Facial paralysis as a presenting symptom of infant leukemia

A case report and literature review

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Abstract

Rationale: Facial paralysis as the initial clinical presentation of infant leukemia (IL) is rare, and the rate of its misdiagnosis is high. Identifying the clinical characteristics of IL with facial paralysis as the initial symptom is necessary to improve the understanding of the causes of facial paralysis and IL.

Patient concerns: A 10-month-old infant had facial paralysis and recurrent fever. He was misdiagnosed as having bacterial meningitis for >2 months.

Diagnoses: The infant was diagnosed as having acute monocytic leukemia (M5) with central infiltration based on examinations of the bone marrow and cerebrospinal fluid by flow cytometry.

Interventions: Before the diagnosis of leukemia, the patient was given meropenem, ceftriaxone, vancomycin, and ampicillin successively for anti-infective treatment for 2 months, and dexamethasone for several days. But he gave up further treatment after confirmed diagnosis.

Outcomes: Our patient discontinued treatment and discharged. From literature review, there were 6 cases (including this case) of IL with facial paralysis as the initial symptom. 80% of patients were misdiagnosis and treated with a corticosteroid in the early stage, and the mortality was 33.3%.

Lessons: The clinical symptoms of IL with facial paralysis are not typical, with a high rate of misdiagnosis. When the cause of facial paralysis is unknown or the advance treatment effect is poor, tumor diseases should be considered. Corticosteroids should be carefully administered to children with facial paralysis.

Abbreviations: ALL = acute lymphoblastic leukemia, AML = acute myeloid leukemia, CSF = cerebrospinal fluid, IL = infant leukemia, M5 = acute monocytic leukemia, MRI = magnetic resonance imaging.

Keywords: corticosteroid, facial paralysis, infant, leukemia

1. Introduction

Infant leukemia (IL), including acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), generally refers to acute leukemia diagnosed in the first 12 months of life.\textsuperscript{[1]} In the United States, the incidence of IL is 4.1/1 million, of which AML and ALL account for 43.75% and 56.25%, respectively\textsuperscript{[2]}; however, such epidemiologic data on IL are not available in China. IL is clinically characterized by high invasiveness, including high leukocyte count, hepatosplenomegaly, lymphadenectasis, central nervous system invasion, and skin invasion.\textsuperscript{[3, 5]} Among them, extramedullary infiltration can occur before peripheral blood abnormalities and hepatosplenomegaly occur; however, IL with facial paralysis as the initial symptom is very rare. Because of atypical symptoms and low incidence of IL, children with this disease may be prone to misdiagnosis. Here, we report about an infant with an earlier age of onset and facial paralysis as the initial symptom who was finally diagnosed as having IL after the misdiagnosis of bacterial meningitis for 2 months at a local, as well as our, hospital. In addition, clinical data were retrospectively analyzed, and the literature was reviewed to improve the understanding of IL with facial paralysis.

2. Case report

This study was approved by the Ethics Committee of the West China Second University Hospital and written informed consent was obtained from parents of the child. A 10-month-old male infant was admitted to our hospital with presentation of an acute onset of right facial droop for 2 months and repeated fever for more than 1 month. Two months before admission, the child had no obvious reason for right facial palsy...
and did not have fever. The local hospital diagnosed the condition as facial paralysis and administered acupuncture treatment for 1 week; however, the patient’s condition did not improve. One month before admission, the child had fever, and routine blood test results revealed elevated white blood cell (WBC) count of $2.07 \times 10^9/L$ (3.6–9.7 $\times 10^9/L$), with the neutrophilic cell (N) count being $13.75 \times 10^9/L$; slightly decreased hemoglobin levels of 106g/L, and platelet (PLT) count of $388 \times 10^9/L$, without unidentified cells. In addition, C-reactive protein (CRP) levels increased to 39mg/L (0–8mg/L). Cerebrospinal fluid (CSF) examination results were as follows: WBC, $860 \times 10^9/L (<15 \times 10^9/L)$, N, 49%, lymphocyte (L), 45%, and monocyte (MN), 6%, with normal biochemical test results and negative smear and culture results. The results of blood EB virus, TORCH, and blood transfusion immunoassay were normal. No abnormalities were found on head magnetic resonance imaging (MRI). Based on these findings, the infant was diagnosed as having bacterial meningitis at the local hospital, which was successively treated with meropenem for 14 days, ceftriaxone for 6 days, and meropenem plus vancomycin for >1 week. The infant’s facial paralysis improved but fever persisted. A rash occurred during vancomycin infusion, with red miliary rashes on the trunk, slightly prominent on the skin surface, and discoloring under pressure, where the inter rash skin was normal. The rash subsided after administering dexamethasone for several days.

