

Vasculitis or ...?!

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62 year-old man with one-year history of progressive upper & lower extremity weakness + purpura + burning pain in legs + Malaise + migratory polyarthralgias + 30 kg weight loss

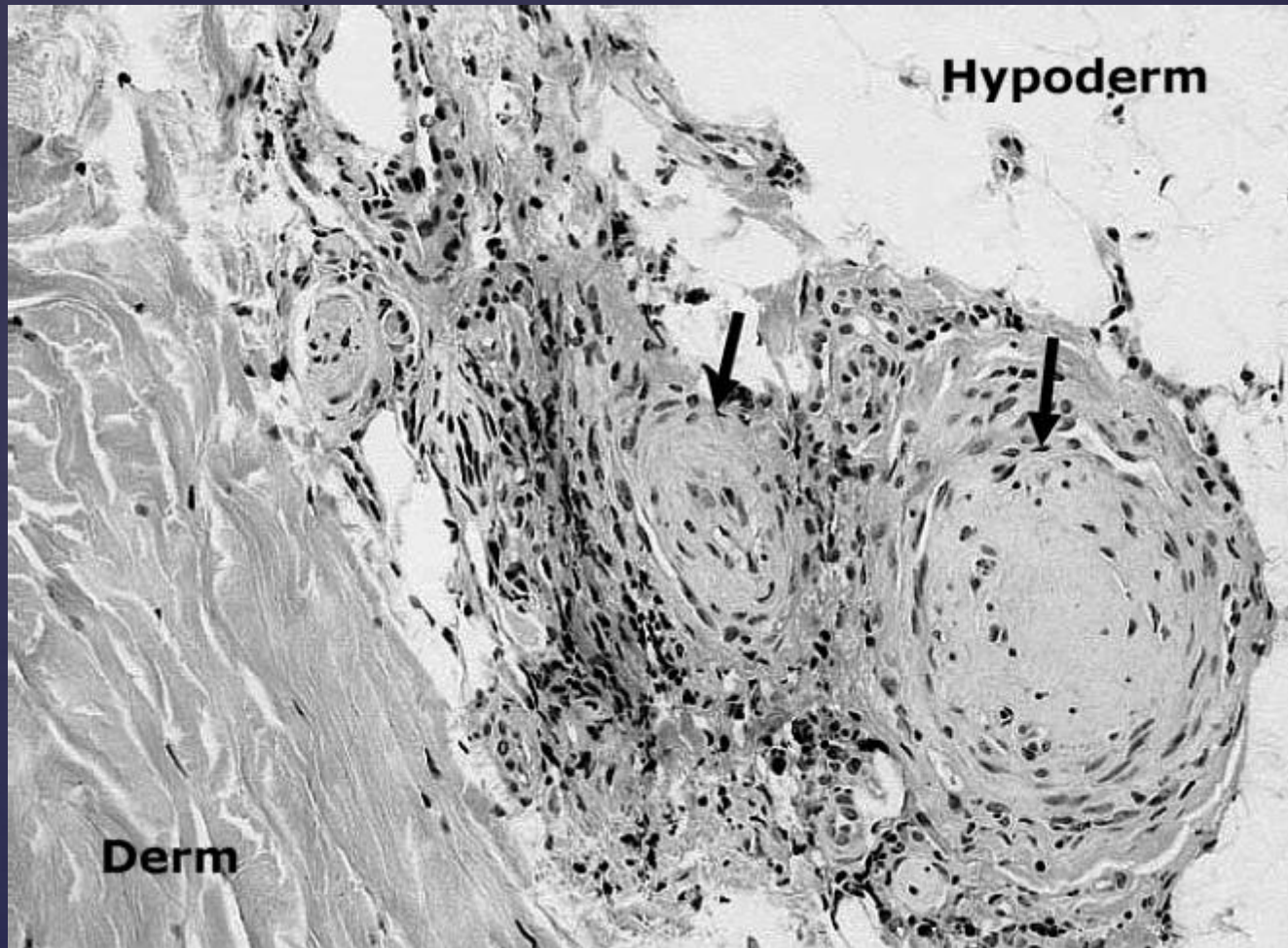
Large erythematous plaque-like skin lesions over both shins + painful dysesthesia in distal lower limbs + bilateral muscle atrophy of limbs + absent DTRs in all limbs

