

Unraveling The Mystery: A Case of Pyrexia Of Unknown Origin Due To Splenic Marginal Zone Lymphoma

Dr. Pravin Selvam^{*1}, Dr. Kuchkar Snehal Sanjay², Dr. S. Moogaambiga³

¹*MD (General Medicine), Associate Professor, Department of General Medicine, Vinayaka Missions Kirupananda Variyar Medical College and Hospitals, Vinayaka Missions Research Foundation (Deemed to be University), Salem, Tamil Nadu, India, Email: pravincapsy@gmail.com, ORCID ID: 0000-0001-5556-5082

²Postgraduate, Department of General Medicine, Vinayaka Missions Kirupananda Variyar Medical College and Hospitals, Vinayaka Missions Research Foundation (Deemed to be University), Salem, Tamil Nadu, India, Email: snehalkuchkar@gmail.com, ORCID ID: 0009-0002-0116-3920

³MD (General Medicine), Professor, Department of General Medicine, Vinayaka Missions Kirupananda Variyar Medical College and Hospitals, Vinayaka Missions Research Foundation (Deemed to be University), Salem, Tamil Nadu, India, Email: mooks.stanlean@gmail.com, ORCID ID: 0000-0003-1807-0093

Abstract

Background: Pyrexia of unknown origin (PUO) continues to pose a diagnostic challenge despite advances in imaging and laboratory diagnostics. The etiological spectrum includes infections, inflammatory disorders, malignancies, and miscellaneous causes.

Case Presentation: A 28-year-old female presented with low-grade continuous fever for one month without localizing symptoms. Extensive evaluation including laboratory tests, cultures, and imaging was performed.

Investigations: Initial investigations were inconclusive. Imaging revealed splenomegaly with focal lesions, prompting further evaluation with contrast-enhanced imaging and histopathological confirmation.

Conclusion: Splenic marginal zone lymphoma, though rare, should be considered in prolonged unexplained fever. A structured diagnostic approach and judicious use of imaging are essential.

Keywords: PUO, Splenic lymphoma, Marginal zone lymphoma, Fever of unknown origin, Splenomegaly.

Introduction

Pyrexia of unknown origin (PUO) is classically defined as:

- Fever >38.3°C on multiple occasions
- Duration >3 weeks
- No diagnosis after 1 week of evaluation

Despite advances in diagnostics, PUO remains complex. Malignancies account for 10–20% of cases, with lymphomas being a significant contributor.

Investigations

1. Laboratory Findings

Case Presentation

A 28-year-old female from West Bengal presented with:

- Fever: Low-grade, continuous, 1 month duration
- No chills, rigor, or diurnal variation
- No systemic symptoms:
 - o No cough, dyspnea
 - o No abdominal pain or urinary symptoms
 - o No neurological deficits
 - o No autoimmune features

Past history:

- Multiple empirical antibiotic treatments → no response

- No TB contact, travel, or high-risk exposure

Clinical Examination

- Vitals: Stable except low-grade fever
- No lymphadenopathy
- Mild splenomegaly (later confirmed on imaging)
- No hepatomegaly or rash

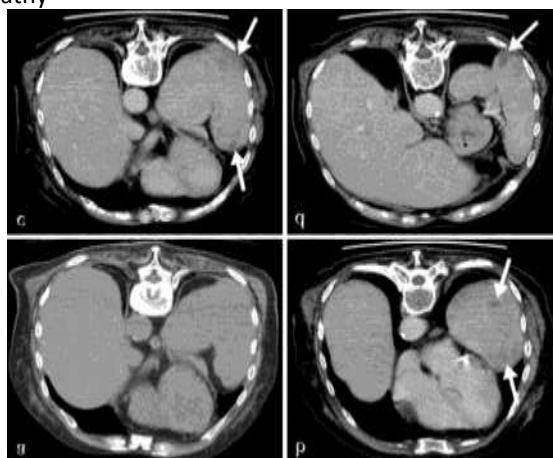
Parameter	Result	Interpretation
Hemoglobin	Mild anemia	Chronic disease
WBC count	Normal/ slightly elevated	Non-specific
ESR/CRP	Elevated	Inflammatory process
Blood cultures	Negative	Infection less likely
LFT/RFT	Normal	No organ dysfunction

