

Solving the Clues for the Triwizard Tournament

Can you figure out the clues and solve the case study?

Micro Case Study

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UW Health

Clinical Case

63 year-old male with hypertension

History of Present Illness:

- 3 months prior: progressive shortness of breath/dyspnea, dry cough, orthopnea
- Diagnosed with COVID-19
- Social History: 3 months prior, visited Laos with his wife for a funeral, stayed 3 weeks

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Medical history:

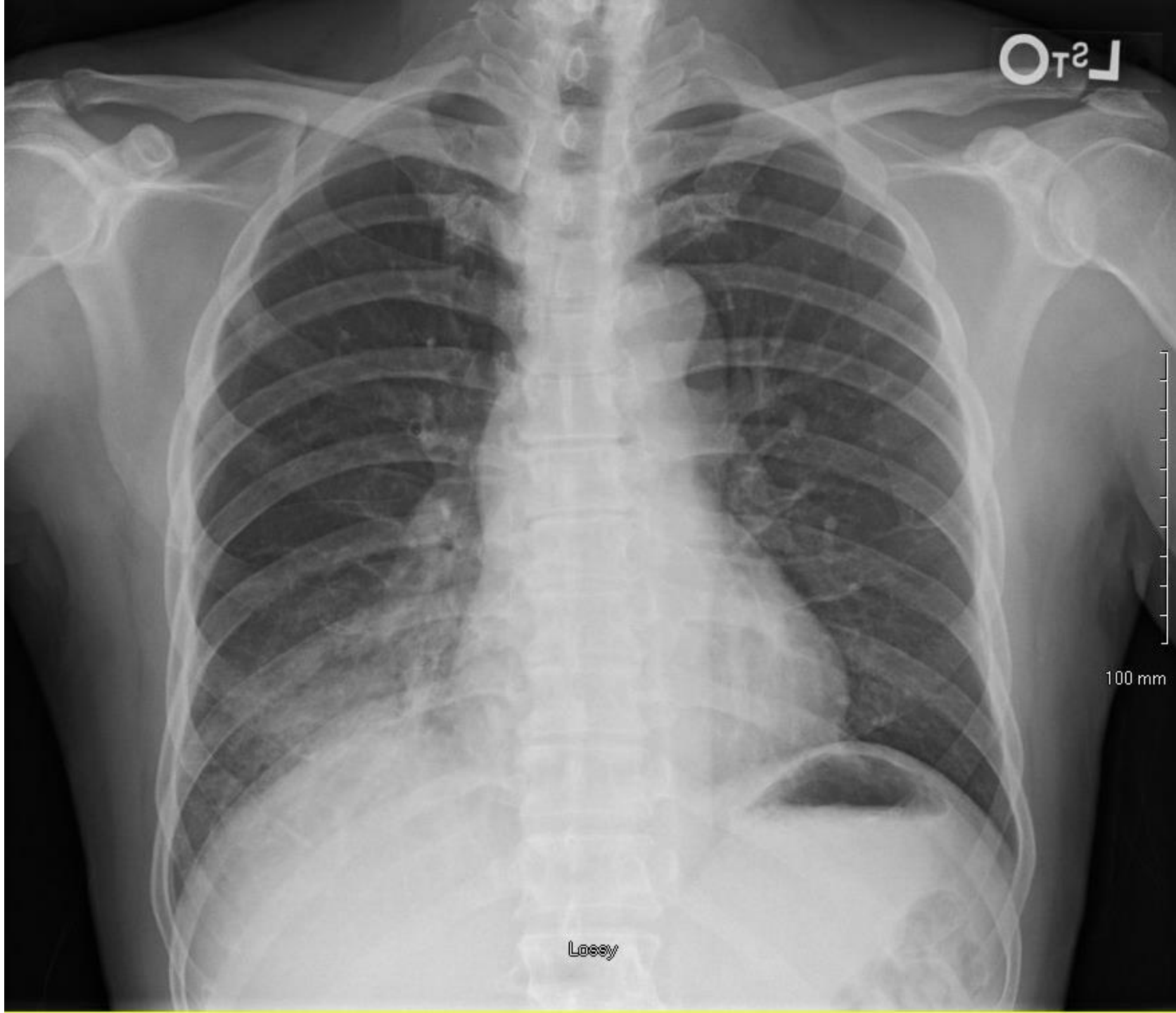
- History of *Listeria monocytogenes* meningoencephalitis
- Chronic eosinophilia

