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Hearing Loss and CLL: a Rare Complication of Leukostasis

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Abstract In chronic lymphocytic leukemia (CLL), hyperleukocytosis has a prevalence of 20-40%, but leukostasis is extremely rare. In this case, a 53-year-old male with no known medical history presented to the emergency department with acute bilateral hearing loss, shortness of breath, diffuse lymphadenopathy, weight loss, and an abdominal mass, and was found to have hyperleukocytosis (WBC: 1075.5 bil/L), anemia (Hb: 2.2 g/dL), and thrombocytopenia (Platelets: 33 bil/L). Flow cytometry and lymph node biopsy found chronic lymphocytic leukemia with a 13q14.3 deletion, and subsequently started on venetoclax resulting in resolution of the leukocytosis and thrombocytopenia. Persistent hearing loss led to attempting oral and intratympanic corticosteroids, which also failed to restore hearing. No lesions were found in the bilateral internal auditory canals on MRI. Unlike previous cases of hearing loss in CLL-related leukostasis, this patient's hearing loss did not resolve with CLL resolution, which suggests that increased viscosity versus other unidentified etiologies are the cause. Further studies need to be conducted in this subset of patients to better understand and combat the mechanisms behind CLL-related leukostasis hearing loss.

Keywords: *CLL, Hearing Loss, Leukostasis, Hyperviscosity, hyperleukocytosis, Leukemia.*

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1. Introduction

Chronic lymphocytic leukemia (CLL) is one of the most frequent types of leukemia with an incidence of 4.9 per 100,000 in the United States. It is characterized by a clonal proliferation of CD5-positive mature B-lymphocytes in the blood, bone marrow, lymph nodes, and spleen. CLL diagnosis is defined as B-lymphocyte count >5000/µL for greater than 3 months. 80% of CLL diagnoses carry one of four common genetic mutations: del(13q14.3), del(11q), del(17p), and/or trisomy 12. Del(13q14.3) is the most common genotype and carries a benign prognosis; del(17p) is associated with chemotherapeutic resistance and a worse prognosis. CLL has a median age of diagnosis of 70 with a male to female predominance of 1.9:1. It is one of the most treatable malignancies with a 5-year survival rate of almost 90% as of 2021 [2].

Hyperleukocytosis is a common complication of leukemic malignancies, with a prevalence of 20-40% and defined as white blood cell (WBC) count >100,000/µL. Leukostasis is a much rarer complication that results in clinical manifestations related to increased leukocyte counts in leukemia. Pathologic diagnosis technically requires the visualization of leukemic stasis and infiltration in capillaries, but the diagnosis is typically made clinically on account of the difficulty in acquiring such a sample. Clinical manifestations of leukostasis are believed to be secondary to microvascular circulatory failure and subsequent end organ hypoperfusion, ischemia, leukocyte extravasation, and systemic inflammation [1]. The most common clinical findings typically have neurologic and pulmonary manifestations like dyspnea, hypoxemia, headache, dizziness, focal deficits, acute respiratory distress syndrome (ARDS), and visual changes. Other organ systems can also be involved such as the cardiac (chest pain, myocardial ischemia), renal (decreased GFR), musculoskeletal (limb ischemia), gastrointestinal (abdominal pain, lactic acidosis), and genitourinary (priapism). Few case reports have reported bilateral hearing loss, usually resolving with treatment.

2. Case Summary

A 53 (now 54) year-old Eastern European-born male with no known medical history presents to the emergency department (ED) with bilateral hearing loss over the preceding three days, shortness of breath, diffuse lymphadenopathy, sore throat, 20-lb weight loss, and an abdominal mass. He was found to have leukocytosis (1,075.5/µL), anemia (Hb: 2.2 g/dL), thrombocytopenia (33 bil/L), transaminitis (ALT 1363 U/L, AST 577 U/L,

