

Diagnosis Under Pressure

Peripheral T-Cell Lymphoma as an Elusive Cause of Progressive Eosinophilic Myocarditis

Dylan Mart, MD; Jacob Luty, M.D.; Cristina Fuss, M.D.; Rebecca Harrison, M.D.

Department of Medicine, Oregon Health and Science University

Introduction

Eosinophilic myocarditis (EM) is a rare cause of progressive myocardial dysfunction that has a broad array of inciting diseases processes and many distinct complications. An elusive cause of EM is peripheral T-cell lymphoma (PTCL), a protean entity with varied presentations. We present a case of PTCL that defied diagnosis, stressing the importance of a broad differential for causes of EM.

Case

Previously healthy 49 year-old Cantonese woman originally presented for evaluation of chest pressure. Multiple previous presentations for progressive fatigue, workup at that time pertinent for:

- Leukocytosis with prominent eosinophilia (69%)
- TTE with preserved EF, but demonstrating apical RV thrombus
- Cardiac MR demonstrating circumferential subendocardial late gadolinium enhancement
- BMBx: basic autoimmune & infectious workup negative,
- FNA of submandibular adenopathy technically suboptimal

Discharged on empiric trial of systemic steroids

Presented again several weeks later with acute-onset substernal chest pain. Objective findings concerning for:

- Lateral ST depressions on EKG, troponemia, leukocytosis with eosinophilia (47%), thrombocytopenia, mild anemia, and LDH 602 U/L
- PET demonstrated avid bulky cervical and periaortic lymphadenopathy with increased hepatic and splenic uptake
- FNA of cervical adenopathy attempted, unrevealing

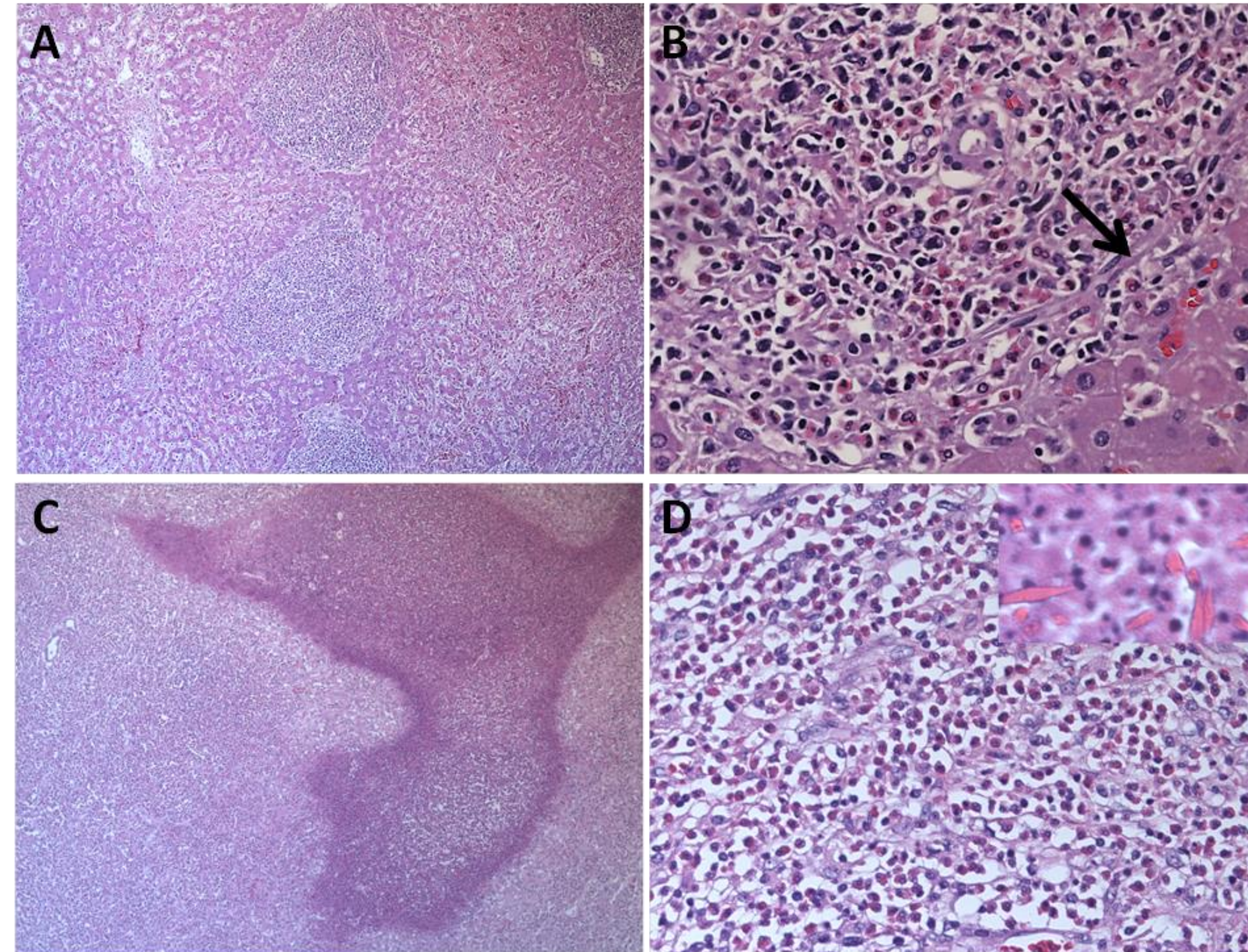
Planned for excisional biopsy, however the patient developed acute hypotension and tachypnea, prompting escalation of care. Bladder pressure obtained given increasing abdominal distension, returned markedly elevated & concerning for intraabdominal hypertension. Emergent ExLap demonstrated evidence of abdominal compartment syndrome, with large-volume ascites.