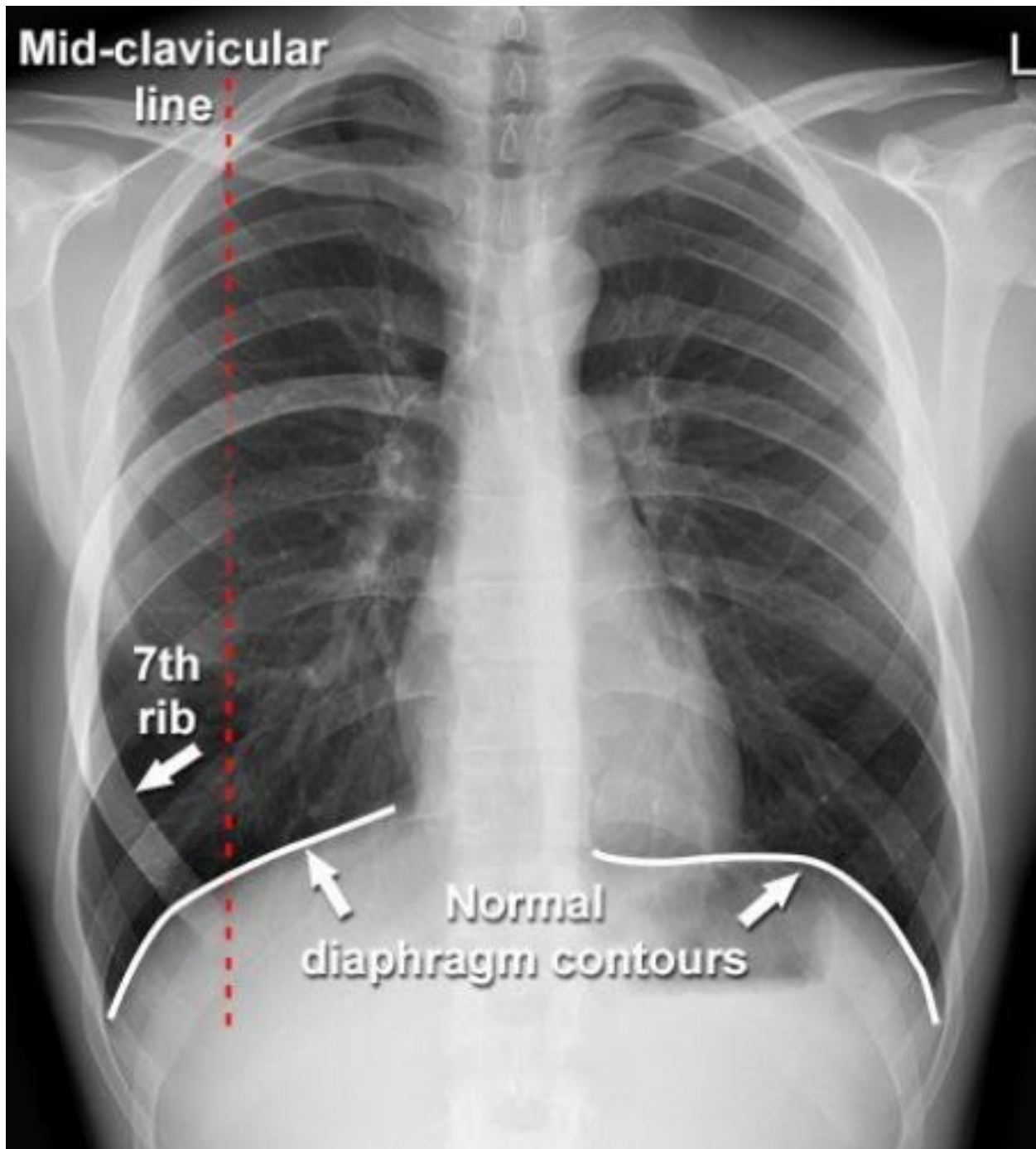
Eosinophil-associated diseases and disorders

