Clinical Case Report

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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.[1] In the United States, the incidence of IL is 41/1 million, of which AML and ALL account for 43.75% and 56.25%, respectively[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.[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

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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 20.75×10^9/L ($3.6–9.7 \times 10^9$/L), with the neutrophilic cell (N) count being 13.75×10^9/L; slightly decreased hemoglobin levels of 106 g/L, and platelet (PLT) count of 388×10^9/L, without unidentified cells. In addition, C-reactive protein (CRP) levels increased to 39 mg/L (0–8 mg/L). Cerebrospinal fluid (CSF) examination results were as follows: WBC, 860×10^9/L ($<15 \times 10^6$/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 621×10^6/L, MN 63%, and protein, 0.46 g/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, 8 kg. 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 not very high, bilateral pupils were equally large and circular, and light reflex was sensitive. Moreover, the check for facial nerve was negative. There was no neck stiffness, and lymph nodes measuring 1×0.5 cm were palpable on the left neck, with soft texture and normal mobility, without tenderness. The double lungs showed coarse respiratory sound with a little sputum. Liver and spleen were not palpable. The residual neurologic examination results were negative. Auxiliary examination results were as follows: routine blood examinations: WBC 14.4×10^9/L; N, 23.3%; L, 68.1%; MN 6.0%; hemoglobin (HGB), 116/L; PLT, 390×10^9/L; and CRP 51.0 mg/L, and abnormal cells were not detected, and CSF examinations: nucleated cells, 620×10^6/L; L, 92%; N, 4%; MN 4%. protein, 928.2 mg/L; sugar, 1.5 mmol/L; chloride, 122 mmol/L; and lactate dehydrogenase (LDH), 127 U/L, with negative smear and culture results. CSF was examined to detect cytomegalovirus, Epstein–Barr virus, herpes simplex virus, and Coxsackie virus, with negative nucleic acid detection of mycoplasma and chlamydia. Results of blood culture for bacteria and fungi, fungus *G* test, mycoplasma antibody test, and polymerase chain reaction analysis did not reveal any abnormalities. Heart color Doppler ultrasound showed nonexpansion of the coronary artery; chest and abdominal computed tomography (CT) revealed a scattered patchy ground glass image of both the lungs; and plain CT scan of the liver, spleen, pancreas, and both kidneys did not show any definite abnormalities. Enhanced head MRI revealed the following: signals in the cortex of the bilateral frontal and temporal lobes as well as the subcortical white matter were abnormal, gap between the white matter around the ventricle and perivascular semioval center was apparent, bilateral cerebral hemispherical sulcus was widened, bilateral ventricle was full, and anterior horn of the lateral ventricle was slightly blunt. 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, 29.0×10^9/L; L, 44.0%; immature cells, 8.0%; abnormal lymphocytes, 5.0%; HGB, 98 g/L; PLT, 513×10^9/L; and CRP, 12.0 mg/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,

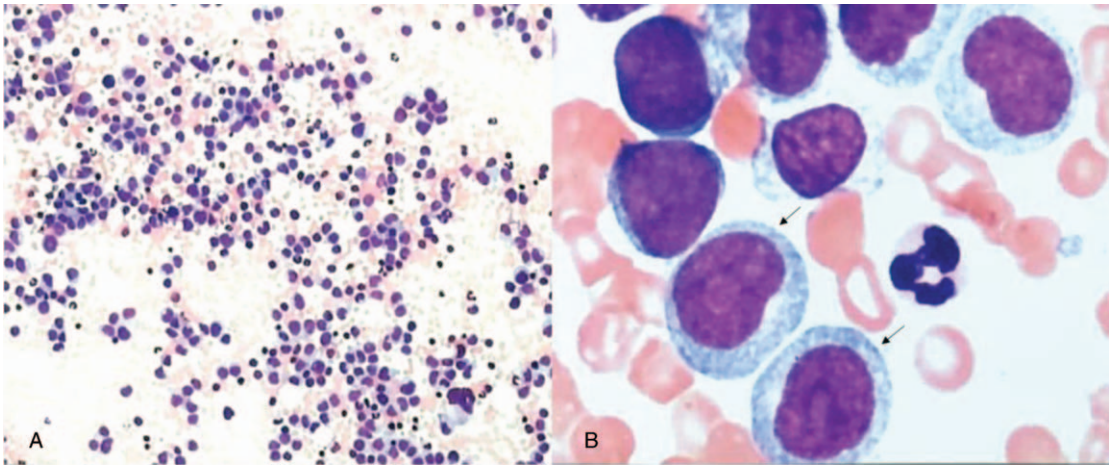

Figure 1. Bone marrow analysis.