WBC=4000/mm³, Hb=8.9 g/dL, ESR=74 mm/h, Cr.=0.5 mg/dL, CPK<20 mg/dL, HIV(-), Hepatitis profile (-), SPEP: MGUS
ANA=1/160, RF(+), ANCA(-)

Clinical Dx. by a rheumatologist: Subacute ascending sensory-motor polyneuropathy

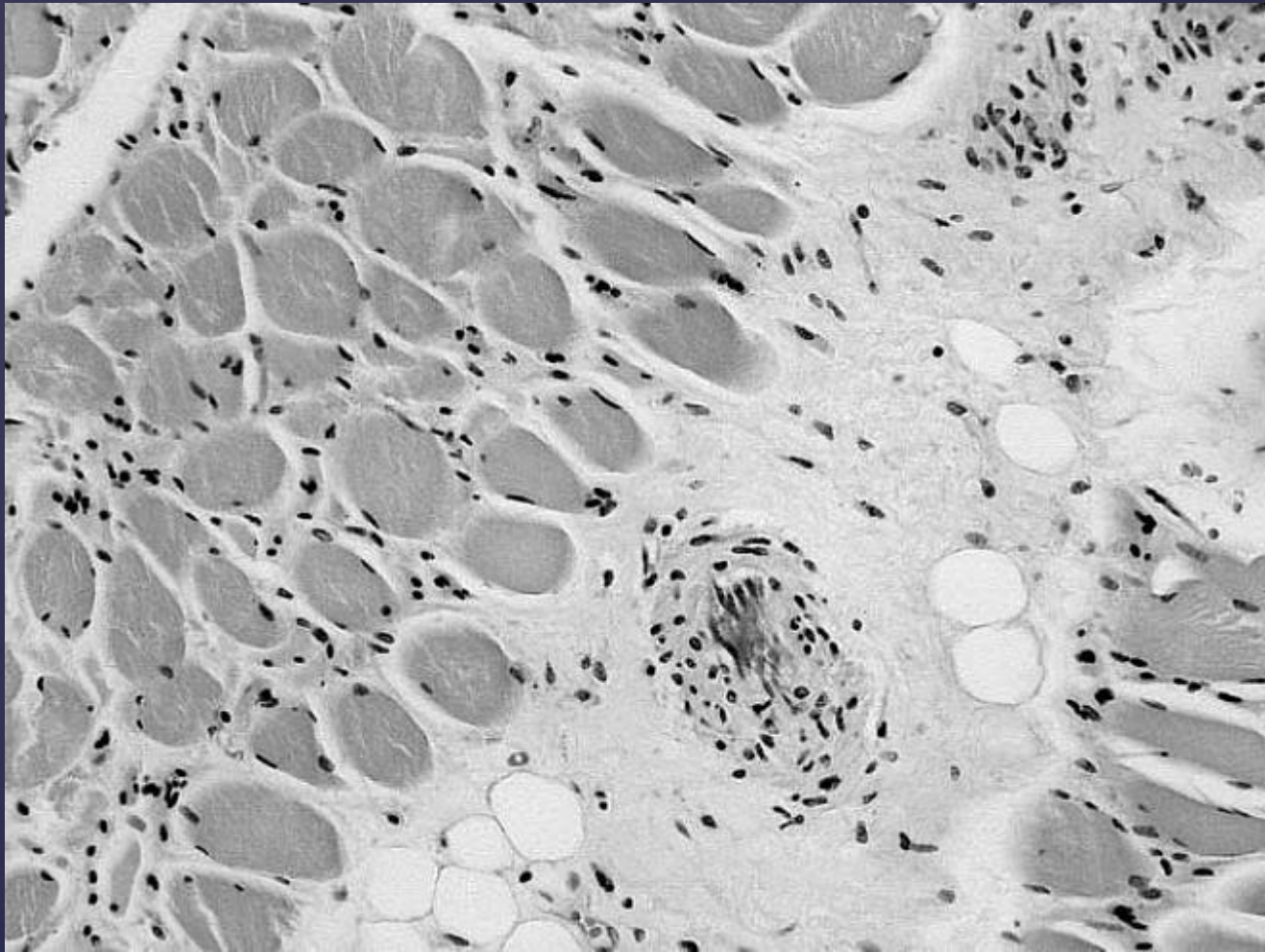
Tx. plan: Six monthly CTX pulses + high dose of steroid

Skin biopsy



Skin biopsy showed mild superficial perivascular dermatitis and couple of occlusive vasculopathies.