2.Imaging Findings Ultrasound Abdomen

- Splenomegaly
- Hypoechoic focal lesions

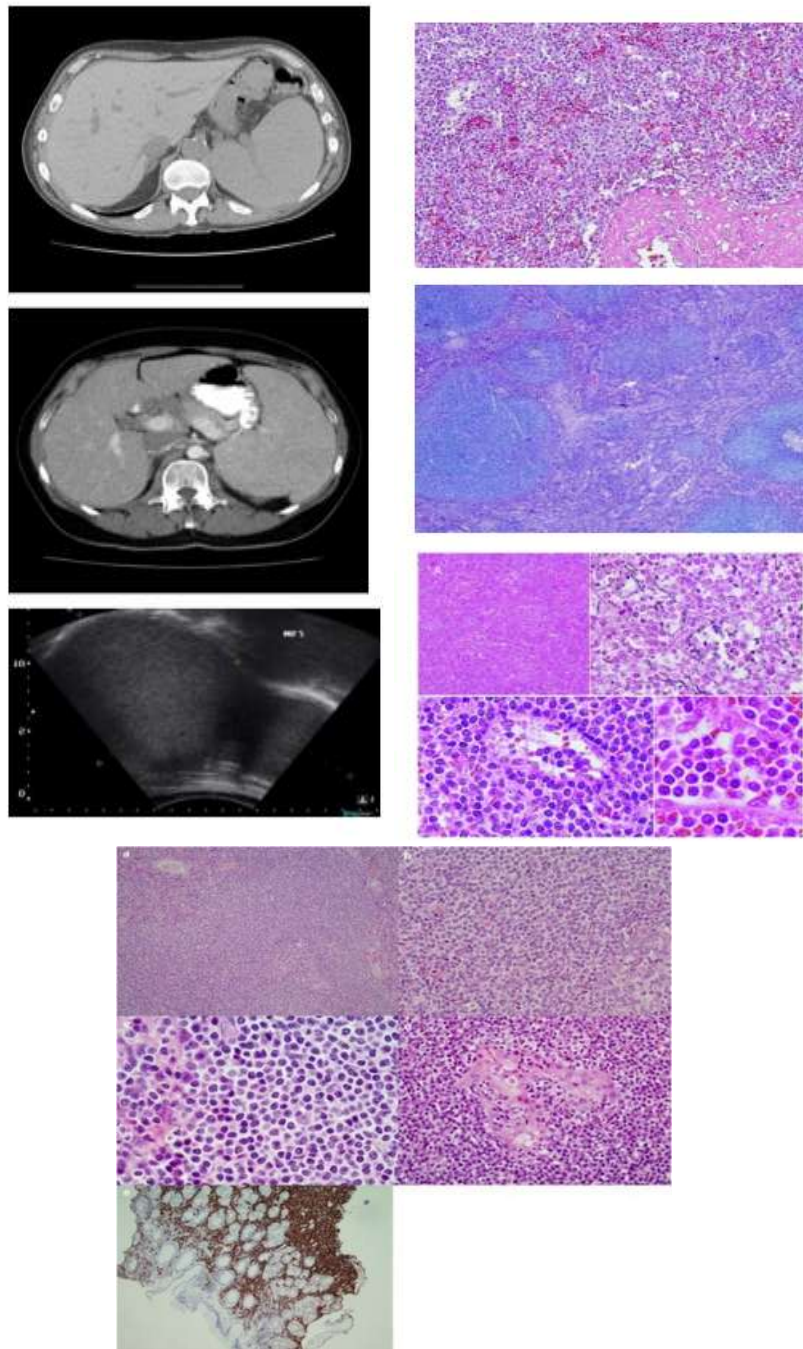
CECT Abdomen

- Enlarged spleen
- Multiple hypodense lesions
- No significant lymphadenopathy



3. Histopathology

- Splenic biopsy
- Features consistent with Splenic Marginal Zone Lymphoma (SMZL)



Inflammatory	SLE, vasculitis
Neoplastic	Lymphoma, leukemia
Miscellaneous	Drug fever

Diagnostic Approach PUO Workup Strategy:

1. Initial labs → inconclusive
2. Cultures → negative
3. Imaging → splenic lesions
4. Targeted biopsy → diagnosis

Timeline of Events

Time	Event
Week 1–2	Fever onset
Week 2–4	Antibiotics (no response)
Week 4	Imaging done
Week 5	Splenic biopsy
Week 6	Diagnosis confirmed

Differential Diagnosis

Graphical Representation

Etiology of PUO (Pie Chart – Suggested Figure)

- Infections – 40%
- Malignancy – 20%
- Inflammatory – 20%
- Miscellaneous – 20%

Diagnostic Yield of Investigations

Modality	Yield
Blood tests	Low
Cultures	Low
Imaging	Moderate

Biopsy	High
--------	------

Discussion

Splenic marginal zone lymphoma (SMZL) is a rare, indolent B-cell lymphoma that:

- Primarily involves the spleen
- Often presents with splenomegaly and cytopenias
- Rarely presents as isolated PUO

Why this case is important:

