A Rare Case of Rapidly Progressive CLL/SLL Presenting as Bilateral Tonsillar Enlargement and Upper Airway Obstruction

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Introduction

- Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) differ in clinical presentation, they are both arise from the same pathologic process, namely the clonal expansion of mature B-cells.[1]
- The introduction of oral targeted therapies, such as the Bruton tyrosine kinase (BTK) inhibitor ibrutinib have supplanted chemotherapy as first line treatment of CLL and greatly improved outcomes.[1]
- Rates of ibrutinib discontinuation due to drug-associated toxicities range from 21-41% in various studies, with one reporting a dose interruption of at least 1 week in 55% of patients.[2-4]
- Rapid disease progression and disease flares that mimic transformation to high-grade lymphomas have been described after ibrutinib discontinuation or medication interruption.[3-6]
- Airway obstruction due to CLL/SLL only accounts for 2% of pulmonary complications and is primarily due to hilar/mediastinal lymphadenopathy.[7]
- CLL/SLL presenting as bilateral tonsillar enlargement is quite rare, with only 13 previously published cases.

Case Report

- 62-year-old male with past medical history of CLL presented to outside facility with 3 weeks of worsening sore throat, painful swallowing, and enlarging neck mass that eventually progressed to shortness of breath and difficulty speaking.
- Patient had been diagnosed with CLL approximately 3 years prior and was started on ibrutinib at that time. He had no issues until about 6 months before presentation when he developed a persistent rash.
- Ibrutinib was discontinued 1 month prior with plans to start acalabrutinib, but he had yet to receive first dose at time of hospital admission.
- On arrival, patient was tachycardic and hypertensive with increased work of breathing, but not hypoxic on room air.
- Initial imaging showed pan-tonsillar enlargement, epiglottis thickening, and lymphadenopathy. Initial labs significant for leukocytosis of 116.91 K/mm^3 and creatinine 1.55 mg/dL.
- Shortly after admission, patient's increased work of breathing continued to worsen, and decision was made for intubation. Due to his significant airway obstruction, an awake fiberoptic nasal intubation was performed.
- On hospital day 2, labs showed potassium of 9.0 mmol/L; however, repeat labs from arterial blood gas (ABG) with chem panel showed potassium of 4.1 mmol/L. Electrolytes were subsequently monitored via ABG the remainder of hospitalization.
- On hospital day 3, patient developed fever of 101.4 F and started on active temperature management, which was continued intermittently throughout hospitalization.
- On hospital day 4, patient underwent successful percutaneous endoscopic gastrostomy (PEG) tube placement, tracheostomy, and tonsillar biopsy. Final biopsy results were consistent with CLL/SLL without definite evidence of transformation or diffuse large B-cell lymphoma.
- Worsening leukocytosis of 439.35 K/mm3 prompted oncology to start chemotherapy on hospital day 10. Treatment included: cyclophosphamide, doxorubicin, vincristine, and dexamethasone (CHOP therapy). Rasburicase and tbo-filgrastim were also added for potential tumor lysis syndrome and chemo-induced neutropenia, respectively.
- After initiation of chemotherapy, patient's leukocytosis initially improved but began to worsen once again on hospital day 14.
- On hospital day 13 patient developed atrial fibrillation with rapid ventricular response, hypotension requiring pressor support, and worsening hypoxia.
- Despite aggressive treatment, family ultimately elected for comfort measures on hospital day 15 and patient passed away shortly after.

Conclusion

- The case presented here is unique not only in the location of the malignancy and clinical symptoms but also in the nature and timing these symptoms arose.
- On extensive literature review, only 13 cases of CLL/SLL causing bilateral tonsillar enlargement were found. Among those cases, this one particularly stands out in severity of clinical presentation.
- Based on the rapid timing of symptom onset after discontinuation of ibrutinib and the biopsy results showing no evidence of transformation, this case likely represents a case of rapid disease progression triggered by the discontinuation of the drug.
- Approximately 25% of patient's experience disease flares with even temporary discontinuation of ibrutinib.[3] These flares can range from mild incidental findings to severe, as in the case presented here.
- Interestingly, this rapid disease progression appears to be improved or reversed when ibrutinib or a similar tyrosine kinase inhibitor is restarted.[3-5]
- This case helps build on the growing body of literature of this potentially devastating phenomenon.

Teaching Points

- As oral targeted therapies become increasingly more commonly used, the number of patients that experience disruptions in treatment will undoubtedly continue to increase.
- This case offers a reminder to clinicians of the potential rapid disease progression associated with discontinuing these medications.
- Given the speed of symptom progression, there was concern for transformation to a high-grade lymphoma. Thus, treatment was not initiated until biopsy results returned. It is unclear how this delay influenced the outcome of this case.
- In severe cases such as this, we propose restarting ibrutinib or other tyrosine kinase inhibitor while waiting for biopsy results. However, further studies are necessary to evaluate this effectiveness of this intervention.

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