# Sudden Hearing Loss as the Initial Manifestation of Chronic Myeloid Leukemia in a Child

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Hearing loss and blindness rarely occur in patients with chronic myeloid leukemia (CML). In this article, we present a 12-year-old girl who had right-side hearing loss as the initial manifestation of CML, followed by left-side hearing loss and blindness of the left eye several days after initiating treatment. The initial white cell count was 181,700/mm$^3$. Audiometry showed severe sensorineural hearing loss of her right ear and moderate mixed hearing loss of the left ear. An ophthalmic examination showed optic neuropathy with subhyaloid hemorrhage in the left eye. A brain magnetic resonance image showed minor hemorrhaging in the right lower frontal area and anterior thalamus. These findings might have implied leukostasis with hyperviscosity syndrome. She died on the 9th hospital day. This case illustrates that CML should be considered 1 of the rare diagnoses in a patient with sudden onset of hearing loss. *(Chang Gung Med J 2004;27:629-33)*

**Key words: chronic myeloid leukemia, deafness, blindness, leukostasis, hyperviscosity syndrome.**

Otolaryngological symptoms and signs such as vertigo, tinnitus, facial weakness, hearing loss, and infections are common in hematologic diseases.[1] However, sudden hearing loss as the first manifestation of hematologic diseases is very rare. These include leukemia, multiple myeloma, and Waldenstrom's macroglobuninemia.[2-4] Furthermore, it is more frequently seen in patients with acute leukemia than in chronic leukemia.[5] Herein, we report on a 12-year-old girl with chronic myeloid leukemia (CML) who presented with hearing loss.

## CASE REPORT

A 12-year-old girl was referred to us because of sudden right-side hearing loss for 2 days. The laboratory data showed a white blood cell (WBC) count of 181,700/mm$^3$ at another hospital. The differential counts tested in our hospital were blasts 2%, promyelocytes 3%, myelocytes 17.5%, metamyelocytes 3.5%, bands 14.5%, segments 45%, eosinophils 3%, basophils 3%, lymphocytes 7%, and monocytes 1.5%. The erythrocyte count (RBC) was $1.67\times10^6$/mm$^3$. The hemoglobin (Hb) was 6.4 g/dl. The platelet count was $2.29\times10^5$/mm$^3$. She was anxious but communicated normally. She had right side tinnitus in the absence of otalgia, vertigo, and blurred vision. On physical examination, she had no otorrhea or nystagmus. The tympanic membrane was normal in the right ear and mildly injected in the left ear. The liver was palpable 12.5 cm below the right costal margin and the spleen was palpable 13.5 cm below the left costal margin. C-reactive protein was 3.1 (normal, < 5) mg/L, uric acid was 576.9 (normal,

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<476) μmol/L, and lactate dehydrogenase was 732 (normal, 47-140) U/L. The prothrombin time and activated partial thromboplastin time were within normal limits. The leukocyte alkaline phosphatase score was 2 (normal, 45-105). Bone marrow examination showed a picture compatible with a diagnosis of CML. The fluorescence in situ hybridization (FISH) technique showed the BCR-ABL fusion gene. Cerebrospinal fluid (CSF) examination revealed a WBC count of 3/mm$^3$ and an RBC count of 8/mm$^3$. CSF cytology showed promyelocytes 2%, myelocytes 18%, metamyelocytes 10%, bands 8%, segments 40%, and lymphocytes 22%. A brain magnetic resonance image (MRI) showed a spindle-shaped hemorrhagic lesion (about 2×0.5 cm) located over the right lower frontal area and a tiny hemorrhagic lesion over the anterior thalamus (Fig. 1). Pure-tone audiometry revealed severe right sensorineural hearing loss and moderate left mixed hearing loss. A tympanogram showed a type A pattern in the right ear and a type B pattern in the left ear. The result of a speech reception threshold test (SRT) was 45 dB in the left ear. The result of a speech discrimination test (SDT) showed no response in the right ear and was 80 dB in the left ear. No acoustic reflex was noted in either ear. An auditory brainstem evoked response study was not performed because the patient was unable to cooperate. We treated her with hydration therapy, allopurinol, and hydroxyurea (30 mg/kg/day, per os). Interferon-alpha (3×10$^6$ units/m$^2$/dose, 3 times per week, subcutaneously) was added 3 days later when the WBC count was still 172,100/mm$^3$. Unfortunately, she gradually lost her hearing in her left ear over the following 3 days. In addition, impaired vision was noted on the 8th day of hospitalization. A visual acuity test showed counting fingers at more than 1 m away in the right eye and no perception of light in the left eye. The pupillary light reflex test showed a normal response in the right eye and a positive Marcus Gunn pupil in the left eye. An ophthalmoscopic examination showed retinal venous stasis and cotton wool spots in the right eye, as well as subhyaloid hemorrhage in the left eye. We performed leukapheresis and added low-dose cytarabine (10 mg/kg/day in 2 divided doses, subcutaneously). However, the clinical course deteriorated. Headaches, irritability, and lip cyanosis suddenly developed and the patient died on the 9th day of hospitalization when the Hb dropped to 3.6 g/dL and the WBC count was still high at 169,600/ mm$^3$.

