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Otological Diseases in Patients with Chronic Myeloid Leukemia

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Abstract

This was a cross-sectional study to determine the pattern of manifestations of otological diseases among patients with Chronic Myeloid Leukemia. A structured questionnaire was administered to assess otological symptoms, followed by a general physical and ear examination. Pure tone audiometry and tympanometry in CML subjects and matched control subjects were also performed.

There were 58 subjects constituting 32(55.2%) males. History of hearing loss and tinnitus was given by 13(22.4%) of the CML subjects. Audiometry however revealed a higher prevalence of 38(65.5%) of hearing impairment. The mode of onset of the hearing impairment in the self-reported cases was sudden in 9(69.2%) and in 7 (53.8%) the hearing loss preceded the diagnosis of CML. Vertigo was seen in 4 (30.8%) of the thirteen CML subjects with self-reported hearing loss. Hearing loss was found to be prevalent in CML despite lower prevalence of self-reported cases was found.

Keywords: Chronic myeloid leukemia; Hearing loss; Tinnitus

Introduction

Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative disorder characterized by proliferation of granulocytic elements at all stages of differentiation [1]. Patients are often discovered incidentally when an elevated White Blood Cell count (WBC) is revealed by routine Full Blood Count (FBC) or when an enlarged spleen is revealed during an abdominal examination. Non-specific symptoms of tiredness, fatigue, and weight loss may occur long after the onset of the disease.

Otologic manifestations have been reported in 15-40% of leukemic patients [2-5]. These include moderate to severe sensorineural hearing loss, tinnitus, vertigo and facial nerve palsy. Other manifestations include finding of *thick red tympanicmembrane*, which typify the ongoing involvement of the middle ear.

The objective of this study is to determine the pattern of otological diseases manifestations found in patients with CML.

Patients and Methods

This was a cross-sectional hospital-based study conducted at the Haematology and Otorhinolaryngology Outpatient clinics of the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife (OAUTHC) in the Nigeria between July 2011 and December 2011. The centre was running the *Glivec International Patient Assistance Program* (GIPAP™) offering free treatment to patients with CML [6].

The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki after obtaining ethical clearance from the Institutional Ethical Committee. Informed consent was also obtained from all subjects.

Fifty-eight consecutive previously diagnosed CML patients in chronic phase with an equal number of age and sex matched controls were recruited. All the CML patients were referred others centers based on symptoms and WBC count above 200,000 cells/mm^3. At our center, they all had bone marrow biopsy and cytogenetic studies with the confirmation of presence of Philadelphia Chromosome (Ph). The control subjects were hospital staffs, medical students and patient relatives. We administered structured questionnaire to consenting CML subjects detailing information on the ear symptoms. This was followed by ear examination, tympanometry and pure tone audiometry using standard protocol [7]. The degree of hearing loss for each subject was based on the World Health Organization (WHO) standard classification [7] .

The variables analysed were age, sex, duration of illness, otological symptoms, examination findings, Pure Tone Average and Tympanometric pattern.

Results were collated and presented in descriptive format and tables. Analysis was done using Statistical package for social sciences (SPSS version 17, Chicago Inc.). Chi-square test was used to determine the differences in prevalence between the study group and the control group. Statistical significance was inferred at $p<0.05$.

Results

There were 32(55.2%) males and 26(44.8%) females. The mean age for the subjects and control group were 47.2 ± 14.4 and 45.9 ± 14.1 respectively. The mean duration of illness was 3.0 years.

The mean packed cell volume (PCV) was 29. 4 ± 7.9 % while the mean white blood cell count was 154, 347 ± 63,050 cells/mm^3. All the subjects were pH positive.

Thirteen (22.4%) subjects self-reported hearing loss. In 7 (53.8%) the hearing loss preceded the diagnosis of CML. All the subjects with self-reported hearing loss also had associated tinnitus and 4(30.8%) gave history of vertigo. Neither tinnitus nor vertigo occurred in any of the 58 subjects in isolation. Nine (69.2%) had bilateral hearing impairment and 4(30.8%) had unilateral hearing loss. Mode of onset of hearing loss was sudden in 9 (69.2%) and gradual in 4(30.8%). (Table 1). The findings at ear examination are summarized in (Table 2).

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Sex	Hearing Loss	Mode of Onset of HL	Tinnitus	Frequency of Tinnitus	Progression of Tinnitus	Vertigo
F	BE	Su	BE	Constant	Stable	NO
F	BE	Su	BE	Constant	worsening	NO
F	BE	Gr	BE	Occasional	worsening	NO
F	BE	Su	BE	Constant	Stable	NO
M	RE	Su	RE	Constant	Stable	NO
F	BE	Su	BE	Constant	Stable	NO
F	BE	Gr	BE	Constant	stable	NO
M	BE	Su	BE	Constant	stable	NO
M	RE	Su	RE	Constant	stable	NO
F	BE	Gr	BE	Constant	worsening	YES
M	BE	Gr	BE	Occasional	worsening	YES
F	LE	Su	LE	Occasional	improving	YES
M	LE	Su	LE	Constant	improving	YES
F=Female; M=Male; LE=Left Ear; RE=Right Ear; BE=Both Ears.						

Table 1: Pattern of presentation in 13 subjects with self reported hearing loss.

