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CASE REPORT

Chronic Myeloid Leukemia Presenting with Visual and Auditory Impairment in an Adolescent: An Insight to Management Strategies

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Abstract A 15-year-old girl presented with progressive deterioration in vision and hearing over 1 week. A huge spleen was palpated below the left costal margin laying down to inguinal region. Blood count showed hyperleukocytosis with a white blood cell count of 455 $\times$ 10^9/l. Peripheral smear yielded myeloid precursor cells with basophilia. Bone marrow aspiration revealed a blast count of 5% morphologically and 4% by flow cytometry. Fundoscopic examination revealed bilateral retinal exudates, edema and hemorhages. Partial sensorioneural hearing loss was also detected on the right ear. The diagnosis of chronic myeloid leukemia was confirmed by positive t(9;22) by RT-PCR. After commencing on hydroxyurea and intrathecal methotrexate-prednisolone, progressive improvement in hearing and vision was obtained. In our brief report, we aimed to emphasize rare presentation with visual and hearing impairment of chronic myeloid leukemia during childhood, especially in "*chronic phase*".

Keywords Chronic myeloid leukemia · Childhood · Leukapheresis · Sensorioneural impairment

Introduction

Chronic myeloid leukemia (CML) in childhood is a very rare condition, occuring approximately in 1–3% of children with leukemia [1]. CML was caused by reciprocal translocation between chromosome 9 and 22 in hematopoietic stem cells. It usually begins with *chronic phase* characterized by neutrophilic leukocytosis and splenomegaly [2]. If left untreated, it rapidly progresses to *accelerated* and *blastic* phase in which the survival measured in months. Patients in chronic phase are usually asymptomatic. When symptomatic, the clinical features include fever, weight loss, night sweats and fatigue like in acute leukemia.

Hyperleukocytosis causes obstruction of the small vessels of mainly brain, lungs and kidneys leading to organ dysfunctions. Headache, convulsions, stroke, papiledema, hearing loss, tinnitus and vertigo constitute the neurological aspect of clinical picture of CML [3, 4].

Herein, we report our treatment experience in an adolescent girl with atypical presentation of CML, including visual impairment and sensorioneural deafness due to hyperleukocytosis.

Case Report

A 15-year-old girl presented with progressive deterioriation in vision and hearing over 1 week. There were no otalgia and otorrhoea but occasional tinnitus. Past history revealed no trauma, intoxication, drug or infection. Family history was also unremarkable.

She was cooperated and orientated. Arterial blood pressure was 110/70 mmHg. She was dyspneic and tachypneic. Pulse oxygen saturation was 88%. A huge spleen was palpated below the left costal margin laying down to the inguinal region. It was firm and non-tender. No hepatomegaly was present. Deep tendon reflexes were normoactive. Cerebellar tests were also normal. Pupils were normoreactive to light bilaterally. Visual acuity was