- Labs now demonstrated profound transaminitis, coagulopathy with evidence of DIC, and metabolic acidosis all concerning for shock liver.

Despite supportive measures, the patient's clinical status deteriorated, and she passed surrounded by family

IHC staining of specimens obtained from liver nodules seen on autopsy:

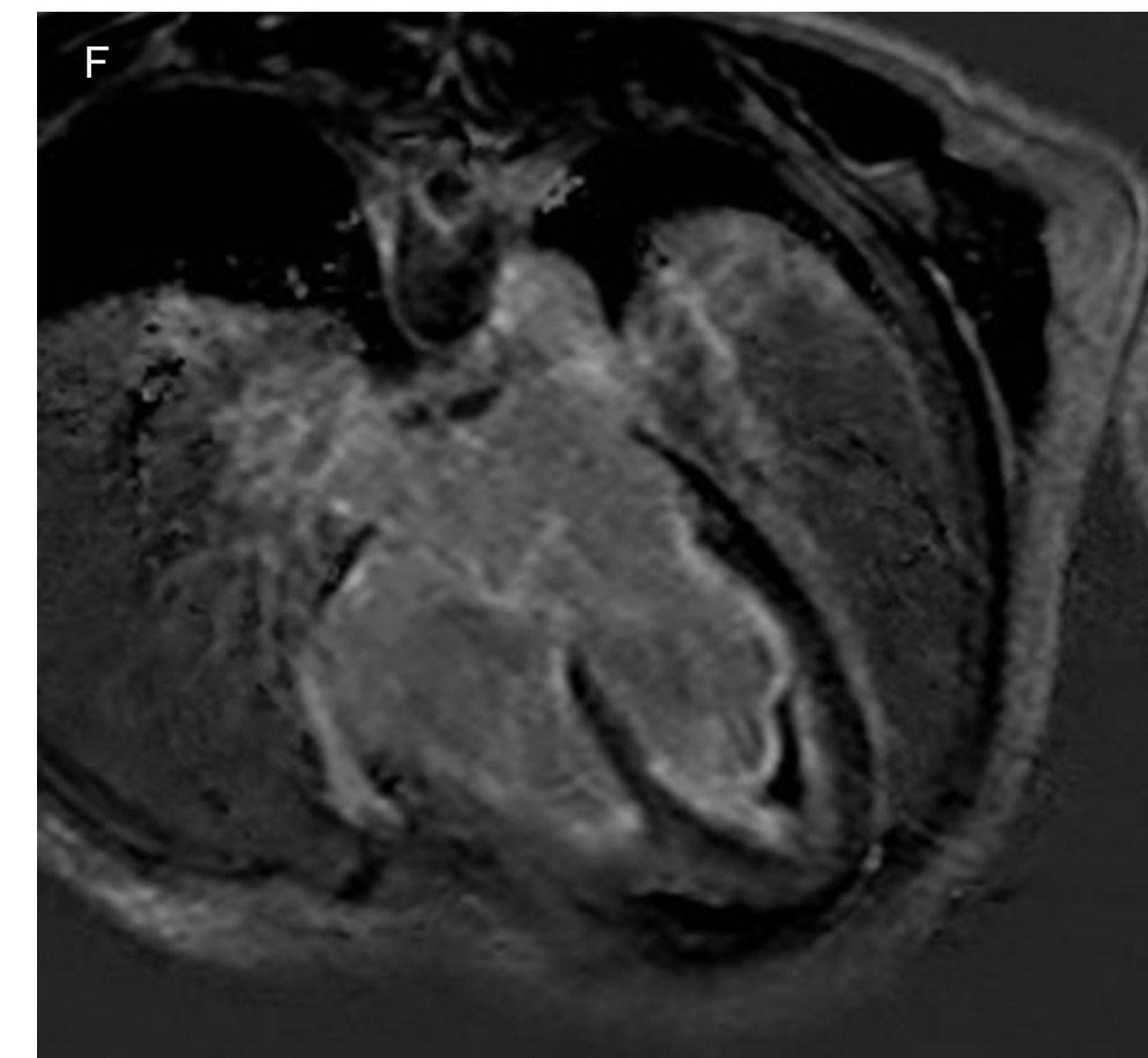
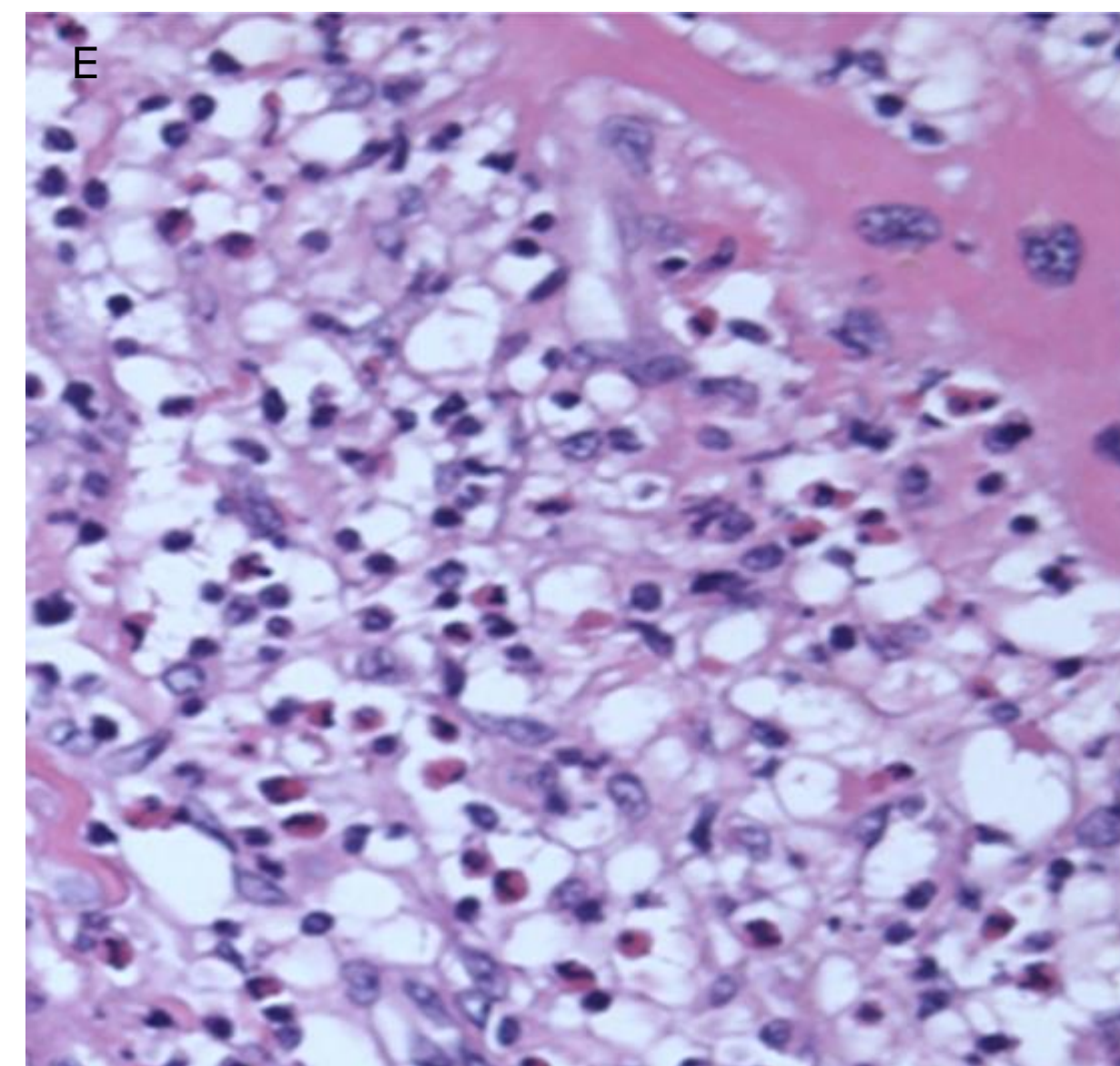
- **Atypical infiltrate with prominent nucleoli and admixed eosinophils, CD3+, CD4+, CD5+, CD8+**
- **Negative for CD56, gamma/delta, CD-19**



