (200) 1 tab po bid pc, Berodual MDI 1 puff prn

ไม่แพ้ยา

Social history: ไม่สูบบุหรี่ ดื่มสุรา ½ ขวดต่อวัน นาน 20 ปี

Physical examination:



General appearance: A middle-age Thai male, good consciousness

Vital signs: BT 37.2°C, RR 18/min, HR 98 bpm, regular, BP 120/80 mmHg,

O2 sat = 96% (at room air)

BW 55 kg, Ht 170 cm, BMI 19.03 kg/m^2

HEENT: Not pale conjunctivae, no icteric sclerae, no enlarged thyroid gland

Lymph node: No cervical lymphadenopathy

CVS: Apical beat at Lt 5th ICS, 2 cm lateral to MCL, no heave, no thrill, palpable P_2

normal S_1, S_2, loud P_2, no murmurs

Lungs: Trachea in midline, fine crepitation both lower lungs

Abdomen: No distension, normoactive bowel sound; soft, not tender,

no hepatosplenomegaly

Ext: Pitting edema over entire left leg; tenderness over both anterior and anterolateral thighs of left side more than right side; no skin lesion

Leg circumference	Right side (cm)	Left side (cm)
Upper leg	43	49
Lower leg	38	43

Neuro: Consciousness: good orientation

No papilledema, normal retinal venous pulsation; pupils 3 mm BRTL, full EOM, no nystagmus, no facial palsy, normal power of mastigation, gag reflex positive both, tongue fasciculation, no uvula/tongue deviation, no tongue atrophy, normal power of sternocleidomastoid muscles

Temperalis, deltoid, supraspinatus, infraspinatus, pectoralis and buttock muscles atrophy both sides

Lower limb muscles especially left side cannot be evaluated well for muscle mass due to marked swelling of legs

Decreased tone of all muscles, no fasciculation

Motor power	Rt	Lt
Neck flexor/ extensor	IV/IV	
Trapizius	V	V
Rhomboid	V	V
Serratus anterior	III	III
Infraspinatus	III	III
Supraspinatus	II	II
Deltoid	II	II
Biceps	V	V
Brachioradialis	V	V

Triceps	V	V
Wrist flexion/extension	V/V	V/V
Hand grip	V	V
Hip flexion/extension	IV/IV	III/III
Hip abduction/adduction	V/V	V/V
Knee flexion/extension	V/V	V/V
Ankle flexion/extension	V/V	V/V
Inversion/eversion	V/V	V/V
EHL	V	V

DTR: 0 all extremities, BBK plantar flexion, clonus negative

Sensory: Normal pinprick sensation, normal propioception both joint position and vibration

PR: normal sphincter tone

Cerebellum: normnal both vermis and hemispheres

Meningeal irritation signs: no neck stiffness and negative Kernig sign

Laboratory investigations:

CBC: Hb 14.4 g% Hct 43.5%, MCV 90.2 fL, MCH 29.9 pg, MCHC 33.1 g/dl, RDW 15.8%,
WBC 5,230 cells/mm3 (PMN 79.1%, L 13.8%, M 3.1%, E 3.8%, B 0.2%) Platelet 209,000 cells/mm^3

PT 12.4/12.2 sec, INR 1.02, PTT 28.40/27 sec

UA: clear yellow color, pH 7, sp.gr 1.015, protein negative, glucose negative, WBC 1-2/HPF, RBC 0-1/HPF,
squamous cell 0-1/HPF

24-hour urine analysis: protein 0.26 g/24h, creatinine 14 mg/dl, volume 3,230 ml, creatinine clearance 92.4 ml/min

FBG 100 mg/dl, BUN 7 mg/dl, Cr 0.42 mg/dl

Electrolytes: Na 135, K 4.4, Cl 98, HCO3 28 mmol/L

Ca 8.8 mg/dl, Phosphate 4.2 mg/dl (2.7-4.5), magnesium 0.84 mmol/L (0.7-1.07)

LFT: TB 0.34 mg/dl, DB 0.14 mg/dl, AST 268 U/L, ALT 101 U/L, ALP 57 U/L, total protein 9.6 g/dl, albumin 3.1 g/dl

