Leukocytosis: Sepsis or Cancer? An atypical presentation of CLL

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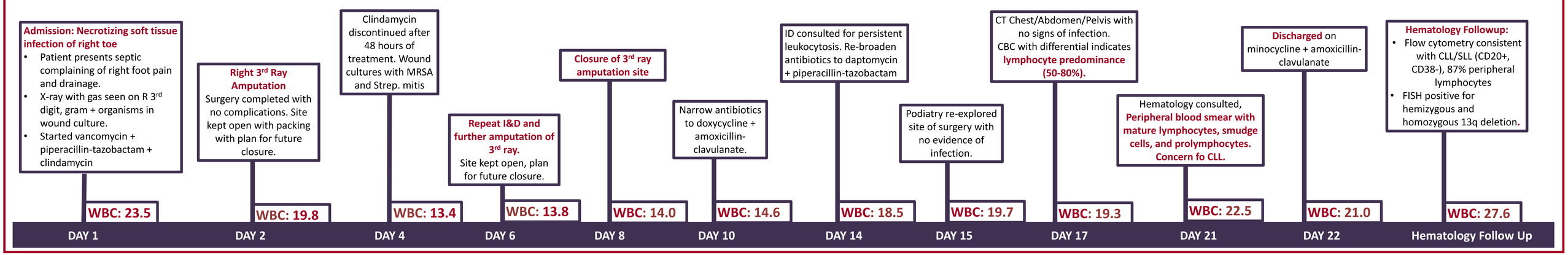
A 65 year-old male with a past medical history of uncontrolled diabetes, hypertension, chronic kidney disease, alcohol use and tobacco use disorder presents complaining of right toe pain…

TIMELINE



INTRODUCTION TO CLL

- Chronic lymphocytic leukemia (CLL) is the most common adult leukemia in Western countries[1], diagnosed in 4.7/100,000 people within the USA per year.[2]
  - Men are at 2x the risk of developing CLL compared to women.[2]
  - Risk of CLL increases with age, median age at diagnosis = 70 years. [2]
- The disease is characterized by functionally incompetent lymphocytes, usually monoclonal in origin.
- The clinical progression of CLL varies: some patients require treatment soon after diagnosis, others have indolent disease that does not require therapy.
- Patients with CLL are hypothesized to be predisposed to developing infections due to hypogammaglobulinemia, increased production of IL-10 by B cells, and impaired cellular immune function secondary to reduced effector function of T cells.[3]
- Patients are more prone to infection with encapsulated bacteria such as Streptococcus pneumoniae and Haemophilus influenzae[4]
  - Neutropenic patients who have had chemotherapy are also prone to infections with Staphylococcus aureus and enteric pathogens (Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae)[4]

References
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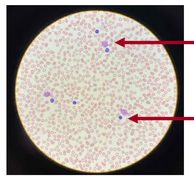
4. Nosari A. Infectious complications in chronic lymphocytic leukemia. *Mediterr J Hematol Infect Dis*. 2012;4(1):e2012070. doi:10.4084/MJHID.2012.070
5. Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Guideline Name V.2.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed [May 21,2023]. To view the most recent and complete version of the guideline, go online to NCCN.org. Hallek M, Cheson BD, Catovsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. *Blood*. 2018;131(25):2745-2760. doi:10.1182/blood-2017-09-806398
6. Hallek M, Cheson BD, Catovsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. *Blood*. 2018;131(25):2745-2760. doi:10.1182/blood-2017-09-806398

DIAGNOSIS OF CLL IN THIS PATIENT[5]

1. Review of peripheral blood smear:



Normochromic RBCs, mild anisocytosis, mild poikilocytosis, no schistocytes. Increased lymphocytes compared to granulocytes. Lymphocytes with "soccer-ball" like appearance with cracked nucleus. A few large atypical lymphocytes with nucleolus, multiple smudge cells, normal granulocytes.

2. Flow cytometry:
   1. CLL diagnosis requires presence of monoclonal B lymphocytes ≥5 x 10^9/L in peripheral blood

Our patient:
A CD5+, CD23+, CD38- monoclonal B cell population is detected with kappa light chain restriction **(75% of the leukocytes).**
Absolute monoclonal B lymphocyte count = 20 x 10^9/L

3. If diagnosis not established by flow cytometry, proceed with lymph node biopsy. – N/A to our patient, flow cytometry was sufficient for diagnosis.
4. Informative prognostic and/or therapy determination:
   a. FISH to detect +12; del(11q); del(13q); del (17p) CpG-stimulated metaphase karyotype
   b. Molecular analysis to detect IGHV mutation status

FISH panel analysis was positive for hemizygous and homozygous loss of 13q14
- Patients with a sole anomaly of del13q have the longest survival time!

Positive for IGHV hypermutation, a marker for good prognosis

INDICATIONS FOR TREATMENT OF CLL[6]

	Our patient:

• Progressive marrow failure:
  • Hgb < 10 g/dL
  • Platelet count <100,000/µL
	Hgb: 11.4 g/dL
	Platelets: 311,000/µL

• Massive (≥6 cm below left costal margin) or progressive/symptomatic splenomegaly.	No significant splenomegaly
• Massive (≥10 cm) or progressive/symptomatic lymphadenopathy.	No palpable lymph nodes
• >50% increase of lymphocytosis over 2 months, or lymphocyte doubling time of <6 months.	None
• Constitutional symptoms (fatigue, night sweats, unintentional weight loss, Fevers	None

CONCLUSION

It is essential to maintain a broad differential to prevent anchoring bias, as seen in the case of this patient who initially presented with leukocytosis thought to be due to infection. However, they developed worsening leukocytosis despite adequate treatment. By maintaining a broad differential for leukocytosis, clinicians were able to diagnose CLL and guide the patient to adequate follow up with hematology for monitoring and further management.