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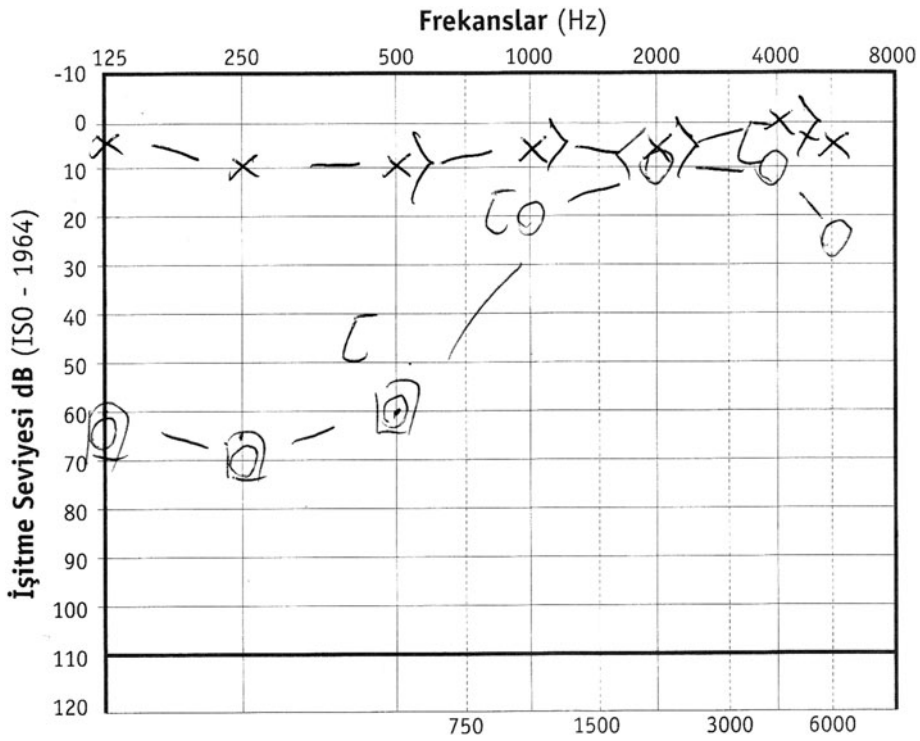

Fig. 1 Odiogram showing hearing impairment on the right ear

determined as counting fingers at 1 m for both eyes. Fundoscopic examination revealed bilateral papilledema, spot hemorrhages and exudates. There were no signs of intraocular inflammation. The rest of the physical examination was unremarkable.

Complete blood count revealed hemoglobin 10.4 g/dl, WBC 455 $\times$ 10^9/l and platelet 868 $\times$ 10^9/l. Peripheral blood smear revealed 18% promyelocyte, 12% myelocyte, 8% metamyelocye, 10% band, 32% mature neutrophil, 16% basophil and 4% eosinophil. Serum urea-creatinine, electrolytes and liver function tests were normal. Lactate dehydrogenase was 2,328 IU/l. Chest X-ray showed bilateral patchy infiltration in lung fields. Abdominal ultrasonography revealed splenomegaly measured as 23 cm in longitudinal axis. Bone marrow aspiration revealed a blast count of 5% morphologically and 4% by flow cytometry pointing out the "*chronic phase*" of chronic myeloid leukemia. t(9;22) analysis by RT-PCR from bone marrow revealed a positivity of 332 copies.

She was admitted to pediatric intensive care unite for leukapheresis. Alkalinized hydration and allopurinol were started promptly. After one cycle of leukapheresis, white blood cell count decreased to 326 $\times$ 10^9/l. Hydroxyurea (40 mg/kg/day, twice a day, p.o) and low dose cytarabine (100 mg/m^2/day, for 3 days) were begun after leukapheresis. Respiratory difficulty dissolved on the 3rd day of admission.

Both external auditory canal and tympanic membranes were examined. Partial sensorioneural hearing loss was detected on the right ear by audiogram (Fig. 1). Cranial MR imaging revealed papillitis (Fig. 2). Intrathecal methotrexate (12 mg) and prednisolone (10 mg) were applied. Five days after the intrathecal chemotherapy, hearing loss of the right ear improved completely. Visual acuity was evaluated as 1/10 on right eye and 3/10 on left eye. There was also decrease in bilateral papilledema on fundoscopic examination.

