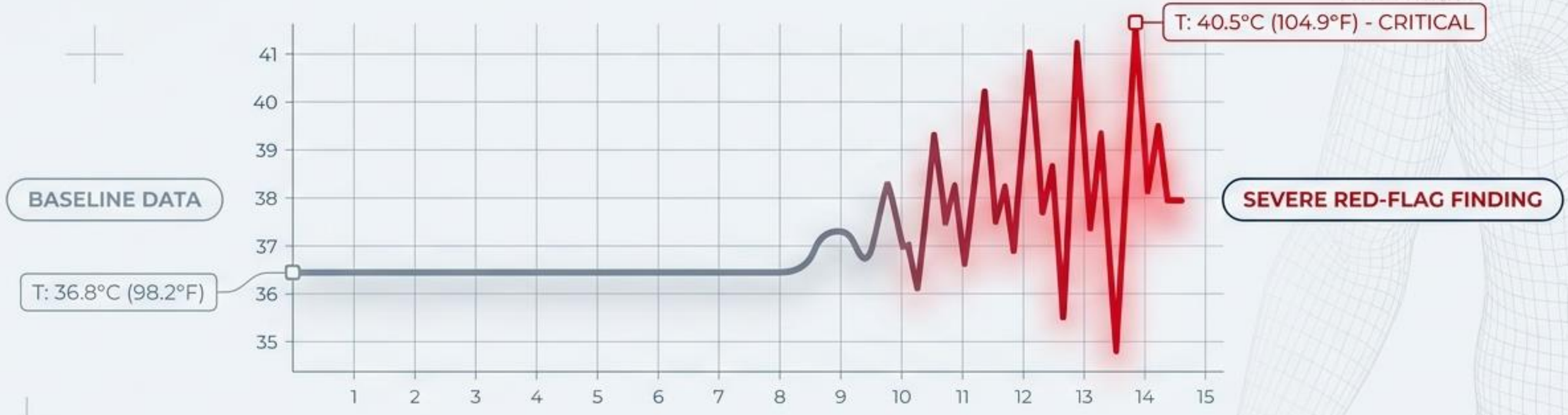
THE MIDNIGHT FEVER

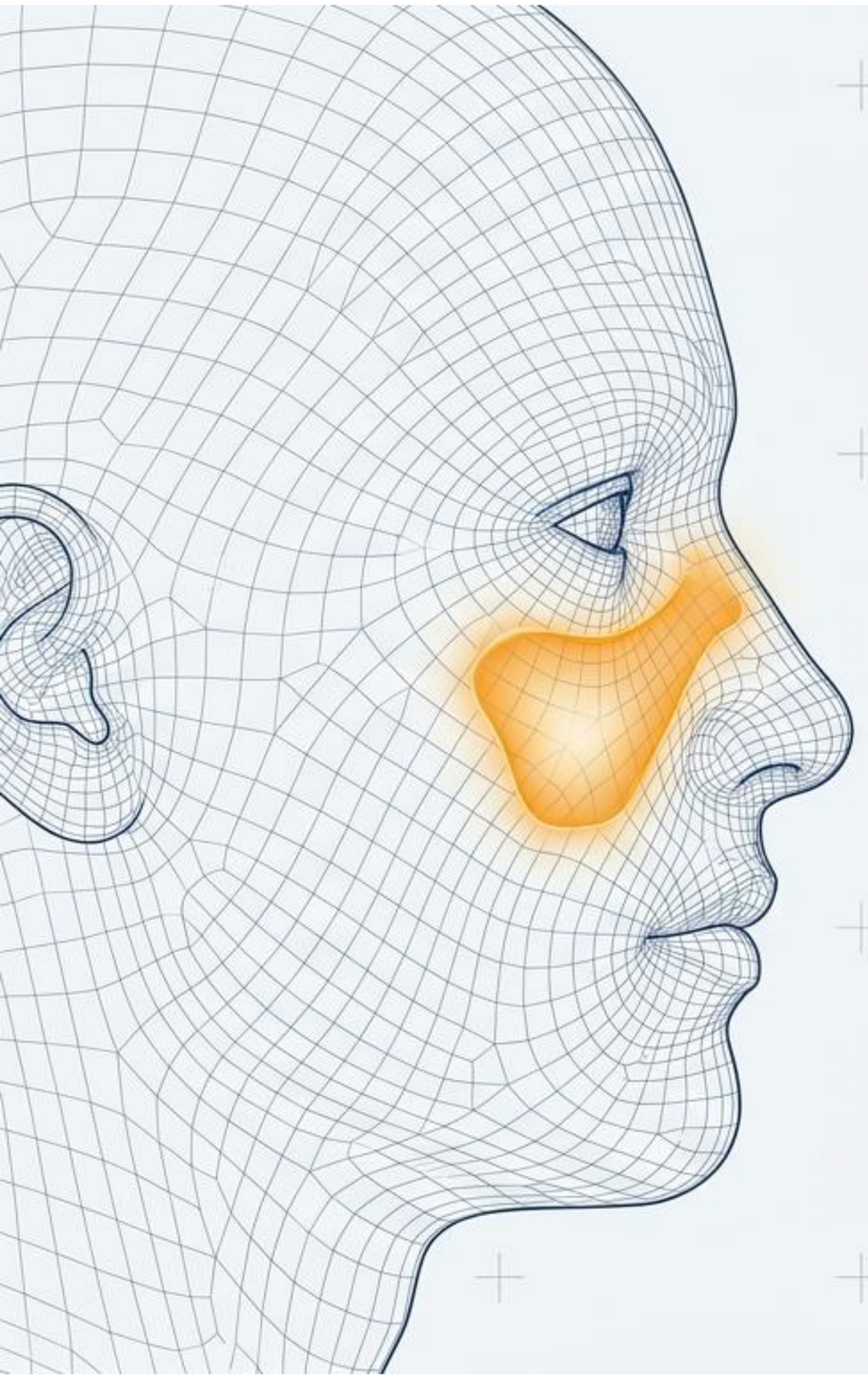
Investigating a 21-Year-Old's Systemic Decline

Clinical Pathological Conference (CPC) | Case Dossier

By : Aynaz Aghdasi



Patient ID: CPC-2024-47X | Presentation: Acute Nocturnal Pyrexia & Rapid Decline



Timeline Node

March 10, 2026 | The Initial Presentation

Patient Baseline 21-year-old previously healthy man.

Initial Symptoms

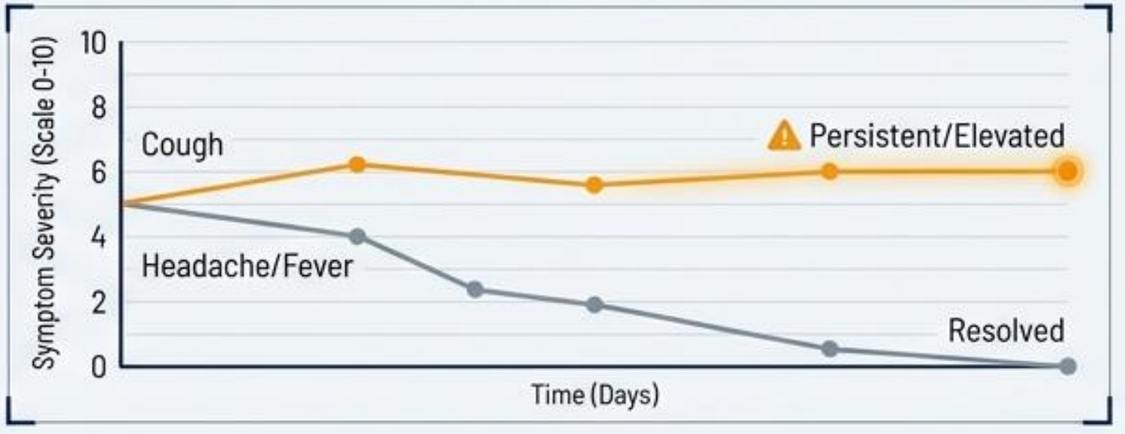
4 days of progressive fatigue, malaise, subjective low-grade fever (responsive to acetaminophen), dry cough, and coryza. Frontal headache and facial fullness over the maxillary region.