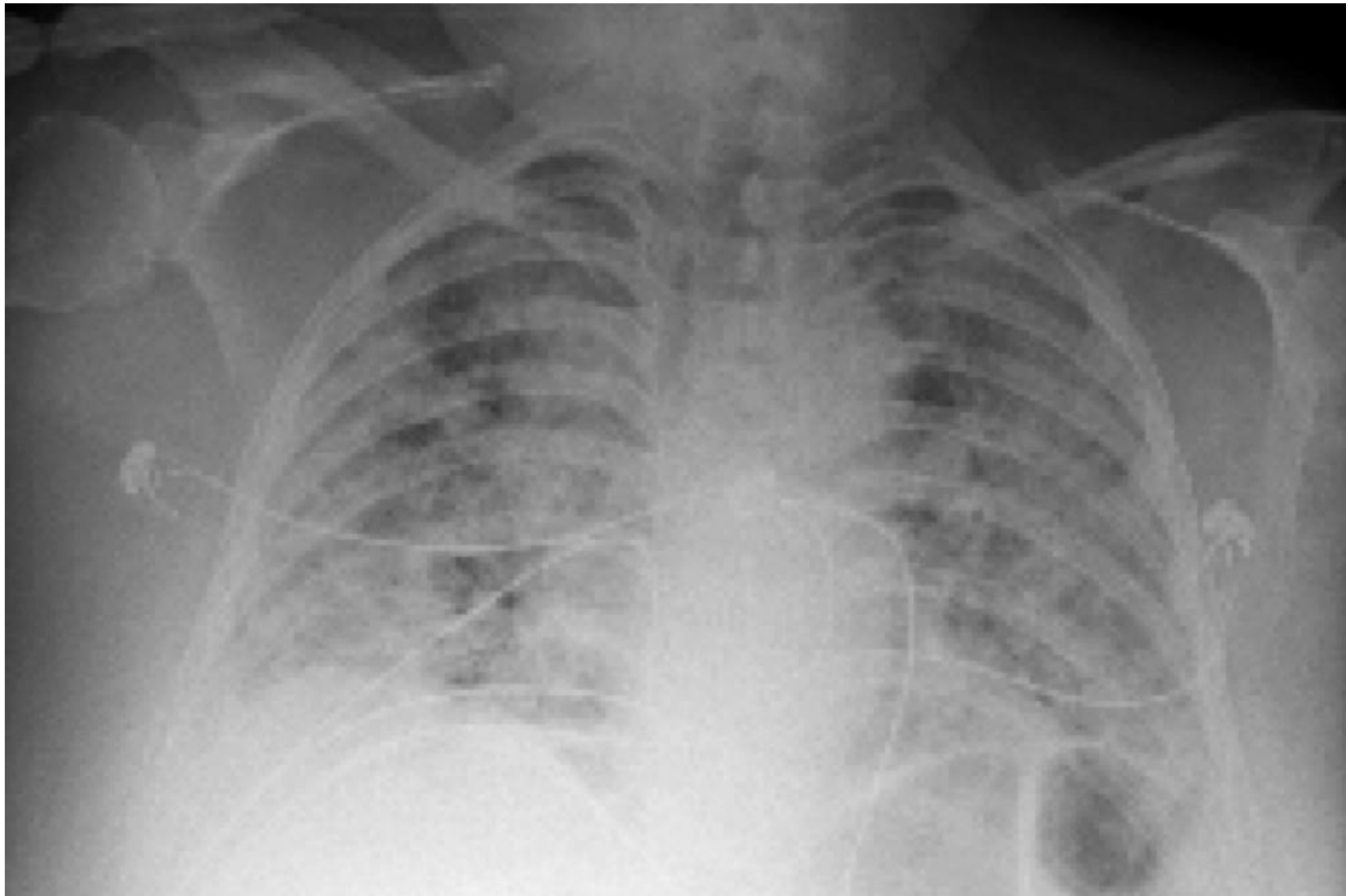
Allergic disorders
Asthma, allergic rhinitis, atopic dermatitis
Drug hypersensitivity (eg, drug reaction with eosinophilia and systemic symptoms [DRESS], eosinophilia-myalgia syndrome, interstitial nephritis, eosinophilic hepatitis)
Infectious diseases
Helminths (eg, strongyloidiasis, trichinellosis, filariasis, toxocariasis, schistosomiasis, hookworm)
Ectoparasites (eg, scabies, myiasis)
Protozoans (eg, isosporiasis, sarcocystis myositis)
Fungi (eg, coccidiomycosis, allergic bronchopulmonary aspergillosis, histoplasmosis)
Viral (eg, HIV)
Neoplastic disorders
Primary hypereosinophilic syndromes (eg, <i>FIP1L1-PDGFRα</i> , <i>-PDGFRβ</i> , <i>-FGFR1</i> rearrangement)
Acute or chronic eosinophilic leukemia
Other myeloid neoplasms (eg, chronic myeloid leukemia, systemic mastocytosis)
Lymphoid malignancies (eg, B cell lymphoma, B or T lymphoblastic leukemia/lymphoma, adult T cell leukemia/lymphoma, cutaneous T cell lymphoma/Sézary syndrome)
Solid tumors (eg, adenocarcinoma, squamous carcinoma)