CPK 3,799 U/L (<190), LDH 1,386 U/L (<480)

Stool exam: yellow, WBC 0/HPF, RBC 0/HPF, not found parasite and oval

CSF profile: OP 9 cmH_20, CP 7 cmH_2O
clear, traumatic CSF, RBC 66 cells/mm^3, WBC 1 cell/mm^3 (PMN 0%, mononuclear 100%)
protein 118 mg/dl (15-45), sugar 53 mg/dl (50-80), DTX = 105 mg/dl

Hemoculture - no growth x 2 specimens, urine culture - no growth, CSF culture – no growth

Sputum: gram stain – no organism, AFB and modified AFB: no organism

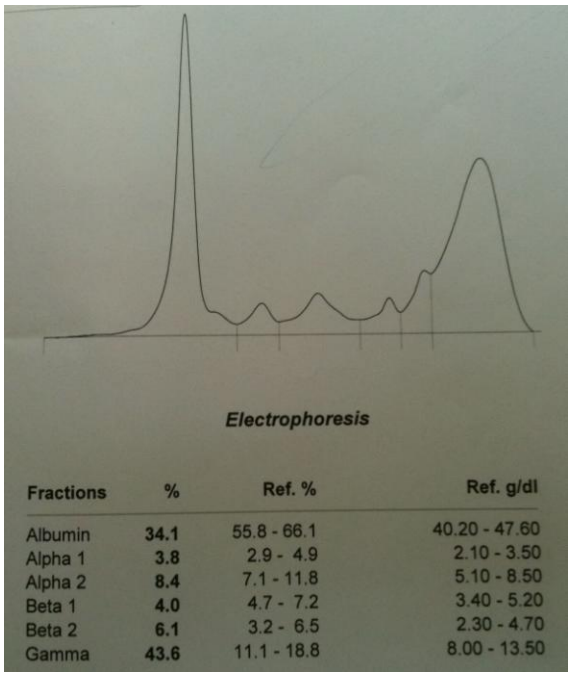
Anti HIV: negative, HbsAg: negative, anti-HBs: positive (1000 mIU/ml), anti-HCV: negative

Cortisol 16.3 µg%, FT4 1.05 ng/dl (0.80-1.80), FT3 2.89 pg/ml (1.60-4.00), TSH 4.850 mU/ml (0.3-4.1)

ESR 71 mm/hr (0-15), D-dimer 3,583 ng/ml (500)

Antinuclear antibody: <80, cytoplasmic staining, Serum cryoglobulin: positive, rheumatoid factor 34.2 IU/ml (<15)

Serum free light chain- kappa 109 mg/L (3.30-19.40), lambda 105 mg/L (5.71-26.30)



Electrophoresis

Fractions	%	Ref. %	Ref. g/dl
Albumin	34.1	55.8 - 66.1	40.20 - 47.60
Alpha 1	3.8	2.9 - 4.9	2.10 - 3.50
Alpha 2	8.4	7.1 - 11.8	5.10 - 8.50
Beta 1	4.0	4.7 - 7.2	3.40 - 5.20
Beta 2	6.1	3.2 - 6.5	2.30 - 4.70
Gamma	43.6	11.1 - 18.8	8.00 - 13.50

IgG 4,360 mg/dL (700-1,600), IgM 174 mg/dL (40-230), IgA 292 mg/dL (70-400), total IgE 478 IU/ml (<100), IgG1 3,300 mg/dL (490-1,140), IgG2 728 mg/dL (150-640), IgG3 178 mg/dL (20-110), IgG4 498 (8-140)

WBC 4,970 cells/mm3, absolute total lymphocyte 611 cells/mm3 (12.3%)

Absolute CD3 177 cells/mm3 (960-2,430) 29% (46.2-82.7)

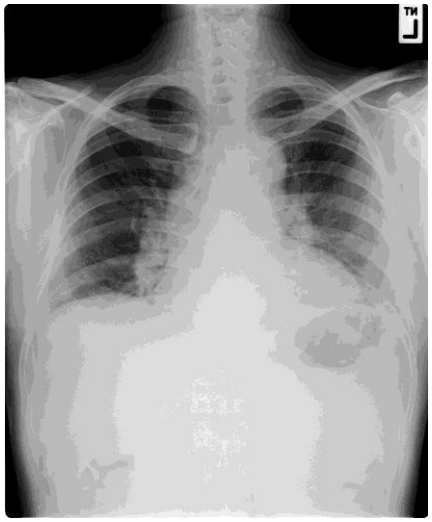
Absolute CD4 110 cells/mm3 (470-1,404) 18% (24.1-50.7)