Presumed Diagnosis & Intervention

Diagnosed as viral upper respiratory tract infection with acute bacterial rhinosinusitis. Treated empirically with amoxicillin, dextromethorphan, cetirizine, guaifenesin, and acetaminophen.

Outcome

Partial improvement: fever, headache, and facial pressure resolved. Persistent nonproductive cough remained.



Timeline Node

April 4, 2026 | The Nocturnal Pivot

Trigger

3 weeks post-initial illness. Persistent dry cough and mild early-morning headache remain unchanged.

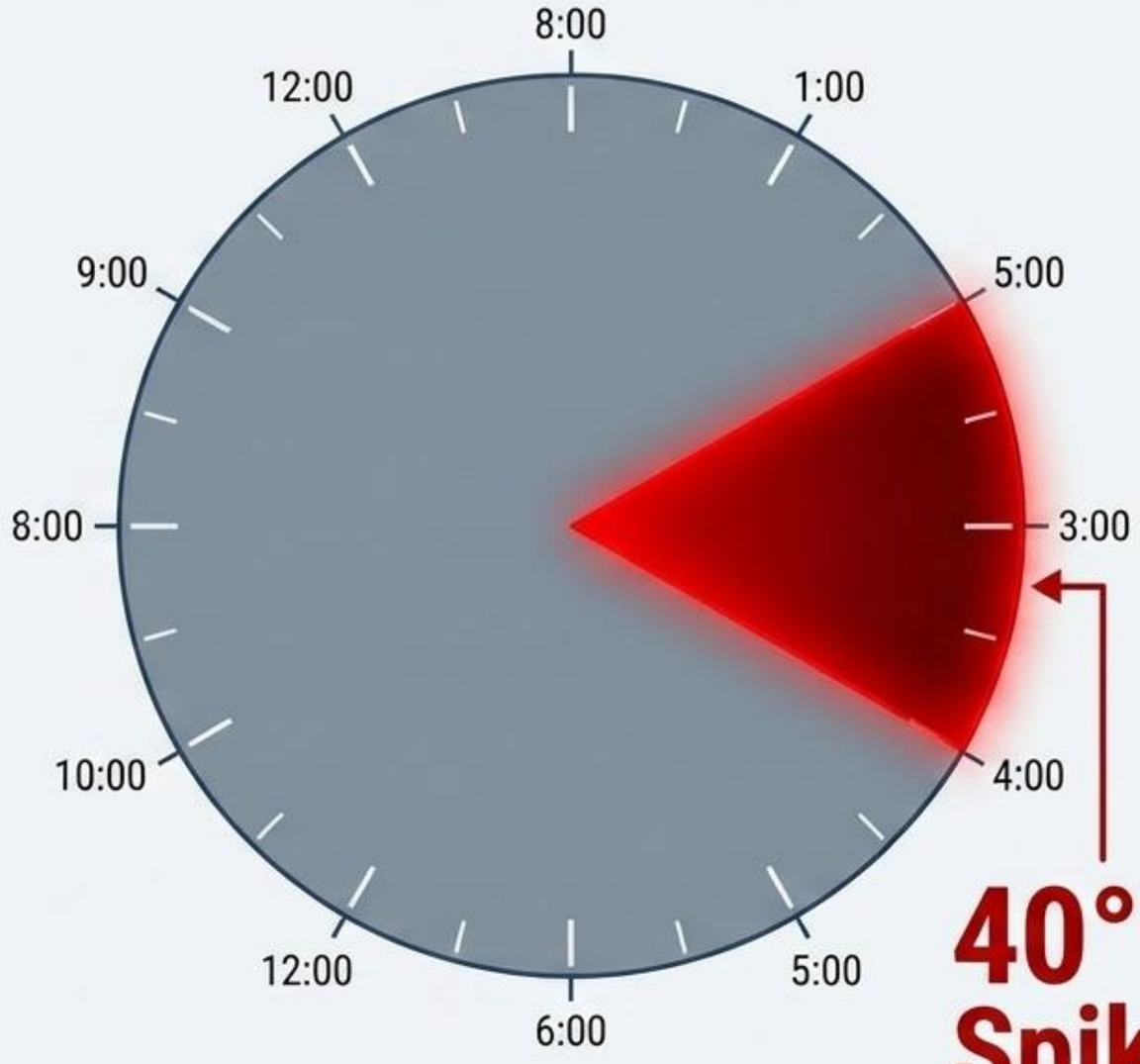
The Anomaly: 3:00 - 4:00 a.m.

- Abrupt awakening, acutely ill
- **High-grade fever (up to 40°C on home digital thermometer)**
- Drenching night sweats
- Shaking chills (rigors)

Daytime State & Intervention

Fever resolves spontaneously after 1-2 hours. Patient experiences persistent fatigue and malaise during the day, with asymptomatic days interspersed.

Outpatient reevaluation led to empiric oral antibiotics, causing a temporary 1-week subsidence of fevers.



Axioms of Pyrexia: Definitions & Red Flags

Core Definitions

- Core temperature ≥38.3°C
- Persistent ≥38.0°C

Fever ≠ Hyperthermia.
History Matters.

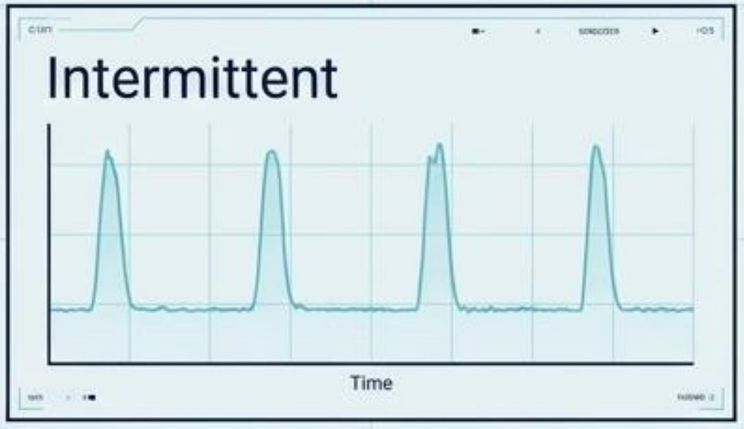
Variables to Track:

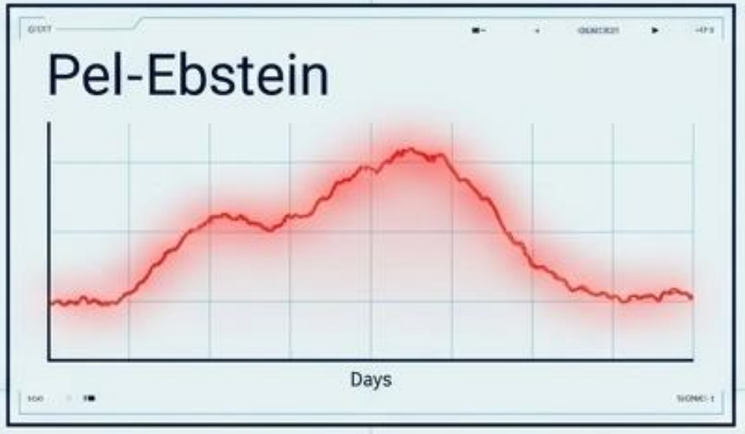
Duration, Pattern, Peak temperature, Rigors, Night sweats, Exposure, Drugs.