Results of the CSF reexamination were as follows: WBC $621 \times 10^9/L$, MN 63%, and protein, 0.46g/L, with normal sugar and chloride levels and negative smear and culture results. The results of blood EB virus, TORCH, and blood transfusion immunoassay were normal. No abnormalities were found on head magnetic resonance imaging (MRI). Based on these findings, the infant was diagnosed as having bacterial meningitis at the local hospital, which was successively treated with meropenem for 14 days, ceftriaxone for 6 days, and meropenem plus vancomycin for >1 week. The infant’s facial paralysis improved but fever persisted. A rash occurred during vancomycin infusion, with red miliary rashes on the trunk, slightly prominent on the skin surface, and discoloring under pressure, where the inter rash skin was normal. The rash subsided after administering dexamethasone for several days.

Results of the CSF reexamination were as follows: WBC $621 \times 10^9/L$, MN 63%, and protein, 0.46g/L, with normal sugar and chloride levels and negative smear and culture results. The infant was referred to our hospital (the West China Second University Hospital of Sichuan University) because CSF examination results and body temperatures did not improve. Results of the physical examination of admission were as follows: temperature, 37.8°C; respiration rate, 35 beats/min; heart rate, 128 beats/min; blood pressure, 87/58 mm Hg; and weight, 8kg. The patient’s spirit was not as good, his complexion was not as ruddy, he was slightly irritable, and his skin did not show the rash. His anterior fontanel was slightly bulging, the tension was full, and anterior horn of the lateral ventricle was slightly blunted. After enhancement, the pia cerebral vessels in the cerebral sulcus were enhanced.

On admission, the diagnosis was bacterial meningitis. Because mononuclear Lester infection could not be excluded, vancomycin + mepem + ampicillin were administered for to treat the infection and provide symptomatic support. Results of the routine blood re-examination on the 16th day of admission were as follows: WBC, $29.0 \times 10^9/L$, L, 44.0%; immature cells, 8.0%; abnormal lymphocytes, 5.0%; HGB, 98g/L; PLT, $513 \times 10^9/L$; and CRP, 12.0mg/L. Bone marrow examination results revealed that mononuclear cells had abnormal hyperplasia and primary mononuclear cells accounted for 68.5% of all nucleated cells (Fig. 1). Peroxidase stain (POX) staining revealed that the positive rate of primitive cells was 2%. Bone marrow flow cytometry (FCM) analysis revealed that the primitive cells accounted for approximately 46.74% of the nucleated cells (Fig. 2). Moreover,
results of the re-examination of CSF were as follows: nucleated cells, 1750 \times 10^6/L; immature cells, 89.0%; L, 8.0%; MN, 2%; protein, 1343.3 mg/L; sugar, 1.8 mmol/L; and LDH, 108 U/L. Immunophenotyping of CSF detected an abnormal cell group in 65.01% of all nucleated cells, which expressed CD45dim, CD13\^+, CD33\^+, CD14dim, CD15\^+, CD16\^+, CD11bdim, CD11c\^+, and cyTdT\^+. Based on these findings, the infant was diagnosed as having M5 with central infiltration. However, the infant’s family decided to discontinue treatment, and thus, the child was discharged.

