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การประชุมใหญ่วิชาการประจำปี ครั้งที่ 45

Bridging science to practice

สมาคมโรคติดเชื้อแห่งประเทศไทย

ID Grand Round

13/10/2019

Lakkana Boonyagars, MD., M.Sc.
Division of Infectious Diseases,
Department of Medicine, Faculty of Medicine,
Vajira Hospital, Navamindradhiraj University

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Patient Profile

- ผู้ป่วยหญิงไทยคู่ อายุ 44 ปี Admit 09/04/62
- อาชีพ รับจ้างทำงานบ้าน
- ภูมิลำเนา กรุงเทพมหานคร
- สิทธิการรักษา ประกันสังคม
- ประวัติได้จากผู้ป่วย เชื่อถือได้มาก

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Patient Profile

- **Chief complaint:** ปวดท้อง 2 สัปดาห์ก่อนมาโรงพยาบาล
- **Present illness:** 2 สัปดาห์ก่อนมาโรงพยาบาล มีปวดท้องด้านขวาล่างและปวดหลังบริเวณบั้นเอว ไม่มีร้าวลงขา มีไข้ไม่ทราบระยะเวลา ไม่มีคลื่นไส้อาเจียน ปัสสาวะอุจจาระปกติ เดินได้ปกติ ไม่มีแขนขาอ่อนแรง ไปพบแพทย์ที่ รพ เอกชนแห่งหนึ่งพบความผิดปกติ จึงส่งมารักษาที่วชิรพยาบาล

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Personal History

- Known case HIV, Dx 2538, previous OI = Cryptococcal meningitis
- รับประทานยา ARV สม่ำเสมอ on GPOvir S30, 8 มค 62 มี lipodystrophy ปรับสูตรยาเป็น TDF/3TC/EFV จนถึงปัจจุบัน ขณะนี้รับยาที่รพเอกชนที่ส่งตัวมา
- ล่าสุด CD4 25/09/61 = 113 cells/mm^3 (10%), HIV VL <20 copies/ml (VL undetectable ตลอดการรักษาที่ผ่านมา)

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Personal/Past History

- แพ้อาหารทะเล มีอาการผื่นคัน
- ปฏิเสธประวัติแพ้ยา สารเคมี
- ปฏิเสธการรับประทานอาหารสุกๆดิบๆ
- ปฏิเสธการใช้ยาชุด ยาแก้อักเสบ ยาลูกกลอน สมุนไพร
- ปฏิเสธการดื่มสุรา สูบบุหรี่
- ปฏิเสธสัมผัสผู้ป่วยวัณโรค

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Familial History

- ปฏิเสธประวัติโรคประจำตัว โรคทางพันธุกรรม โรคมะเร็งในครอบครัว

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Physical Examination

- **Vital signs:** BT 39.5°c, PR 110 bpm regular, RR 20 bpm, BP 130/70 mmHg, body weight 63 kg, height 165 cm, BMI 23.1 kg/m^2
- **GA:** Thai female, good consciousness, mild pallor, no jaundice, no cyanosis
- **HEENT:** Mild pale conjunctivae, anicteric sclerae, no OC, no OHL, no oral ulcers, no cervical and supraclavicular lymphadenopathy
- **Heart:** Normal S1S2, no murmur

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Physical Examination

- **Lung:** Clear, no adventitious sound
- **Abdomen:** Mass at RLQ diameter ~10 cm, fixed, mild tender at mass area on palpation, CVA mild tender at right side

- **Skin:** no rash, no petechiae/purpura/ecchymosis
- **Neurological examination:** Alert, cranial nerves; grossly intact, motor power; grade V all extremities, no stiffness of neck

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Investigations

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Complete Blood Count (09/04/62)

Hb 9.8 g/dL, Hct 29.7%, MCV 91.4 fl, RDW 11.9%

WBC count 12,520 cells/mm^3, PMN 83.6%, Lymphocyte 9.8%, Eosinophil 0.6%, Monocyte 5.8%, Basophil 0.2%