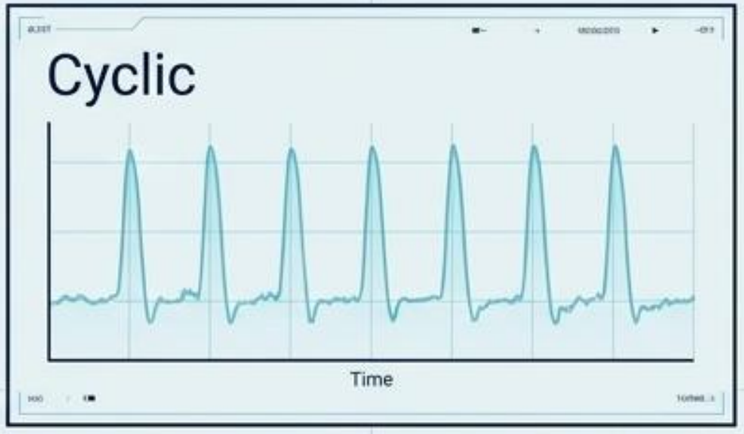
Diagnostic Red Flags

- >39–40°C
- Persistent fever
- Drenching night sweats
- Weight loss
- No obvious source
- Constitutional symptoms

Topography of Temperature







Clinical Axiom: Pattern alone is rarely diagnostic.

Timeline Node

April 23 – Early May | Systemic Progression

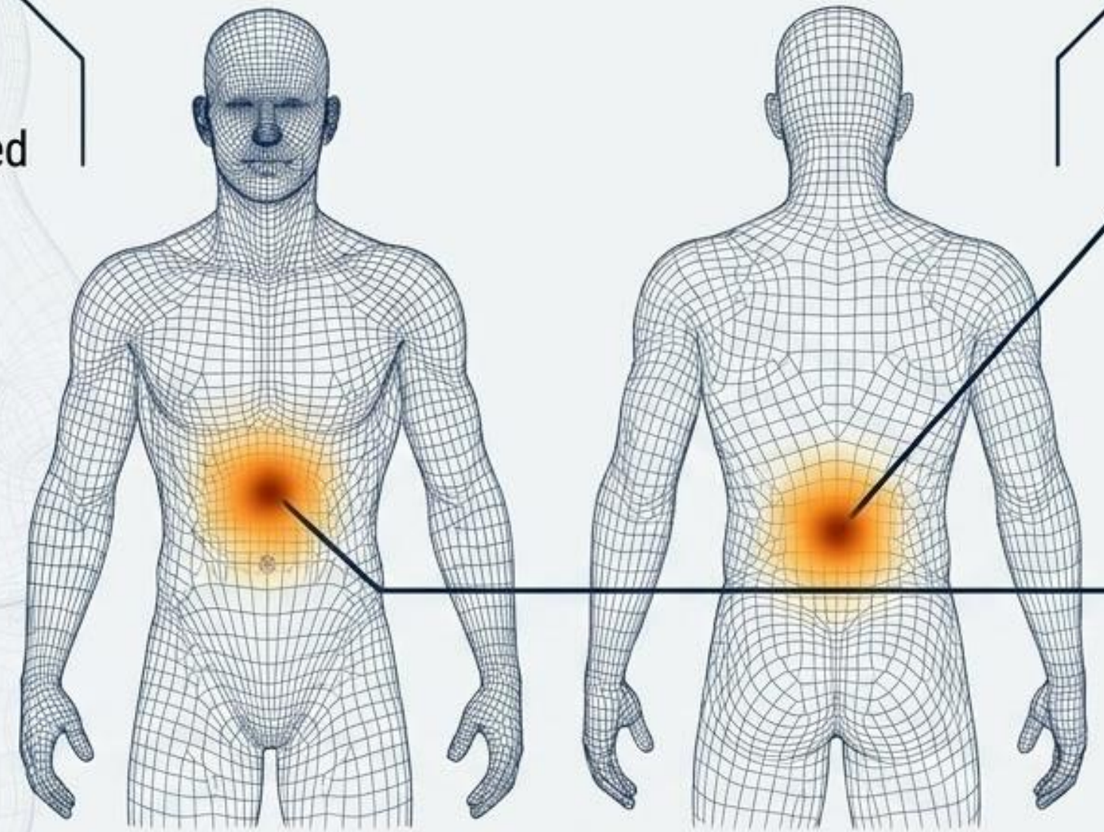
General Status

Progressive fatigue, generalized weakness, and notable functional decline.

Febrile episodes initially reduced to 1-2x/week, then returned to nightly. Dry cough intensified.

Systemic Impact

Unintentional 5 kg weight loss since illness onset.



New Localizations

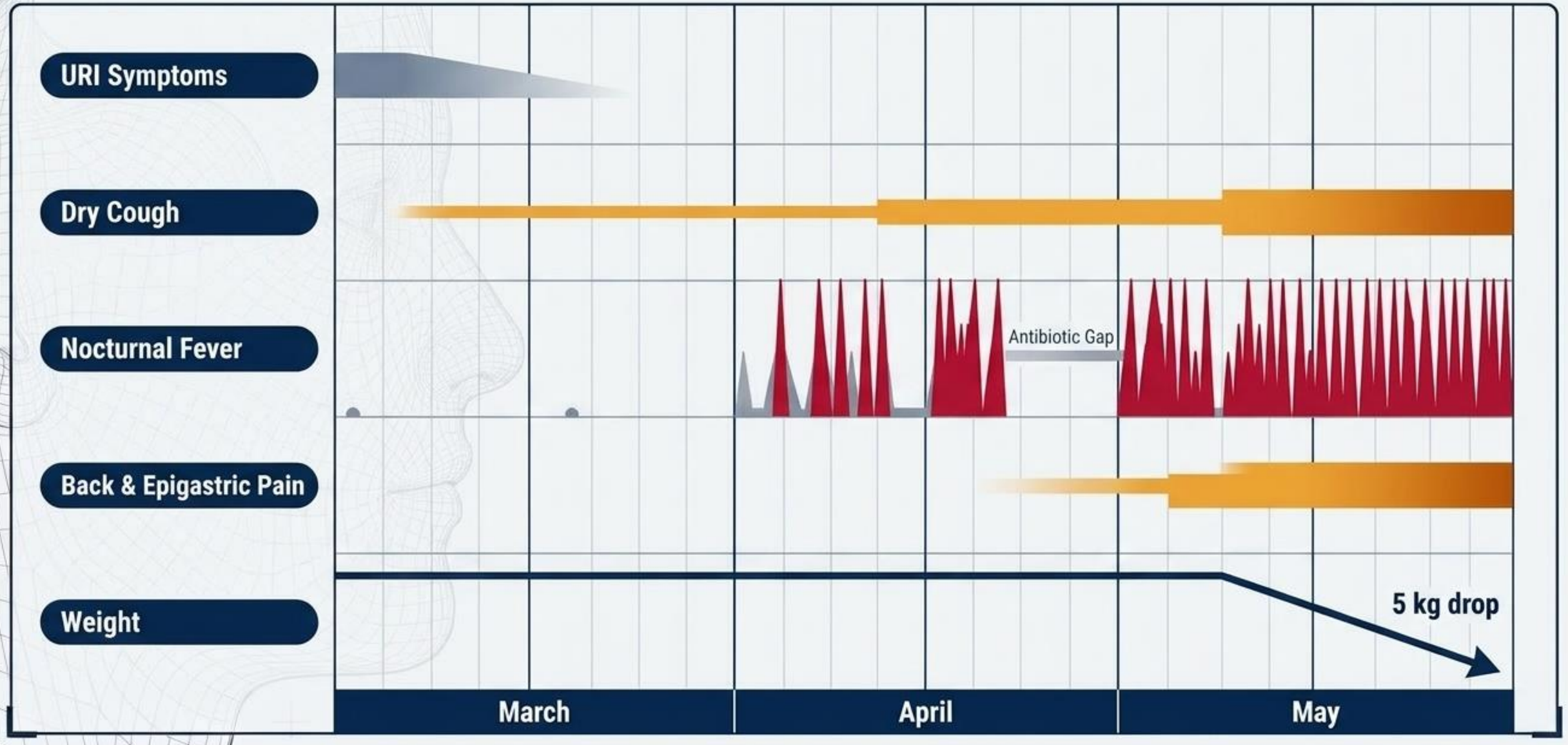
Lower Back Pain

Insidious onset, dull, non-radiating, unrelated to activity or position, present most of the day. No trauma history.