Muscle & Sural Nerve Biopsy



Perivascular & intraluminal lymphocytic infiltration of small arteries consistent with lymphocytic vasculitis

Based on biopsy results, patient discharged with low-dose oral CTX (75 mg/d) along with prednisolone 30 mg/d.

One month afterwards, purpuric skin lesions and burning pain in legs had improved but he continued to have marked generalized weakness.

Two months later he presented with acute abdominal pain, nausea, vomiting and diarrhea.

T=40 C, PR=137/min. , BP=116/76 mmHg, RR=26/min.

Abdomen was distended and had rebound tenderness.

WBC=1000/mm³, Hb=7.5 g/dL, plt count=36,000/mm³

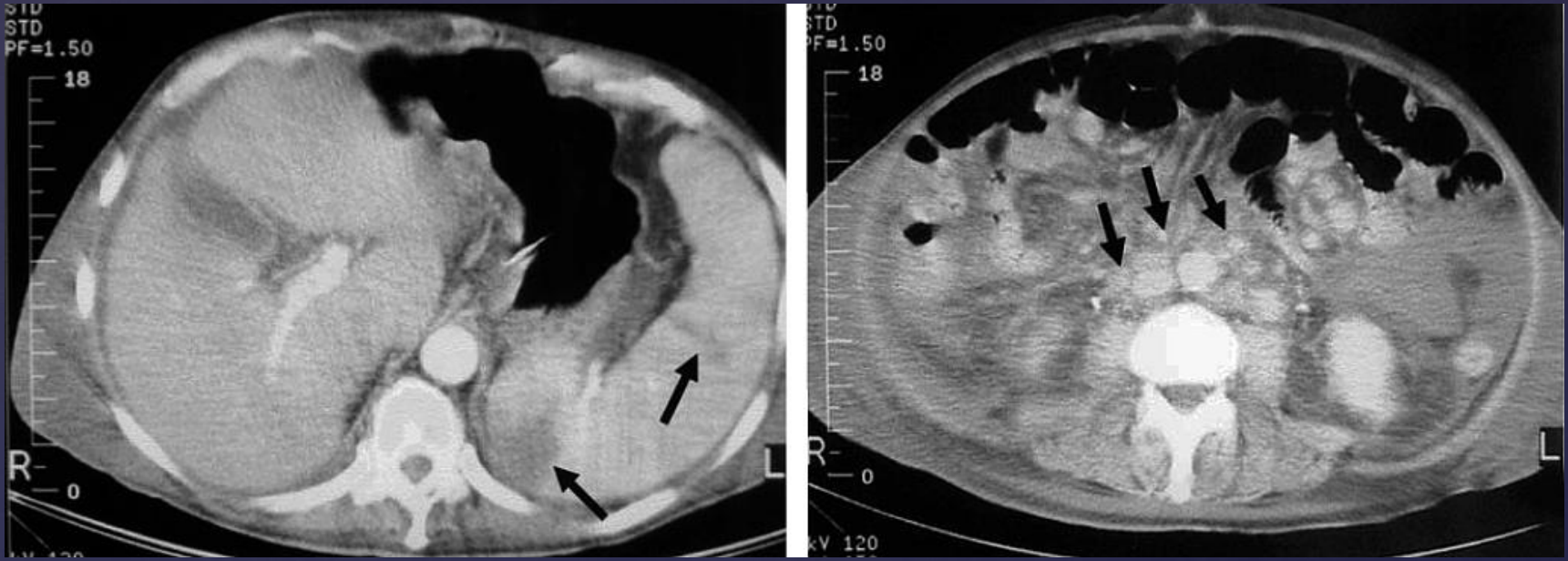
There was no free air in plain abdominal radiograph

He was intubated & admitted to ICU and IV antibiotics started for presumed sepsis.

Emergent exploratory laparotomy found no bowel perforation or other significant pathologies besides small amount of ascites. No biopsy was done.

The next day, he developed GI bleeding and Lansoprazole infusion started. On ICU day#2, a CT scan of abdomen and pelvis performed.

Abdominal CT Scan



Bilateral pleural effusion

Ascites

Splenomegaly with two hypodense lesions in the spleen that were consistent with splenic infarction

No intraabdominal lymphadenopathy was reported at the time.