	CML Subjects		Controls		P value
	N	(%)	N	(%)	
EARS					
Pinna/ EAC swellings	2	3.4	0	0.0	0.496
CerumenAuris	10	17.2	11	19.0	0.500
EAC Otorrhea	0	0.0	0	0.0	*NA*
Thick Red TM (Evidence of leukemic infiltration)*	10	17.2	0	0.0	0.001
Dull TM	4	6.9	3	5.2	0.500
Right Rinne's Test					
Negative	0	0.0	0	0.0	*NA*
No Response	6	10.3	0	0.0	*NA*
LeftRinne's Test					
Negative	0	0.0	0	0.0	*NA*
Response	7	12.1	0	0.0	*NA*
Weber's Test					
Lateralized	0	0.0	0	0.0	*NA*
Not heard	7	12.1	2	3.4	*NA*
Facial Nerve Palsy	0	0.0	0	0.0	*NA*
NA: Not applicable					

Table 2: Findings at ear examination.

	CML Subjects N=58				Normal Control N=58			
	R	L	Bil	Total	R	L	Bil	Total
Mild	9	5	6	**20**	0	1	6	**7**
Moderate	4	0	0	**4**	0	0	0	**0**
Moderately Severe	1	4	1	**6**	0	0	0	**0**
Severe	2	1	0	**3**	0	0	0	**0**
Profound	0	1	4	**5**	0	0	0	**0**
Total	**16**	**11**	**11**	**38**	**0**	**1**	**6**	**7**
R=Right; L=Left; Bil=Bilateral.								

Table 3: Classification of degree of hearing loss among CML subjects and control subjects.

Among the CML subjects the pure tone average in the right and left ears were 35.6 ± 26.3 dB HL and 35.9 ± 25.0 dB HL respectively whereas in the control subjects the values were 24.3 ± 6.4 dB HL and 25.8 ± 8.2 HL. No significant air-bone gap was recorded in any of the subjects and tympanometry was type A in all the CML subjects and control subjects.

Thirty-eight (65.5%) CML subjects showed varying degree of hearing loss whereas 7(12.1%) of the control subjects demonstrated hearing loss (Table 3).

The 13 CML subjects with self-reported hearing loss showed significantly higher mean pure tone average (right: 74.1 ± 31.6 db HL; left: 75.0 ± 32.5 db HL; $p<0.001$) compared to the 25 CML patients with hearing impairment detected only by audiometric assessment (right: 29.2 ± 7.2 db HL; left: 28.1 ± 5.2 db HL).

Discussion

This study showed the prevalence of self-reported hearing impairment in the CML subjects to be 22.4%. Audiometry assessments however showed higher prevalence of hearing loss of 38(65.5%). In the control group, only 7(12.1%) had hearing impairment and all were mild. The prevalence obtained is higher than what was reported locally by Joseph and Durosinmi [5] and Druss [2]. Comparable higher prevalence of hearing loss were reported by [4], [8] and [3] but these studies included all forms of leukemia.

In the majority of the cases of self-reported hearing impairment, the mode of onset was sudden and the mean pure tone averages of both ears were within range of severe hearing loss. In addition, all were sensorineural hearing loss.

The foregoing shows that hearing loss is common in patients with CML and by the time a patient with CML is self-reporting hearing loss, it may indicate involvement of both ears or increase in severity of the hearing loss. Hearing loss in CML is described as being sensorineural, unilateral or bilateral. It may also start as unilateral and progressing to become bilateral. It can be a presenting complaint or develop during the course of the disease. The mode of onset is usually sudden but may be gradual [5,9-14]. Hearing impairment as initial manifestation of CML has been reported in the literature [12,13,15,16]. This mode of presentation however is said to be rare [13]. In more than one half of the 13 subjects with severe hearing loss, hearing impairment heralded the diagnosis of CML. This shows that hearing impairment as initial manifestation of CML is not rare and that a patient with CML may present first to an Otorhinolaryngologist. The significance of this is that ENT surgeon should be aware that CML manifestation can be localized mainly in the ear in the early stages of CML. The otological manifestations may thus be worsened by the routing practice of steroid administration in cases of Sudden Sensorineural Hearing Loss (SSNHL) because this causes leukemoid reaction which worsens CML.

Thirteen subjects with self-reported hearing loss had associated severe tinnitus. The tinnitus in these subjects may equally be as worrisome as the hearing impairment. Based on the finding that all self-reported hearing loss had tinnitus and subjects with self-reported hearing loss in this study had more severe degree of impairment, it is possible that tinnitus may be the actual pointer to the worsening of hearing in CML patients. This finding is consistent with what is reported in literature [5,9-12].

Four subjects who presented with vertigo were also part of the subjects with severe hearing loss and tinnitus. We did not explore this further because at the time of assessment, none of the subjects could describe their last episode with certainty. Vertigo has been reported as one of the otological features seen in CML [5,10,17,18].

Swelling on the pinna and EAC was found in 2(3.4%) of the subjects. Similar swellings have been reported to be granulocytic sarcoma in the literature and one could conclude that this was likely the case in this study [19].

Ten (17.2%) of the CML subjects showed the characteristic which *red thick tympanic membrane*. This finding however did not have any effect on the findings at tympanometry as the subjects had the normal

Type Atympanogram and we did not find any subject with conductive hearing loss. The red thick tympanic membrane noted in leukemia has been linked to possible to leukemic infiltration of the middle ear extending to the TM [20,21]. It is possible that the occurrence of thick red TM may be sign of otological affectation in progress and significance needs further evaluation.

Conclusion

Hearing loss is more common in patients with CML than generally reported since patients may not report mild to moderate hearing loss. Since patient with CML may present with severe to profound SSNHL and tinnitus preceding the diagnosis of CML, it is important that Otorhinolaryngologist perform routine WBC in patients with SSNHL before commencing steroid administration. We also recommend that patients with CML should have regular otological assessment.

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