Platelet count 487,000 cells/mm^3

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Blood Chemistry (09/04/62)

BUN 11 mg/dL, Cr 1.06 mg/dL, BS 102 mg/dL

Na 136 mmol/L, K 4.1 mmol/L, Cl 100 mmol/L, HCO3 24 mmol/L

AST 156 U/L, ALT 139 U/L, ALP 328 U/L

Total protein 8.4 g/dL, Alb 2.8 g/dL, Glb 5.6 g/dL

Total bilirubin 0.3 mg/dL, direct 0.15 mg/dL, indirect 0.15 mg/dL

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Urinalysis	Hepatitis Profile	Coagulogram
Yellow, clear	HBsAg: negative	PT 13.1 sec (10.5-13.5)
sp.gr. 1.015	Anti-HBs: negative	INR 1.09
WBC 3-5/HPF	Anti-HBc: negative	aPTT 25.8 sec (22.0-30.0)
RBC 0-1/HPF	Anti-HCV: negative	
Nitrite negative		

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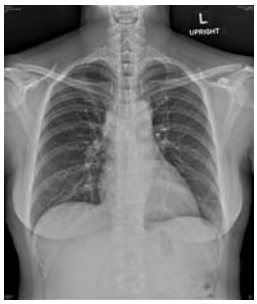
Chest X-ray (02/04/62)



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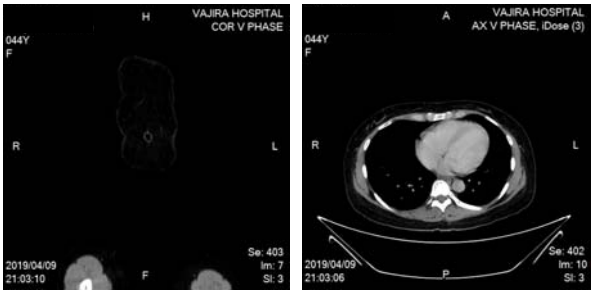
CT Abdomen (09/04/62)



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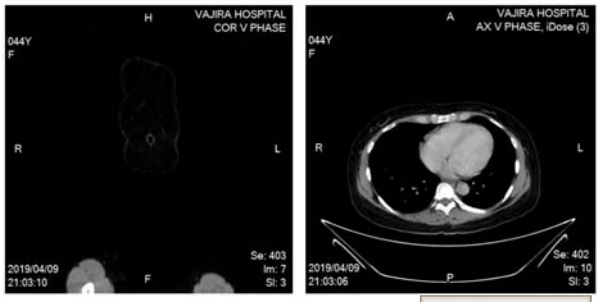

Discussion

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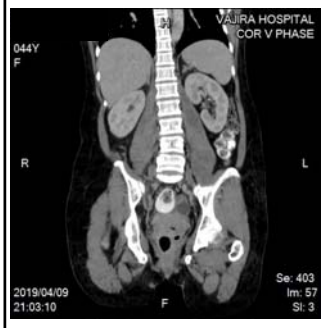
CT Abdomen (09/04/62)



- Multi-located bilateral iliopsoas abscesses measuring about 8x7x14 cm, 5x4x10 cm & 4x2x3 cm in size at Rt side, Lt anterior and Lt posterior aspects, respectively, with minimal surrounding fat stranding
- Abnormal heterogeneous enhancing lesion at the left adrenal gland measures about 2.6x2x4.4 cm in size
- Multiple matted enhancing LN are seen along paraaortic, aortocaval, retrocaval, bilateral common iliac and internal iliac regions.

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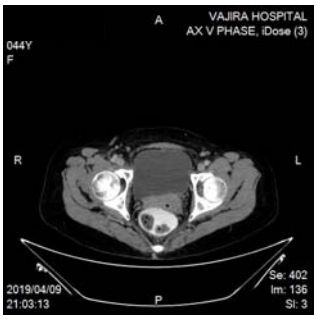
CT Abdomen (09/04/62)



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- Multiple matted enhancing LN are seen along paraaortic, aortocaval, retrocaval, bilateral common iliac and internal iliac regions.