Absolute CD8 55 cells/mm3 (360-1,250) 9% (17.1-44.6)

%CD 19 (B cell) 57% (7.7-25.4)

%CD56 (NK cell) 13% (3.9-38.5)

CXR:



Cardiomegaly with rapid attenuation of pulmonary vasculature is noted. No pulmonary infiltration or pleural effusion is noted. The mediastinum, diaphragm and bony thorax are intact.

Impression: Cardiomegaly with pulmonary arterial hypertension.

Histopathologic studies:

Bone marrow aspiration:

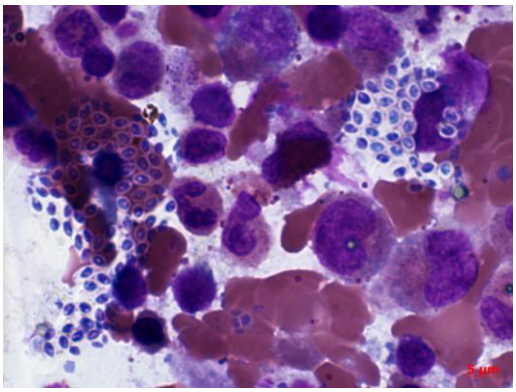
Mild hypercullular marrow, M:E = 2:1, iron 4+, ring sideroblast: negative

Megakaryopoiesis: normal

Granulopoiesis: promyelocyte 10%, myelocyte 22%, metamyelocyte 0%, PMN 51%, eosiniphil 1%

Erythopoiesis: increased

Lymphopoiesis: -



Bone marrow biopsy:

Microscopic examination:

Cellularity: cell:fat ratio = 60:40 myeloid:erythoid ratio = 4:1

Erythoid series: unremarkable

Myeloid series: unremarkable

Megakaryocyte: mildly increased

Megakaryocyte morphology: unremarkable

Lymphoid cell: not increased

Plasma cell: not increased

Fibrosis: no

Granuloma: no

Diagnosis: normocellular trilineage marrow with histologically normal maturation

No histologic evidence of lymphoma

Bone marrow immunohistochemistry:

CD20: highlighting some interstitial small B-cells without abnormal expansion and significant cytologic atypia

CD3 (mono): highlighting some interstitial small T-cells without abnormal expansion and significant cytologic atypia

CD3:CD20 = 2:1 of lymphoid cells

Kappa: highlighting some interstitial mature plasma cells without Dutcher bodies

Lambda: highlighting some interstitial mature plasma cells without Dutcher bodies

Kappa:Lambda = 1:1 of plasma cells

IgG: highlighting some interstitial mature plasma cells without Dutcher bodies

IgA: highlighting some interstitial mature plasma cells without Dutcher bodies

IgM: highlighting some interstitial mature plasma cells without Dutcher bodies

Diagnosis: no histologic and immunohistochemical evidences of lymphoproliferative disorder and plasma cell neoplasm

Molecular technique (in situ hybridization for immunoglobulin light chain)

Polyclonal plasma cells, no evidence of plasma cell neoplasm

Bone marrow: Giemsa staining: negative, GMS: negative

Muscle biopsy:

Microscopic examination:

I. Left deltoid: sections show striated muscle. Myofibers vary minimally in size and shape. Interstitial connective tissue is increased, and mild lymphocytic infiltrates noted. Regenerating myofibers are occasionally sen.

II. Left vastus lateralis: sections show striated muscle. Granulomata are seen, containing epithelioid histiocytes. One of the granulomata contains a central area of necrosis. Myofibers vary in size and shape, and are intervened by fibrous connective tissue. Regenerating myofibers are also seen. No organism is detected by AFB, GMS and giemsa stains.

III. Right vastus lateralis: sections show striated muscle. Myofibers vary in size and shape, and interstitial connective tissue increased. Mild lymphocytic infiltrates is observed in the endomysium. No organism is detected by AFB, GMS and geimsa stains.

