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CASE REPORT

Chronic Myeloid Leukemia (CML) with Permanent Hearing Loss

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Abstract

Objective: The present case study aims to discuss a rare case of chronic myeloid leukemia causing bilateral hearing impairment, tinnitus, and vertigo.

Introduction: Chronic Myeloid Leukemia (CML) or chronic granulocytic leukemia is a type of blood cancer that affects the bone marrow. It results in an overproduction of immature White Blood Cells (WBCs) that typically happens throughout or after middle age, and adolescents are rarely affected. The genetic mutation that causes CML is known as the BCR-ABL fusion gene.

Case Presentation: In this case report, a 30-year-old female presented to the hospital of Jazan, Saudi Arabia, with sudden hearing impairment and other symptoms, leading to a CML diagnosis. The patient had no prior hearing impairment background, and the otoscopic scanning was normal. The Pure Tone Audiometry (PTA) showed profound sensorineural hearing loss on both sides. Blood tests revealed hyperleukocytosis with marked neutrophilia, mild basophilia, and eosinophilia and a BCR-ABL quantitation of 85%. Bone marrow aspiration showed granulocytic hyperplasia, mild left-shifted maturation, and less than 1% blasts.

Results: The patient was started with options including Tyrosine Kinase Inhibitors (TKIs) such as Imatinib, which target the BCR-ABL fusion gene, reducing the number of leukemia cells and improving her white blood cell count. However, her deafness persisted, and she became dependent on hearing aids.

Discussion: CML presenting with hearing loss is rare, with only a few reported cases in the literature. It is believed to be related to the infiltration of leukemic cells in the inner ear or the microvascular complications associated with the disease. Hearing loss can be reversible or permanent, depending on the severity and duration of the disease. Treatment of CML with tyrosine kinase inhibitors such as Imatinib can improve the hematologic parameters, but the effect on hearing loss is uncertain.

Abbreviations

CML: Chronic Myeloid Leukemia; TKIS: Tyrosine Kinase Inhibitors; PTA: Pure Tone Audiometry; CNS: Central Nervous System

Introduction

Initially, leukemia was a term coined by Rudolf V [1], who related the association between an enlarged spleen and leukocytosis. Chronic myeloid leukemia was first observed in the early 19th century as an outcome of

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astute clinical observations [2]. Leukemias were later recognized as a unique nosological entity with the advent of clinical microscopy and the application of aniline-based dyes to stain human tissues; several of the earliest initiatives were on therapy and resulted in the development of compounds of arsenic for relieving pain in the latter 19th century. It wasn't until 1960 that significant advancements in cytogenetics technology allowed for identifying a consistent chromosomal abnormality in the bone marrow cells of CML patients. This finding marked a turning point in the disease's management and our awareness of how it works; therefore, it was eventually given the name "Philadelphia" or "(Ph) chromosome" to honor the location of the research [3].

Chronic myeloid leukemia is characterized as a myeloproliferative illness, malignant tumors of the hematopoietic system primarily descended from granulocytic stem cells, infiltrating the bone marrow, plasma, and other tissues and organs [4]. It is marked by an early chronic stage that is docile and simple to treat, evolving to a blastic, chemotherapy-resistant phase, often accompanied by an increased pace [4,5]. Hyperleukocytosis (WBC > 100 000/mm³) is caused by the disease's clonal expansion of myeloid cells, which replace all other hematopoietic products; Leukostasis, a reduction in microcirculation blood flow, may result from acute hyperleukocytosis, making the blood functionally more viscous. Vascular constriction leads to tissue ischemia and infarction after that, particularly among the lungs and the cerebellum (CNS) [6,7].

Blindness and hearing loss are the symptoms that infrequently occur in Chronic Myeloid Leukemia patients (CML); however, otolaryngological manifestations and indications, i.e., vertigo, tinnitus, facial weakness, and hearing loss, are usual in hematologic diseases [8,9]. This case report explained bilateral profound sensorineural hearing impairment diagnosed in a 30-year-old female.