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Problem lists

- Bilateral psoas abscess with multiple intraabdominal lymphadenopathies
- Known case HIV infection with good virological control

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First Admission (9-17/04/62)

- ATB แรกรับ ceftriaxone + metronidazole
- **Set PCD at Rt psoas abscess 11/04/62** ได้ pus 50 cc (send for gram, AFB, mAFB, c/s for aerobes, c/s for mycobacterium/fungus, PCR TB)
- Discharges 17/04/62 (ไปฉีดยา รพ ใกล้บ้าน)

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Pus from Psoas Abscess (11/04/62)

Gram stain, AFB stain, mAFB stain: **not found organisms**

Culture for aerobes: **no growth**

Culture for mycobacterium/fungus: **pending**

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Pus from Psoas Abscess (11/04/62)

PCR TB: Negative

PCR NTM: Negative

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Hemoculture (11/04/62)

Hemoculture x II: No growth in 3 days

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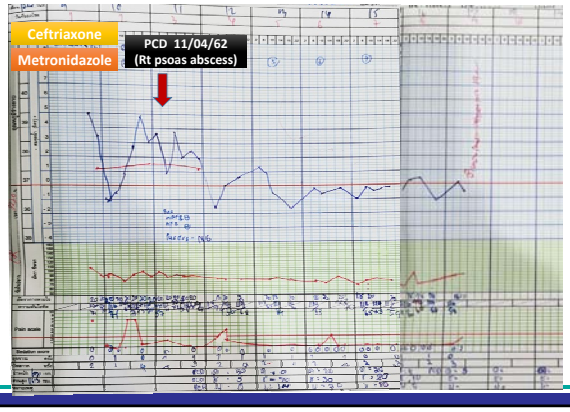

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Second Admission (22/05-24/07/62)

- หลังจากกลับจากการนอน รพ (d/c 17/04/62) ผู้ป่วยกลับไปเข้ารับการรักษา รพ เอกชนเดิมต่ออีก 10 วัน และได้กลับบ้านไป หลังกลับบ้าน ให้ประวัติมีหนองออกจากสายด้านขวาทุกวัน วันละประมาณ 20 cc ไม่มีไข้ ไม่มีปวดขาหนีบ เหยียดขาได้ปกติ ไม่มีปวดบริเวณอื่นอีก
- วันนี้แพทย์นัดมาใส่สายระบายหนองด้านซ้าย
- เริ่มสังเกตว่ามีต่อมน้ำเหลืองที่คอซ้ายโตมากขึ้น ไม่ปวด

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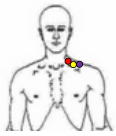
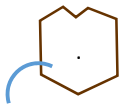
Second Admission

❖Physical examination:

- ❑ Lt cervical/supraclavicular lymphade-nopathies 3 ก้อน (diameter ~ 1.5-2 cm, rubbery consistency, not tender)





Rt PCD

Pus from psoas abscess (Rt PCD) (11/04/62)

❖c/s for mycobacterium/fungus

- ❑ No growth

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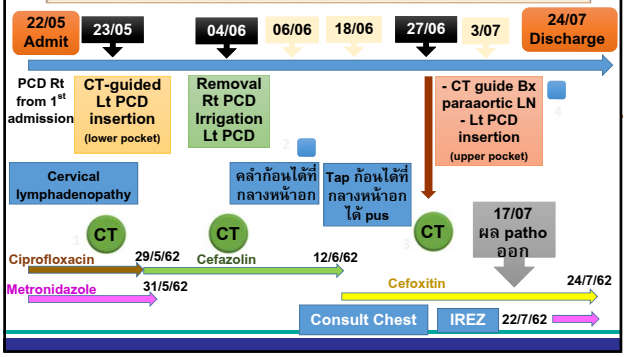
Admission Course (22/05 - 24/07/62)



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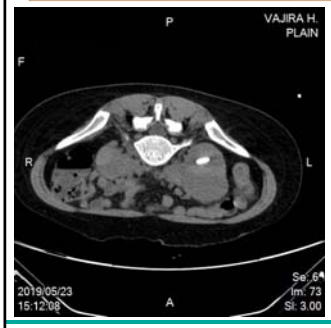
23/05/62: Lt PCD Insertion (lower pocket)



Ultrasound and CT guidance Lt PCD insertion (lower pocket)

❖US revealed the target lesion of left iliopsoas abscess, which considered as the target lesion for drainage.

