Case 5: Answer

from University of Tsukuba Hosp.

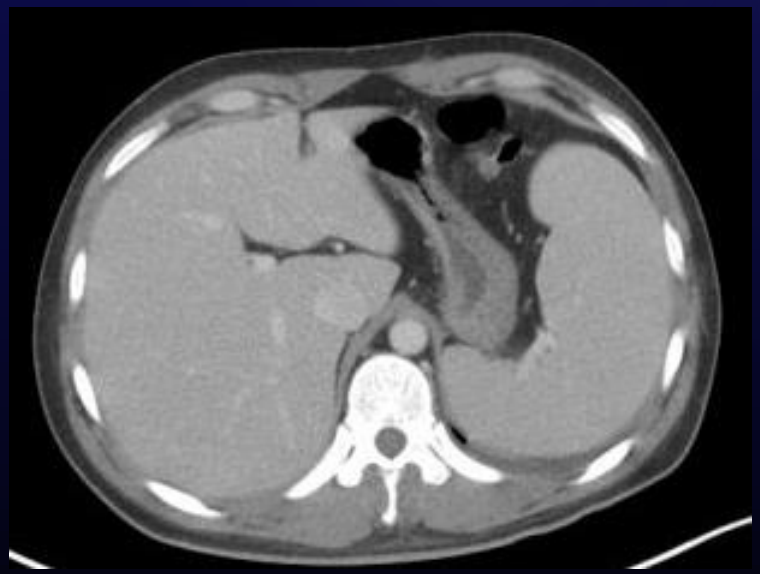
We deeply appreciate Dr. Masato Sugano, Dept. of Pathology, Univ. of Tsukuba Hosp. for his assistance of this presentation.

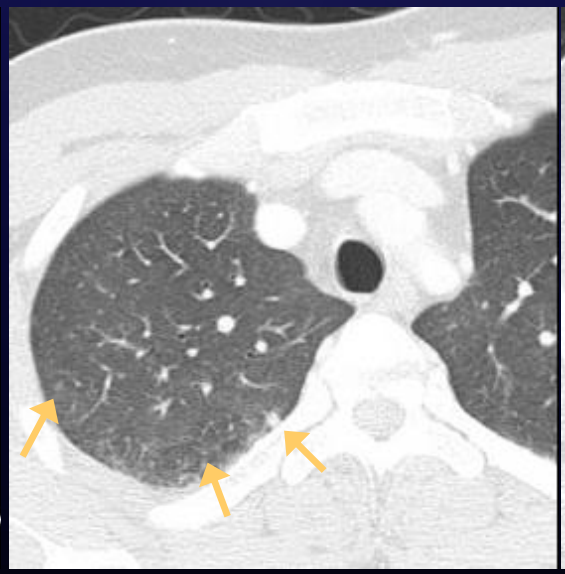
Summary: clinical & laboratory findings

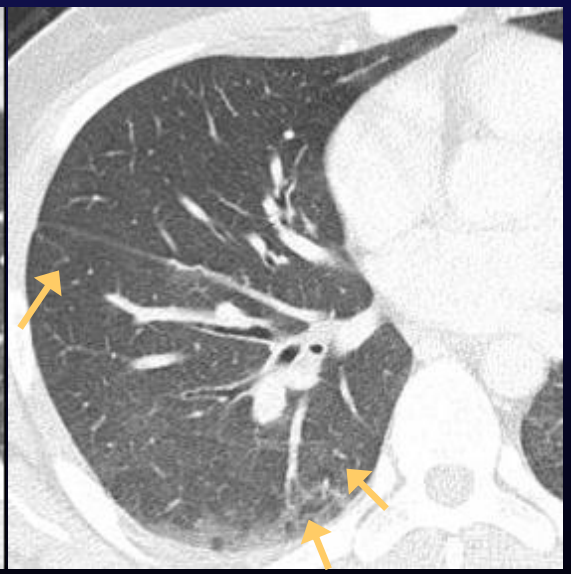
- 33-year-old man, previously healthy
- fever (>38.0° C) since 1 month ago, no response to AB
- productive cough, RR 24/min, SpO_2 97%
- CRP 8.05 μg/mL ↑
- RBC 403X10^4/μL↓, Hb 10.8 g/dL↓, Ht 31.7%↓, mildly microcytic (MCV 78.6↓), Fe 24 μg/dL↓, TIBC 238 μg/dL↓, ret 29‰↑
- Plat 13.6X10^4/μL↓, WBC 5300/μL
- Progressive abdominal distention (hepatosplenomegaly)
- LDH 644 U/L↑
- no lymphadenopathy/skin lesions/neurological abnormalities.