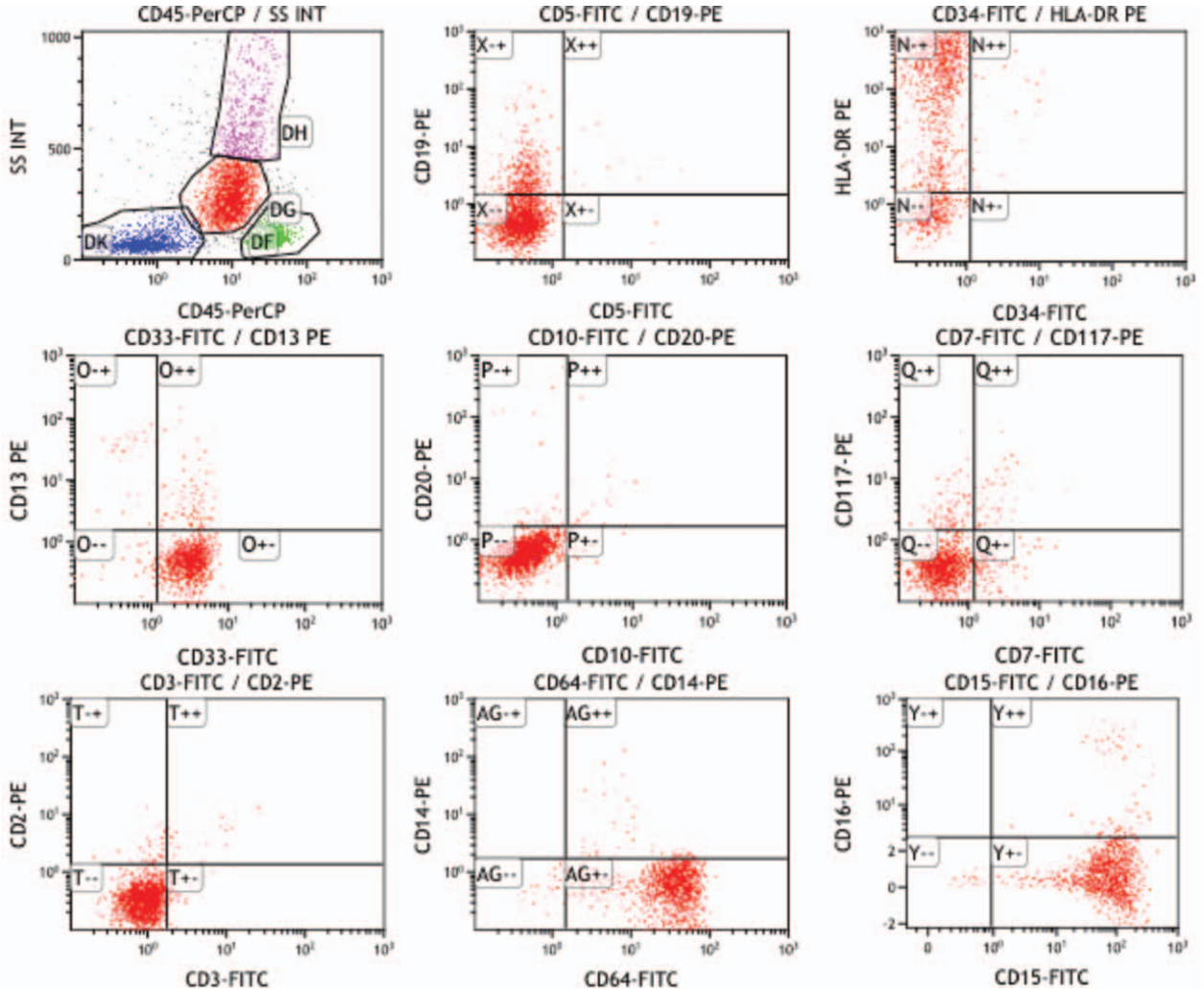

Figure 2. Flow cytometry analysis.