Immunologic disorders
Immunodeficiencies (eg, DOCK8 deficiency, hyper-IgE syndrome, Omenn syndrome)
Autoimmune and idiopathic disorders (eg, sarcoidosis, inflammatory bowel disease, IgG4 disease, other connective tissue disorders)
Eosinophilic disorders
Idiopathic hypereosinophilic syndrome
Eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss syndrome)
Eosinophilic gastrointestinal disorders
Miscellaneous
Radiation exposure
Cholesterol emboli
Hypoadrenalism
IL-2 therapy

HIV: human immunodeficiency virus; *FIP1L1-PDGFR α* : FIP1-like-1-platelet-derived growth factor receptor alpha; *FIP1L1-PDGFR β* : FIP1-like-1-platelet-derived growth factor receptor beta; *FGFR1*: fibroblast growth factor receptor 1; DOCK8: dedicator of cytokinesis 8; IgE: immunoglobulin E; IgG4: immunoglobulin G4; IL-2: interleukin 2.









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- Diagnosed with COVID-19
- Resolved, unclear if patient took paxlovid

- Social History: 3 months prior, visited Laos with his wife for a funeral, stayed 3 weeks

Clinical Case

63 year-old male with hypertension

History of Present Illness:

- Worsening: dyspnea, orthopnea
- Presents to Meriter, where a CT scan shows **pericardial effusion** and bilateral pleural effusion
- No cultures positive at the time in and around hospitalization

- Social History: 3 months prior, visited Laos with his wife for a funeral, stayed 3 weeks

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- Worsening: dyspnea, orthopnea
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- Successive indeterminate quantiferon results

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Clinical Case

63 year-old male with hypertension

History of Present Illness:

- COVID-19 + Pneumonia in April
- Meriter hospitalization in May
- June, returned cough + SOB continued to progress

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Clinical Case

63 year-old male with hypertension

History of Present Illness:

- COVID-19 + Pneumonia in April
 - Meriter hospitalization in May
 - June, returned cough + SOB continued to progress
 - Lymphadenopathy + worsening pleural effusions
-
- Social History: 3 months prior, visited Laos with his wife for a funeral, stayed 3 weeks

Labs at UW Health

- CBCs w/ differential: Elevated WBCs, including elevated Neutrophils and Eosinophils
- May 8 – Sinus culture (*S.aureus* and endogenous flora)
- May 26 – Blood cultures, negative
- May 27 – Pericardial fluid
 - Bacterial culture – *C. acnes* (34-37° C)
 - Fungal culture- negative (28 days at 29-31° C)

Labs at UW Health

- June 16 – Pleural fluid
 - Bacterial culture – POSITIVE
 - Fungal culture – Negative
- June 16 – GI Pathogen Panel (*Y. enterocolitica*)
- June 17 – Blood cultures negative
- June 19 – Lymph node biopsy – Bacterial culture POSITIVE
- June 26 – Pleural Fluid – Bacterial culture POSITIVE
- June 27 – Pleural fluid
 - Bacterial culture and fungal cultures - Negative

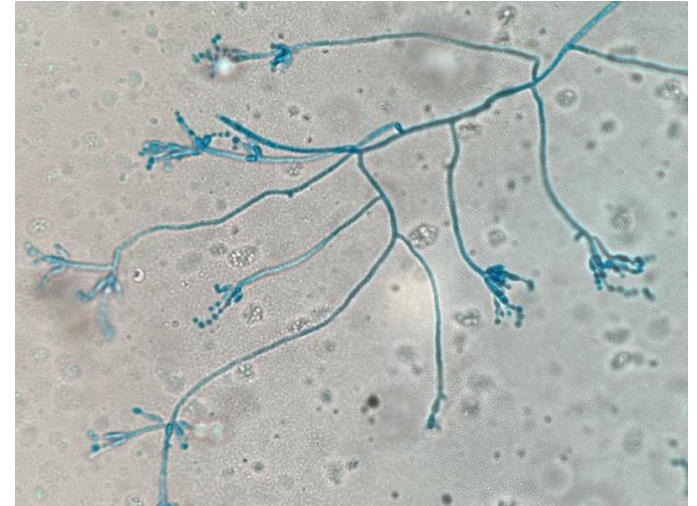
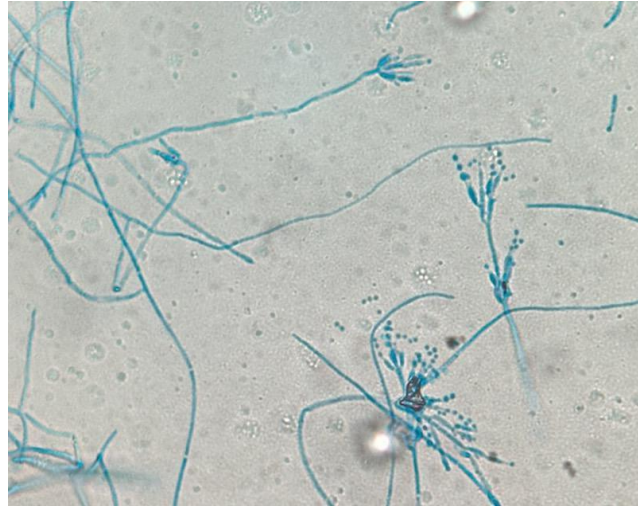
Labs at UW Health

