Facial palsy as the presenting symptom of acute myeloid leukemia in children: Three cases with stem cell transplantations

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Abstract

Facial palsy as the presenting symptom of leukemia is very rare, especially in acute myeloid leukemia. A review of the medical literature identified reports on 8 children with AML who had facial paralysis as the presenting sign. Whole brain irradiation (WBI) has been applied in most cases. We present the cases of 3 such children. Achieving a remission without WBI, the patients underwent stem cell transplantations (SCTs). Two patients remain event-free 52 months and 62 months after allotransplants. Facial palsy was the harbinger of leukemic relapse in one case after autotransplant. This patient is disease-free 59 months after unrelated SCT rescue. Facial palsy persisted in 2 cases. Allogeneic SCT without WBI may be an effective therapy in patients presenting with facial palsy. A brief review of the literature is presented here. (Korean J Pediatr 2009;52:713-716)

Key Words: Facial palsy, Acute myeloid leukemia, Whole brain irradiation, Stem cell transplantation, Children

Introduction

Facial palsy is not well recognized as a presenting symptom of childhood leukemia, especially in acute myeloid leukemia (AML). A review of the medical literature identified eight children with AML who had facial paralysis as the presenting sign. Most such cases have blast cells in the cerebrospinal fluid (CSF) and are treated with systemic and intrathecal chemotherapy, and whole brain irradiation (WBI) for recovery of facial palsy.

This report describes three children with AML who presented with facial palsy but no blast cells found in the CSF. Following systemic and intrathecal chemotherapy the patients were effectively rescued by allogeneic stem cell transplantations (SCTs), avoiding WBI.

Case report

1. Patient 1

A 4-year-old girl presented with intermittent right otalgia of 1-month. Right facial paralysis developed 1 day before admission. No other neurological abnormality was present. The white blood cell count was 13,400/µL with 74% myeloblasts, and she was diagnosed to have AML-M4Eo. The temporal bone CT revealed bilateral mastoiditis without destructive bony lesions. The CSF analysis was normal with no leukemic cells found. With induction chemotherapy followed by cyclic consolidations, the facial palsy improved by 3 months. The patient underwent a matched sibling bone marrow transplantation (BMT) in the first complete remission (CR), 4 months after the diagnosis. The conditioning regimen consisted of intravenous busulfan and cyclophosphamide. A total of six intrathecal triple chemotherapy (methotrexate, cytarabine and hydrocortisone) was given, two doses as conditioning and additional 4 doses every 3 months after transplantation. The patient remains event-free 52+ months following transplant without evidence of facial palsy.
2. Patient 2

A 10-year-old girl was admitted because of a left facial palsy of 1 month's duration. Having elevated white cell counts, she was diagnosed to have AML-M4Eo with a CBG/MYH11 rearrangement. Magnetic resonance imaging (MRI) of the brain revealed bilateral mastoiditis and a soft tissue mass in the left auditory canal, but no evidence of meningeal or facial nerve enhancement. The CSF analysis was normal without leukemic cells. After achieving a remission, she underwent a matched sibling BMT 4 months after diagnosis. The conditioning regimen consisted of cytarabine, cyclophosphamide, and total body irradiation (12 Gy in 6 fractions). A total of six intrathecal therapy was given, as in case 1. The patient is in remission for 62+ months after transplant with remaining facial nerve palsy as evidenced by incomplete wrinkling on her forehead.

3. Patient 3

A 10-year-old boy presented with left facial palsy and cervical lymphadenopathy. The brain MRI was normal. The patient was diagnosed with AML, M2. The CSF analysis was normal without leukemic cells. During induction, 4 doses of intrathecal cytarabine were added. After achieving a remission, 4 cycles of consolidation chemotherapy was administered as a matched sibling was not available. The facial palsy improved by 4 months after the chemotherapy.