results of the re-examination of CSF were as follows: nucleated cells, 1750×10^6/L; immature cells, 89.0%; L, 8.0%; MN.0, 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 of CD45dim, $CD13^-$, $CD33^+$, $CD64^+$, 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

Table 1

Clinical information of infant leukemia patients complicated with facial paralysis.

Case	Author (date of publication)	Age	Sex	Clinical manifestation	Time of diagnosis	Leukocyte ($\times 10^9$/L)	Immature cells in peripheral blood	Cerebrospinal fluid	CNS findings by imaging	Disease classification	Use of hormones	Treatment and prognosis
1[11]	Krishnamuthy et al (2002)	11 mo	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[11],*	Krishnamurthy et al (2002)	11m	M	Right facial paralysis, with irritability and hepatosplenomegaly	3 wk	14.9	45% primitive cells	Normal	MRI: Normal	AML	Yes	Chemotherapy + radiotherapy, Remission
3[12]	Bilavsky et al (2006)	8 mo	F	Right facial paralysis, growth and development stagnation, without fever, hepatosplenomegaly or lymphadenectasis	3 wk	7.0	None	–	MRI: No evidence of facial nerve or meningeal enhancement	M4	Yes	Chemotherapy
4[13]	Ranta et al (2017)	8 mo	M	Bilateral facial paralysis, with exophthalmos	–	–	–	–	Orbital tumor infiltrating the nasal cavity; solid tumor compressing the spinal cord	M5	–	Died after remission of chemotherapy
5[14]	Li et al (2004)	4 mo	M	Left facial paralysis, with irritability, without fever, hepatosplenomegaly or lymphadenectasis	28 d	24.1	None	Normal	CT: little subdural effusion	M2b	Yes	Died
6	This case	10 mo	M	Right facial paralysis, with late fever, rash and irritability, irritation, without hepatosplenomegaly or lymphadenectasis	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.

the 7early stage and 4 (66.7%) had no hepatosplenomegaly, of which all 4 cases (100%) had increased peripheral WBC count ($>10 \times 10^9$/L), although none of them had hyperleukocyte acute leukemia. Of 5 cases, 4 (80%) did not have abnormal cells in the peripheral blood at the first visit. The misdiagnosis rate1detection of IL; furthermore, facial paralysis caused by acute leukemia may be accompanied by surrounding meningeal involvement and direct leukemic infiltration to the tympanic cavity and temporal bone.[15] It is necessary to improve the understanding, early diagnosis, and treatment of IL to improve its prognosis.

Corticosteroids were frequently used in the early stage for children with a diagnosis of Bell paralysis or with the occurrence of rashes during the course of a disease (the use rate in this group of children is 80%), which may provide temporary relief of the symptom but is also one of the reasons for the misdiagnosis of IL. In terms of Bell paralysis, the use of corticosteroids in adult patients may improve the prognosis by reducing inflammation and edema in the myelin sheath of facial nerves.[16,17] However, currently, the use of corticosteroids for children remains controversial. Babl et al affirmed the effectiveness of hormones in treating Bell paralysis in children in a multicenter, randomized, controlled trial study.[18] But Pitaro et al and Salman and MacGregor et al stated that there was insufficient evidence for the beneficial effects of corticosteroids and did not recommend the routine use of it in children.[19,20] Therefore, considering the higher incidence of central nervous system leukemia in the infant group and the disadvantages of delayed diagnosis and treatment of children with leukemia after using corticosteroids, it is necessary to consider the possibility of neoplastic disease in infants with facial paralysis.