At this point, the impression was overwhelming infection, bowel ischemia due to abdominal vasculitis, and/or malignancy infiltration.

A peripheral blood smear showed for the first time the presence of some atypical lymphocytes.

BM biopsy was consistent with reactive process (EBV, CMV, Toxoplasmosis, treated CLL, or ...).

On ICU day#14, patient passed away after a massive GI bleeding and the ensuing CV collapse, despite full attempt at his resuscitation.

Autopsy Findings

The cause of death was multiorgan failure: Ischemic enteritis, Diffuse alveolar damage, CMV & fungal bronchopneumonia, Renal failure.

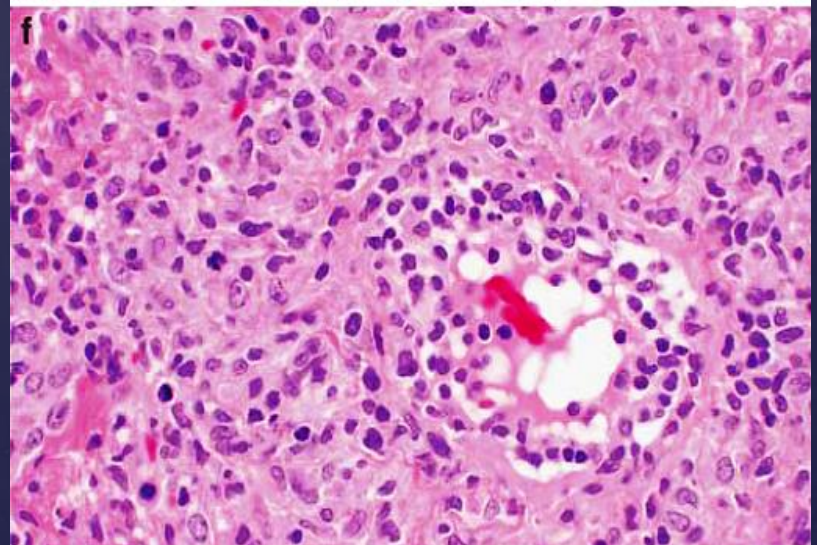
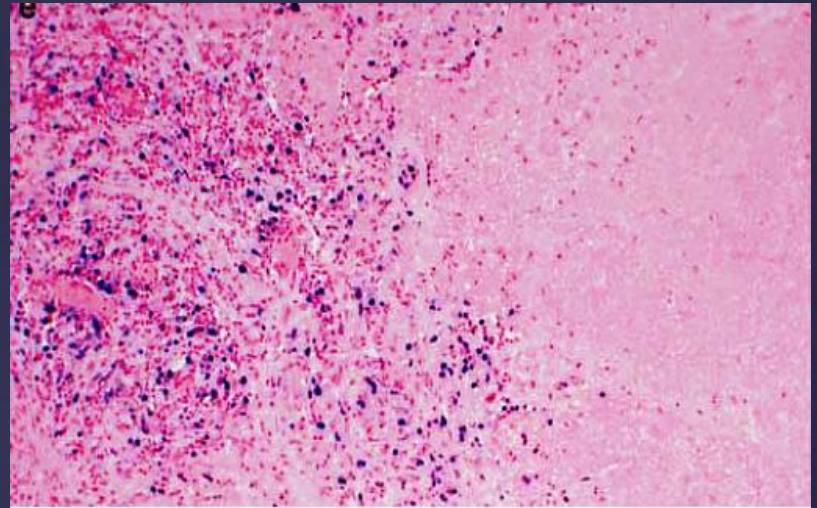
There was striking paraaortic, omental and mesenteric lymphadenopathies. The lymph node, BM, spleen and intestinal examination showed malignant lymphoma, with abundant EBV-infected B lymphocytes .