- Pleural Fluid Culture (June 19):
 - 2 colonies on direct chocolate plate on day 4, possible feet starting
 - Aerobic Bactec Bottle Positive at 2 days, 20.7 hours
 - No organisms seen, AO negative
 - 2nd positive alert: "looks like funky yeast"
 - Subculture plates growing 2 days later, feet noted.
 - Following day tech noted that this does not look like yeast or typical feet. Gram stain showed possible fungus, possible fungus balls noted in Bactec bottle held at bench
 - Subcultured to Mycology media and referred to Mycology
- Lymph Node Biopsy (June 19):
 - Thio broth positive for growth on day 4, subcultured, determined to be same organism as growing in pleural fluid
- Lymph node biopsy pathology:
 - The core biopsy shows small (2-5 microns) round to elongated yeasts. No budding is seen. One yeast form shows a division plane with a dividing septa.

Mycology Workup

- Manual exam/workup
- Fungal MALDI extraction – score of 1.52

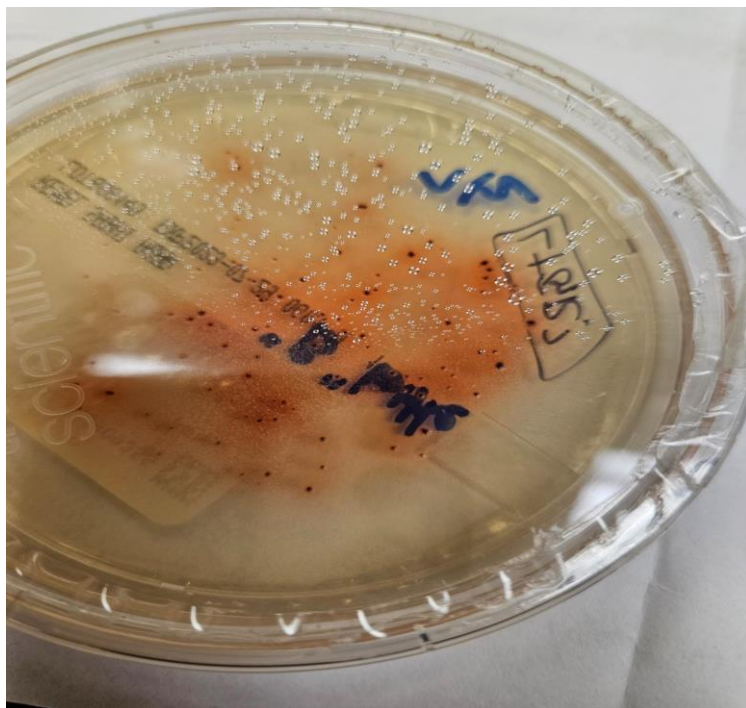
LPCB to verify Genus