3. Discussion

Facial nerve paralysis in children is a common condition, with its annual incidence being 6.6 to 20/100,000. Facial nerve paralysis can be divided into peripheral and central facial paralysis based on the sites of nerve damage. Peripheral facial paralysis mainly includes Bell paralysis, trauma, infection, and a few congenital malformations and tumors, with Bell paralysis accounting for approximately 70% of the cases.\(^6,7\) Central facial paralysis mainly includes cerebrovascular lesions and intracranial tumors. The symptoms of our case were in line with the characteristics of peripheral facial paralysis, with no finding of intracranial mass and cerebral vascular lesions on cerebral MRI. Therefore, the reason of peripheral facial paralysis was considered because of meningitis or Bell paralysis. However, bacterial meningitis was not the common cause of facial paralysis. A literature review revealed that children with tuberculous meningitis, Salmonella typhi meningitis, and meningococcal diplococcus complicated with cerebral infarction could be complicated with facial paralysis.\(^8\)–\(^10\) Bacterial meningitis treatment had poor effects in our case, and clinical and laboratory test results showed no evidence of tuberculosis, fungi, or mycoplasma infection; thus, the diagnosis of meningitis was doubtful. Therefore, the possibility of other rare reasons, particularly a tumor, being the cause of facial paralysis should be highly suspected. Our case was finally diagnosed as M5 based on bone marrow examination, bone marrow FCM, and re-examination of tumor cells in the CSF.

A literature search revealed that 6 cases of IL with facial paralysis, including our case, have been reported from 1984 to 2017\(^11\)–\(^14\) (Table 1), and the proportion of male and female patients was 5:1. AML accounted for 83.3% of all cases. The clinical manifestations of IL include unilateral facial paralysis (83.3%), irritability (60%), growth development retardation (20%), and rash (20%). Of 6 cases, 5 (83.3%) had no fever in
Clinical information of infant leukemia patients complicated with facial paralysis.

| Case | Author (date of publication) | Age (mo) | Sex | Clinical manifestation | Time of diagnosis | Leukocyte (×10^9/L) | Immature cells in peripheral blood | Cerebrospinal fluid | CNS findings by imaging | Disease classification | Use of hormones | Treatment and prognosis |
|------|-----------------------------|----------|-----|-----------------------|------------------|-------------------|-----------------------------|-----------------|----------------|----------------------|---------------|------------------------|
| 1    | Krishnamurthy et al (2002)  | 11m      | M   | Left facial paralysis without fever or hepatosplenomegaly | 5 d             | 18.0             | 50% lymphoblastic cells     | Normal          | MRI: No evidence of facial nerve or meningeal enhancement | ALL           | No Chemotherapy | Remission             |
| 2    | Krishnamurthy et al (2002)  | 11m      | M   | Right facial paralysis with irritability and hepatosplenomegaly | 3 wk            | 14.9             | 45% primitive cells         | Normal          | MRI: No evidence of facial nerve or meningeal enhancement | AML           | Yes Chemotherapy + radiotherapy | Remission Chemical therapy |
| 3    | Bilacevich et al (2006)     | 8 mo     | F   | Right facial paralysis, growth and development stagnation, without fever, hepatosplenomegaly or lymphadenopathy | 3 wk            | 7.0              | None                        | Normal          | Orbital tumor infiltrating the nasal cavity; solid tumor compressing the spinal cord | M5            | – Died after remission of chemotherapy |
| 4    | Ranta et al (2017)          | 8 mo     | M   | Bilateral facial paralysis, with exophthalmos | –               | –                | –                           | –              | –                           | M5            | – Died after remission of chemotherapy |
| 5    | Li et al (2004)             | 4 mo     | M   | Left facial paralysis, with irritability, without fever, hepatosplenomegaly or lymphadenopathy | –              | –                | –                           | –              | –                           | M2b           | Yes Died |
| 6    | This case                   | 10 mo    | M   | Right facial paralysis, with late fever, rash and irritability, infection, without hepatosplenomegaly or lymphadenopathy | 2 m            | 20.75            | None                        | Abnormal        | MRI: abnormal                | M5            | Yes Abandoned |

ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; CNS = central nervous system; MRI = magnetic resonance imaging.

*The child was diagnosed as Bell's palsy in local hospital, where the blood routine was not available, administered with hormones for treatment.

In conclusion, IL associated with facial palsy is extremely rare, with a higher incidence of central nervous system leukemia in the treatment group and the disadvantages of delayed diagnosis in the control group. Early diagnosis and timely treatment are crucial for the prognosis and management of IL. Further studies are needed to elucidate the mechanisms underlying the association between facial palsy and IL, focusing on factors such as immune-related processes and genetic predispositions. The authors hope that this study will contribute to a better understanding of the relationship between facial palsy and IL, and will help to improve the diagnosis and treatment of IL patients.
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