Case Presentation

A 30-year-old female was presented in the Emergency Room (ER) of Prince Mohammad Bin Naser, Hospital in Jazan, Saudi Arabia, with a one-week history of vertigo, tinnitus, generalized body weakness, and abrupt hearing impairment on both sides. There was no history of hearing discomfort, exposure to loud noise, ear trauma, evidence of a foreign body in the ear, facial pain, or any report

of nose or throat issues that occurred. Moreover, there were no prior indications of bleeding from any craniofacial orifices or slow bleeding from the pierced area. A history of radiation exposure and a record supporting the respiratory complaint were absent. It is unknown if the patient has hypertension, diabetes mellitus, or any evidence of surgery or blood transfusions.

Initial examination revealed that the young female was conscious and alert. The body's vital indicators were normal. Although the spleen was roughly 16 cm below the costal border, no hepatomegaly existed. Otosopic scanning is normal, and Pure Tone Audiometry (PTA) performed by the audiologist by the standard method with averaging thresholds at 250, 500, 1000, 2000, 4000, 6000, and 8000Hz, indicated bilateral profound sensorineural hearing impairment, which is more severe in the right than in the left ear, following Word Recognition Scoring (Table 1).

Full blood count results were as follows: WBC 719.4 x 10⁹/L, blast cell 4%, promyelocyte 12%, myelocyte 8%, metamyelocyte 10%, segmented neutrophil 42%, lymphocyte 12.3%, monocyte 4%, basophil 4%. Peripheral blood film revealed hyperleukocytosis reflected mainly by marked neutrophilia with moderate left-shifted granulocytic cells and rare circulating blasts (<1%), mild basophilia 11%, and eosinophilia. Red cells showed a hypochromic microcytic picture with mild to moderate anisopoikilocytosis, few elliptocytes, few teardrop cells, occasional fragmented red cells, and rare spherocytes. Platelets were increased with occasional large forms.

Bone marrow aspiration was non-articulated and partially hemodiluted with granulocytic hyperplasia 84% with mild left-shifted maturation. Blast represented less than 1% of all nucleated bone marrow cells. Rare megakaryocytes were seen. Erythroid precursor 1%, lymphocytes 4.5%, and basophils 6%. BCR-ABL Quantitation had been detected at a level of 85%. Her brain's Magnetic Resonance Imaging (MRI) showed normal mastoids, cerebellopontine angle, and other posterior fossa structures. There are bilateral tiny sub-cortical cerebral hyper signal foci, seen by T2 and flair DW that are not restricted by diffusion and not enhanced after injection; the contrast as nonspecific foci that could be seen by broad spectrum MRI brain studies, i.e., chronic demyelinating diseases or small vessels disease. Neurological consultation

Table 1: Pure-tone audiometric approach and word recognition scores in quiet (Record quieted in NU-6 Lists).

Right Ear Hearing Threshold (dB HL)									
Date	250 Hz	500 Hz	1 kHz	2 kHz	3 kHz	4 kHz	6 kHz	8 kHz	Word Recognition Score (%)
18/2/22	20	25	55	55	45	50	35	40	83
1/3/22	20	30	60	50	40	55	40	45	95
6/4/22	15	25	60	50	45	55	35	50	68
7/5/22	10	25	55	60	45	55	35	45	92
23/5/22	15	20	60	50	45	50	35	50	100
22/11/22	10	25	60	50	50	55	35	45	96
Left Ear Hearing Threshold (dB HL)									
Date	250 Hz	500 Hz	1 kHz	2 kHz	3 kHz	4 kHz	6 kHz	8 kHz	Word Recognition Score (%)
18/2/22	20	30	55	10	30	80	65	40	73
1/3/22	35	25	60	10	40	65	40	65	76
6/4/22	25	10	10	5	25	65	60	50	100
7/5/22	30	40	55	5	35	70	65	65	83
23/5/22	30	25	60	20	35	40	75	60	92
22/11/22	25	30	55	5	50	55	65	45	96