Epigastric Pain

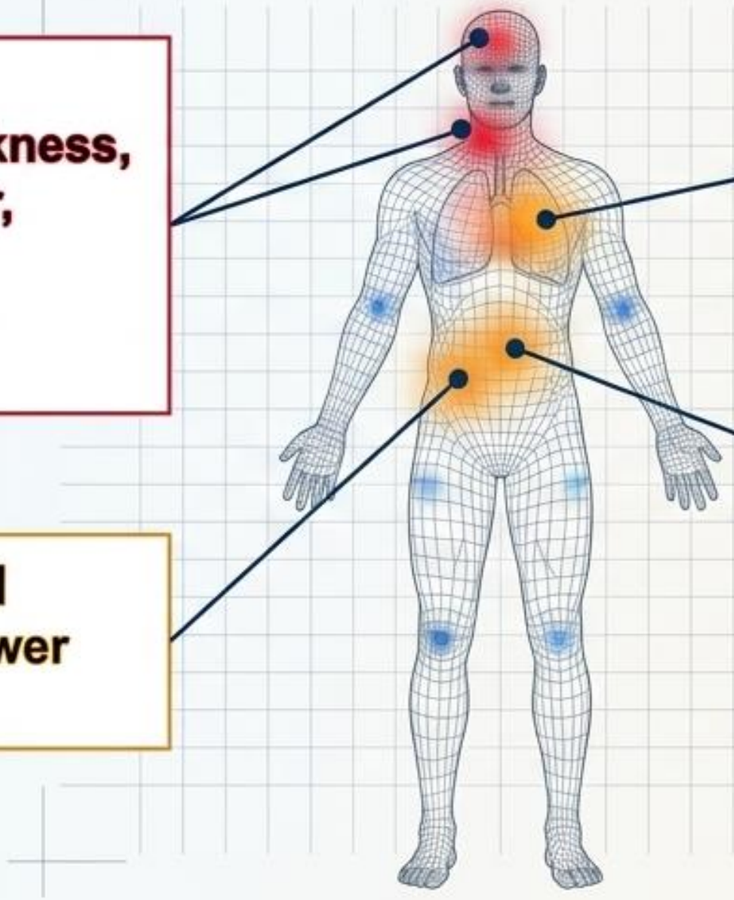
Dull, poorly localized abdominal pain. Unrelated to meals. Accompanied by anorexia and intermittent nausea.

Timeline of Symptom Evolution (March – May)



Review of Systems | The Subjective Burden

Anatomical Heat Map



Constitutional
Progressive fatigue/weakness, recurrent nocturnal fever, drenching sweats, unintentional 5-kg loss, anorexia.

Respiratory
Persistent dry cough, mild exertional dyspnea.

Gastrointestinal
Mild epigastric pain, intermittent nausea.

Musculoskeletal
Persistent dull lower back pain.

Negative Systems

ENT: No sore throat/dysphagia. **Skin:** No rash/ulcers.
Genitourinary: No dysuria/hematuria. **Neurologic:** No focal deficits.

Patient Dossier: Baseline & Exposures

Past Medical History

- Previously healthy
- No prior hospitalizations
- No chronic medications
- No known drug allergies

Family History

- Hypertension & dyslipidemia in parents
- Negative for malignancy
- Negative for autoimmune disease
- Negative for hereditary disorders
  use.

Social History

- **Occupation:** Clothing store salesman
- **Substances:** Occasional alcohol (1-2 drinks/month), Occasional vaping (1-2 sessions/month). Denies cigarette smoking or illicit drug
- **Exposures:** No recent travel. No animal exposure. No known TB contact. No high-risk sexual behavior.

Physical Examination | The Illusion of Normal

General Appearance & Vitals

General Appearance
Ill-appearing, alert, oriented, no acute distress.
Note: Despite the absence of striking physical findings, the patient appeared noticeably unwell.

Vital Signs	
Temp: 37.0°C (Axillary)	**HR**: 91/min
BP: 100/60 mmHg	**RR**: 19/min
SpO2: 98% (Room Air)	

Systemic Exam Findings

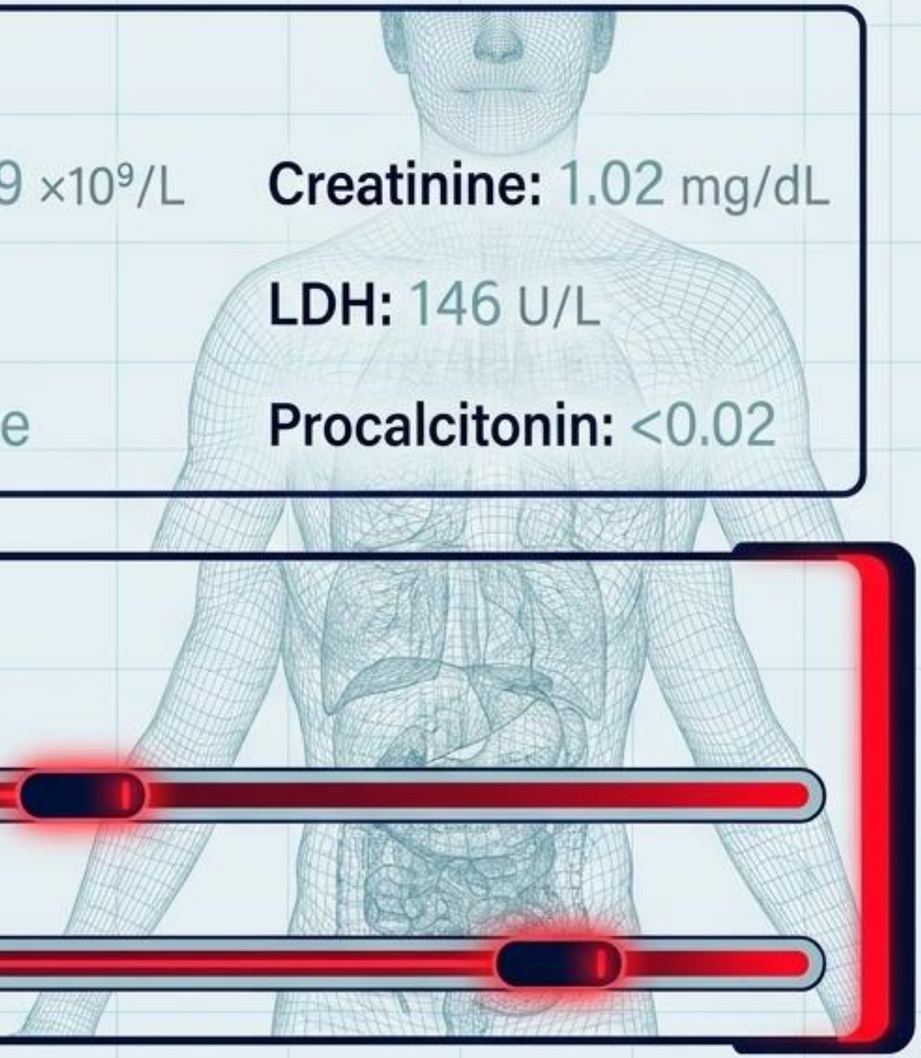
- **Head/Neck**: No lymphadenopathy.
- **Cardiovascular**: Normal rhythm, S1/S2, no murmurs. Stigmata of infective endocarditis absent.
- **Respiratory**: Clear bilaterally, symmetric, no crackles/wheezing.
- **Abdomen**: Soft, mild epigastric tenderness. No hepatosplenomegaly.
- **Musculoskeletal**: Mild diffuse lower lumbar discomfort, no point tenderness, negative straight-leg raise.
- **Neurologic & Skin**: Completely normal.