Eight months after completing the chemotherapy, however, the right facial nerve palsy and otalgia reappeared. The blood counts were normal and blast cells were not present on the blood smear. The CSF was normal but the brain MRI revealed involvement of the right petrosal bone and adjacent meninges, and accompanying mastoiditis (Fig. 1A). The bone marrow (BM) exam showed 11% blast cells. After achieving a second CR, the patient underwent an autologous peripheral blood SCT without radiation. The patient remained in remission for subsequent 4 years. However, the facial palsy was present over 2 years following transplant.

Four years after initial transplant, the right facial palsy reappeared. Even though the BM and CSF exam showed no leukemic cells, the temporal MRI revealed a 3×4 cm mass involving the right upper neck and skull base (Fig. 1B). An incisional biopsy of the mass showed a localized leukemic mass. The patient received radiation of 36 Gy to the right neck and parapharyngeal space. The facial palsy partially improved. However, he developed a second BM relapse with recurring right facial palsy at 4 months after the radiation therapy.

The patient underwent a reduced-intensity matched unrelated BMT after achieving the third CR. The conditioning regimen consisted of fludarabine, busulfex, antithymocyte globulin and two doses of intrathecal cytarabine. Extensive chronic GvHD involving the skin and mucous membranes developed, which is now under control with mycophenolate mofetil and prednisolone. After the second transplantation, the patient is alive in CR for 59 months and attending a college with remaining partial facial palsy with incomplete eye closure.

![Fig. 1. Patient 3. (A) MRI performed at the time of the first relapse shows increased signal intensity of the right petrosal bone and adjacent meninges, and mastoiditis on T2WI suggesting leukemic involvement. (B) MRI performed at the time of the second relapse revealed leukemic infiltration in the deep space of the right upper neck and skull base.](image-url)
Facial palsy as the presenting symptom of acute myeloid leukemia

**Discussion**

Cranial neuropathies, especially of the seventh nerve, occur in children with central nervous system leukemia caused by leukemic infiltration; however, they are extremely rare as the presenting sign of the disease. Facial palsy in lymphoid malignancies has been reported in the medical literature and in many cases, there is accompanying meningeal involvement. Among 1,895 children with acute lymphoblastic leukemia (ALL) and non–Hodgkin lymphoma (NHL) 45 children had cranial nerve palsy: 22 at diagnosis (9 ALL, 13 NHL). The facial nerve was the most frequently involved (15 of 22 cases).

However, there are only a few reports where children with myeloid leukemia have presented with a facial palsy. A review of the medical literature identified eleven children with AML who had facial paralysis as the presenting sign. These patients are summarized in Table 1. Six of 11 children did not have blast cells in the CSF.