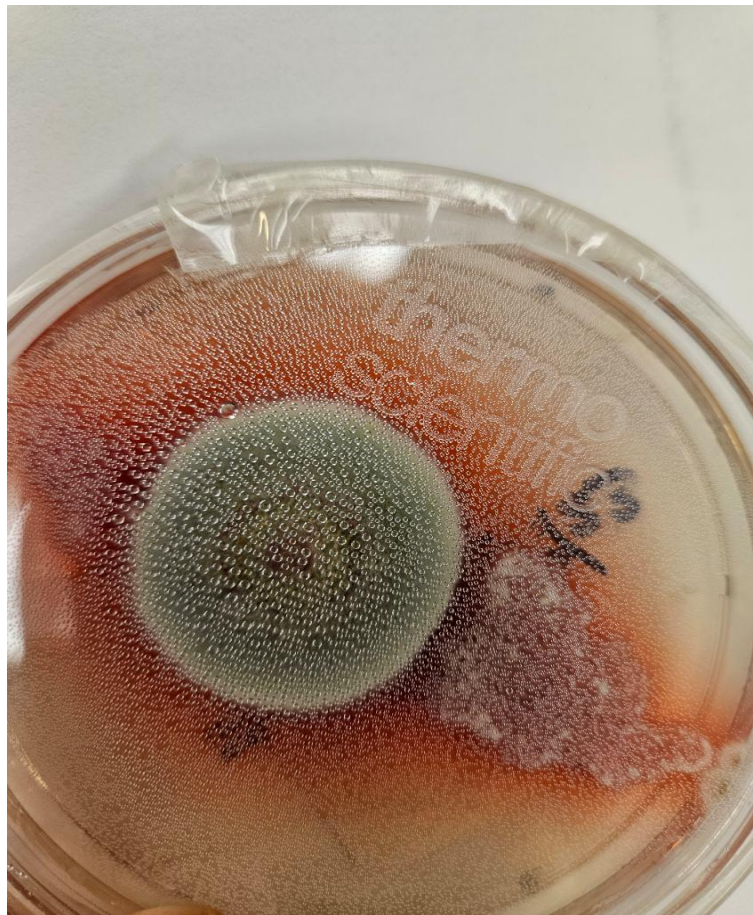
LPCB to verify Genus



Colony Morphology for Species



Colony Morphology for Species



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Colony Morphology for Species



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Talaromyces (Penicillium) marneffe

- Kingdom: Fungi
- Division: Ascomycota
- Class: Eurotiomycetes
- Order: Eurotiales
- Family: Trichocomaceae
- Genus: *Talaromyces*

- Thermally dimorphic fungus identified in 1956

Epidemiology, Pathology, Pathogenesis

- Identified in 1956 and isolated from hepatic lesions in rats infected with various *Talaromyces* species in Vietnam
- First case recorded was from laboratory acquired infection (handling animals) but the first naturally derived case from person with Hodgkin lymphoma
- Historically, thought to be exclusively restricted to patients with HIV or AIDs
- Endemic in tropical regions: especially Thailand, Vietnam, northeastern India, Southern China, Hong Kong, Taiwan, Laos, Malaysia, Myanmar, Cambodia and Laos