Summary: imaging findings

- Mild bil. pulm. hilar lymphadenopathy
- Mild pleural effusion, no ascites
- Moderate hepatosplenomegaly
- Mild diffuse thickening of bronchovascular bundles
- Multiple tiny nodules, multifocal faint irregular GGOs
- No bone abnormality
- Diffuse irregular BM enhancement

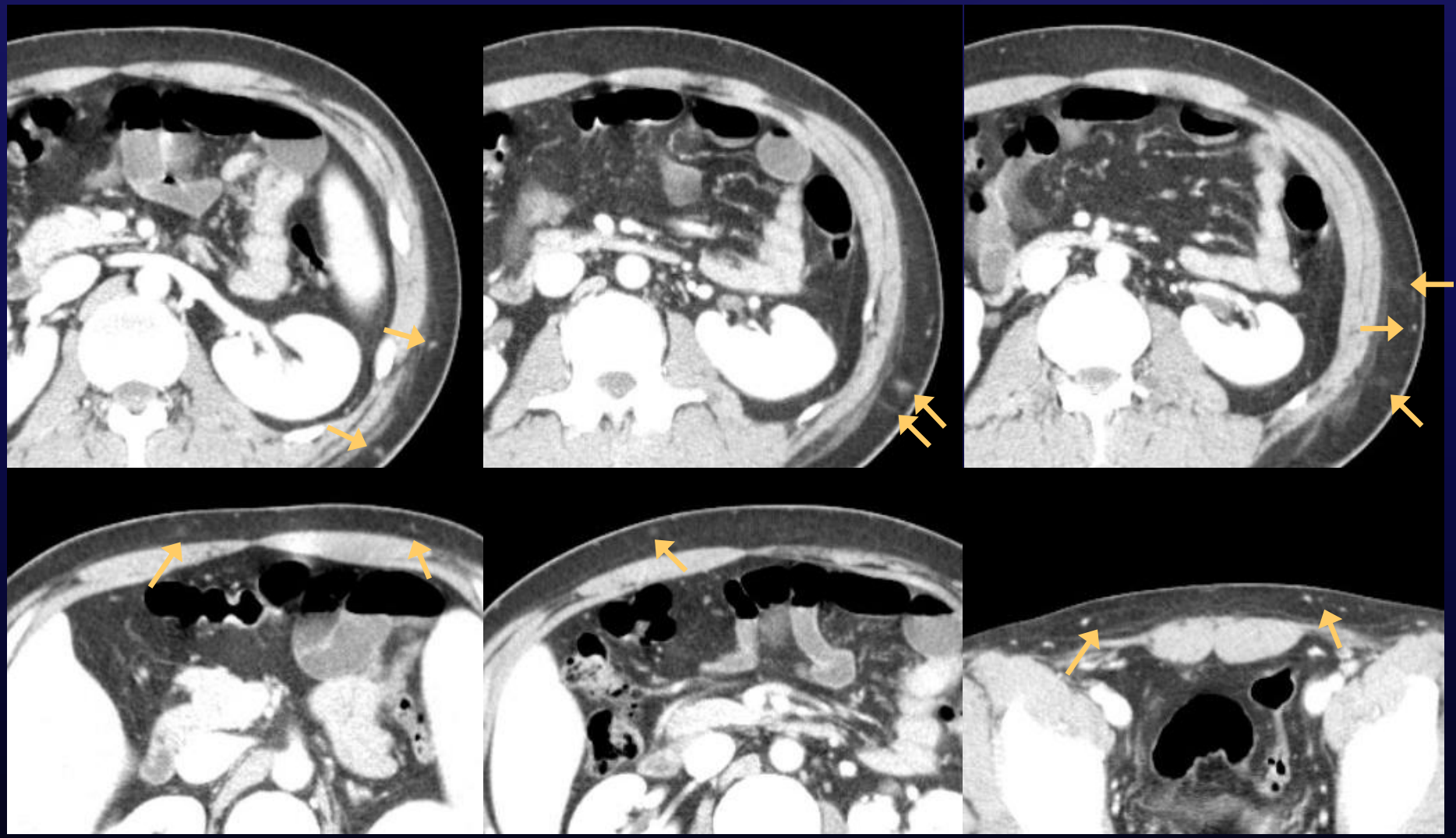






Summary: imaging findings

Postcontrast CT in September (fat window)