**Table 1. Summary of Cases with Facial Palsy as the Presenting Symptom of Acute Myeloid Leukemia in Children**

<table>
<thead>
<tr>
<th>Ref. No</th>
<th>Year of pub.</th>
<th>Age at diagnosis</th>
<th>Interval</th>
<th>Type of leukemia</th>
<th>Brain MRI or CT finding at diagnosis</th>
<th>Additional finding</th>
<th>CSF Blast</th>
<th>Treatment</th>
<th>Interval from treatment to improvement of facial palsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1971</td>
<td>7 yr</td>
<td>1 week</td>
<td>AML</td>
<td>ND</td>
<td>Right mastoiditis</td>
<td>UK</td>
<td>S+C+RT</td>
<td>UK</td>
</tr>
<tr>
<td>2</td>
<td>1984</td>
<td>13 yr</td>
<td>1 week</td>
<td>AML</td>
<td>ND</td>
<td>Chloroma involving mastoid and mesotympanum</td>
<td>No</td>
<td>C+IT+RT</td>
<td>6 months</td>
</tr>
<tr>
<td>3</td>
<td>1986</td>
<td>5.5 yr</td>
<td>1 day</td>
<td>AML</td>
<td>ND</td>
<td>Chloroma involving mastoid Cells</td>
<td>UK</td>
<td>C</td>
<td>1 month</td>
</tr>
<tr>
<td>4</td>
<td>1990</td>
<td>6 yr</td>
<td>1 day</td>
<td>AML</td>
<td>ND</td>
<td>Chloroma overlying the VII nerve</td>
<td>UK</td>
<td>C</td>
<td>3 months</td>
</tr>
<tr>
<td>5</td>
<td>1995</td>
<td>16 yr</td>
<td>1 day</td>
<td>AML</td>
<td>Left mastoiditis with granulation tissue occluding the middle ear</td>
<td>UK</td>
<td>S+C</td>
<td>UK</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2001</td>
<td>17 yr</td>
<td>1 month</td>
<td>AML</td>
<td>Bilateral maxillary sinus involvement, bilateral mastoiditis</td>
<td>Chloroma on T4 spinal cord</td>
<td>UK</td>
<td>C</td>
<td>2 months</td>
</tr>
<tr>
<td>7</td>
<td>2002</td>
<td>11 mo</td>
<td>5 days</td>
<td>AML</td>
<td>Normal</td>
<td>No</td>
<td>C+IT+RT</td>
<td>Not improved but CR state of leukemia</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2006</td>
<td>8 mo</td>
<td>3 weeks</td>
<td>AML</td>
<td>Normal</td>
<td>No</td>
<td>C+IT</td>
<td>UK</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>2008</td>
<td>4 yr</td>
<td>1 day</td>
<td>AML</td>
<td>Bilateral mastoiditis</td>
<td>No</td>
<td>C+IT+SCT</td>
<td>3 months</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>2008</td>
<td>10 yr</td>
<td>1 month</td>
<td>AML</td>
<td>Bilateral mastoiditis with intact ossicles and Chloroma in the left external auditory canal</td>
<td>No</td>
<td>C+IT+SCT</td>
<td>4 months</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; C, chemotherapy; IT, intrathecal chemotherapy; RT, radiation therapy; S, surgery; SCT, stem cell transplantation; ND, not done; UK, unknown

*Interval from onset of facial paralysis to diagnosis

The brain imaging results were reported in 7 patients at the time of diagnosis: 4 patients had findings of mastoiditis but others were normal. Acute otomastoiditis subsequent to leukemic infiltration of the temporal bone may be implicated with facial and acoustic nerve paralysis. However, the clinical findings of facial paralysis were not always associated with radiological findings.

The time from the appearance of facial paralysis to the diagnosis of leukemia varied from 1 day to 1 month. In four cases, idiopathic facial palsy was suggested, and steroid medication was administered in three of them. The steroid therapy might have resulted in a partial remission of facial palsy, thus delaying the diagnosis of leukemia. Recurrent facial palsy was reported in some cases on follow-up. In our Case 3, facial palsy preceded every relapse of the leukemia. The facial palsy usually improved by 1 to 6 months after beginning chemotherapy (Table 1). One AML patient did not show improvement of facial palsy after radiotherapy, despite a CR of the leukemia in the BM. Thus, long–term remission of leukemia can be obtainable.
despite incomplete recovery of facial palsy, as shown in our Cases 2 and 3.

In lymphoma and leukemia patients with symptomatic cranial nerve palsy, CNS irradiation has been reported to be effective. Among 28 adult patients (17 ALL, 9 AML, 2 chronic myelocytic leukemia), 14 complete and 8 partial responses were documented following intrathecal (6 patients), or systemic (5 patients) chemotherapy, or both (17 patients) in addition to the radiotherapy of 24 Gy. On the contrary, most AML patients reported in Table 1 (8/11) were treated without radiotherapy. For our three patients, AML was effectively treated by the SCT. Sparing radiotherapy to the brain, especially for children is important to prevent the potential long-term sequelae on cognitive and endocrine function, and to reduce the development of secondary malignancies.

In conclusion, facial palsy may be the presenting sign of AML, and also the harbinger of leukemic relapse. Allogeneic SCT without WBI may be feasible and effective way to treat these rare AML patients presenting with facial palsy.

References