NORMAL

Initial Laboratory Intel: Hematologic vs. Inflammatory

Hematology, Hepatic, Renal, Serology

WBC: 8,900 /µL	**Hb:** 14.7 g/dL	**Platelets:** 369 $\times 10^9$/L	**Creatinine:** 1.02 mg/dL
Urea: 21 mg/dL	**AST:** 36 U/L	**ALT:** 20 U/L	**LDH:** 146 U/L
PT/INR: Normal	**Wright/Coombs/2ME:** Negative		**Procalcitonin:** <0.02

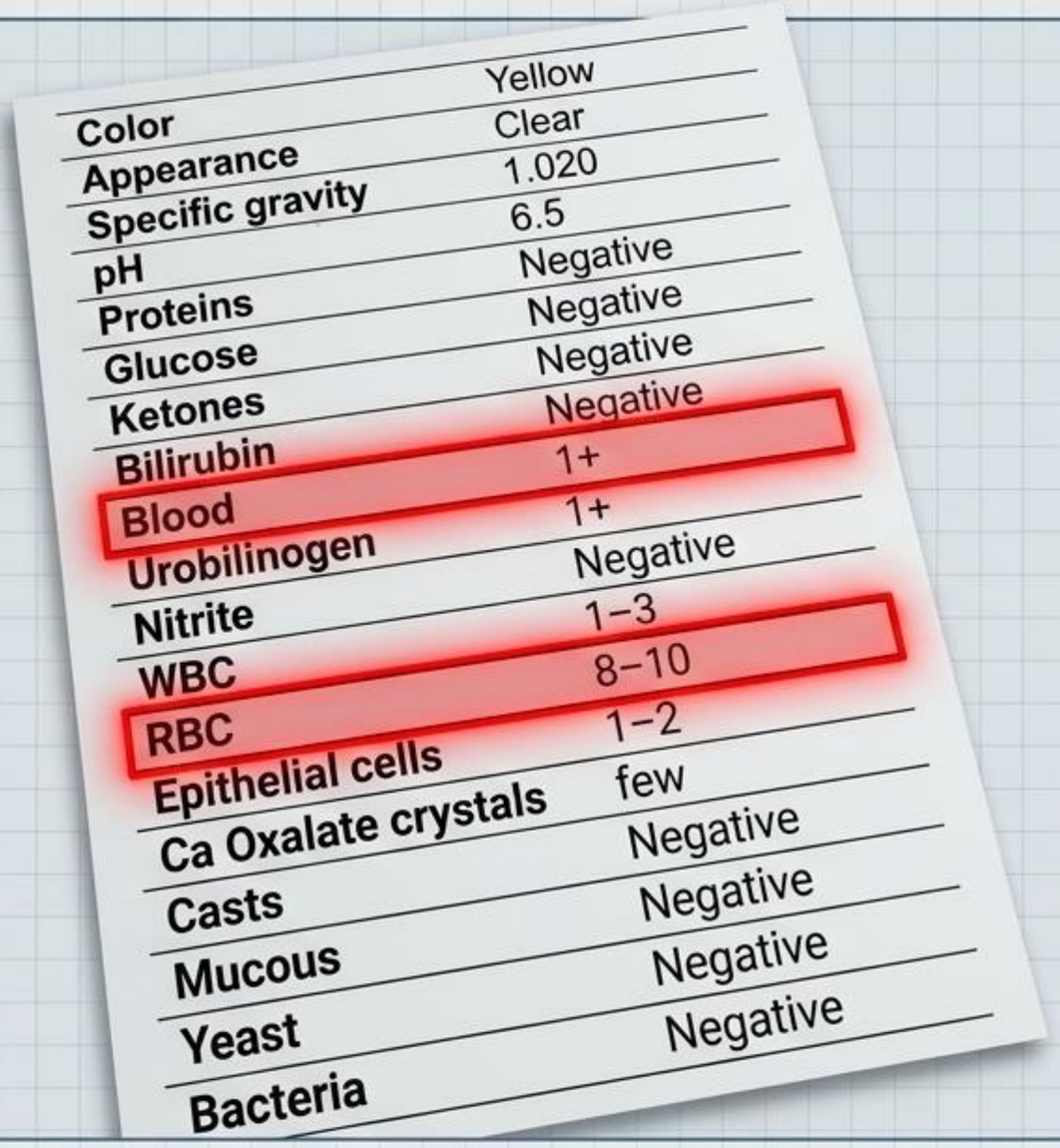


Inflammatory Markers

ESR: 65 mm/hr (Systemic Inflammation)

CRP: 73 mg/L (Systemic Inflammation)

URINALYSIS EVIDENCE | THE FIRST MICROSCOPIC CLUE



Color	Yellow
Appearance	Clear
Specific gravity	1.020
pH	6.5
Proteins	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	1+
Urobilinogen	1+
Nitrite	Negative
WBC	1–3
RBC	8–10
Epithelial cells	1–2
Ca Oxalate crystals	few
Casts	Negative
Mucous	Negative
Yeast	Negative
Bacteria	Negative

Extracted Data Block

Macroscopic:
Color: Yellow | Appearance: Clear | Specific gravity: 1.020 | pH: 6.5

Chemical: Protein / Glucose / Ketones / Bilirubin / Nitrite: Negative.
Blood: 1+ **Urobilinogen: 1+**

Microscopic:
WBC: 1–3 | Epithelial cells: 1–2 | Ca Oxalate crystals: few | Casts / Mucous / Yeast / Bacteria: Negative.
RBC: 8–10

Clinical Takeaway: Unexplained microscopic hematuria requires systemic correlation.

The Problem Representation

Caseboard Summary

- Recurrent nocturnal high-grade fever
- Drenching night sweats
- Progressive fatigue and constitutional symptoms
- Persistent dry cough
- Non-mechanical low back pain
- Epigastric abdominal pain
- Unintentional 5-kg weight loss
- Elevated ESR and CRP
- Normal CBC and organ function
- No obvious infectious focus

Clinical Reasoning Framework

Occam's Razor

One patient, one disease—until proven otherwise.

Seeking a single unifying systemic disease to explain the cough, fever, back pain, and weight loss.

Single Diagnosis

Hickam's Dictum

Patients can have as many diseases as they damn well please.

Allowing for concurrent, independent conditions.

Multiple Concurrent Diseases

"Occam is a starting point, not a rule."

The Differential Matrix | Suspect Board

Infection

- Tuberculosis — Prime Suspect 1
- Infective Endocarditis — Prime Suspect 3
- Occult abscess
- Brucellosis
- Fungal infection
- HIV

Autoimmune / Inflammatory

- Granulomatosis with Polyangiitis (GPA) — Prime Suspect 2
- SLE
- Adult-onset Still disease
- Sarcoidosis
- IgG4 disease

Malignancy

- Lymphoma — Prime Suspect 4
- Leukemia
- Metastatic cancer

SUSPECT PROFILE ANALYSIS | TB VS. GPA

Tuberculosis (The Disease Behind the Phenotype)

Pathophysiology

The Host–Pathogen Battle.

Epidemiology

Why TB Still Matters.

Core Insight

TB is not simply a pulmonary infection. It is an immunologic disease whose clinical and radiologic phenotype reflects the interaction between the organism, the host, and the tissue.

VS

Granulomatosis with Polyangiitis (GPA)

Pathophysiology

What Actually Happens?
(Pulmonary–Renal–ENT triad).