Final Dx.: Lymphomatoid Granulomatosis

Histology of Lymphomatoid Granulomatosis

Angiocentric & angiodestructive process composed of a mixed population of lymphoreticular cells, lacking true granulomatous features, resulting in vascular invasion and necrosis

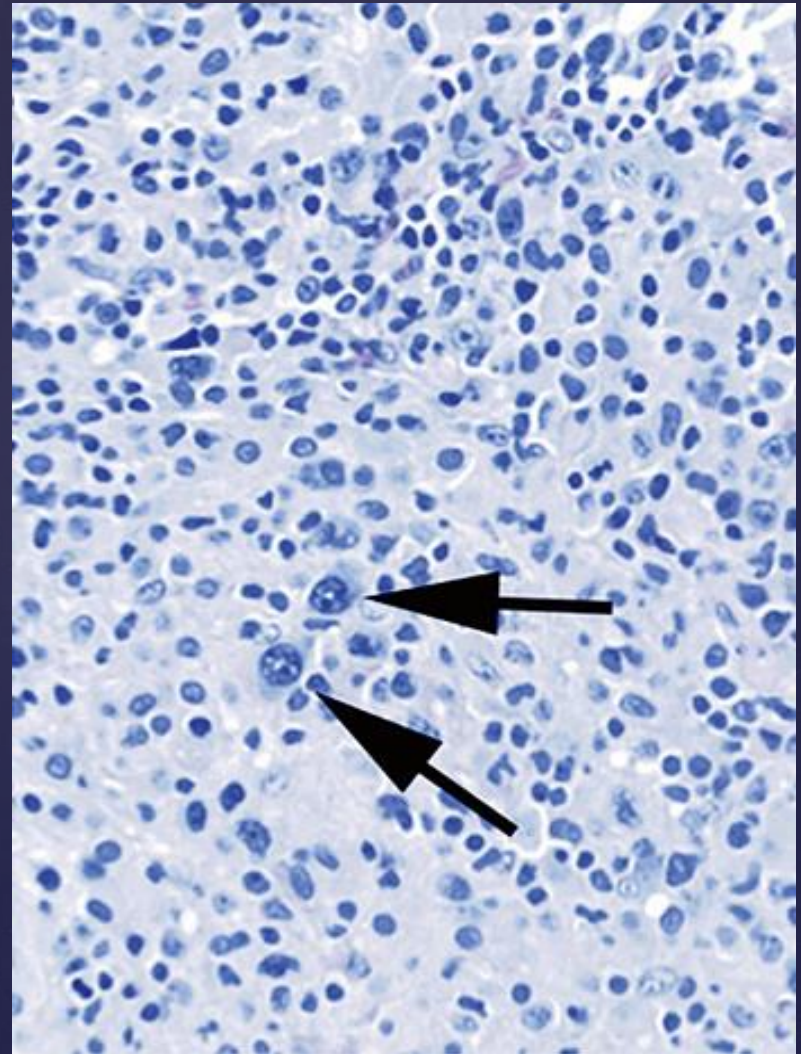
The transformed cells are EBV-infected large B-lymphocytes that are atypical and the vascular invasion is done by abundant reactive T-lymphocytes.



LG versus large B-cell Lymphomas

The polymorphous background cellular infiltration and the EBV-positivity is necessary for the diagnosis of LG, and to distinguish it from other large B-cell lymphomas.

According to WHO, a lymphoma composed of a uniform population of atypical EBV-positive B-cells without a polymorphous cellular background should be classified as diffuse large B-cell lymphoma.



Clinical Features of LG

- ❖ Generally occurs in 4th-6th decades of life with 2-3/1 male predominance.
- ❖ Most commonly presents with cough, dyspnea, fever, fatigue, malaise and weight loss.
- ❖ Lung is by far the most commonly involved organ. Lung lesions are bilateral parenchymal nodules favoring the lower zones.
- ❖ CNS involvement occurs in up to one third of cases, carries poor prognosis, LP is usually not diagnostic, and imaging shows nodular lesions.
- ❖ Lymph nodes become more involved as the disease progresses.
- ❖ The clinical course is varied according to the grading of the lesion, based on the number of EBV-positive cells in the lesion.
- ❖ The largest reported series of 152 patients, reported a 67% mortality rate and a median survival time of 14 months.

Skin in Lymphomatoid Granulomatosis

- ❖ Patchy, occasionally painful, erythematous macules, papules, and plaques typically involve the gluteal regions and extremities.
- ❖ Erythema may involve nodosum-like subcutaneous nodules that may ulcerate but are often truncal.
- ❖ Isolated cutaneous lymphomatoid granulomatosis has been reported.