❖Nearly resolve of the right iliopsoas abscess with in placed prior PCD tip.

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Pus from Psoas Abscess Lt PCD (23/05/62)

Gram stain, AFB stain, mAFB stain: **not found organisms**

Culture for aerobes: **no growth**

Culture for mycobacterium/fungus: **pending**

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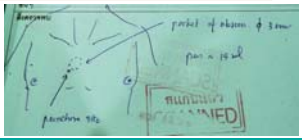
6/6/62

❖คลำก้อนได้ที่กลางหน้าอก

❖**Ultrasound chest wall**: Heterogeneous echoic mass at Rt upper chest wall with connecting to intercostal space, measured about 4.7x2.3x4.7 cm, DDx abscess, soft tissue tumor

18/6/62

❖ Tap ก้อนที่กลางหน้าอก ได้หนอง 15 cc



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Pus from Chest Wall Abscess (18/06/62)

Gram stain, AFB stain, mAFB stain: **not found organisms**

Culture for aerobes: **no growth**

Culture for mycobacterium/fungus: **pending**

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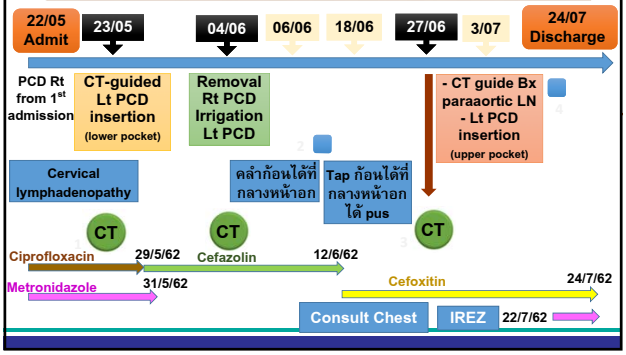
Admission Course (22/05 - 24/07/62)



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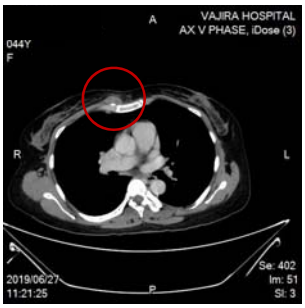
27/06/62: F/U CT Chest & Abdomen



Findings: The chest study;

- A rim-enhancing turbid fluid collection at subcutaneous layer of mid-to-right parasternal area (size 2x5x4 cm) with suspected extending through right costochondral junction into the prevascular space
- Multiple mediastinal LN at prevascular, both paratracheal, paraaotic, and subaortic regions, with central necrosis

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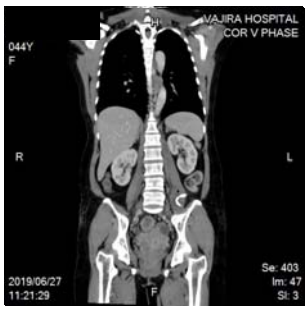
27/06/62: F/U CT Chest & Abdomen



Findings: The abdomen study;

- Slightly decrease in size of the posterior pocket of left psoas abscess that placed PCD tip inside (4x3→3x2 cm). Also slightly decreased of the undrained anterior pocket of left psoas abscess (6x4→5x3 cm).
- Totally resolve of the right iliopsoas abscess.
- No significant change in size and numbers of the multiple matted lymphadenopathies.
- No significant change of a large heterogeneous left adrenal mass