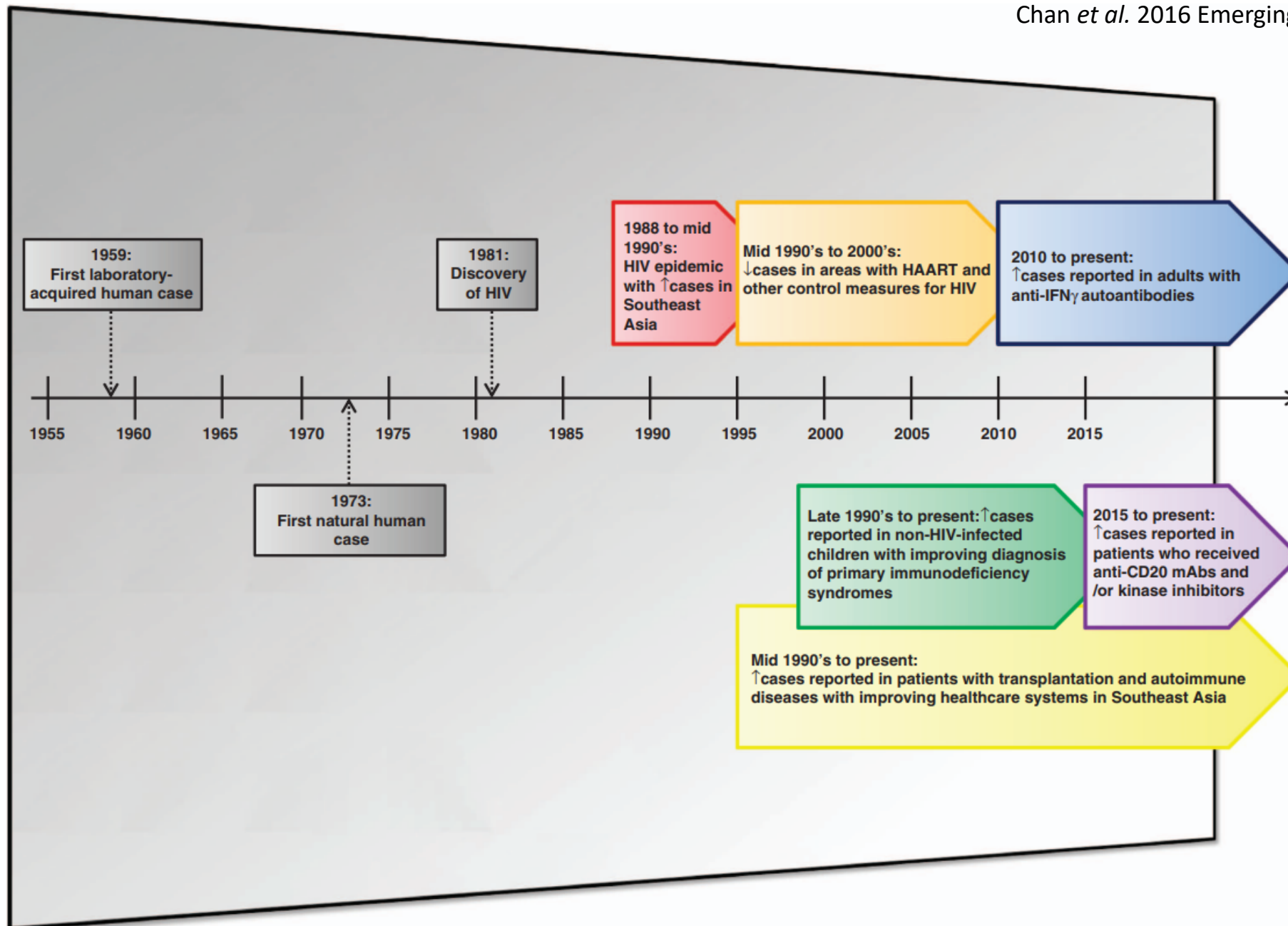


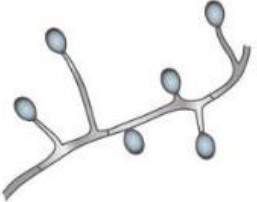
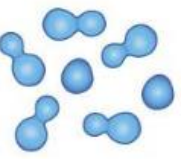
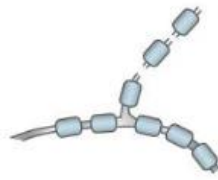

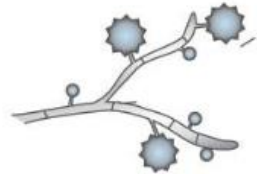

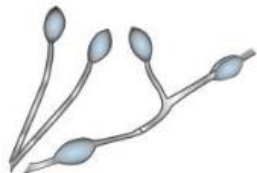



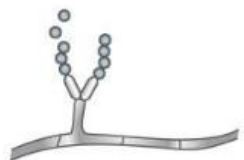

Figure 2 Major milestones in the changing epidemiology of *Talaromyces marneffei* infection. HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; IFN- γ , interferon-gamma; mAb, monoclonal antibodies.