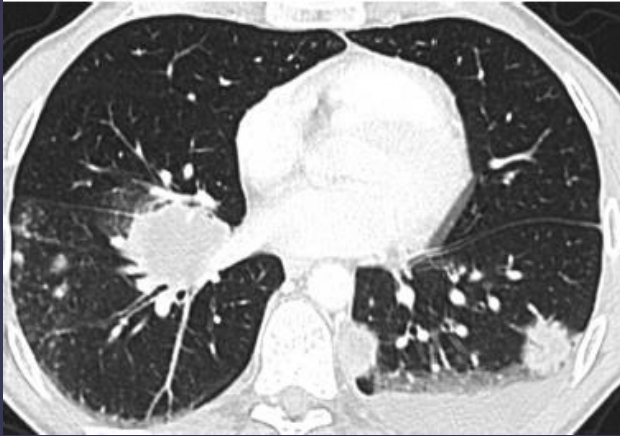


Lung Involvement in LG

Organ System Involved	Clinical Features	Diagnosis
Pulmonary (lung and mediastinal lymph nodes)	-Dyspnea, Cough, Chest pain, Fatigue, Non-productive cough -Constitutional symptoms -rarely, asymptomatic -Underlying Immunodeficiency e.g. AIDS - may clinically mimic pneumonia or interstitial lung disease [5]	-Chest Radiograph-non specific - Differential Diagnosis: Pseudolymphoma, Interstitial Pneumonia, Wegener's Granulomatosis, Sarcoidosis, Metastasis [8] -High Resolution CT chest-peribronchovascular distribution of nodules and coarse irregular opacities, small thin walled cysts, and conglomerating small nodules [8]

Lung CT & PET Scan in LG

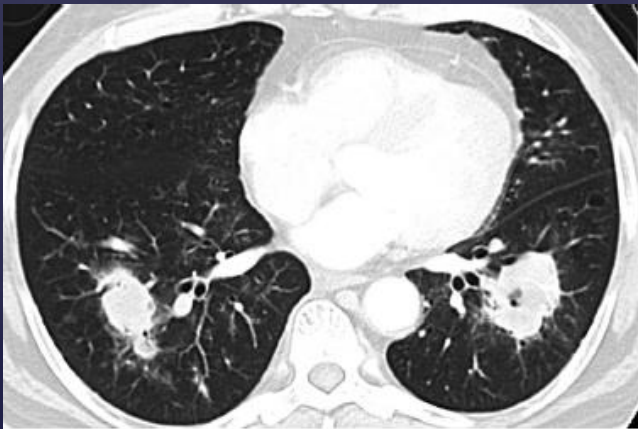
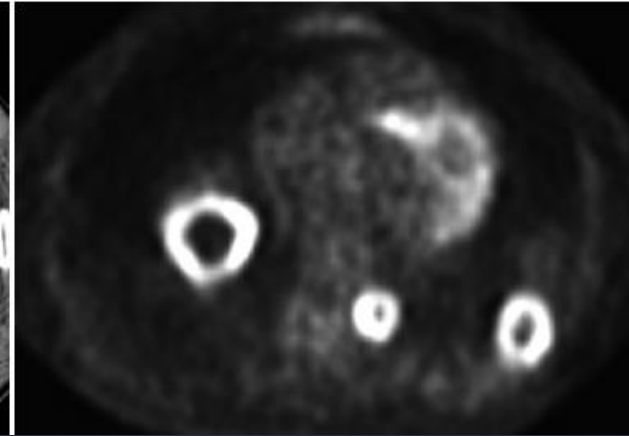
Ground glass pattern adjacent to the lesion