During clinical follow-up, white blood cell count decreased progressively and no tumor lysis or related nephropathy developed. On the 10th day of admission,

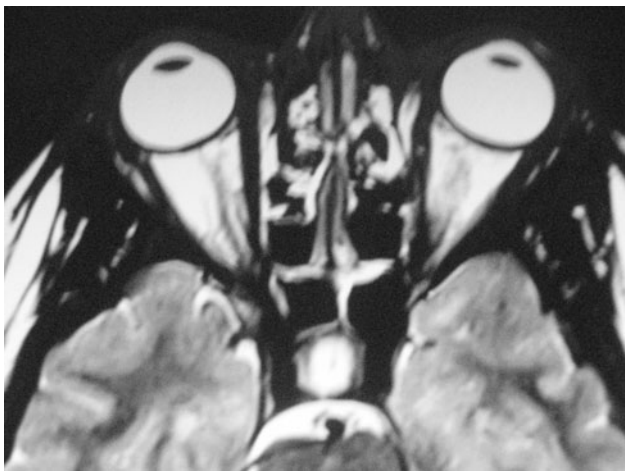

Fig. 2 Cranial MRI pointing papillitis

white blood cell and platelet counts were 8.1 $\times$ 10^9/l and 446 $\times$ 10^9/l, respectively.

Imatinib mesylate was started at a dose of 400 mg/m^2 after obtaining positive test results for t(9;22). Hematopoietic stem cell transplantation from a martched related donor was scheduled.

Discussion

Hyperleukocytosis (HL)—leukemoid reaction—is usually encountered during infections and acute inflammatory conditions in children. Leukemoid reaction is generally not accompanied by splenomegaly and basophilia like in CML and white blood cell count does not increase above 70 $\times$ 10^9 /l. HL is also seen in 5–20% of newly diagnosed children with acute leukemia and points poor prognosis [5, 6]. Complications of HL due to CML such as leukostasis due to occlusion of small arterioles of vital organs are very rare during childhood. Our knowledge on treatment and outcome of organ dysfunction due to HL in CML is based on a few case reports unlike that of adults [3]. Neurological involvement including deafness, blindness and tinnitus was reported as 15.5% in a series of 33 adults with CML. Cochlear and retinal blastic infiltration may also cause sensorioneural deficit other than leukostasis in CML [7]. Unfortunately, improvement to pre-morbid condition is more difficult despite the disease control in '*blastic phase*' [4].

Vigorous hydration, urine alkalinization, allopurinol treatment and leukapheresis are the mainstays of treatment in the case of HL. Leukapheresis is the removal of leukocytes or blasts with re-infusion of leukocyte poor plasma. Although there were no guidelines in children for when to start or when to stop leukapheresis, it is generally not done unless symptoms of leukostasis develop or leukocyte count exceeds 200 $\times$ 10^9/l [8]. We performed leukapheresis due to the presence of neurologic complications and high leukocyte count. But, firstly we applied alkalinated hydration to expand the intravascular volume for 6 h in order to avoid central nervous system complications of leukapheresis.

The duration of HL is also of paramount importance. The longer duration increases the risk of development of infarcts on retina and cochlea leading to the permanent impairment. Leukapheresis may provide improvement in visual disturbance, whereas improvement in visual acuity in a child without leukapheresis has been reported [9]. If the leukocytoreductive treatment fails to improve the hearing loss, alternative treatment modalities can be performed. Intratympanic dexamethasone has been performed in an adult with CML but unfortunately no improvement was obtained [10]. On the other hand, a dramatic improvement in hearing has been obtained in a case with CML after intrathecal methotrexate suggesting blastic infiltration of cochlea [11].

Systemic steroids are known to be used for treatment of idiopathic sensorio-neural hearing loss [12]. But, neutrophilia may be exaggrated and the clinical course may worsen by systemic steroids in CML. We performed methotrexate and prednisolone intrathecally and we obtained prominent improvement in hearing and vision within 5 days. Here, we thought prednisolone and methotrexate may have acted their anti-inflammatory and/or anti-neoplastic effects directly around her cochlea and retina through circulation of cerebrospinal fluid.

To the best of our knowledge, this is the first pediatric CML presenting with both hearing and visual impairment. Here, we also would like to emphasize our experience with intrathecal prednisolone treatment in the light of current literature. The severe visual, auditary and possibly pulmonary involvements in the present case at chronic phase of disease is also a point of interest in this case.

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