In conclusion, IL associated with facial palsy is extremely rare, with its clinical symptoms being atypical and having a high rate of misdiagnosis. In addition, clinicians treating children with facial paralysis should pay attention to excluding the possibility of neoplastic disease when the cause of the disease remains unknown or the treatment effect is poor, and they should administer corticosteroids carefully before a definite diagnosis is made.

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References

[1] Biondi A, Cimino G, Pieters R, et al. Biological and therapeutic aspects of infant leukemia. Blood 2000;96:24–33.
[2] Howlader N, Noone AM, Krapcho M, et al. Previous version: SEER cancer statistics review, 1975-2010[OL]. 2013-06-14. http://seer.cancer.gov/archive/csr/1975_2010(/2016-01-06).
[3] Creutzig U, Zimmermann M, Bourquin JP, et al. Favorable outcome in infants with AML after intensive first-and second-line treatment: an AML-BFM study group report. Leukemia 2012;26:654–61.

[4] Hilden JM, Dinndorf PA, Meerbaum SO, et al. Analysis of prognostic factors of acute lymphoblastic leukemia in infants: report on CCG 1953 from the Children's Oncology Group. Blood 2006;108:441–51.
[5] Ibagy A, Silva DB, Seiben J, et al. Acute lymphoblastic leukemia in infants: 20 years of experience. J Pediatria 2013;89:64–9.
[6] Reddy S, Redett R. Facial paralysis in children. Facial Plastic Surg 2015;31:117–22.
[7] Wolfovitz A, Yehudai N, Luntz M. Prognostic factors for facial nerve palsy in a pediatric population: a retrospective study and review. Laryngoscope 2017;127:1175–80.
[8] Chiu CH, Lin TY, Huang YC. Cranial nerve palsies and cerebral infarction in a young infant with meningococcal meningitis. Scand J Infect Dis 1995;27:75–6.
[9] Suri S, Bhasin A, Srivastava VK. Salmonella typhi meningitis with facial nerve palsy. Indian Pediatr 1992;29:901–2.
[10] Fukui K, Nagata E, Kobari M, et al. A case of tuberculous meningitis associated with facial nerve paralysis and MRI findings of brain stem lesion [in Japanese]. Nihon Naika Gakkai Zasshi 1995;84:1731–3.
[11] Krishnamurthy S, Weinstock AL, Smith SH, et al. Facial palsy, an unusual presenting feature of childhood leukemia. Pediatr Neurol 2002;27:68–70.
[12] Bilavsky E, Scheuerman O, Marcus N, et al. Facial paralysis as a presenting symptom of leukemia. Pediatr Neurol 2006;34:502–4.
[13] Ranta S, Palomäki M, Levinsen M, et al. Presenting features and imaging in childhood acute myeloid leukemia with central nervous system involvement. Pediatr Blood Cancer 2017;64:
[14] Li ZX, Lin XJ, Zheng L, et al. A case of infant acute myeloid leukemia (M2b) which developed initially facial nerve palsy [in Chinese]. Zhonghua Er Ke Za Zhi 2004;42:912.
[15] Kubota K, Ozeki M, Hori T, et al. Facial palsy as an unusual presenting symptom associated with acute myeloid leukemia. Pediatr Int 2014;56: e37–40.
[16] Madhok VB, Gagyor I, Daly F, et al. Corticosteroids for Bell's palsy (idiopathic facial paralysis). Cochrane Library 2016;Epub ahead of print.
[17] Gagyor I, Madhok VB, Daly F, et al. Antiviral treatment for Bell's palsy (idiopathic facial paralysis). Sao Paulo Med J 2015;133:383–1383.
[18] Babl FE, Gardiner KK, Kochar A, et al. Bell's palsy in children: current treatment patterns in Australia and New Zealand. A PREDICT study. J Paediatr Child Health 2017;53:339–42.
[19] Pitaro J, Waissbluth S, Daniel SJ. Do children with Bell's palsy benefit from steroid treatment? A systematic review. Int J Pediatr Otorhinolaryngol 2012;76:921–6.
[20] Salman MS, MacGregor DL. Should children with Bell's palsy be treated with corticosteroids? A systematic review. J Child Neurol 2001;16:565–8.