Peripheral contrast enhancement of the nodule

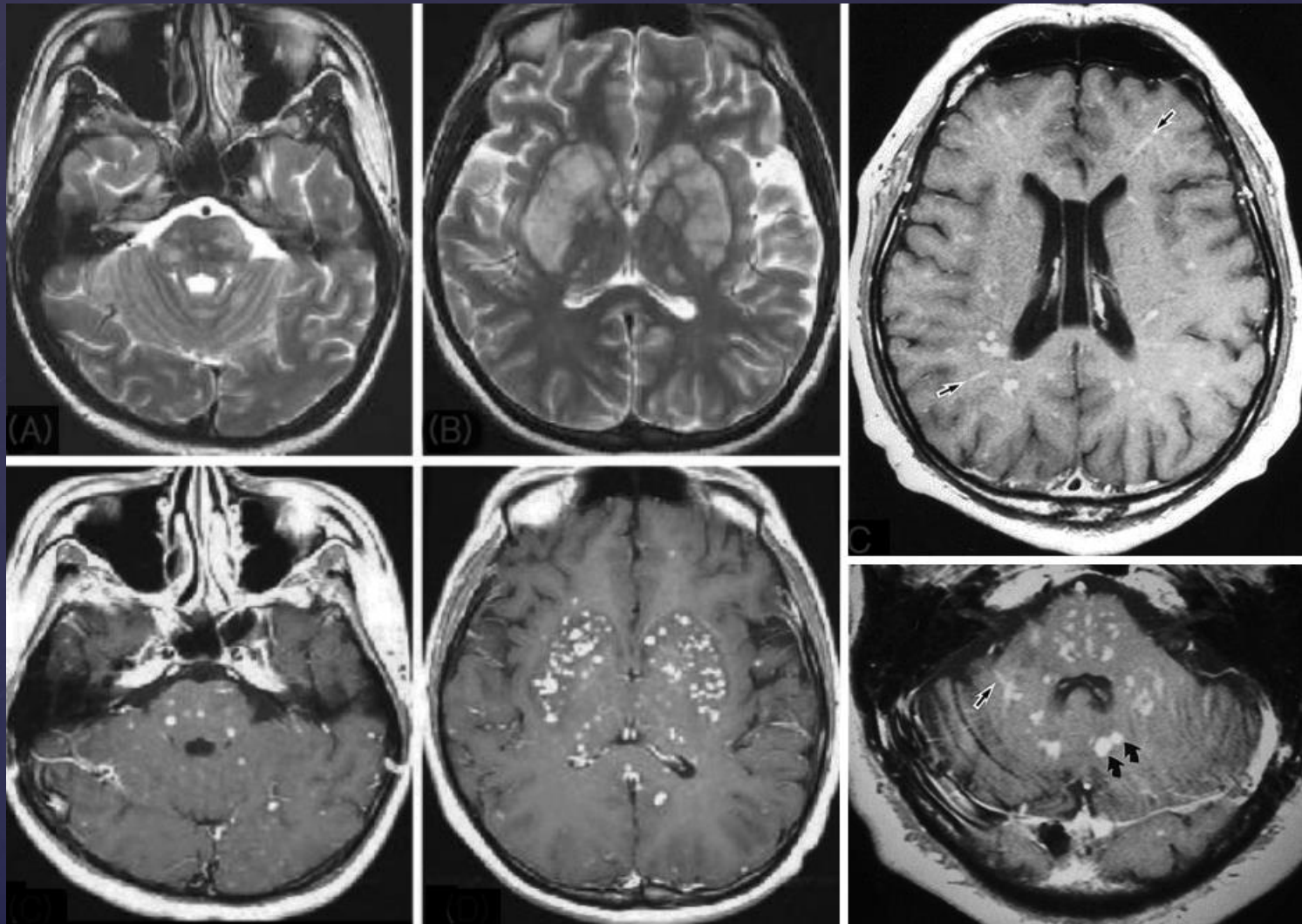


Peripheral FDG uptake of nodules in PET scan



Peribronchovascular distribution of nodules, their tendency for central cavitation, and peripheral ground glass lesions

Brain MRI in LG



Although the MR appearance of LG of the brain varies, multiple punctate or linear enhancements that reside along the perivascular space suggest LG.

References:

- 1) Lymphomatoid granulomatosis: a rare mimicker of vasculitis
Journal of Rheumatology (2005) 32: 11, 2242-2245
- 2) Current histological diagnosis of lymphomatoid granulomatosis
Modern Pathology (2012) 25, S39-S42
- 3) Lymphomatoid Granulomatosis: CT and FDG-PET Findings
KJR (2011), 12(6): 671-678
- 4) Lymphomatoid granulomatosis – A rare pulmonary lymphoproliferative disease
Rev. Port. Pulm, (2016) 22(4): 248-251
- 5) Clinical Mimics of Lymphoma
The Oncologist (2004) 9:406-416
- 6) Lymphomatoid Granulomatosis: Abnormalities of the Brain at MR Imaging
Radiology (2005) 237:265–273
- 7) FDG-PET findings of the brain in lymphomatoid granulomatosis
Annals of Nuclear Medicine (2006) 20, 10, 683–687
- 8) The radiological spectrum of pulmonary lymphoproliferative disease
The British Journal of Radiology (2012) 85, 848-864