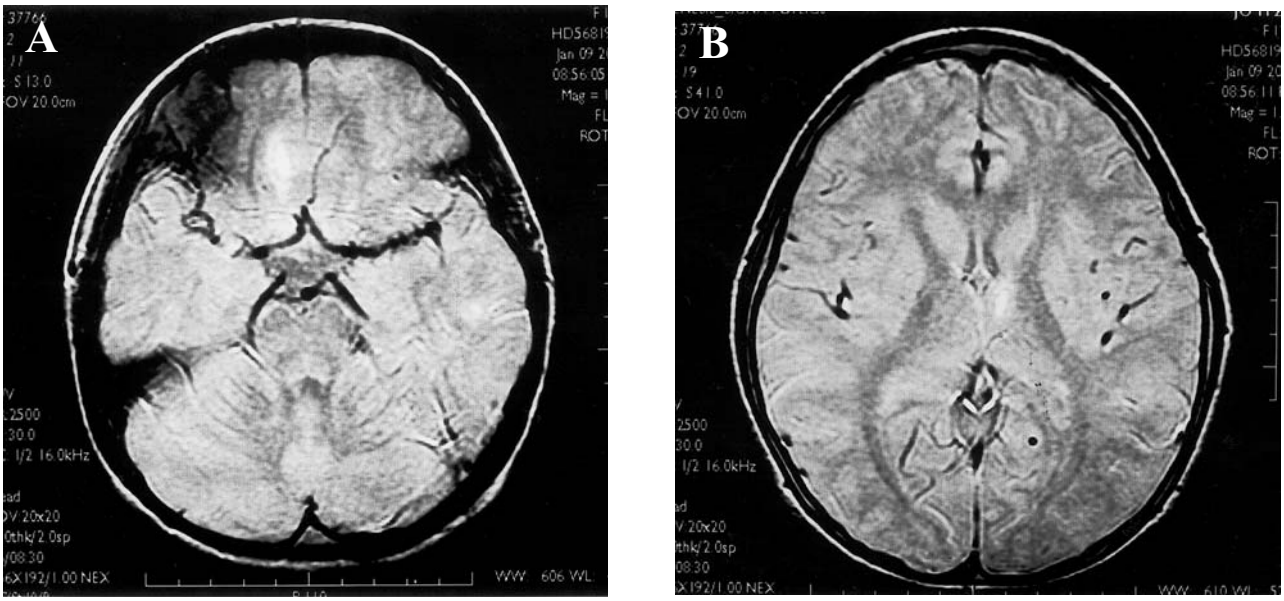


**Fig. 1** Axial proton density brain magnetic resonance image showing a spindle-shaped hemorrhagic lesion (about 2×0.5 cm) located over the right lower frontal area (A) and a tiny hemorrhagic lesion over the anterior thalamus (B).

## DISCUSSION

In 1856, Vidal first described the relationship between leukemia and deafness.[1] Deafness occurring in patients with CML is very rare, and to the best of our knowledge, only 29 patients have been reported in the literature.[6,7]

Druss et al. found leukemic infiltration of both inner ear apparatuses and the middle ear space and acute otitis media in sectioned temporal bone.[1] The pathogenesis of hearing loss in patients with leukemia is complex. Many studies have revealed histopathologic changes of the temporal bones and can be classified into 4 main categories: 1) leukemic infiltration, 2) hemorrhage, 3) infection, and 4) hyperviscosity.[1,5,8,9] Resende et al. reported a case of sudden bilateral deafness in a CML patient and speculated that deafness had occurred as a result of hyperleukocytosis with leukostasis and hyperviscosity in the labyrinth artery and other small arteries of the vertebrobasilar region.[6] In our patient, a brain MRI showed hemorrhagic lesions over the right lower frontal lobe and the left anterior thalamus. Marcus Gunn pupil of the left eye was an optic neuropathy due to ischemia while the subhyaloid hemorrhage was due to leakage of retinal venous blood. In the right eye, the findings of retinal venous engorgement and cotton wool spots were due to infarction in the retinal nerve fiber layer. On the last day of hospitalization, the patient developed headaches, irritability, and sudden onset of lip cyanosis with decreased Hb, so that intracranial hemorrhage could be considered as the direct causes of her death. All of these findings suggest that hyperleukocytosis with leukostasis and hyperviscosity syndrome had occurred. In addition, leukemia infiltration of the temporal bone could also have played a role in the pathogenesis of deafness in this girl.

The biological mechanism of leukostasis remained unclear. It was traditionally related to "overcrowding" of leukemic cells in the capillaries of the microcirculation. The WBC counts are generally higher in CML patients with leukostasis.[10] Recent investigations have indicated that leukostasis might also result from endothelial damage in addition to the number of circulating blasts.[11,12]

Leukapheresis has a rapid cytoreductive effect, but it is an invasive procedure. We do not routinely perform leukapheresis as a primary procedure. Porcu et al. reported that efficient leucoreduction could not assure better survival, and the recovery of hearing was also variable after disease control.[13] If hyperleukocytosis is complicated with central nervous system or respiratory events in CML patients, early leukapheresis and high-dose chemotherapy may be considered because conventional chemotherapy is rarely effective.[8,10] In conclusion, acute onset of hearing loss is a rare initial presentation of CML. This case illustrates that CML should be considered one of the possible etiology in patients with hearing loss.

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# 一位兒童之突發性聽力喪失爲慢性骨髓性白血病最初徵候

蔡璟忠 黃崇濱 沈俊明 魏秀惠 蕭志誠

聽力喪失和視力喪失在慢性骨髓性白血病相當罕見。在這篇文章，我們報告一位12歲慢性骨髓性白血病的女孩最初以右側聽力喪失來表現，後來發生兩側聽力喪失以及左側視力喪失。純音聽力檢查顯示左耳感覺神經性聽障以及右耳混合性聽障。眼科檢查顯示左眼視神經病變以及玻璃體膜下出血。腦部磁振影像顯示右下額葉以及左側視丘前部出血。這些表現可能與白血球黏滯合併高黏度症候群有關。希望藉此病例能提供關於急性聽力喪失診斷上的另一個考量。(長庚醫誌 2004;27:629-33)

**關鍵字**：慢性骨髓性白血病，聽力喪失，視力喪失，白血球黏滯，高黏度症候群。

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