Clinical Phenotype

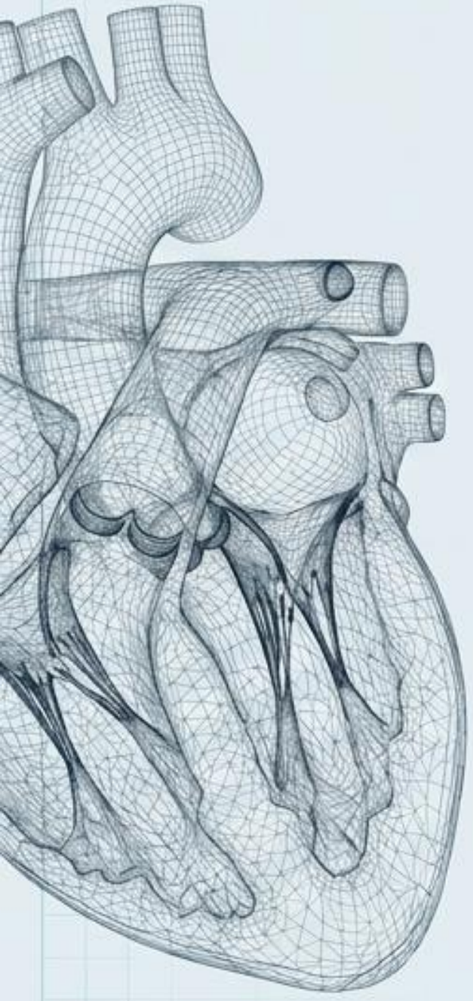
Look for the Triad, plus
“The Hidden Clues” in other organs.

Diagnostic Pitfall

Don’t Let ANCA Do the Thinking.

Differential Matrix: Endocarditis

Infection or Systemic Thromboinflammation? (Fever 77.7%, Murmur 64.5%, Emboli 25.3%)



	Infective Endocarditis	NBTE
Vegetation	**Infectious**	Sterile
Composition	Microorganisms + fibrin/platelets	Mainly fibrin + platelets
Fever	**Common**	Usually not dominant
Blood cultures	Often positive	**Negative**
Embolization	Common	Very prominent
Valve destruction	Can be substantial	Usually limited
Major associations	Bacteremia, valve/device risk	Cancer, SLE, APS, DIC
Key clinical clue	Fever + bacteremia	Recurrent/multifocal emboli + hypercoagulability

Differential Matrix: Hodgkin Lymphoma

When Malignancy Mimics Infection

1. **Pathophysiology:**
   The Tumor Is Not What It Seems.
2. **Epidemiology:**
   Why This Patient Fits.
3. **Clinical Phenotype:**
   The B-Symptom Syndrome.
4. **Diagnosis.**

> A patient can look profoundly inflammatory while having a nearly normal CBC.

INPATIENT RE-EVALUATION | ESCALATING SYSTEMIC INFLAMMATION

HEMATOLOGY SHIFT

WBC: 14.7 (H) — Shifted from Normal to High

Hemoglobin: 12.7 **(Drop)**	
Hematocrit: 38.5	
MCV: 82.5	MCH: 27.1
MCH: 27.1	MCHC: 32.9

Platelets: 413 — **Trending Up**

INFLAMMATORY SPIKE

ESR (1st hr): 101 (H) (Massive spike)

CRP Quantitative: 70 (H)

Ferritin: 452.3 (New marker)

NEGATIVE INFECTIOUS WORKUP PANEL

- Sputum AFB smear, Mycobacterial culture, PPD (Pending/Implied Negative).
- Wright Tube Neg, 2ME Neg, Widal Neg, Brucella IgG 0.1, Brucella IgM 0.5, ImmunoCapture Neg.

REPEAT URINALYSIS NOTE

Blood (Hb) Positive, RBC 10-12.

Structural Intel: Cardiovascular & Abdominal Scans

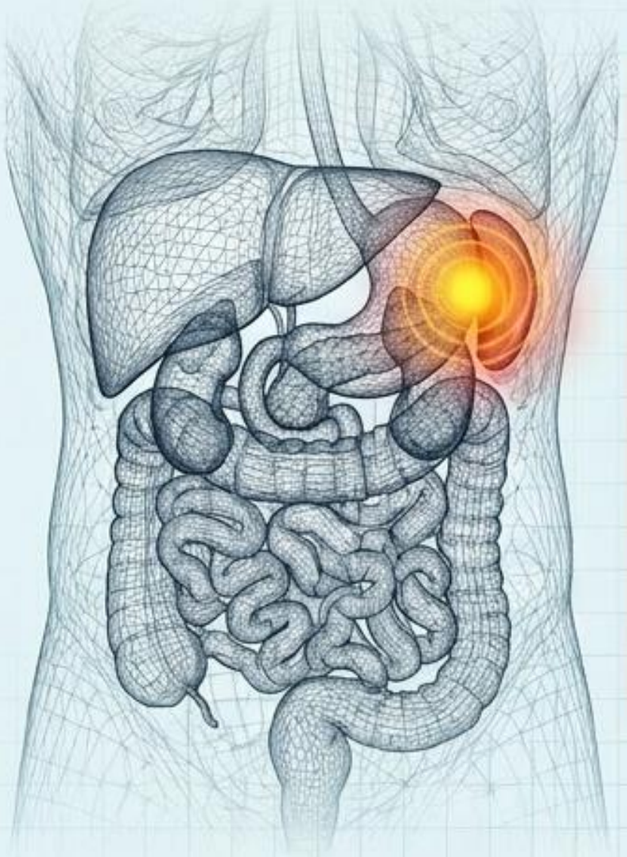
Transthoracic Echocardiography

Clear Status

Sinus tachycardia (~110 bpm).
Normal LV/RV.
Mild-to-mod TR.

NO vegetations, masses, or thrombi.
(Effectively rules out Suspect 3: Endocarditis).

Abdominal Ultrasound



Clear Organs:
Liver, Gallbladder, Pancreas, Kidneys normal.

Splenic Anomaly:
Normal size (106mm) BUT heterogeneous echotexture. No focal lesion or abscess.

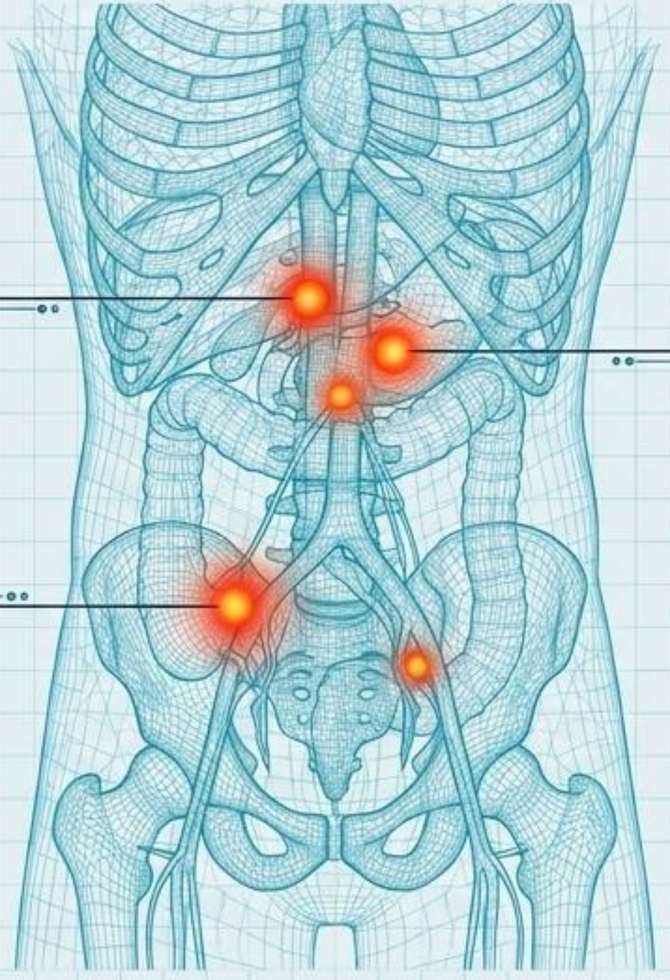
Topographical Mapping: Contrast-Enhanced CT Abdomen/Pelvis

Solid Organs: Liver, spleen, pancreas, kidneys normal. Incidental enlarged pancreatic head.

Multiple para-aortic lymphadenopathies (Max: 17 mm)

Adjacent pancreatic node (26 × 20 mm)

Left iliac-chain lymphadenopathy (30 × 17 mm & 11 × 10 mm)



Additional Find: 5-mm solid nodule in Right Lower Lobe (RLL).