ALP 227 U/L), hyperbilirubinemia (3.0 mg/dL), and AKI (Cr 1.34 mg/dL). Computed tomography (CT) of the abdomen and pelvis found extensive lymphadenopathy within the central mesentery, retroperitoneum, pelvis and inguinal regions; a large mass in the right hemipelvis; abdominal and pelvic ascites; hepatosplenomegaly; splenic infarction; a necrotic right kidney mass; right adrenal nodule; and cholelithiasis. Abdominal ultrasound (US) showed similar findings along with pleural effusions, multiple hepatic masses and gallbladder wall thickening. CT of the head was negative for intracranial process; subsequent MRI showed a 1.1x1.1 cm right occipital lobe lesion with surrounding edema without other infarctions, hemorrhage, or lesions in the bilateral internal auditory canals. There was also bilateral retinal hemorrhages, vitreous hemorrhage and cataracts with associated bilateral visual loss. Flow cytometry and lymph node biopsy found chronic lymphocytic leukemia with a 13q14.3 deletion. The patient received multiple transfusions of pRBCs and leukapheresis, as well as treatment with Venetoclax for CLL causing resolution of the leukocytosis and thrombocytopenia. Oral and intratympanic corticosteroids were attempted with no effect on the patient's hearing. Biopsies of the right kidney mass, right occipital lobe, liver, and adrenal nodule were not performed due to thrombocytopenia and anemia throughout hospital admission.

3. Discussion

Hearing loss is a very rare complication of leukostasis from CLL with only 6 documented cases found, compared with other leukemias that have a much higher propensity for leukostasis and associated symptoms like acute myeloid leukemia (AML). This may be explained by the small size and low rigidity of lymphocytes as opposed to other cell lines that predominate in other leukemias [1,6]. These small, more flexible lymphocytic cells are therefore less likely to physically occlude vessels significantly to cause neurologic symptoms [1,6]. This may explain why most of the cases of hearing loss were associated with hyperleukocytosis, because higher WBC counts may be needed to cause such occlusive symptoms [1,2,3,4,5]. Other potential reasons for the rarity of leukostasis in CLL include less rapid cell growth, decreased endothelial adhesion factor expression and activation, and less favorable cytokine production in relation to other leukemias [1,6,8].

What was unique in this case, was not only because leukostasis is uncommon in the context of CLL, but also hearing loss that was refractory to treatment [3,4,5,6,7]. In the 6 published case reports, 4 of 6 patients recovered hearing after treatment, with two cases after leukapheresis and two after chemotherapy. These findings highlight the uniqueness of our case, because our patient received both of these treatments with persistent deafness.

Finally, it is interesting that this case and the previous cases appear to suggest an alternate explanation to hearing loss in CLL leukostasis other than leukostatic hyperviscosity. In our case, hearing was not recovered even after reduction of cell counts to normal limits. In the 6 previous cases, 4 had WBC counts >500/µL, 2 of which recovered hearing ability after treatment, while the other 2 did not (1 case was treated with leukapheresis and 1 was treated with chemotherapy plus radiation). This observation calls into question whether hearing loss in these cases can solely be attributed to vasoocclusion because resolution of the hyperleukocytosis was not consistently linked to resolution of deafness in patients with WBCs >500/µL. Further, 2 cases of deafness were found in CLL patients with WBC counts <500/µL, and both of these cases had resolution of symptoms with treatment.

Since leukostasis is rarely seen in CLL with WBC counts <1 million/µL and since the symptoms resolved with treatment, this indicates that hearing loss is a possible complication of CLL even when cell counts are not increased to a leukostatic degree. Taken together, these findings point to the existence of an additional explanation for hearing loss in leukostatic CLL. Leukostatic extravasation of lymphocytic cells has been proposed as an explanation, although radiologic confirmation of such mechanisms has been inconsistent [6]; in our case there was no radiologic evidence of such a process. More in-depth studies need to be conducted in order to elucidate whether and to what degree other mechanisms are at play in the pathogenesis of hearing loss in this disease process.

4. Conclusion

Patients with CLL can present with hearing loss, either due to leukostasis, infiltration of lymphoid cells, or other yet unknown factors. Early diagnosis by using imaging techniques, and treatment with chemotherapy or leukapheresis depending on the total WBC can be very crucial to avoid progression of hearing loss to permanent deafness.

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