suggests peripheral vestibular disorder. The Ear, Nose, and Throat (ENT) consultant advised using a hearing amplification device. She began receiving her regular CML treatment, which included hydroxyurea, IV fluids, and allopurinol. Her WBCs count reached 75000 x 109/L. She was started on oral Imatinib (400mg once daily). Additional neuro stimulants added to the treatment regimen include nicotinic acid and neurobion. The patient improved her count and mild to moderate response with hearing aids. At her outpatient follow-up, audiometry was completed during the last visit 3 months ago and showed only mild hearing recovery, as explained in table 1; she had a stable count but was hearing aids dependent.

Discussion

Chronic Myeloid Leukemia (CML) is a hematopoietic stem cell illness characterized by malignant cells of the hematopoietic system, primarily of granulocytic origin, infiltrating the plasma, bone marrow, and certain other organs [4]. Only 2-5% of pediatric leukemias are CML, typically an adult disorder. In the chronic stage of CML, over 50% of patients are asymptomatic. Anemia and signs of an enlarged spleen (pain, swallowing, and abdominal discomfort), when present, are among the clinical characteristics. Owing to hypermetabolism, temperature, bodyweight reduction, and night sweats were frequent findings. Individuals with hyperleukocytosis may experience alterations to their mental state, headaches, papilledema, hemorrhage, cerebellar symptoms, and dysmenorrhea. The

condition causes restriction of blood in the brain, lungs, and other organs [10].

In between 16 and 40 % of leukemia patients, otological abnormalities such as infection, vertigo, tinnitus, and abrupt hearing impairment were discovered. Deafness is a relatively uncommon first sign of this illness, though. Hearing impairment caused by CML can be sensorineural, unilateral, bilateral, or begin unilaterally before progressing to bilateral [6]. Leukapheresis and chemotherapy might help certain CML patients who have experienced an unexpected hearing impairment. Several people with hyperviscosity disease have been able to do this, indicating that this kind of impairment is recoverable [10]. When WBC levels exceed 500 000/L, "hyperviscosity" is reported to develop [11]. It's noteworthy that hyperleukocytosis doesn't result in hyperviscosity in physiological tests. Because the rise in leukocytes is accompanied by a compensatory drop in the relative proportion of red blood cells (erythrocyte), on the other hand, hematopoietic white blood cells cannot properly deform to traverse the microcirculation, making them susceptible to establishing disruptive blood clot.

Additionally, because of their high oxygen uptake, they compete with normal hemoglobin for this limited supply, causing local hypoxemia and ischemic stroke [7]. Leukemic infiltration, middle and inner ear bleeding, leukostasis, or pathogens all seem to play a role in the pathophysiology causing leukemic otologic signs [11,12]. In our case, the patient's deafness

occurred due to hyperviscosity and hyperleukocytosis with leukocytosis in other tiny arteries of the vertebrobasilar area, including the labyrinth artery. Tyrosine kinase inhibitors like Imatinib, used to treat CML, can improve certain hematological metrics, yet it's unclear how they will affect hearing impairment. The usage of hearing aids can enhance our patients' living conditions.

Conclusion

This case report enlightens the significance of considering CML in the differential diagnosis of sudden hearing loss, even in the absence of other symptoms. It also emphasizes the potential for permanent hearing loss as a complication of CML, which may require long-term hearing support. Early diagnosis and prompt treatment of CML with tyrosine kinase inhibitors such as Imatinib are crucial to improving the hematologic parameters and preventing further complications. Still, the effect on hearing loss is uncertain. The use of hearing aids can enhance the patient's life expectancy.

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Ethical Approval

This study was approved by the Research and Ethical Committee ofIRB#..?

Informed Consent

Written informed Consent was obtained from the patient to publish this case report, including the images.

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