Topographical Mapping: High-Resolution CT Pulmonary & Sinus

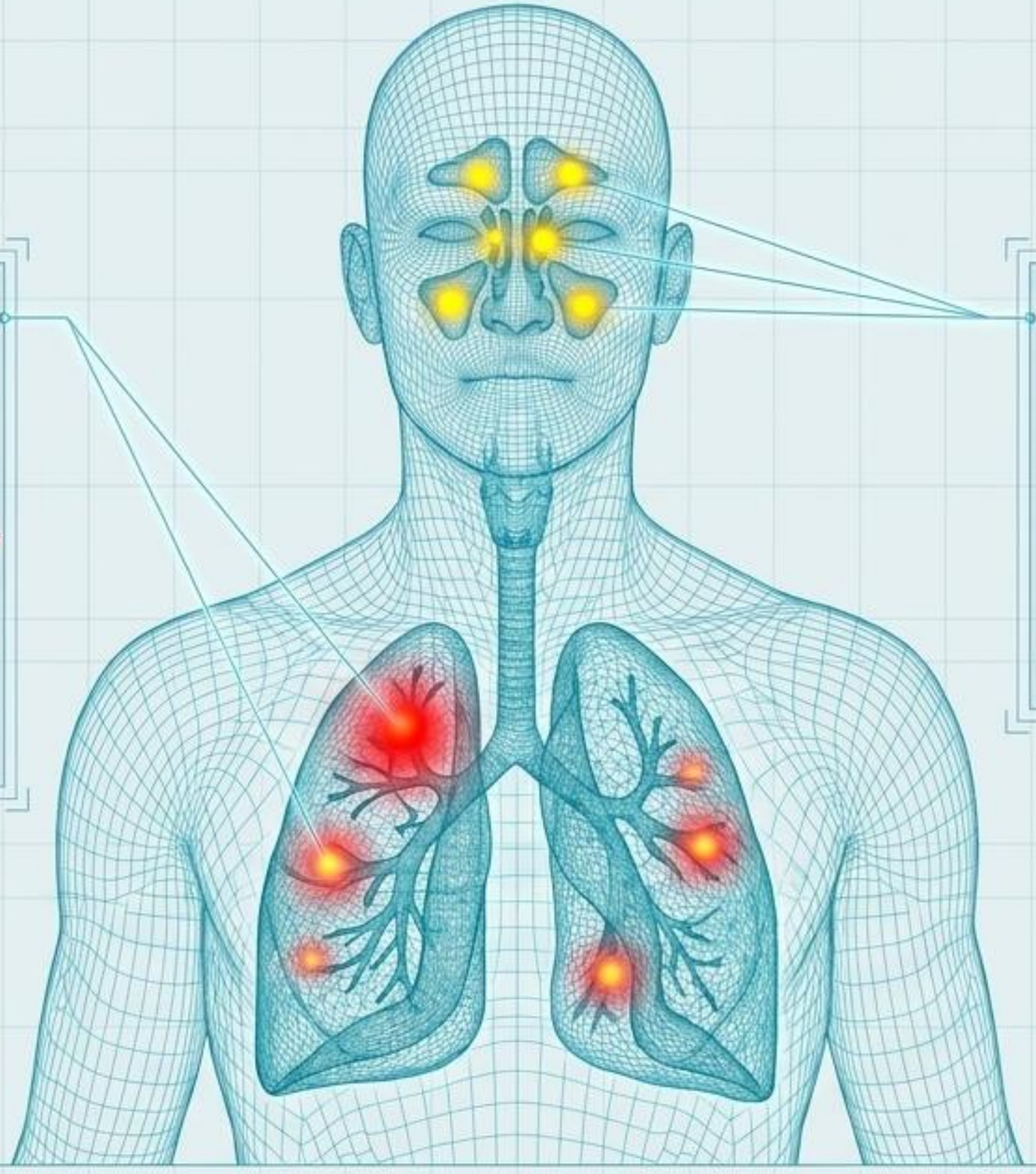
Pulmonary Findings

Multiple bilateral solid nodules (right-predominant, 7mm in LUL).

20 × 14 mm cavitary lesion in RUL.

2-mm calcified nodule in RML.

No pleural effusion or definite mass.



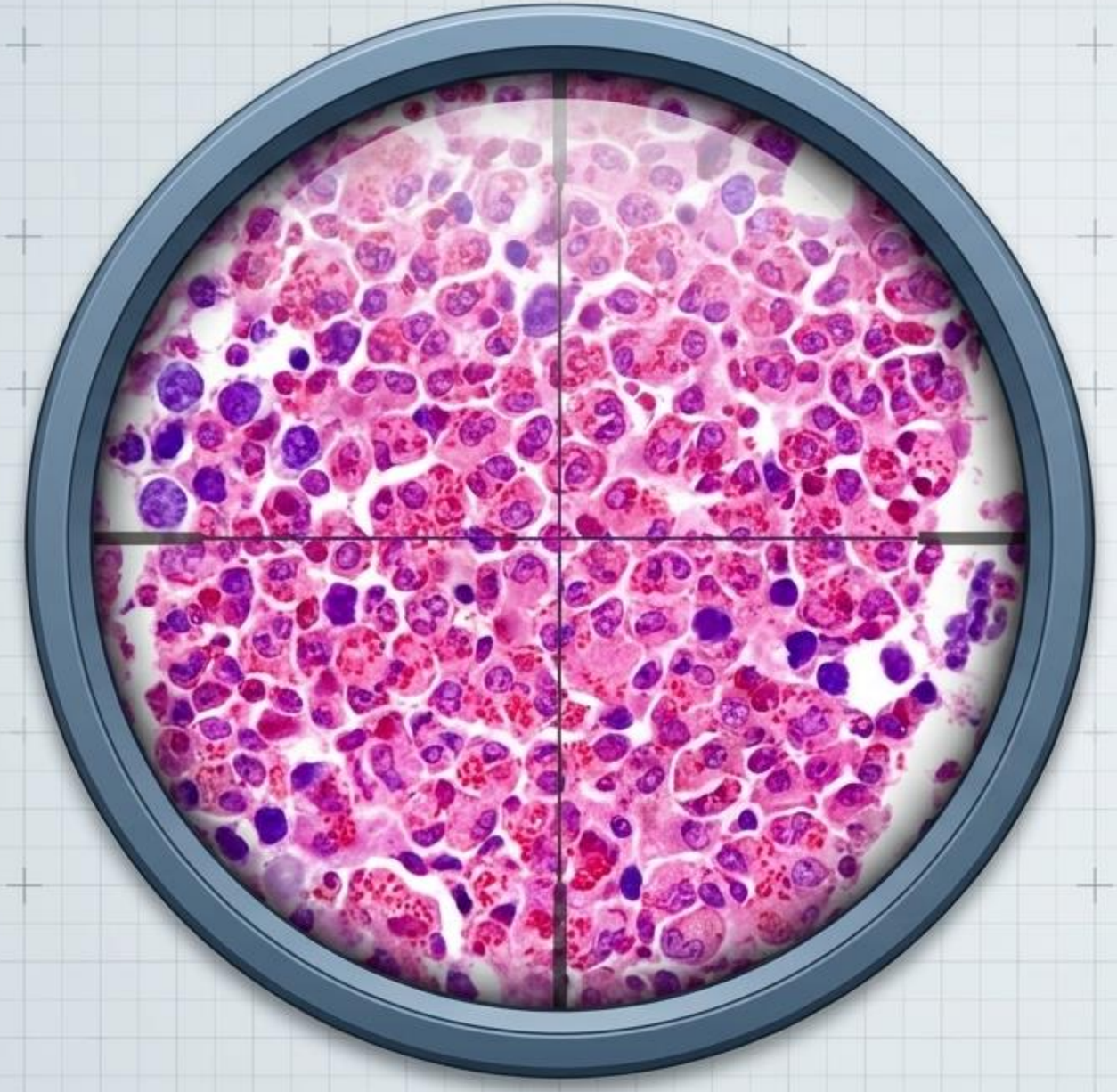
Sinus Findings

Bilateral maxillary mucosal thickening + retention cysts.