- No lymphadenopathy
- No B symptoms (weight loss/night sweats)

- Only presenting feature → prolonged fever

Radiological significance:

- Splenic lesions in PUO should raise suspicion of:
 - o Lymphoma
 - o Granulomatous disease
 - o Metastasis

Learning Points:

- Avoid empirical antibiotic overuse
- Early imaging is crucial
- Biopsy remains gold standard

Conclusion

This case emphasizes:

- Importance of structured PUO evaluation
- Role of imaging in narrowing diagnosis
- Need to consider rare malignancies like SMZL

Early diagnosis prevents:

- Delayed treatment
- Unnecessary antibiotic exposure

Figures

1. Figure 1 – CT abdomen showing splenic lesions
2. Figure 2 – Ultrasound spleen
3. Figure 3 – Histopathology slide
4. Figure 4 – PUO diagnostic flowchart
5. Figure 5 – Pie chart of PUO causes
6. Figure 6 – Timeline graph

References

1. Petersdorf RG, Beeson PB. Fever of unexplained origin.
2. Cunha BA. Fever of unknown origin.
3. Arcaini L et al. Splenic marginal zone lymphoma.
4. Habermann TM. Lymphoma overview.

5. Durack DT, Street AC. Fever of unknown origin—reexamined and redefined. *Curr Clin Top Infect Dis.* 1991.
6. Bleeker-Rovers CP et al. A prospective multicenter study of patients with fever of unknown origin. *Medicine (Baltimore).* 2007.
8. Vanderschueren S et al. From prolonged febrile illness to fever of unknown origin: the challenge continues. *Arch Intern Med.* 2003.
9. Knockaert DC, Vanderschueren S, Blockmans D. Fever of unknown origin in adults: 40 years on. *J Intern Med.* 2003.
10. Wright WF, Auwaerter PG. Fever and fever of unknown origin: review, recent advances, and lingering dogma. *Open Forum Infect Dis.* 2020.
11. Mulders-Manders CM et al. Fever of unknown origin. *Clin Med (Lond).* 2015.
12. Cunha BA, Lortholary O, Cunha CB. Fever of unknown origin: a clinical approach. *Am J Med.* 2015.
13. Zhang S et al. Splenic marginal zone lymphoma: a case report and literature review. *World J Surg Oncol.* 2020. (PubMed)
14. Santos TS et al. Splenic marginal zone lymphoma: diagnostic and therapeutic challenges. *Rev Bras Hematol Hemoter.* 2017. (PubMed)
15. Traverse-Glehen A et al. Splenic marginal zone lymphoma: a distinct clinical and pathological entity. *Lancet Oncol.* 2011.
16. Matutes E et al. Splenic marginal zone lymphoma proposals for a revision of diagnostic criteria. *Leukemia.* 2008.
17. Piris MA, Onaindia A, Mollejo M. Splenic marginal zone lymphoma. *Best Pract Res Clin Haematol.* 2017.
18. Arcaini L et al. Splenic marginal zone lymphoma: clinical presentation, prognostic factors and treatment. *Blood.* 2006.
19. Kalpadakis C et al. Treatment of splenic marginal zone lymphoma: should splenectomy be abandoned? *Leuk Lymphoma.* 2013.
20. Rossi D, Gaidano G. Genetic basis of marginal zone lymphomas. *Blood.* 2013.
21. Salido M et al. Cytogenetic abnormalities in SMZL (7q deletion). *Blood.* 2010.
22. Baseggio L et al. Revised diagnostic criteria for SMZL. *Haematologica.* 2010.
23. Bennett M et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. (latest edition)
24. Mollejo M et al. New insights into biology and diagnosis of SMZL.
25. Cancers (Basel). 2021. (PMC)
26. Depowski PL et al. Splenic marginal zone lymphoma: case report and literature review. *Arch Pathol Lab Med.* 2002. (PubMed)
27. Iannitto E, Tripodo C. How I diagnose and treat splenic marginal zone lymphoma. *Blood.* 2011.
28. Thieblemont C et al. Management of marginal zone lymphomas. *Hematology Am Soc Hematol Educ Program.* 2016.
29. Olszewski AJ, Castillo JJ. Survival of marginal zone lymphoma—population-based study. *Blood.* 2013.
30. Parry-Jones N et al. Splenic lymphoma with villous lymphocytes and SMZL spectrum. *Br J Haematol.* 2003.
31. Warshawer DM, Hall HL. Solitary splenic lesions. *Radiographics.* 2004.
32. Thut D et al. Imaging of splenic lymphoma. *AJR Am J Roentgenol.* 2015.
33. Mortelé KJ et al. CT features of splenic lymphoma. *Radiology Clinics of North America.* 2004.