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03/07/62

- **CT guide biopsy paraaortic node biopsy**
  - Tissue pathology
  - Gram stain, AFB, c/s aerobes, c/s mycobacterium and fungus
- **PCD at Lt psoas abscess (upper pocket)**
  - Pus was sent for gram stain, AFB, c/s, c/s for mycobacterium and fungus

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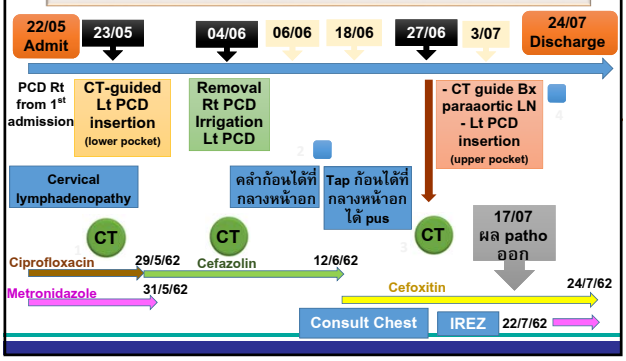
Admission Course (22/05 - 24/07/62)



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Paraaortic LN Biopsy: Initial Report

- วันที่รับสิ่งส่งตรวจ : 03/07/2562, รายงานผล 17/07/2562
- **GROSS:**
  - Four pieces of rubbery cores light brown tissue from needle biopsy.
- **MICROSCOPIC FINDINGS:**
  - The section shows fragments of fibroadipose tissue containing aggregates of epithelioid cells and multinucleated giant cells with central caseous necrosis. The surrounding tissue contains moderate chronic inflammatory infiltrates. No malignancy is seen.
- **DIAGNOSIS:**
  - **Caseating granulomatous inflammation**

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Admission Course (22/05 - 24/07/62)

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Paraaortic LN Biopsy: Final Report

- รายงาน **24/7/62** Patho S5381/62 (จาก tissue 3/7/62)
- Tissue from psoas area, core biopsy (S62-4987)
  - Caseating granulomatous inflammation
  - ส่งย้อม stain เพิ่มเติม

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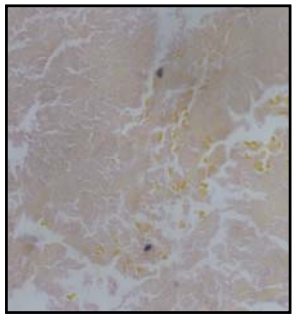
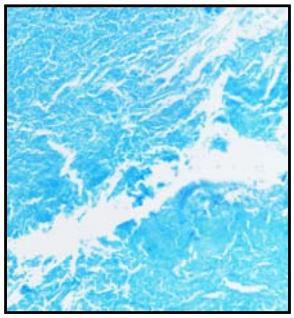
Mucin



AFB



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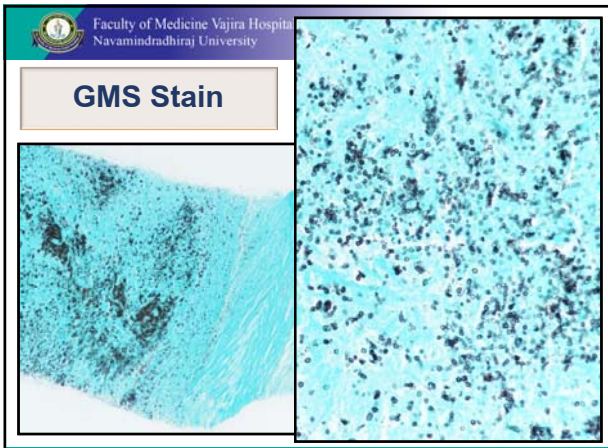
GMS Stain



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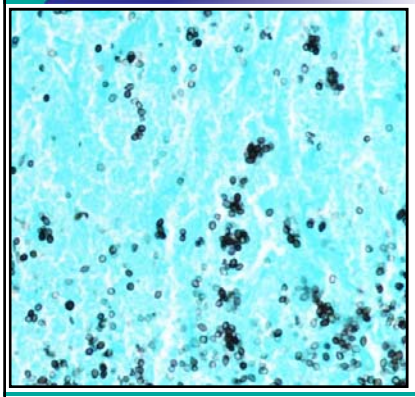

