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...

INTRODUCTION TO CLL

- Chronic lymphocytic leukemia (CLL) is the most common adult leukemia in Western countries, diagnosed in 4.7/100,000 people within the USA per year.
- Men are at 2x the risk of developing CLL compared to women.
- Risk of CLL increases with age, median age at diagnosis = 70 years.
- 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.
- Patients are more prone to infection with encapsulated bacteria such as Streptococcus pneumoniae and Haemophilus influenzae.
- Neutropenic patients who have had chemotherapy are also prone to infections with Staphylococcus aureus and enteric pathogens (Pseudomonas aerugiosa, Escherichia coli, Klebsiella pneumoniae)

DIAGNOSIS OF CLL IN THIS PATIENTS

1. Review of peripheral blood smear

- Smudge Cells
- Predominant lymphocytes with sparse cytoplasm
- Neutrophils RBCs, mild anisocytosis, mild poikilocytosis, no schistocytes.
- Increased lymphocytes compared to monocytes. Lymphocytes with “screw-ball” like appearance with condensed nucleus. A few large mononucleated lymphocytes are seen with nucleolus, small to medium-sized cells, and prolymphocytes.

2. Flow cytometry:

- CLL diagnosis requires presence of mononuclear B lymphocytes ≥ 10% in peripheral blood
- If diagnosis not established by flow cytometry, proceed with lymph node biopsy – N/A to our patient, flow cytometry was sufficient for diagnosis.
- Inflammatory and/or therapy determination:
  - FISH to detect +12; del(13q); del(17p); del (17p)CGH-stimulated metaphase karyotype
  - Molecular analysis to detectIGHV mutation status

Out patient:
- FISH (13q), (13q), (12q) mononuclear cell population is detected with kappa light chain restriction (75% of the leukocytes).
- Absolute mononuclear B lymphocyte count = 20 x 10^3/L

FISH panel analysis was positive for hyperdiploidy and monosomy of 13q14
- Patients with a sole anomaly of del(13q) have the longest survived time
- Positive GHR hyperpmentation, a marker for good prognosis

INDICATIONS FOR TREATMENT OF CLL

- Progressive marrow failure:
  - High <10 x 10^6/L
  - Platelet count <100,000 x 10^6/L
  - Massive (≥6 cm below left costal margin) or progressive/symptomatic splenomegaly
- Massive (≥10 cm) or progressive/symptomatic lymphadenopathy
- >50% increase in lymphocytosis over 2 months, or lymphocyte doubling time <6 months.
- Constitutional symptoms (fatigue, night sweats, unintentional weight loss, Fever)

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.

PA-ACP Southeastern Philadelphia, PA
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Admission: Necrotizing soft tissue infection of right toe
- Patient presents septic: complaining of right foot pain and drainage.
- X-ray with gas seen on R 3rd digit, gram + organisms in wound culture.
- Started vancomycin + piperacillin-tazobactam + clindamycin

Right 3rd Ray Amputation

- Surgery completed after 48 hours of treatment. Wound cultures with MRSA and Strps. mils.
- Clandamycin discontinued after

Closure of 3rd ray amputation site

Repeat I&D and further amputation of piperacillin-tazobactam + clindamycin

Recurrent cellulitis at amputation site

CT Chest/Abd/Pelvis with no signs of infection. CBC with differential indicates lymphoedema predominance (50-80%).

Discharged on monocybine + amoxicillin-clavulance

Hematology Follow up:
- Flow cytometry consistent with CLL (D12q, -13q, -17p). 87% peripheral lymphocytes.
- FISH positive for hyperdiploidy and monosomy 13q deletion.

Hematology Consulted, Peripheral blood smear with mature lymphocytes, smudge cells, and polynuclears. Concern fo CLL.

TImeline

DAY 1

- WBC: 23.5

DAY 2

- WBC: 19.8

DAY 4

- WBC: 13.4

DAY 6

- WBC: 13.8

DAY 8

- WBC: 14.0

DAY 10

- WBC: 14.6

DAY 14

- WBC: 18.5

DAY 15

- WBC: 19.7

DAY 17

- WBC: 19.3

Hematology Followup:

- Clindamycin
- Tazobactam
- Doxycycline + amoxicillin-clavulanate
- Amoxicillin + clavulanate
- minocycline + amoxicillin-clavulanate
- bismuth subcitrate + tetracycline + metronidazole

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