- **Multiple faint/tiny subcutaneous lesions**

Dx: fever of unknown origin

Then,

We requested random skin biopsy

Hepatologists did liver biopsy

→ Neutro. Infiltration

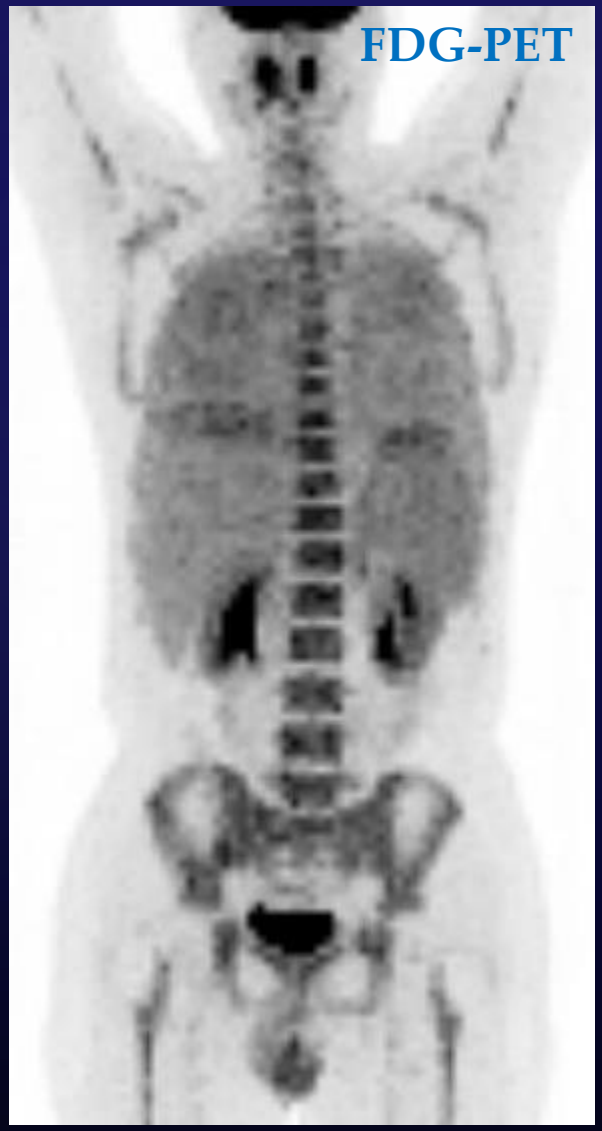
Hematologists did BM biopsy

→ hypercellular marrow

Surgeons did splenectomy

→ cogestion, no malignancy

Pulmonologists did TBLB



SALT & PEPPER Diagnosis in Imaging

by Manabu Minami, M.D.

S: Sarcoidosis
A: Amyloidosis/AIDS
L: Lymphoma
T: Tuberculosis

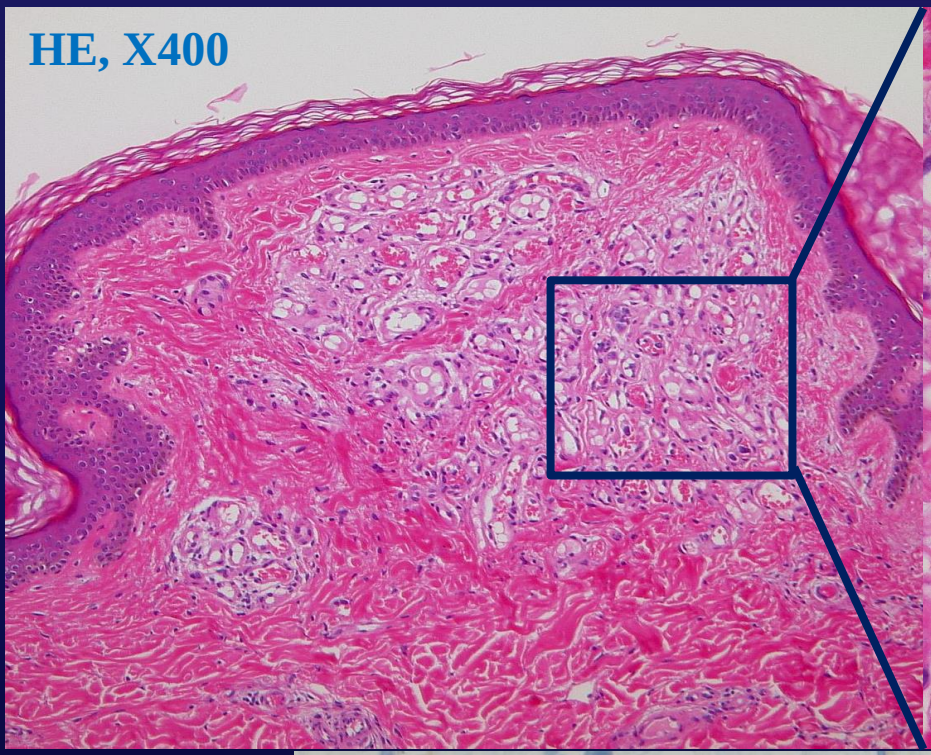
can show any varieties of image findings.