GMS Stain

- **Positive results for GMS**
  - In granulomatous area, numerous small yeasts are found, disseminated fungal infection is suspected

Histoplasma capsulatum

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Third Admission (13/08-31/08/62)

- นัด admit หลังทราบผล tissue pathology paraaortic LN
- Serum Cryptococcal Ag neg
- Follow up CT abdomen (14/08/62)
- **15/8/62** start Amphotericin B 0.7 mg/kg/d x 14 days
- **18/8/62** รับย้าย med
- **23/8/62** ก้อนที่คอซ้ายโตมากขึ้น ปวด บวม ร้อน มี fluctuation

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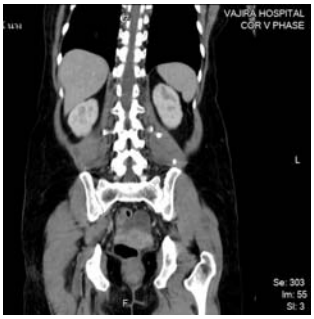
14/8/62



Findings;

- Decrease in size of the posterior pocket and near total resolution of anterior pocket of left psoas abscess
- No significant change in size and numbers of the multiple matted lymphadenopathies at paraaortic, aortocaval, retrocaval, and bilateral iliac lesions change of a large heterogeneous left adrenal mass

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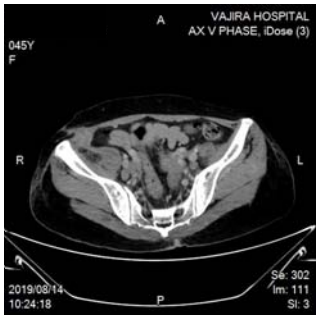
14/8/62



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Third Admission (13/08-31/08/62)

- นัด admit หลังทราบผล tissue pathology paraaortic LN
- Serum Cryptococcal Ag neg
- Follow up CT abdomen (14/08/62)
- **15/8/62** start Amphotericin B 40mg/d x 14 days
- **18/8/62** รับย้าย med
- **23/8/62** ก้อนที่คอซ้ายโตมากขึ้น ปวด บวม ร้อน มี fluctuation

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23/08/62

- Aspirate Lt cervical LN ได้ pus 20 cc ส่ง GMS stain
  - Moderate yeast with budding

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Third Admission (13/08-31/08/62)

- Pus culture for fungus from Lt supraclavicular LN and Lt PCD (26/8/19), reported 02/09/19
  - No growth
- Hemoculture for fungus/mycobacterium (16/08/19), reported 30/08/19
  - No growth
- **28/8/26** Off amphotericinB, start Itraconazole
- Discharge 31/08/62

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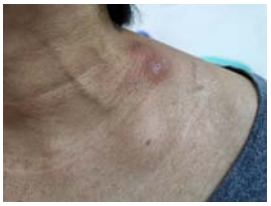

OPD F/U 10/09/62

- Continue itraconazole and ARV

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Last Follow Up 24/09/62

- Drain ยังออกเล็กน้อย plan remove PCD ถ้า drain ไม่ออก

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Final Diagnosis

HIV infection with subacute progressive disseminated histoplasmosis

(involve psoas abscess, intraabdominal LN, cervical LN, chest wall and Lt adrenal gland)

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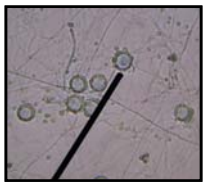
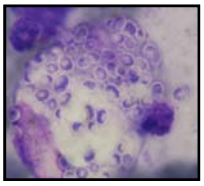
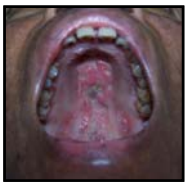
Histoplasmosis