Right OMC obliteration, Left OMC narrowing.

Bilateral concha bullosa.

BONE MARROW INTERROGATION | THE EOSINOPHILIC TWIST



PATHOLOGY REPORT

ASPIRATION FINDINGS

Hypercellular marrow, preserved myeloid-to-erythroid ratio.
Mild left shift (myelocytes/promyelocytes).
Hypereosinophilia. Megakaryocytes present. No blasts.
Occasional binucleated Reed–Sternberg-like cells.

TREPHINE BIOPSY FINDINGS

Eosinophilia with focal eosinophil aggregates.
Occasional histiocytic collections.
Crucially: No evidence of leukemic or lymphomatous involvement identified.

PATHOLOGIC IMPRESSION

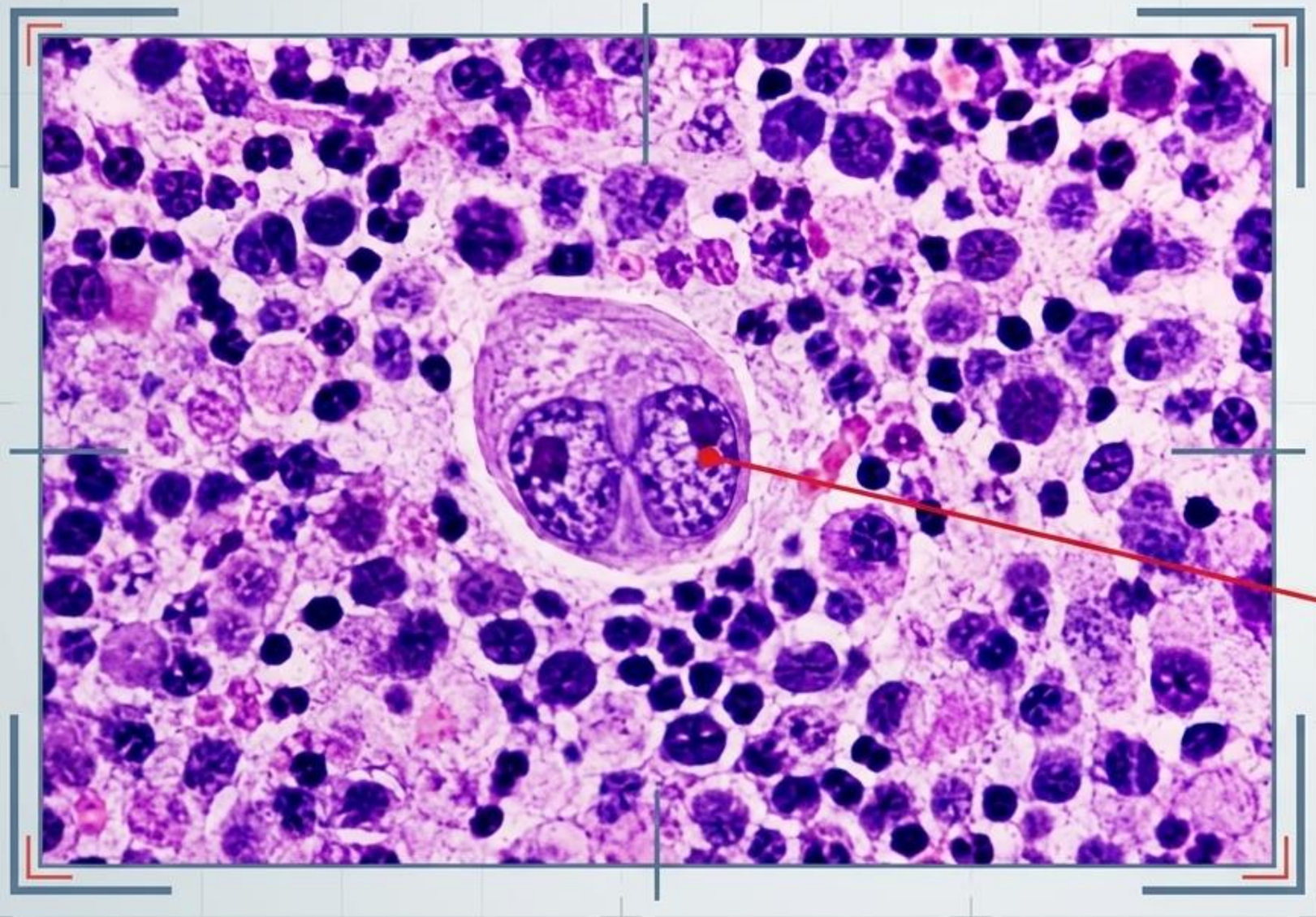
Hypercellular marrow with eosinophilia.

SUGGESTED DIFFERENTIAL

Reactive/allergic disorders vs. Parasitic infection vs. Hodgkin lymphoma (less likely based on marrow alone).

ACTION MANDATE: Proceed to direct biopsy of enlarged lymph node.

THE DEFINITIVE TEST | PARA-AORTIC LYMPH NODE BIOPSY



PATHOLOGY REPORT SUMMARY

- Complete **effacement of lymph-node architecture**.
- **Polymorphous inflammatory background** (numerous eosinophils, histiocytes, and plasma cells).

THE SMOKING GUN

Abundant **Reed–Sternberg cells** (bilobed / multinucleated nuclei) – The classic 'Owl-Eye' appearance.

CASE RESOLVED | FINAL DIAGNOSIS

CLASSICAL HODGKIN LYMPHOMA

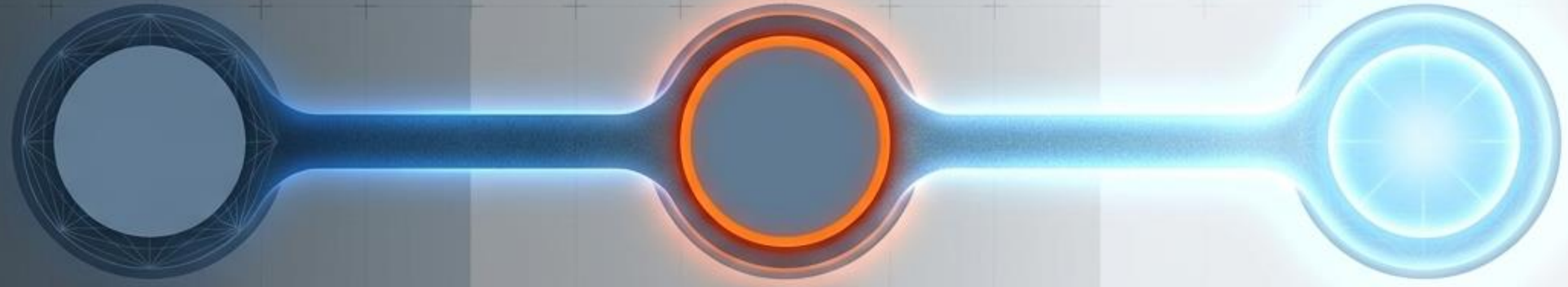
MIXED CELLULARITY SUBTYPE

Diagnostic Synthesis: Tying it all together—The recurrent nocturnal fevers, the escalating inflammatory markers (ESR 101), the hidden retroperitoneal lymphadenopathy, and the profound marrow eosinophilia are all unified under the B-symptom driven phenotype of Mixed Cellularity CHL, perfectly demonstrating how this malignancy expertly mimics a systemic infection.

CASE CLOSED.

HODGKIN LYMPHOMA | MANAGEMENT & OUTCOMES

> "The goal is not merely to cure Hodgkin lymphoma, but to preserve the life and health of the survivor."



Step 1: Staging & Risk Stratification

Step 2: Prognosis & Outcomes

STEP 3: LONG-TERM FOLLOW-UP & SURVIVORSHIP