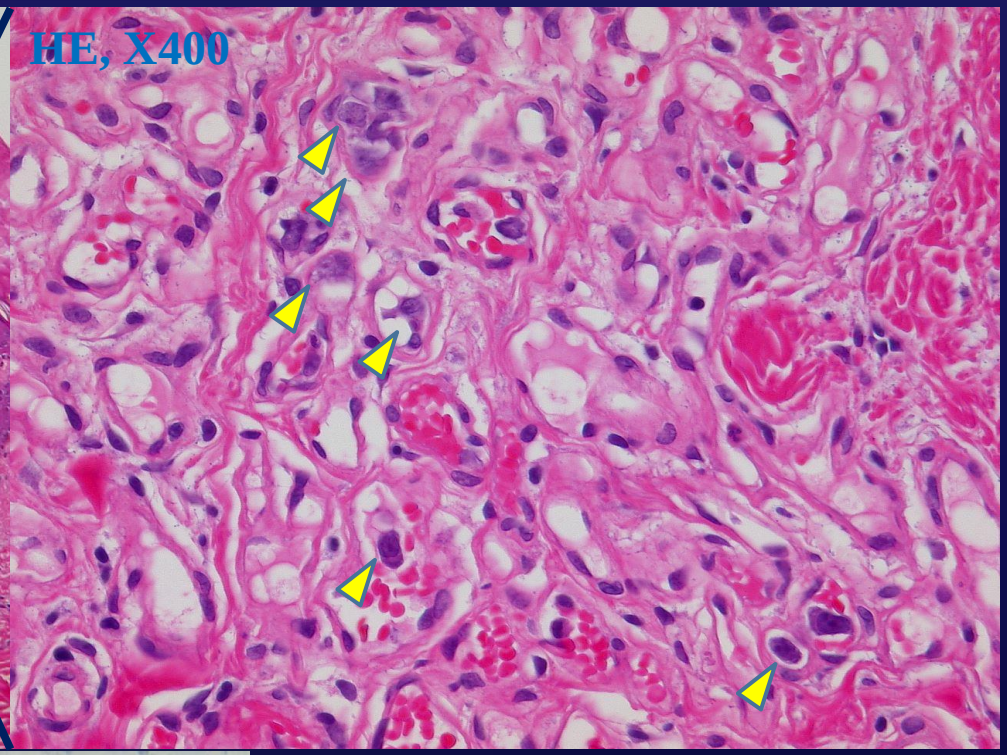
&

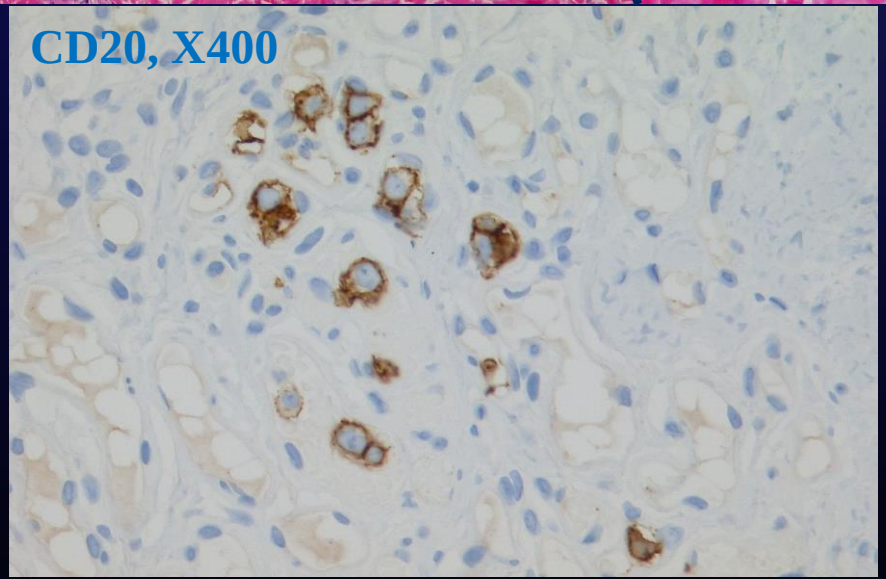
P: Parasites
E: Extrinsic (foreign bodies, iatrogenic)
P: Phacomatosis
P: Pharmacological (drugs)
E: Environmental /poisoning
R: Rare skin tumors (melanoma, etc.)

can be when you see very peculiar image findings.