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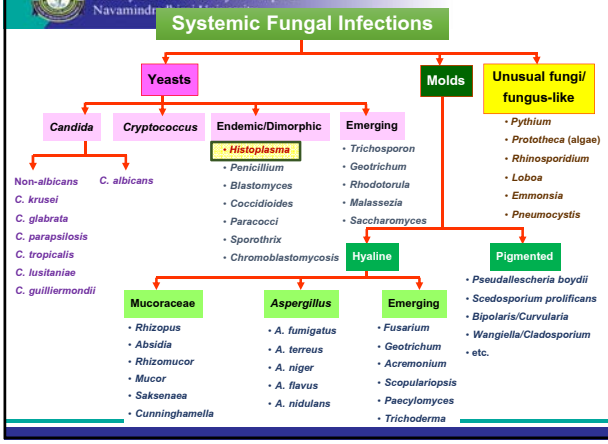

Histoplasmosis

- Broad spectrum of clinical manifestations
  - Ranging from a self-limited, acute, influenza-like illness to a progressive disseminated infection that is life-threatening
- **Pathogenesis**
  - Conidia settle into the alveoli
  - Following transformation of conidia into yeasts in the lungs, yeasts migrate, presumably intracellularly, to local draining lymph nodes and subsequently to distant organs rich in mononuclear phagocytes (e.g., liver, spleen)
  - Activation of cellular immunity is necessary for restricting growth

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Risk Factors

Risk factors for histoplasmosis

Epidemiologic Factor	Host Factors	Pathogen Factors
Endemic area • Ohio and Mississippi River basins (US) • Puerto Rico & Caribbean • Central and South America • Southeast Asia • Oceania • Africa (*H var duboisii*) Bird and Bat guano exposure • Spelunking Aerosolized soil exposure • Construction • Landscaping • Strong winds	HIV/AIDS (especially CD4 count <150 cells/mm^3) TNF-alpha inhibitors Solid organ transplantation Bone marrow transplantation Extremes of age (<2 or>50 y) Other causes of cellular immune suppression or dysfunction	Size of inoculum Inherent virulence

Azar MM, Hage CA. Clin Chest Med. 2017;38(3):403–15.

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Clinical Syndromes

- **Pulmonary histoplasmosis**
  - Acute pulmonary histoplasmosis
  - Subacute pulmonary histoplasmosis
  - Chronic pulmonary histoplasmosis
  - Pulmonary nodules
- **Mediastinal Histoplasmosis**
  - Mediastinal adenitis
  - Mediastinal granuloma
  - Mediastinal fibrosis
- **Progressive disseminated histoplasmosis**
- **Other sites;** uncommon organ involvement

Azar MM, Hage CA. Clin Chest Med. 2017;38(3):403–15.

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Uncommon Organ Involvement

- **Other sites**; include
  - Thrombotic microangiopathy
  - Hemophagocytic syndrome
  - Hypercalcemia due to calcitriol production by activated macrophages
  - Chorioretinitis
  - Pleuritis
  - Pericarditis
  - Peritonitis
  - Pancreatitis and cholecystitis
  - Panniculitis
  - Mastitis
  - Osteomyelitis and septic arthritis
  - Tenosynovitis
  - Prostatitis, epididymitis, or involvement of the penis or vagina

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Progressive Disseminated Histoplasmosis (PDH)

- Yeast cells migrate from the lungs to organs rich in mononuclear phagocytes
- Reactivation vs. New Exposure
- **Three forms,**
  - Acute PDH
  - Subacute PDH
  - Chronic PDH