Diagnosis:

1. Left deltoid muscle biopsy: mild muscle damage with mild chronic inflammation
2. Left vastus lateralis biopsy: necrotizing granulomatous inflammation, negative AFB, GMS and geimsa stains. Negative real-time PCR for mycobacterial tuberculosis.
3. Right vastus lateralis biopsy: muscle damage with mild chronic inflammation, negative AFB, GMS and geimsa stains.

Electrodiagnosis report (first time)

Summary of finding

1. Sensory nerve conduction study of bilateral median, right ulnar and sural nerve is normal except mildly prolonged left median distal latency.
2. Motor nerve conduction study of 4 nerves of bilateral upper extremities with stimulation up to the Erb's point is normal, except mildly prolonged right median distal latencied and slow conduction velocities across the elbow of bilateral ulnar nerves. MCNS of right common peroneal nerve is normal. MCNS of left tibial nerve shows reduced distal CMAP amplitiude, this could be from leg and foot edema. In addition, motor nerve conduction study of right axillary and bilateral musculocutaneous nerves shows normal distal latencies.

3. EMG of the right iliacus shows moderate degree of spontaneous activities in the form of PSW and fibrillation potentials; most of the MUAPs are short duration and normal duration polyphasic; with early recruitment pattern.EMG of the right vastus medialis and right gluteus maximus shows no spontaneous activities with some polyphasic MUAPs. EMG of the right deltoid shows rare spontaneous activities in the form of PSW, MUAPs. Many normal-increased duration polyphasic MUAPs are sen; recruitment pattern is mixed pattern some area normal and some of reduced. EMG of the right FDI and biceps br. Also showed polyphasic MUAPs. EMG of the left lower extremities are not performed due to leg and thigh edema.

Interpretation:

This bed side electrodiagnostic test shows electrodiagnostic evidences of

1. Rather irritative myopathy; this is mainly based of the findings at the right iliacus plus many polyphasic MUAPs elsewhere.
2. Bilateral ulnar neuropathies at the elbows and right sensory motor median neuropathy at the wrist, likely subclinical entrapment neuropathies.

   The mixed recruitment pattern at the right deltoid/biceps may suggest concurrent neurogenic process; however, the spontaneous activity is scanty to support this diagnosis. Please note that EMG of the bilateral spinati and left deltoid is not done.

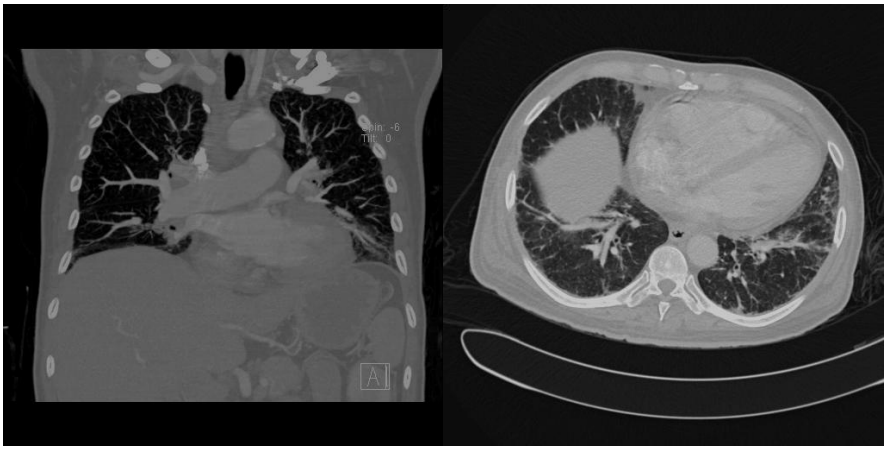
   No electrodiagnostic evidence of large fiber sensory and motor polyneuropathy is demonstrated.

Color Doppler ultrasonography of deep veins of left lower extremities:

The study reveals normal diameter, color flow and spectral waveform of left common femoral veins (CFVs), great saphenous veins (GSVs), deep femoral veins (DFVs), superficial femoral veins (SFVs) and popliteal arteries. There are normal diameter and color flow of right anterior tibial veins, tibioperoneal veins, posterior tibial veins and peroneal veins. Normal compressibility and response to augmentation of left CFVs, SFVs and popliteal veins are noted. No intraluminal thrombus is detected.