Microscopic findings in the liver. **A)** Portal tracts expanded by cellular infiltrate. **B)** Portal infiltrate contains cells with enlarged, hyperchromatic atypical nuclei, eosinophils, and a compressed portal vein radical. **C)** An area of geographic necrosis. **D)** The necrotic parenchyma is replaced by a dense collection of eosinophils containing Charcot-Leyden crystals



FDG PET-CT above demonstrating increased uptake in cervical & periaortic lymphadenopathy, as well as liver and spleen.



E) Microscopic findings in the heart, Eosinophilic interstitial infiltrate in myocardium. **F)** PSIR image captured on cardiac MRI demonstrating late-phase subendocardial gadolinium enhancement involving both the right and left ventricles, which does not respect a vascular territory. The differential includes eosinophilic myocarditis and amyloid deposition.

Discussion

PTCL describes a collection of disease entities with no defining clinical or phenotypic features, and constitute 4-10% of NHL overall¹. There is an elevated incidence in Asian populations, as PTCL constitutes approximately 20% of all NHL² presenting in that group.

Presenting symptoms are non-specific: Classic "B symptoms" only present in 35% of cases³. Extra-nodal involvement is present in 49% of cases, solid organ involvement in 17%.

Lab findings:

- Elevated LDH ~50% of cases
- Thrombocytopenia ~25% cases
- Anemia ~25% of cases
- Eosinophilia – Variable

Histology:

- Pleomorphic cell types, most commonly resembling T-cell phenotype
- Variable findings on immunohistochemistry, characteristically lack typical "B" markers, and variably express mature T-cell markers (CD4,5,8, etc)

Adverse prognostic indicators³:

- Low IPI
- Bulky adenopathy
- Thrombocytopenia

Take home points

- PTCL refers to an array of NHL variants of various phenotypes
- PTCL can manifest with seemingly idiopathic eosinophilia as a paraneoplastic phenomenon: A reactive process generated by constitutive expression of IL-3, which is incompletely responsive to steroids⁴
- The prevalence of PTCL in Asian populations is pronounced, accounting for ~20% of NHL, and special consideration should be given for an atypical phenotype when there is clinical concern for lymphoma.
- The diagnosis is suggested by histology demonstrating a pleomorphic cellular infiltrate of nodal and solid-organ involvement without expression of B-cell associated antigens on IHC, and variable expression of mature T-cell markers
- Diagnostic yield of FNA is low. Excisional biopsy offers more favorable operating characteristics, and should be pursued if possible.⁵

References:

1. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, Advani R, Ghielmini M, Salles GA, Zelenetz AD, Jaffe ES. *Blood*. 2016 May 19;127(20):2375-90.
2. International peripheral T-cell and natural killer/T-cell lymphoma study: pathology findings and clinical outcomes. Vose J, Armitage J, Weisenburger D. *International T-Cell Lymphoma Project*. *J Clin Oncol*. 2008 Sep 1;26(25):4124-30.
3. Peripheral T-cell lymphoma, not otherwise specified: a report of 340 cases from the International Peripheral T-cell Lymphoma Project. Weisenburger DD, Savage KJ, Harris NL, Gascoyne RD, Jaffe ES, MacLennan KA, Rüdiger T, Pileri S, Nakamura S, Nathwani B, Campo E, Berger F, Coiffier B, Kim WS, Holte H, Federico M, Au WY, Tobinai K, Armitage JO, Vose JM. *International Peripheral T-cell Lymphoma Project*. *Blood*. 2011 Mar 24;117(12):3402-8. doi: 10.1182/blood-2010-09-310342.
4. Peripheral T-cell lymphoma—not otherwise specified. Savage KJ, Ferreri AJ, Zinzani PL, Pileri SA. *Crit Rev Oncol Hematol*. 2011 Sep;79(3):321-9.
5. Utility of fine-needle aspiration as a diagnostic technique in lymphoma. Hehn ST, Grogan TM, Miller TP. *J Clin Oncol*. 2004 Aug 1;22(15):3046-52.