Epidemiology, Pathology, Pathogenesis

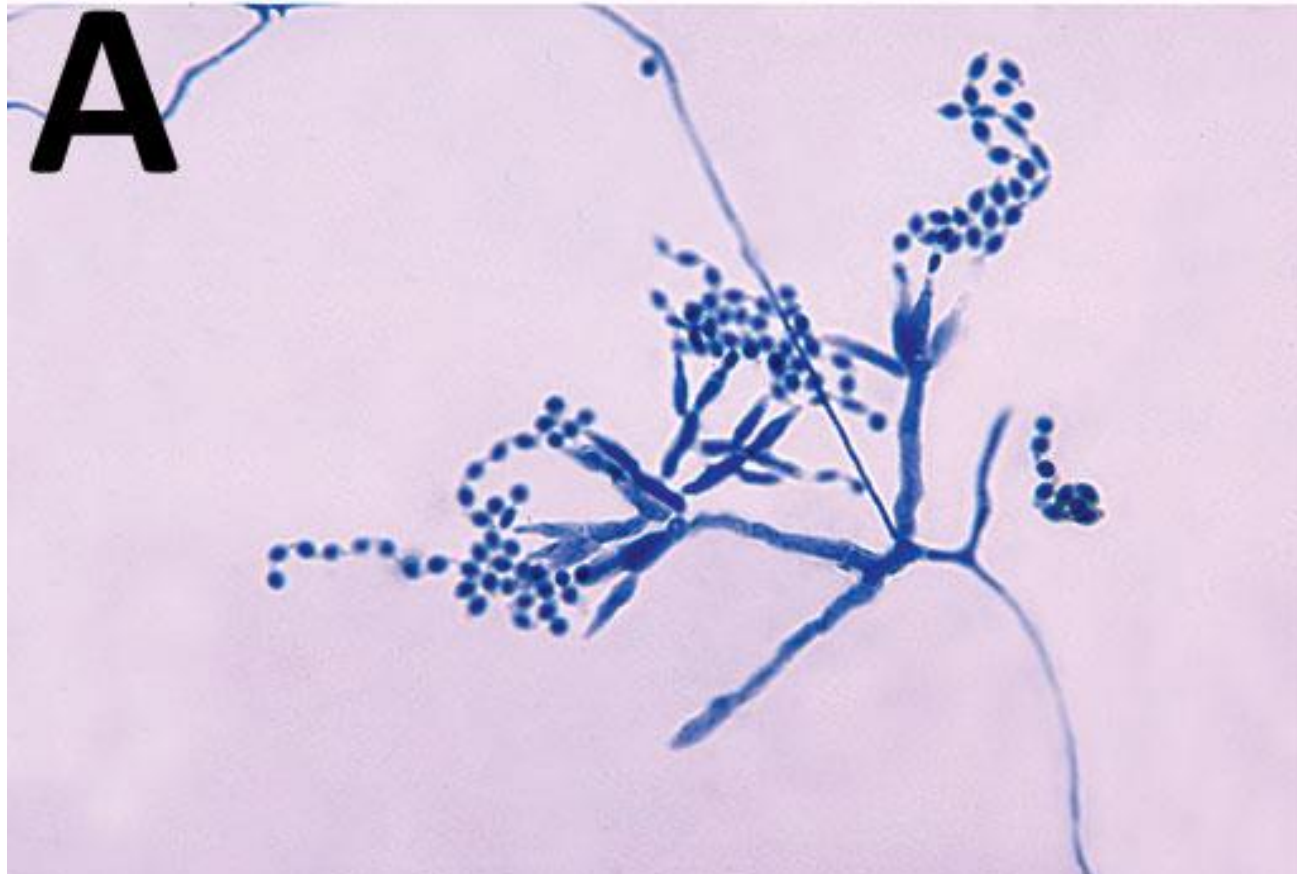
- Proliferate in macrophages and disseminates via the reticuloendothelial system
- Invades multiple body organ systems
- Activation of macrophages by T-lymphocyte-derived cytokines, especially those of the Th1 response such as: interleukin (IL)-12, IFN- γ and tumor necrosis factor (TNF)- α is important for host defense against *T. marneffe* infection

Growth, Culture, Differentiation

- Mold in the environment and yeast at tissues at 37 °C, *marneffeii* is the only dimorphic species in the genus
- Divides by septation and not budding in contrast to other dimorphic fungi
- At 25°C, *T. marneffeii* grows as multinucleate, septate, branched hyphae with tear drop shaped conidia overlying flask shaped phialides
- At 37 °C, show globe-shaped to sausage-shaped yeast cells
- It produces a distinctive red diffusible pigment, which is visible on agar media
- Determined to be genetically distinct from other *Penicillium* species (Samson *et al.* 2011b)

	Environment	Host (37°C)
<i>Blastomyces dermatitidis</i>		
<i>Coccidioides immitis/posadasii</i>		
<i>Histoplasma capsulatum</i>		
<i>Paracoccidioides brasiliensis/lutzii</i>		
<i>Sporothrix schenckii</i>		
<i>Talaromyces marneffeii</i>		





Case Resolution

- Treated with liposomal amphotericin B for 2 weeks, 3 weeks of itraconazole
- Daily electrolytes while on LAMB, renal toxicity
- Recommended at least 12 weeks of treatment in total
- Family history of Anti-TNF autoantibodies, found to have as well

Take Home Points

- Dimorphic fungus endemic to tropical Southeast Asia not commonly encountered in North America
- Fungus has ability to proliferate inside macrophages, with an ability to cause disease in virtually any organ
- A T-cell mediated cytokine response is needed to mount an effective response
- Progression to systemic disease is common if initial source is not controlled