Impression: No evidence of deep vein thrombosis

CT angiography of the pulmonary artery:



The pulmonary trunk is enlarged, approximately 4.0 cm in caliber. The right and left main pulmonary arteries are dilated. There is neither filling defect nor arterial web in the pulmonary trunk and its branches.

Mild cardiomegaly is seen. There is minimal pericardial effusion.

There are multiple highest mediastinal, prevascular, right paratracheal, subcarinal and both axillary nodes, up to 1.3 cm in short axis diameter.

There is diffuse interlobular septal thickening with some ground glass opacities of both lungs predominantly at both lower lobes.

The trachea and major bronchi are patent.

There is minimal atelectasis in both lower lungs. There is no pleural effusion. There is no osteolytic or osteoclastic lesion.

Impression:

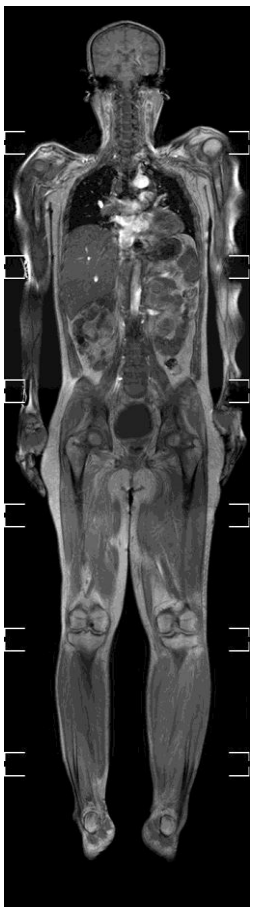
- Multiple small mediastinal nodes, probably representing reactive nodes
- Probably pulmonary hypertension
- Diffuse interlobular septal thickening with some ground glass opacities of both lungs predominantly at both lower lobes suspecting of NSIP
- No evidence of pulmonary embolism

CT whole abdomen:

Few small non-enhancing hypodense nodules are at segment VIII and VI of right hepatic lobe, probably hepatic cyst, size0.5 and 0.8 cm.

Unremarkable otherwise.

MRI whole body:



Increased SI of bilateral upper thighs and left leg, more pronounced on the anterior muscular group og left thigh and lateral muscular group of left leg and mild subcutaneous edema at left lower extremity, possibly inflammatory myositis.

Degenerative discs at C3/4, C5/6, C6/7 and L4/5 levels

Mild herniated discs at C5/6 and C6/7 levels

Three small hepatic lesions in both lobes, measured about 0.5-0.8 cm.

MRI whole spine:

Degenerative discs at C2/3-C6/7 and L4/5 levels

Mild focal central disc protrusion at C3/4, C5/6 and C6/7 levels and stenosis of left C5/6 and bilateral C6/7 neural foramina due to protruded discs

A 1.0-cm lesion at left side of vertebral body at T12 level which shows hyperSI on T1W, T2W, T2W with FS and enhancement on post-contrast study as well as central low SI without enhancement, possibly hemangioma

No evidence of abnormal SI of spinal cord

Transthoracic echocardiogram

Normal LV size and systolic function (LVEF = 70% by Teicholz's method). No RWMAs. LV d-shape during systole compatible with LV pressure load. Normal LA size. Normal diastolic function (E/e' = 5)

Dilated RA and RV size (RVD1 =51, RVD2 = 39, RVD3 = 89 mm). normal RV systolic function (TAPSE = 26 mm, lateral tricuspid annulus S' = 19 cm/s)

Normal MV. No MS. No MR. Normal leaflets AV. No AS. No AR. Structurally normal TV and PV. Moderate TR. Mild PR. Estimated PAP = 73/22 mmHg. Dilated MPA. Consistent with severe pulmonary hypertension

Minimal pericardial effusion (maximum thickness 1 mm) adjacent to LV posterior wall without tamponade physiology

No intracardiac thrombus

Saline agitation test: no negative contrast from LA to RA via A4C.

Questions

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