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PDH

	Acute PDH	Subacute PDH	Chronic PDH
Settings	- **Severely immunosuppressed, esp. AIDS and hematologic malignancies**		- **Previously normal adults**
Sign	- **Abrupt onset (few days)** - Fever (90%) & malaise, followed by weight loss, cough, and diarrhea -	- Fever(~50%), weight loss	- Malaise, lethargy - Fever (<30%), often low grade
Organ involvement	- Rales, hepatosplenomegaly, and lymphadenopathy (esp. cervical LN) - **Oropharyngeal ulcers (<20%)** - **Cutaneous lesions (MP, petechiae, or ecchymosis)** - Other unusual manifestations (colonic masses, perianal ulcers, chorioretinitis, meningitis, encephalitis)	- Hepatosplenomegaly and oropharyngeal ulcers - **Focal lesions in various organ systems, including the GI tract, endovascular structures, CNS, and adrenal glands**	- **Oropharyngeal ulcer (50%, well circumscribed, indurated, deep and painless)**, also tongue, buccal mucosa, larynx, gums, & lip - Hepatosplenomegaly (~30%) - Chronic meningitis or granulomatous hepatitis - **Absence of disease involvement of other organ (CNS, heart, adrenals)**
Lab	- **Hematologic abnormalities,** anemia (>90%), leukopenia and thrombocytopenia (>80%) - Abn LFT (ALT/ALP) - CXR (patchy pneumonitis with mediastinal & hilar node enlargement)	- Less striking than in acute PDH -Hematologic abnormalities, anemia & leukopenia (~40%), thrombocytopenia (~20%)	- Hematologic abnormalities, uncommon & often not significant - This illness may persist for years, there may be an abrupt worsening caused by involvement of a particular organ (CNS, adrenals, or heart)

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PDH: Adrenal Glands Histoplasmosis

- **Incidence**
  - Although symptoms arising from involvement of adrenal glands are not frequent, autopsy series indicate that yeasts invade adrenal glands ~80% of cases
- **CT findings**
  - Display enlarged adrenals (esp. in subacute PDH)
- **Pathological findings (DDx with TB)**
  - Macrophages containing yeasts are found scattered throughout the parenchyma of the adrenal gland
  - Tissue necrosis is seen but usually involves only a small portion of the gland. Grossly, the adrenal glands are enlarged.
- Overt Addison's disease is uncommon (<10%)

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Morphology Differential Diagnosis

Organism	Size (um)	Shape	Attachment of Buds	Cell Wall Thickness	GMS	PAS	Mucin
H. capsulatum var. *capsulatum*	2–4	Globose or ovoid	Narrow base	Thin	Positive	Positive	Negative
H. capsulatum var. *duboisii*	~ 6–12 or larger	Ovoid	Narrow base	Thick, refractile	Positive	Positive	Negative
C. glabrata	2–5	Ovoid	Narrow base	Thin	Positive	Positive	Positive
C. neoformans and *C. gattii*	3–8	Globose or ovoid	Narrow base	Thin	Positive	Positive	Positive
Leishmania spp. (amastigotes)	<4	Ovoid	N/A	N/A	Negative	Negative	Negative
P. jirovecii (cyst forms)	5–8	Rounded, irregular	N/A	Thin	Positive	Positive	Negative
T. gondii (bradyzoites)	<4	Ovoid	N/A	N/A	Negative	Negative	Negative
Trypanosoma cruzi (asmastigotes)	<4	Ovoid	N/A	N/A	Negative	Negative	Negative

Wheat LJ, et al. Infect Dis Clin North Am. 2016 Mar;30(1):207–27.

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Histoplasmosis: Treatment

Clinical Practice Guidelines for the Management of Patients with Histoplasmosis: 2007 Update by the Infectious Diseases Society of America — IDSA GUIDELINES

Table 2. Indications for antifungal therapy.

Definite indication, proven or probable efficacy
- Acute diffuse pulmonary infection, moderately severe symptoms, or severe symptoms
- Chronic cavitary pulmonary infection
- Progressive disseminated infection
- CNS infection

Manifestation	Treatment	Class
Progressive disseminated histoplasmosis		
Moderately severe to severe	Liposomal AmB[a] (3.0 mg/kg daily), AmB lipid complex[a] (5.0 mg/kg daily), or deoxycholate AmB[a] (0.7–1.0 mg/kg daily) for 1–2 weeks, followed by Itra[a] (200 mg twice daily for at least 12 months)	A-I
Mild to moderate	Itra (200 mg twice daily for at least 12 months)	A-II

Clinical Infectious Diseases 2007; 45:807-25

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