Random Skin Biopsy







TBLB also showed IVL, corresponding to diffuse FDG uptake in both lungs on PET.

Intravascular Lymphomatosis (IVL)

synonyms: intravascular ML, malignant angioendotheliomatosis, angiotropic large-cell L, intravascular B-cell L

- rare, intravascular proliferation of malig. lymphoid cells with predilection for CNS and skin, malig. cells occlude & distend small arteries, veins & capillaries, NHL characterized by angiotropic growth (usually B-, can be T-, rarely NK-cell)
- may affect any organs besides brain (kidneys, BM, breast, uterus, testes, lungs, larynx, adrenal, --), possibly with EBV (esp. NK-IVL)
- 5^{th}-7^{th} decade; mean 63 y.o., slight M predom.
- dementia (most common), confusion, memory loss, cognitive failure, focal deficits, seizure, fever, CNS involved in > 30% of cases
- skin: raised plaques or nodules over abdomen & thighs (50%)
- Dx may be made by skin or brain biopsy
- CSF: may show ↑protein, no malignancy in peripheral blood or BM

Intravascular Lymphomatosis (IVL)

- T2/FLAIR: multifocal hyperintensities in deep white matter, cortex, & basal ganglia
- may mimic infarct (1/3 cases), diffusion restriction common
- typically with linear & punctate CE, often mimics vasculitis
- may show meningeal &/or dural CE
- spinal cord can be involved
- DSA: often mimics vasculitis, alternating stenosis and dilatation, "beading," primarily involving 2nd-3rd order branches
- FDG-PET helpful in diagnosing IVL in bone marrow & kidneys

DDx: vasculitis, multi-infarct dementia, primary CNS lymphoma, neurosarcoidosis, hemophagocytic lymphohistiocytosis

- Px: mean survival: 7-13 month, mortality rate> 80%, spontaneous regression rarely occurs, Dx often made postmortem (underDx)

However, the presentation in this case is quite different!

There has been reported another type of IVL: an Asian variant!

(lymphoma associated with hemophagocytic synd./malig. histiocytosis)

Asian variant	Symptoms & signs	Classical (Western) type
fever, CRP↑, hepatosplenomegaly	Clinical manifestation	embolic/vasculitis-like symptoms
hemophagocytosis, pancytopenia, LDH/IL2R↑	Laboratory data	LDH/IL2R↑
rare	Small vessel involvement	Frequent in the brain/skin (rash)
exertional dyspnea, liver dysfunction, pancytopenia	Lung/liver/BM lesions	rare
no LN swelling	Lymphadenopathy/tumor	sometimes
Randomly skin/lung/BM	Recommended biopsy site	Skin lesions/brain

Transition from the Asian variant to the classical type has been reported.

Final Diagnosis

Intravascular large B-cell lymphoma (IVL)

Asian variant

Take Home Points

- **Elevated LDH is a good clue for the diagnosis of hematologic disorders including IVL.**
- **Imaging findings of classical type IVL are nonspecific, but it should be considered in patients with dementia or multifocal enhancing lesions which resembles brain infarcts or vasculitis.**
- **Recently, a new type of IVL, Asian variant, has been recognized, which mainly involves the lung, liver, and bone marrow showing different features from the classical IVL.**

References

1. Fonkem E, Lok E, Robison D, et al: The natural history of intravascular lymphomatosis. Cancer Med. 2014;3(4):1010-24.
2. George MR: Hemophagocytic lymphohistiocytosis: review of etiologies and management. J Blood Med. 2014;5:69-86.
3. Martin-Duverneuil N, Mokhtari K, et al: Intravascular malignant lymphomatosis. Neuroradiology. 2002;44(9):749-54.
4. Murase T, Nakamura S: An Asian variant of intravascular lymphomatosis: an updated review of malignant histiocytosis-like B-cell lymphoma. Leuk Lymphoma. 1999;33(5-6):459-73.